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ECTMIH2015 Plenary Sessions

PL2 Disease Systems

INV.PL2.001
Medical HIV prevention: science, public health and medical ethics

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The HIV pandemic remains a public health challenge; the number of new infections continues to excess the number starting antiretroviral therapy (ART). The relative efficacy of medical interventions reducing risk of HIV transmission varies from >99% (durable suppression of HIV replication by ART), 80–90% (pre-exposure prophylaxis (PrEP) or consistent condom use), to approximately 50% (male circumcision, treatment of STD). No effective vaccine has yet been discovered. UN-defined strategy to control global transmission is to exponentially increase the number of infected on ART over next decade while maintaining focus on diversified prevention efforts. HIV incidence continues to increase despite increasing ART coverage in key affected populations in some but not all settings; global uniform decrease in mother-to-child transmission by use of ART in pregnant HIV+ women is seen. Further increase in ART coverage rate is projected to eventually result in population transmission control. Use of ART in early HIV infection was until recently ethically challenged; however, a favourable benefit: risk profile from use of ART for the individual has been established and hence aligns the personal with the preventive benefit. Novel testing and linkage to care strategies are required for ensure diagnosis and ART for the large fraction of the infected population yet to be diagnosed. For HIV negative persons at high risk of HIV infection, PrEP is a useful option. Expanding use of ART will require restructuring of health systems to ensure continued good care quality despite increasing case load. In summary, a scenario is emerging to suggest possible control of the HIV pandemic; this will require continued research to innovate effective and simple implementation tools and increased investment.
DISCLOSURE Nothing to disclose.

PL7 Health systems

INV.PL7.001
Gender sensitivity in health systems: why does it matter?

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This keynote address examines the evidence for gender sensitivity in health systems and what we know about how much difference it makes to health and other outcomes. Based on the abundant literature on gender and health that has emerged over the past two decades, it uses WHO's health system building blocks framework to review how gender sensitivity has been found to influence its six areas (governance, health financing, service delivery, health workforce, medical products and technology, and research, surveillance, monitoring and evaluation), and identifies gaps in this literature. It further examines which aspects of this literature have been reviewed systematically and what results remain valid under the scrutiny of systematic reviews. It then asks to what extent robust findings and recommendations from these reviews have been put into place in health systems, whether there is evidence that they make a difference, and if so, in what ways. The paper also examines to what extent a tool for incorporating of gender into health systems, developed by WHO, SIDA and UNHR in 2011, has been used and concludes with some positive examples of well documented, gender sensitive health interventions from low and middle income countries.
DISCLOSURE Nothing to disclose.

PL8 Disease systems

INV.PL8.001
NCD policy in South Africa: progress and challenges using fiscal, legislative and regulatory levers

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Addressing the non-communicable disease (NCD) epidemic is critical to a virtuous cycle of improved health outcomes and better economic growth. 40% of deaths in South Africa (SA) result from NCDs. GDP losses between 2006–2015 from diabetes, stroke and coronary heart disease are estimated to cost US $1.88 billion. Obese workers cost their employers 50% more in paid time off than non-obese colleagues. While workplace wellness programs are growing, the urban poor have little access. The NCD epidemic is a greater burden because it is occurring concurrently with an aging HIV-positive population.

Fiscal, regulatory and legislative levers could impact NCDs and lessen the burden on fragile health services. Mandatory salt regulation was passed in 2013 and evidence on the cost savings and impact on stroke played a key role for policy makers. The National Department of Health also considers taxing unhealthy foods – specifically those 'high in fats and sugar' – to be very cost-effective but significant resistance can be expected from industry. These countervailing pressures need to be understood before government can strategically embark upon policies involving sugar regulation. Modeling shows a 20% sugar sweetened beverage (SSB) tax would reduce obesity by close to a quarter of a million a year, while the cost of inaction would increase obesity by the same magnitude. The regulation of widely consumed, harmful substances other than sugar is not unprecedented: alcohol and tobacco areregulated and 'sin' taxes are considered a 'best buy'.

Before adopting and implementing sugary drink taxes, complex obstacles remain, mainlyfrom vested interests. Aggressive marketing and advertising campaigns, including corporate social responsibility initiatives, ensure that excessive consumption remains a social norm especially in emerging economies with growing populations that can afford SSBs and other low-cost, high-sugar foods. Current consumption trends, if allowed to continue unchecked, will in part lead to unprecedented rates of obesity related NCDs. Many other countries in the global South are

already taking action to bring sugar consumption in line with new WHO recommendations. SA can leverage this inflection point by systematically addressing these challenges.
DISCLOSURE Nothing to disclose.

PL9 Health systems

INV.PL9.001
Achieving effective community participation for health under resource constraints

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Global health practitioners are in quasi-agreement on the importance of involving beneficiaries of programs in their design and implementation. The approach is embodied in the concept of community participation (CP) – a promise of Alma Ata that underlines the importance of ownership and participation; which has further evolved to include the paradigms of empowerment and rights.

However, involvement of beneficiaries in health and development projects globally has met with varying levels of success. In part, this is a function of the complexity of defining 'community' and 'participation' as well as the heterogeneity of communities and contextual interpretation of participation. Nevertheless, the definition of Susan Rifkin et.al (1988), 'Community participation is a social process whereby specific groups with shared needs, living in a defined geographic area actively pursue identification of their needs, take decisions and establish mechanisms to meet these needs' is adopted for this address.

Literature on CP in resource constrained settings suggests that weak health systems could be strengthened by a cadre of workers at the community level variously named community health workers (CHWs), village health workers (VHWs) and health extension workers (HEWs), among other names. The literature also highlights the contribution of CHWs on a range of health services, illustrating this cadre is the critical link that embodies community engagement and participation in health care.

As a result, there seems to be added urgency to strengthen, integrate and/or institutionalize CHWs into health systems. This in an effort to increase their numbers, expand their roles and maximize their value; and ostensibly increase their effectiveness in engaging communities not only on current health issues, but also on the expected changes in the global health landscape post-2015.

This address critically reviews the proposed global efforts for CHW scale-up post-2015 in light of effective CP including their representation, remuneration, level and quality of participation in decision making and remit expansion. It posits that there are a number of unresolved and ongoing challenges that need to be acknowledged and addressed in order to achieve effective CP. The global health community has registered considerable progress in several areas of health. Meaningful community engagement and participation is necessary going forward if these gains are to be enhanced, maintained and sustained.
DISCLOSURE Nothing to disclose.

PL11 Disease systems

INV.PL11.001
The global strategy 2016–2030: accelerating towards elimination

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BRIEF INTRODUCTION In June 2013, WHO began a global consultative process involving Member States and stakeholders, including scientific and research groups, nongovernmental organizations and implementing partners. Between March and June 2014, seven regional consultations were held on a draft version of the strategy, at which more than 70 Member States were represented and more than 400 technical experts provided input. To supplement these consultations, the Secretariat hosted an online public consultation between 11 July and 15 August 2014, during which further comments were received.
METHODS AND MATERIALS The draft malaria strategy 2016–2030 provides a comprehensive framework for countries to develop tailored programmes for accelerating towards malaria elimination. It emphasizes that progression towards malaria-free status does not consist of a set of independent stages but is a continuous process requiring a structuring of programmes in line with subnational stratification by malaria risk. It underlines the need to ensure universal coverage of core malaria interventions, and proposes milestones and goals for 2020, 2025 and 2030. It also identifies areas where innovative solutions will be essential to achieve the goals, and outlines the global financial implications of implementing the strategy.
RESULTS The vision of WHO and the global malaria community is a world free of malaria. The four global goals with intermediate milestones and 2030 targets are to reduce malaria mortality rates and case incidence by at least 40% (2020), 75% (2025), and 90% (2030) compared with 2015; to elimination malaria from at least 10 (2020), 20 (2025) and 35 (2030) countries in which malaria was transmitted in 2015; and to prevent re-establishment of malaria in all countries that are malaria-free. The three pillars of the strategy are: ensure universal access to malaria prevention, diagnosis and treatment, accelerate efforts towards elimination and attainment of malaria-free status, and transform malaria surveillance into a core intervention. The two supporting elements are: harnessing innovation and expanding research, and strengthening the enabling environment.
CONCLUSIONS In January 2015, the WHO Executive Board endorsed the draft and submitted it to the World Health Assembly for consideration in May 2015. The strategy provides the technical underpinning for the Roll Back Malaria Partnership's Action and Investment to Defeat Malaria 2016–2030.
DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

Society Sessions

SS1 Société de Pathologie Exotique (SPE), Italian Society of Tropical Medicine and Global Health (SIMET) and Sociedad Espan~ola de Medicina Tropical y Salud Internacional (SEMTSI): Rapid diagnosis tests (RDTs) in tropical infectiology I

O.SS1.003

Performance comparison of three rapid diagnostic tests for the serodiagnosis of hepatic cystic echinococcosis in humans

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INTRODUCTION The diagnosis of cystic echinococcosis (CE) is based on imaging, in particular ultrasound (US) for abdominal CE, complemented by serology when US features are unclear. In rural endemic areas, where expertise in US diagnosis of CE may be scant and conventional serology techniques are unavailable due to the lack of laboratory equipment, Rapid Diagnostic Tests (RDTs) for CE are appealing. However, the performances of immunoassays are heterogeneous and influenced by many variables, and the interpretation of results may be difficult especially in case of small young or inactive cysts. We evaluated the performance of 3 commercial RDTs for the diagnosis of hepatic CE.
MATERIALS AND METHODS Sera from 59 patients with single hepatic CE cysts (38 active and 21 inactive) and 25 patients with non-parasitic cysts were analysed by RDTs VIRapid HYDATIDOSIS (Vircell, Spain), Echinococcus DIGFA test (Unibiotest, China), ADAMU-CE (ICST, Japan), and by RIDASCREEN Echinococcus IgG ELISA (R-Biopharm, Germany), routinely used in our lab. Sensitivity (Se), specificity (Sp) and ROC curves were compared with McNemar and *t*-test. For VIRapid and DIGFA tests, correlation between semiquantitative results and ELISA OD values was evaluated by Spearman's coefficient. Reproducibility was assessed on 16 randomly selected sera with Cohen's Kappa coefficient.
RESULTS Se and Sp of VIRapid (74%, 96%) and ADAMU-CE (57%, 100%) did not differ from ELISA (69%, 96%) while DIGFA (72%, 72%) was significantly different ($P = 0.045$). ADAMU-CE test was significantly less Se in the diagnosis of active cysts ($P = 0.019$) while DIGFA was significantly less Sp ($P = 0.014$) compared to ELISA. All tests were poorly Se in diagnosing inactive cysts (33.3% ELISA and ADAMU-CE, 42.8% DIGFA, 47.6% VIRapid). ROC curves of VIRapid (AUC = 0.851) and DIGFA (AUC = 0.722) were significantly different ($P = 0.042$). The reproducibility of all RDTs was good ($k = 0.62$ DIGFA; $k = 0.71$ ADAMU-CE) to very good ($k = 1$ VIRapid). Band intensity of VIRapid and DIGFA correlated with ELISA OD values ($r = 0.76$ and $r = 0.79$ respectively, $P < 0.001$).
DISCUSSION RDTs may be useful in resource-poor settings to complement US diagnosis of CE in doubtful cases. In this regard, VIRapid test appears to perform best among the examined kits, but all tests are poorly Se in presence of inactive cysts, which may pose considerable problems of differential diagnosis.
ACKNOWLEDGEMENTS This work was partly funded by FP7 (HERACLES) g.a. 602051 (to EB).
DISCLOSURE Vircell is SME partner in HERACLES project but it had no role in the design, analysis and discussion of this work and the VIRapid tests were purchased independently.

SS5 Symposium 10th Anniversary Swiss School of Public Health (SSPH+): SSPH+ perspectives on global health challenges

O.SS5.002

Setting priorities for dementia research: a global health perspective

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INTRODUCTION Dementia has a significant impact on patients, families and society, and is a recognized global health priority. The first Ministerial Conference on Global Action Against Dementia held in March 2015 at the WHO, in Geneva has been an historic event that culminated in a call for a global set of actions to raise awareness about dementia and to reduce its burden in all world regions. The need to position dementia high in the global health agenda has been recognized by representatives of more than 80 countries. In this context, investment priorities in dementia research must be identified to inform governments on a more rational use of funds and resources aimed at reducing the global burden of dementia. In 2014 the WHO convened 13 world experts in dementia to outline a method to identify global dementia research priorities using a transparent, systematic, rigorous, replicable, fair and legitimate process.
METHODS A structured exercise modified from the Child Health and Nutrition Research Initiative (CHNRI) methodology has been conducted involving hundreds of researchers, clinicians, stakeholders and policy makers from all world regions. The CHNRI consists of five steps:
1 Scope definition.
2 Collection of research topics from a wide range of identified researchers and stakeholders.
3 Consolidation of research topics.
4 Scoring of consolidated research topics.
5 Computation of scores to produce the priority list.
RESULTS More than 200 researchers and stakeholders, identified using Web of Science and other sources, suggested research questions. We will present the process of consolidation

of research questions and their allocation to pre-defined research categories (basic, clinical-translational and implementation), their grouping in overarching 'goals' and the scoring according to five criteria (i.e. potential for success, impact on burden reduction, potential for paradigm shift, potential for translation and equity), and finally illustrate the key research priorities identified using the CHRNI exercise.
CONCLUSION Application of a modified CHNRI methodology to identify dementia research priorities provided clear indications to optimize investments and concert efforts to respond to the current and future impact of dementia on patients, families and societies worldwide. The implications of our findings will be discussed and contextualized with respect to the global health agenda.
DISCLOSURE Nothing to disclose.

O.SS5.003

Cancer risk factors – a global challenge

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Chronic diseases are no longer only a problem of developed countries. The incidence of cardiovascular diseases and cancer is rising in low- and middle-income countries due to increased life expectancy, but also changes in lifestyle habits. Common cancer risk factors such as smoking, obesity, high alcohol consumption, and unhealthy diet are important contributors to this development. For example, smoking prevalence rates have been increasing, in particular among men, in many low- and middle-income countries, and, thus, lung cancer is becoming a major public health challenge in countries like China. A second example is increased consumption of red meat in many middle-income countries. Red meat consumption is linked to increased colorectal cancer incidence, but also with overall mortality. Although less strongly linked with cancer risk than smoking, changes in food consumption patterns, such as higher meat, lower fish, and lower fruit and vegetable consumption, may thus contribute to changes in cancer burden. The aim of the presentation is to show changes in the prevalence of common cancer risk factors worldwide and how they are linked to changes in cancer patterns.
DISCLOSURE Nothing to disclose.

O.SS5.004

Transportation noise: 'neglected exposure' on a global scale

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BACKGROUND Epidemiological research on health effects of transportation noise is mainly restricted to Europe and North America. As a consequence, little is known about noise exposure and its health effects in other parts of the world. Transportation noise is not even considered as a risk factor in the most recent global burden of disease study.
OBJECTIVE To estimate life years lost due to transportation-related noise and air pollution in Switzerland and to evaluate the results with respect to global implications.
METHODS Spatially resolved noise and air pollution models for the year 2010 were derived for road, rail and aircraft sources in Switzerland. Average day-evening-night sound level (Lden) and particulate matter (PM_{10}) were selected as indicators, and population-weighted exposures derived by traffic source. Cause-specific exposure-response functions for mortality were derived from a meta-analysis for noise and literature review for PM_{10}. Life years lost were calculated using life table methods.
RESULTS Total transport-related burden in Switzerland in 2010 amounted to 17 682 years of life lost (69% air pollution; 31% noise). Taking into account noise-induced sleep disturbances and annoyance, economic burden for noise were similar to air pollution (ca. 1.8 billion CHF per year).
CONCLUSIONS Although air pollution and noise levels in Switzerland tended to be lower than in many urban areas worldwide, health impact is substantial. Outside Europe and North America noise effects are mostly neglected and need a more careful evaluation.
DISCLOSURE Nothing to disclose.

O.SS5.005

The challenges of global health research from an ethical and legal point of view

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During the last 50 years, the ethical and legal framework of research involving human participants has experienced several phases. In 1964, the World Medical Association adopted the Declaration of Helsinki that soon became the main document of reference for the protection of human participants. It is also in the early sixties that in the USA the FDA requested clinical data prior to register new medicinal products, the same requirement being introduced in the European regulation in 1965. This corresponded with a dramatic increase of clinical trials together with the industrialization and globalization of research at the international level. At that time the normative framework of research involving human participants was mainly focusing on drug trials. The pharmaceutical industry learned to cope with those requirements and promoted the adoption and implementation of Good Clinical Practice or GCP during the nineties (ICH GCP 1996). In 1997, the Council of Europe adopted in Oviedo the Convention of Human Rights and Biomedicine. This is one of the first regulations that considers the protection of the research participants in a human right point of view. Since then, many countries, both in the North and in the South, adopted specific legislation on biomedical or health research. In Switzerland the new Federal Act on Research Involving Human Beings entried into force on January 1, 2014.

This evolution was not without impact for the researchers. For instance, in Europe, the adoption of the Clinical Trial Directive in 2001 created difficulties within the academic community confronted to the fact it was bound to respect the same law than the industry. In spite of serious efforts, many questions remain open in the field of public health research. The legislations are based on the GCP model that is adapted to drug trials but not to global health research. Some adaptations seem inevitable. In its 2013 Health Report on « Research for Universal Health Coverage », the WHO stressed the need to develop more researches that are addressing the needs of the world's population. Beyond the need to guarantee the protection of the research participants and the quality of the research, a growing attention should be paid to the fact the proper resources are made available to conduct research in fields where there are the highest public health needs.
DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

SS6 Swiss Society of Tropical Medicine and Parasitology (SSTMP): Helminthiases: from drug discovery to policy

O.SS6.002

The 'Magic Glasses' research programme for the global control of intestinal worms

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INTRODUCTION The soil-transmitted helminths (STH) are a significant public health concern globally. Our research team developed and evaluated (via a cluster RCT) the impact of a video-based health educational intervention package on STH incidence, knowledge and hygiene behaviour in Chinese primary school children aged 9–10 years (grades 4–5). Results showed an unprecedented (for educational interventions targeting STH) 50% decrease in the incidence of STH infection (OR = 0.5, 95% CI 0.35–0.7, $P < 0.0001$) in the intervention schools compared with the control schools (published in the *New England Journal of Medicine*). This provided proof of principle that the video-based health educational package widens student knowledge and changes behaviour, resulting in fewer STH infections. Our central thesis is that this package, developed by our group, targeting schoolchildren, can influence their behaviour in a way conducive to the prevention of parasitic worm infections, thereby playing a pivotal role in the sustainable control and prevention of NTDs globally.
METHODS AND MATERIALS To evaluate the potential for up-scaling of our video-based health educational package as a universal school-focused educational tool forming part of multi-component sustainable integrated NTD control programs, we wish to assess the generalisability of our findings in different geographical areas with a high force of infection (high prevalence) and different ethnic groups. As such, we are currently undertaking two cluster RCTs in Yunnan Province, China; and Laguna Province, Philippines.
RESULTS Here we will give a general overview of the entire research programme, describe the baseline results of the Yunnan trial; and discuss the development of the 'Magic Glasses: Philippines' cartoon video.
CONCLUSION This study will provide an evidence base for translation of our video-based educational package into public health policy and practice in the Asian region and beyond.
DISCLOSURE Nothing to disclose.

O.SS6.003

WASH for WORMS: a cluster randomised controlled trial of the impact of a community-based WASH programme on soil-transmitted helminth infections in Timor-Leste - mid-point results at six months follow-up

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INTRODUCTION Soil-transmitted helminths (STH) infect more than two billion people worldwide, causing considerable morbidity, including malnutrition and anaemia. STH are most prevalent in communities lacking adequate clean water, sanitation and hygiene (WASH). Deworming programmes with anthelminthic drugs are highly effective in reducing morbidity but rapid reinfection occurs if there is no reduction in environmental contamination with infective stages, impeding the sustainability of STH control programmes based on deworming alone. Therefore, provision of water, sanitation and hygiene (WASH) programs is of critical importance in the sustainable control of STHs.
METHODS AND MATERIALS 'WASH for Worms' is a cluster randomised controlled trial (RCT) assessing the impact of a community-based WASH intervention, implemented by WaterAid Australia, on infection with intestinal parasites following mass albendazole (ALB) chemotherapy in villages in Timor-Leste. In this trial, initiated in 2012, twelve intervention villages receive the WASH programme and ALB treatments every six months. Twelve control villages receive only the six-monthly ALB. All villages are followed-up for 2 years after the first ALB distribution. Infection prevalence and intensity is measured by a modified qPCR.
RESULTS An overview of the study design and implementation progress will be presented. Additionally, the prevalence and intensity of STH infections at baseline and after the first (6-monthly) follow-up will be discussed and compared across trial arms. At baseline the prevalence of STH in the 24 villages was high, with more than 70% of the 2225 participants who provided stools infected with at least one STH, mostly comprising *Necator americanus* (62.3%) followed by *Ascaris lumbricoides* (30.4%). At the first follow-up the overall prevalence of STH infection decreased to 46.3%, with 34.6% of the 1630 participants who provided stools infected with *N. americanus* and 21.0% infected with *A. lumbricoides*. In the intervention arm, *N. americanus* decreased from 62.8% to 32.2% whereas *A. lumbricoides* decreased from 31.6% to 22.0%. In the control group, *N. americanus* decreased from 61.8% to 36.9% whereas *A. lumbricoides* decreased from 29.2% to 20.1%.
CONCLUSION This trial is the first reported RCT evaluating the impact of integrated WASH and deworming programmes on infection with STHs; and will provide essential evidence for scaling up integrated programmes for STH control.
DISCLOSURE Nothing to disclose.

O.SS6.004

Individual-based modelling of hookworm infection: predicted feasibility of achieving control and elimination by 2020

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Globally, 440 million people are infected with hookworms, the majority living in developing countries. High parasite loads contribute to development of anaemia, particularly in children and women of childbearing age (WCBA). In recognition of the hookworm disease burden, the WHO has set the target to implement annual or semi-annual preventive chemotherapy (PCT) for preschool and school-aged children and WCBA in endemic areas with an overall coverage of at least 75% by 2020. The associated parasitological goal is to achieve <1% prevalence of heavy hookworm infection in these PCT target populations (and thus prevent most morbidity). As part of the NTD Modelling Consortium, we evaluated the feasibility of achieving control (prevalence of heavy infection <1%) or even elimination of hookworm infection, given currently recommended intervention strategies. To this end, we developed an individual-based model for transmission and control of soil-transmitted helminths that synthesizes all relevant available information on hookworm biology, and captures heterogeneities in transmission and PCT participation. Model predictions were compared to longitudinal parasitological data spanning 5 years, collected pre-control and during PCT. In general, model predictions suggest that elimination of hookworm infection is not possible by means of PCT, unless a broader age group is targeted (e.g. including all adults). Controlling levels of heavy infection (<1%) is however very well possible through annual or semi-annual PCT (depending on pre-control endemicity) applied to current target populations at 90% coverage. Sensitivity analysis showed that individual systematic non-participation is a key determinant for achieving control, and in particular, elimination. In conclusion, we present the first individual-based model for hookworm infection and a first-time comparison of mathematical model predictions to longitudinal data. Model predictions suggest that hookworm infection can be controlled with PCT, but probably cannot be eliminated with the current strategy.

DISCLOSURE Nothing to disclose.

SS11

Be-cause Health (Belgian Platform for International Health): integrated mental health care: finally a different perspective towards a more human health care?

O.SS11.004

Fostering mental health services development in rural Cambodia: an NGO perspective

T. Khem

Louvain Cooperation, Phnom Penh, Cambodia Dramatic events which occurred during three decades of civil war including Khmer Rouge regime have decimated Cambodian experts and intelligentsia, leaving the country with a lack of trained people in many fields including mental health (MH). Currently there are only 56 psychiatrists in the whole country, corresponding to a ratio of 0.33 per 100 000 persons and psychiatric nurses are even rarer with 0.26 per 100 000 persons. Psychologists, social workers and other paramedical professionals are in a similar situation. A psychiatric morbidity study at household levels already showed a decade ago the burden of MH with 42.4% of the respondents reporting symptoms of mental disorders and about 25% reporting being socially impaired. Although health strategic plan, national guidelines, and policies exist, MH remains a low priority for the government with a poor implementation of MH services at the health facilities especially in rural areas. Transcultural Psycho-social Organization (TPO) Cambodia and Louvain Cooperation (LD) NGOs collaborated since June 2006 to strengthen the quality of MH services in terms of medical approaches and also to integrate non-medical approaches into public MH facilities in rural Cambodia. To date, MH services were set up in five referral hospitals (RHs) and 12 health centres (HCs) in three provinces. From 2008 until 2014, the project reached over 28 572 consultations and 3153 home visits and the quality of consultations, counselling, psycho-educations and home visits increased remarkably. Lessons learnt from this long experience reveals that investing in MH services for a low resource country like Cambodia is relevant if compared with population's needs and is also feasible. Training on non-medical interventions to both patients and community does not require highly qualified people or long training and is relatively inexpensive. Nevertheless, there is still a long way to go for Cambodia in developing quality MH services in response to the demand of the population. Challenges encompass various aspects including the availability of human resources, the quality, the accessibility and the financial viability of the services. The future trend of Cambodian MH should embrace the concept of an integrated MH care approach where MH facilities and the community level are working more together, where medical and non-medical approaches are combined, and where skills are transferred from highly qualified people to less qualified health workers.

DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

Stellite sessions

SAT1 Co-infections: its impact on neglected tropical diseases

SAT1.002

The double jeopardy of having female genital schistosomiasis in poorly informed and resourced health systems in Ghana

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Within the last decade in Ghana, the Neglected Tropical Disease (NTD) Program has successfully broken transmission in 69 out of the 98 Districts endemic for Lymphatic Filariasis (LF), dramatically reduced Onchercerca prevalence from 45.2% in 2007 to 2.7 % and reduced community microfilaria load from 20.1% to 0%. Recent surveys have indicated that trachoma is nearing elimination and school based distribution of Praziquantal for schistosomiasis has been implemented in 107 out of 240 districts. Despite the above achievements, in the last year the program has become concerned about the fate of women who suffer silently from Female Genital Schistosomiasis (FGS) a condition that exists in Ghana whose signs and symptoms are no different from other female gynaecological problems (post coital bleeding, irregular menstruation, dysmenorrhea, dyspareunia, lower abdominal pain and vaginal discharge) and may end up being treated as such. Currently 49 districts in Ghana have a prevalence of over 50% for schistosomiasis and 10 of these districts are co-endemic with LF and Onchocerciasis. A recent study of the Volta Basin of Ghana estimates a 24.8% prevalence among women aged 15–49 years. Due to lack of funds and drugs the NTD program in Ghana focuses only on school based distribution of praziquantel, rather than employing community based mass treatment. This presents a serious challenge for a woman whose livelihood depends on the river from which she gets infected and who may end up never getting appropriately diagnosed and treated due to lack of awareness about the problem among community members and health care providers. The COUNTDOWN research consortium will be working in Ghana over the next 5 years and will seek to document the extent to which the problem of FGS exists, explore in-depth community and health worker understanding of the issue, identify blockages which prevent the roll out of programs for FGS, and suggest appropriate interventions to address the problem. Preliminary findings of the inception phase of the study will be shared.
DISCLOSURE Nothing to disclose.

SAT1.003

Paediatric schistosomiasis- effects on overall host health

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BACKGROUND An important disease affecting child health and development in sub-Saharan Africa is schistosomiasis. Schistosomes also exacerbate pathology and disease due to other parasites, including *Plasmodium falciparum*, alter host physiology and general immune response, and interfere with diagnosis of other conditions such as allergy. Nonetheless, the wider health implications of paediatric schistosome infection for other infectious and noninfectious diseases remain un-studied and there is paucity of research on possible indirect health effects and in the effects of the current practise of delayed treatment of infected children. We have been investigating the effects of paediatric schistosomiasis and subsequent antihelminthic treatment on general non schistosome-specific inflammatory immunological and biochemical attributes mediating infectious and non-infectious disease pathology.
MATERIALS AND METHODS A longitudinal study of 346 Zimbabwean children; (1–10 years old) measured levels of inflammation biomarkers (C-reactive protein (CRP), Chitnase-3-Like 1- protein (CHI3L1P), Resistin, Ferritin, Secretory leukocyte protease inhibitor (SLPI) (measured by enzyme linked serological assays) and microhaematuria, albuminuria (albuminto- creatinine ratio) and proteinuria (via urinalysis). The correlation and multivariate analyses were conducted to determine the relationship between the serological markers, urine attributes and schistosome infection. The effects of antihelminthic treatment with the drug praziquantel (PZQ) on these variables were also tested.
RESULTS Our studies show, distinct inflammatory response profiles in children infected with schistosomes. Furthermore, schistosome-infected children are positive for microhaematuria, proteinuria and albuminuria. Curative PZQ treatment of schistosome infection resulted in a significant ($P < 0.001$) decline in the levels of proteinuria and albuminuria 12 weeks posttreatment, a decrease maintained for over a year. Significant treatment effects on microhaematuria prevalence were observed 12 months post-treatment.
CONCLUSION Schistosome infection is associated with altered inflammatory response profiles as well as altered physiology. Antihelminthic treatment significantly reduced serological markers of inflammatory responses and restored the urine protein and haemoglobin excretion and creatinine-albumin ratio to levels similar to uninfected children.
DISCLOSURE The study was support by a grant to FM by the Thrasher Medical Research Fund.

SAT1.004

Challenges of Visceral Leishmaniasis (VL) and HIV co-infection

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The emergence of HIV in the VL endemic areas in East Africa has resulted in increasing coinfection rates, at some point as high as 20–40% observed in Ethiopian VL patients. Major challenges in the management of HIV/VL are the recurrent relapses, and the poor effectiveness of available anti-leishmanial drugs. Pentavalent antimonials (SSG), the mainstay of VL treatment in Africa, have shown to be poorly tolerated, with high toxicityinduced mortality in co-infected patients. Other anti-leishmanial

drugs (miltefosine, liposomal amphotericin B) have shown to be safer than SSG, but lacking efficacy when used as mono-drug therapy, resulting in high treatment failure rates. A compassionate combination treatment of liposomal amphotericin B plus miltefosine, two drugs that had proven to be safe and well-tolerated in HIV co-infected VL patients, was introduced by MSF. The experiences with this combination regimen are very promising, with higher initial cure rates and lower failure rates, especially in relapse patients. Miltefosine seems to enhance the efficacy of AmBisome, and prevents the rapid emergence of unresponsiveness in relapse patients. Based on these promising initial results a multi-centre randomised clinical trial has started in Ethiopia, comparing the combination regimen with the WHO recommended AmBisome mono-therapy.

VL cannot be permanently cured in HIV-infected patients, resulting in repeated relapse and rapid development of drug unresponsiveness, even when patients are on antiretroviral treatment. Pentamidine secondary prophylaxis for HIV co-infected VL patients with high risk of relapse has been used in Europe but not yet in Africa; its efficacy, safety and feasibility in the African setting is currently being evaluated in a collaborative multi-centre observational study.

DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

Oral Sessions

TRACK 3: Disease systems and their determinants
3.1.1. HIV/AIDS from research to implementation

O.3.1.1.002
Challenges in estimating death and retention rates in a longitudinal cohort of HIV-infected persons in rural Tanzania

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INTRODUCTION The Kilombero-Ulanga Antiretroviral Cohort (KIULARCO) is an open, prospective cohort since 2005 of people living with HIV in rural southern Tanzania. In resource-limited settings, high loss to follow up (LTFU) leads to challenges in estimating outcomes. Substantial improvements in KIULARCO since 2013 include implementation of electronic medical records, referral from hospital wards through provider-initiated counselling/testing, and active participant tracking. Our aim was to assess changes in mortality and LTFU over time.
METHODS We included adults (≥16 years) enrolled in 2005–2014. Individuals were defined LTFU if >60 days late for visit (every 3 and 6 months for those on and not on ART). Participants who were not reported as dead, LTFU or transferred out were included with follow-up to 31 Dec. 2014. Time periods were 2005–07, 2008–09, 2010–12, and 2013–14. We assessed time to death with LTFU as a competing risk.
RESULTS Of 7207 adults, 65% were female; median age was 37 (IQR 31–45) years. Median CD4 count remained relatively stable over time [217 (88–413) cells/mm^3] while disease stage varied (46%, 38%, 36% and 48% WHO stage 3/4 over the time periods). The proportion of patients referred from hospital wards quadrupled in 2013–14 versus earlier years. 802 (11%) died and 2626 (36%) were LTFU. The probability of death by 12 months was 12.3% (95% CI 10.8–13.9), 6.1% (5.2–7.2), 3.0% (2.2–3.9) and 17.3% (15.0–19.7) over the time periods. The corresponding values for LTFU were 20.6% (18.7–22.5), 23.5% (21.8–25.3), 22.7% (20.6–24.9) and 19.1% (16.4–21.9). The mortality results were reflected in the unadjusted model (sub-hazard ratio 2.13 [95% CI 1.79–2.54], 0.48 [0.37–0.64] and 2.86 [2.35–3.48] for the time periods with 2008–09 as reference), and somewhat attenuated after adjustment for sex, age, WHO stage and in-patient referral [1.78 (1.46–2.18), 0.52 (0.39–0.70) and 2.73 (2.21–3.37)].
CONCLUSIONS Despite improvements in patient care, the data suggest that death rates have increased in 2013–2014, even after adjustment for patient health status. However, death rates in later years are likely to be more accurate than earlier years, due to improved tracking processes, and as reflected in the lower LTFU rates in 2013–14. There is likely a survivor bias due to sicker patients being less likely to link to care in earlier years as well as residual confounding. Additional time-dependent modelling is needed to obtain accurate outcome estimates.
DISCLOSURE Nothing to disclose.

O.3.1.1.003
Are we doing it right? Accuracy of 2013 WHO recommendations for switch to second-line ART in children: a prospective multi-center study from rural Lesotho

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BACKGROUND As recommended by the World Health Organization (WHO) 2013 Guidelines on anti-retroviral therapy (ART) for HIV Infection in resource-limited settings, children on ART should receive viral load (VL) monitoring. Those with VL ≥1000 copies/mL (c/mL) at two consecutive measurements should be switched to 2nd-line. The new empiric 2nd-line regimens (ESLR) consist of a protease inhibitor, lamivudine, and a new empirically chosen nucleoside reverse transcriptase inhibitor (NRTI).
METHODS To assess the utility of the VL cut-off at 1000 c/mL and accuracy of recommended ESLR, children <16 years of age, on first-line ART for ≥6 months with no previous access to VL testing in 10 rural clinics in Lesotho received a first VL. Those with detectable VL (≥80 c/mL) received adherence support and a second VL after 3 months. Those with 2 detectable VLs received a genotypic resistance test (GRT). Using as cut-off 'low-level resistance' according to the Stanford HIV Drug Resistance Database, GRT were classified as resistant if HIV presented resistance-mutations against ≥2 drugs of the current 1st-line regimen. The ESLR was classified 'suboptimal' if GRT revealed at least 'low-level resistance' to both NRTIs used in the new regimen. Study-ID: NCT02126696 (www.clinicaltrials.gov).
RESULTS VL-testing of 191 children revealed an unsuppressed viremia in 28% (53/191), 24% (46/191) with VL ≥1000c/mL. After 3 months of adherence support 49 received follow-up VL (1 died, 3 lost). VL was again >1000 c/mL in 61% (30/49), 80–999 c/mL in 12% (6/49), and undetectable in 27% (13/49). Among the 29 with follow-up VL ≥1000 c/mL and GRT, a virus resistant to current therapy was detected in 69% (20/29). In the 5 with follow-up VL 80–999 c/mL and GRT four presented with resistant virus. Among the 34 children with available GRT, 59% (20/34) would empirically have been switched to a suboptimal ESLR as their virus already presented with at least 'low-level resistance' for both NRTIs of the to be chosen ESLR.
CONCLUSIONS The cut-off of 1000 copies/mL when treatment failure is suspected, as stated in the 2013 WHO-guidelines, may misclassify a substantial proportion of children with relevant resistances as their low-VL treatment failure will not lead to a switch to 2nd-line ART. Also, ESLR without GTR may lead to a high number switches to a suboptimal 2nd-line regimen while

HIV is already resistant against both NRTIs. The true clinical impact of the latter remains to be further explored.
DISCLOSURE Nothing to disclose.

O.3.1.1.004

Effect of current usage of contraceptives on HIV-1 shedding in late breastfeeding

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BACKGROUND Oestrogen containing oral contraceptives (OC) are known to inhibit lactation. Mammary gland environment regulates HIV-1 load in breast milk (BM). However, the effect of contraception on HIV-1 shedding (detectable HIV-1 RNA or DNA) in BM has never been described.
MATERIALS AND METHODS We nested a cross-sectional study in the Zambian cohort of the ANRS12174 trial which compared two infant prophylaxis drugs to prevent post natal mother-to-child transmission of HIV-1. Frozen acellular left and right BM samples collected at week 38 (W38) from all mothers who breastfeed for more than 9 months were tested for HIV-1 RNA and subclinical mastitis [SCM; defined as sodium/potassium ratio (Na^+/K^+ ratio) ≥0.6 in lactoserum (LS) from at least one breast]. Corresponding breast milk cell (BMC) pellets were tested for HIV-1 DNA. All tests were done using commercially available kits and reagents. Data on social, demographical, biological and clinical characteristics of the mothers were extracted from the ANRS12174 trial data base. Binary logistic regression was used to assess the association of contraceptives and HIV-1 shedding in BM.
RESULTS We tested 537 samples from 270 mothers. None of the mothers took antiretroviral drugs during breastfeeding. At W38, 18.9% (95% CI: 14.2–23.6%), 20.0% (95% CI: 15.2–24.8%) and 7.9% (95% CI: 4.7–11.2%) mothers were using OC, injectable contraceptives (IC) and intrauterine device (IUD) respectively. HIV-1 RNA was detectable in LS from at least 1 breast of 66.4% (95% CI: 60.7–72.1%) mothers while HIV-1 DNA was detectable in BMC pellets from at least one breast of 61.9% (95% CI: 56.0–67.7%) mothers. Overall, 79.8% (95% CI: 75.0–84.7%) mothers had detectable HIV-1 RNA or DNA in at least one breast. In univariate analyses OC were associated with HIV-1 shedding in BM whereas IC and IUD were not. After controlling for plasma HIV-1 viral load, CD4 count, BMC and SCM, OC remained significantly associated with HIV-1 shedding in BM [adjusted odds ratio (AOR): 0.365; 95% CI: 0.164–0.813]. This association was strong for HIV-1 RNA (AOR: 0.372; 95% CI: 0.181–0.767) and marginal for HIV-1 DNA (AOR: 0.567; 95% CI: 0.284–1.132).
CONCLUSION In this observational study we report a strong association between use of OC in late breastfeeding and reduction of HIV-1 shedding in BM. If this relationship is shown to be causal, OC may complement maternal HAART or infant peri-prophylaxis in the fight against transmission of HIV-1 through breastfeeding.
DISCLOSURE Nothing to disclose.

O.3.1.1.005

Acceptability of lifelong treatment (Option B+) among HIV-positive pregnant and lactating women in selected sites in Malawi

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OBJECTIVE To explore the acceptability of the new WHO guideline Option B+ and the barriers and facilitators that affect a woman's decision to initiate lifelong antiretroviral therapy (ART).
METHODS Data were collected using convenience sampling from two rural sites and two urban sites in the districts of Dedza, Mchinji and Lilongwe between September-December 2013. Eighteen in-depth interviews (IDIs) and 4 focus-group discussions (FGDs) were conducted with pregnant women, 21 IDIs and 8 FGDs with lactating women and 4 FGDs with health care workers (HCWs). Eligible pregnant and lactating women were ≥18 years old, HIV-positive, on ART ≥1 month and with a child ≤18 months for lactating women. HCWs identified and referred eligible participants to data collectors. Eligible HCWs worked in the ANC/ART for ≥6 months and were referred by the head nurse. All study participants provided written informed consent.
RESULTS Women reported difficulty around learning their HIV status and initiating ART on the same day. They were overwhelmed with the information, needed time to think about ART initiation and wanted to first discuss with their partners before committing to lifelong treatment. Disclosure had both a positive and negative effect. Those who disclosed discussed being supported by the partner/family and those who did not disclose discussed challenges with initiating and adhering to ART. HCWs reported women taking the medication home and waiting to initiate until they felt ready. According to the women, knowing other women who had a positive experience with Option B+ made it easier to initiate. All groups emphasized a strong need for increased community sensitization about Option B+.
CONCLUSION In order to maximize the impact of Option B+, it is important to address challenges faced by women starting on lifelong therapy. Methods need to be developed to strengthen initiation and adherence of Option B+.
DISCLOSURE Nothing to disclose.

3.1.2. Implementation research for malaria elimination. Emerging results from Malaria Eradication Scientific Alliance (MESA) – supported projects

INV.3.1.2.001

Efficacy and safety of high-dose ivermectin for reducing malaria transmission: a dose finding study

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In western Kenya the prevalence of malaria in <5 year olds has fallen from 70% in 1997 to 40% in 2008, where it has now stagnated. Innovative approaches are needed to continue towards elimination. Ivermectin is a broad spectrum antiparasitic endectocide widely used for the control of onchocerciasis and lym-

phatic filariasis at a dose of 150–200 μg/kg. Ivermectin at this dose has a potent, but short-lived effect for 6–11 days on mosquito survival, egg-laying, and parasite sporogony. Higher doses are needed to prolong its mosquitocidal effects. Regulatory studies have shown ivermectin is very well tolerated and safe even up to 2000 μg/kg. We will conduct dose finding studies to evaluate the transmission blocking effect of high-dose ivermectin to define the optimal dose for future use of ivermectin in combination with artemisinin-based combination therapy (ACT) for mass drug administration (MDA) for malaria in Kenya. This study explores a research question of global relevance. A prolonged transmission blocking effect of ivermectin could have substantial consequences for malaria control in the next decades.
DISCLOSURE Funding: Malaria Eradication Scientific Alliance (MESA).

INV.3.1.2.003

Active detection of infection for malaria elimination in South Cotabato, Mindanao, The Philippines: performance of LAMP for screening people in their home villages

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The development of a malaria LAMP test kit permits rapid, highly sensitive detection of malaria infection in finger-prick samples. We tested the performance of this format in 3 villages of South Cotabato Province for a test and treat approach to malaria elimination, in which asymptomatic people were asked to provide finger-prick samples for cross-sectional LAMP testing. Over 500 tests were successfully performed in each village, and the sensitivity and specificity is being compared against standard nested PCR performed *post hoc* on duplicate filter paper samples. Preliminary data will be presented, and the utility of this approach to surveillance for elimination discussed.
DISCLOSURE Nothing to disclose.

INV.3.1.2.004

Targeting pregnant women to assess malaria transmission

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New metrics for malaria transmission are needed for malaria elimination. *Plasmodium falciparum* infection during pregnancy is associated with a strong antibody response against VAR2CSA (pregnancy-specific antigen expressed by the parasite on the erythrocyte membrane that binds to placental Chondroitin Sulphate A), suggesting that detection of these antibodies in pregnant women at antenatal clinics could be used for surveillance of malaria. *Plasmodium falciparum* qPCR-positivity in women from Manhiça (Mozambique) at delivery decreased from 33% in 2003 to 2% in 2010 and increased to 6% in 2012, with antimalarial IgGs against VAR2CSA mirroring these malaria trends. To select antigens with the highest potential for a VAR2CSA-based serological test, we measured IgGs in Mozambican pregnant women, as well as in non-exposed individuals, using a quantitative suspension array technology that included 46 peptides from both conserved and semi-conserved regions of VAR2CSA, 3 recombinant proteins (DBL3X, DBL5ε, DBL6ε) and non-pregnancy specific antigens. Dynamics of antibody responses during pregnancy were also determined to assess acquisition and longevity of antibody responses. We first excluded those antigens that were a) poorly recognized by plasmas from pregnant women with high antibody levels against a VAR2CSA-expressing parasite line (CS2) (n = 106); b) recognized by Mozambican men (n = 102) and Spanish individuals (n = 100) and c) not associated with antibody acquisition in women infected with *P. falciparum* during pregnancy (n = 252, longitudinal cohort with 3 time-points per women). Among the 25 antigens selected, antibodies against 17 peptides, DBL3X and DBL5ε mirrored falls and rises in malaria prevalence in Manhiça during 2003–2012 (n = 654). Finally, 9 out of the 17 peptides, DBL3x and DBL5ε were selected based on high boosting of antibody by malaria infection, low time to double the levels when infection occur (rapid generation of antibodies) and short half-life (detectable during one pregnancy). We have evaluated the potential of such a tool to reflect malaria transmission in malaria endemic countries as well as to detect recent changes in *P. falciparum* exposure associated with the use of intermittent preventive treatment with different antimalarials. This pregnancy-specific serological test could be placed into action to provide information for malaria surveillance in elimination campaigns.
DISCLOSURE Nothing to disclose.

O.3.1.2.005.LB

Malaria and the mobile and migrant population in Cambodia: a population movement framework to inform strategies for malaria control and elimination

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The relationships between human population movement (HPM) and health are a concern at global level. In the case of malaria, those links are crucial in relation to the spread of drug resistant parasites and to the elimination of malaria in the Greater Mekong sub-Region (GMS) and beyond. The mobile and migrant populations (MMP) who are involved in forest related activities are both at high risk of being infected with malaria and at risk of receiving late and sub-standard treatment due to poor access to health services. In Cambodia, in 2012, the National Malaria Control Programme (NMCP) identified, as a key objective, the development of a specific strategy for MMPs in order to address these challenges. A population movement framework (PMF) for malaria was developed and operationalized in order to contribute to this strategy.

A review of the published and unpublished literature was conducted. Based on a synthesis of the results, information was presented and discussed with experienced researchers and programme managers in the Cambodian NMCP and led to the development and refinement of a PMF for malaria. The framework was 'tested' for face and content validity with national experts through a workshop approach.

In the literature, HPM has been described using various spatial and temporal dimensions both in the context of the spread of

anti-malarial drug resistance, and in the context of malaria elimination and previous classifications have categorized MMPs in Cambodia and the GMS through using a number of different criteria. Building on these previous models, the PMF was developed and then refined and populated with in-depth information relevant to Cambodia collected from social science research and field experiences in Cambodia. The framework comprises of the PMF itself, MMP activity profiles and a Malaria Risk Index which is a summation of three related indices: a vulnerability index, an exposure index and an access index which allow a qualitative ranking of malaria risk in the MMP population. Application of currently available data to the framework illustrates that the highest risk population are those highly mobile populations engaged in forest work.

The framework has been used to develop more targeted behaviour change and outreach interventions for MMPs in Cambodia and its utility and effectiveness will be evaluated as part of those interventions.

DISCLOSURE Nothing to disclose.

3.1.3. Malaria elimination: getting there and staying there

INV.3.1.3.003

Ivermectin to reduce malaria transmission, prospects and challenges

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Ivermectin is an anti-parasitic drug commonly used for the treatment and control of onchocerciasis and lymphatic filariasis. In this context, over 2000 million doses have been safely used in the last 30 years.

In parallel, it has been noted that *Anopheles* mosquitoes feeding on ivermectin-treated humans have a reduced lifespan. For this reason, the potential use of ivermectin at a population level to impact on malaria vectors is under investigation. There are several theoretical benefits: it could target mosquitoes escaping core interventions (i.e. residual transmission); as a novel mechanism of action, it would have function even in the context of insecticide resistance, and finally, it could be a new tool to support vector control in areas of high transmission.

There are key knowledge gaps to be able to interpret even available data. First, what is the correlation of ivermectin blood levels with mosquito mortality; second, what are the target dose and treatment regimens needed to help interrupt transmission in different settings? And finally, what would be needed to turn this into an implementable and scalable tool?

Ivermectin's short half-life poses a technical challenge since the dose and formulation currently used in mass drug administration (MDA) campaigns would result in mosquito-killing levels lasting only a few days. The options being explored include multiple-dose schemes, novel long-lasting formulations and the effect of a single dose on the age structure of the mosquito population.

Additional technical challenges include the safety of new dose MDA campaigns targeting malaria, the procurement of the drug for a larger population and the potential appearance of ivermectin resistance in mosquitoes or filariae.

From the regulatory point of view, ivermectin MDA would constitute an altruistic intervention since the benefit for the person taking the drug would stem from a community effect on the mosquito population. Direct benefits would include impact on filariae, helminths and ectoparasites, but no effect is expected on the malaria parasite within the human. The ethics and regulatory pathway of such an intervention have been explored during the development of transmission-blocking vaccines, but constitute nonetheless an important challenge.

Lastly, the effectiveness, safety, acceptability and costs-effectiveness of an ivermectin-based tool will need to be contrasted with alternative tools to reduce transmission.

DISCLOSURE Nothing to disclose.

O.3.1.3.005.LB

Decline in the burden of malaria in pregnancy in Southern Mozambique: evidence from a 14-year period and implications for malaria elimination

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BACKGROUND Knowledge of the trends in malaria transmission is essential to evaluate the impact of elimination campaigns. Pregnant women are especially vulnerable to malaria and have been suggested as a potential reservoir of *Plasmodium falciparum* parasites. The objective of this study was to describe changes in the burden of malaria in pregnancy and its maternal and infant adverse consequences over a 14-year period in a semi-rural area of southern Mozambique.

METHODS The study was designed as a retrospective pooled analysis of data collected in five studies that enrolled pregnant women of all gravidities between 1998 and 2012. Temporal changes of maternal *P. falciparum* infection and pregnancy outcomes, as well as the effect of gravidity and HIV infection on the changes on malaria burden were assessed over the 14-year period.

RESULTS A total of 4973 pregnant women contributed to this analysis; 27.2% of them were primigravidae and 29.3% were HIV-infected. A significant drop in peripheral parasitemia prevalence was found between 1998 and 2010 (from 15.3 % to 0.5% $P < 0.001$) with a slight but significant rebound in 2012 (to 3.5%, $P = 0.003$). The geometric mean *P. falciparum* parasite density in peripheral blood was higher in 2010 compared with that in 1998 (66 683 vs. 4667.9 parasites/μl, $P < 0.001$). The prevalence of placental infection also significantly drop during the study years (from 50.7% in 2003 to 3.5% in 2012, $P < 0.001$).Primigravidae had higher prevalence of *P. falciparum* infection than multigravidae across all studied periods ($P < 0.001$). Overall, no significant differences were found in the prevalence of peripheral parasitemia between HIV- infected and uninfected pregnant women. Maternal anemia ranged between 57.4% and 37.4% with no specific pattern over the study years. The prevalence of low birth weight decreased during the study period (from 19.8% in 2003 to 6.1% in 2012, $P < 0.001$).

CONCLUSIONS A significant decrease in the malaria burden in pregnancy was observed in this area of southern Mozambique over a period of 14 years. Importantly, the increase in *P falciparum* infection found at the end of the 14-year period calls for the need of continuous monitoring and surveillance of malaria transmission in pregnant women.

DISCLOSURE Nothing to disclose.

3.1.4. *P. vivax* – and it's importance

O.3.1.4.002

Malaria elimination in the Asia-Pacific: addressing the *P. vivax* challenge

I. Mueller[1,2] and The TransEPI Consortium

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After a decade of significant successes in malaria control, the East Asian leaders have committed themselves in 2014 to a malaria-free Asia Pacific by 2030. *Plasmodium vivax* is now the predominant parasite throughout the region and its elimination will be the major challenge in meeting this ambitious deadline. Its high transmissabilty and ability to relapse from long-lasting liver stages render *P. vivax* significantly more resistant to elimination than *P. falciparum*. Our studies in PNG and Thailand have shown that relapses cause up to 80% of *P. vivax* blood stage infections and that even sub-microscopic, asymptomatic *P. vivax* infections can successfully infect mosquitoes. A rapid path to elimination will thus require a direct attacking on the hidden hypnozoite reservoir with mass-drug administration (MDA). Given the challenges of MDA with an 8-aminoquinoline, novel methods to determine population at risk and individuals that carry hypnozoites are urgently needed.

DISCLOSURE Nothing to disclose.

O.3.1.4.003

Killing the hypnozoite: drug discovery approaches to prevent relapse in *Plasmodium vivax*

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Malaria remains a disease of devastating global impact, killing more than 600 000 people every year—the vast majority being children under 5 years old. *Plasmodium vivax* puts as many people at risk as *P. falciparum* and is more prevalent outside of sub-Saharan Africa. In 2007, the call for malaria eradication was made to researchers in the malaria community. However, the eradication of malaria will only be possible if effective, well-tolerated medicines that kill hypnozoites in vivax malaria – and thus prevent relapses – are available to patients. Over the last decade there has been an increased investment in antimalarial research and development through the work of organizations such as the Medicines for Malaria Venture (MMV), their partners, and others; new molecules with new modes of action are entering into preclinical development and beyond. Despite progress in the 8-aminoquinoline series, with tafenoquine in Phase III showing clear benefits over primaquine, the drug discovery challenge to identify new hypnozoiticidal or hypnozoite-activating compounds has been hampered by the dearth of biological tools and affordable *in vitro* assays fit for screening large libraries of chemical compounds. This is due mainly to the immense scientific and logistical challenges associated with accessing relevant human tissue and sporozoites. There are now emerging good quality and exciting tools that have recently demonstrated the proof of concept that such robust assays could be developed. This presentation will review the current Global Malaria Portfolio focusing on drugs in development that target *P. vivax* liver stage, with a particular focus on the promising drug tafenoquine, and on the MMV strategy to increase the number of new hypnozoiticidal drug candidates. As part of this, the recent progresses on the delivery of accessible *in vitro* decision-making assays for *P. vivax* liver stages and our efforts to team up together with academic researchers, industrial partners, non-governmental agencies, foundations and funding agencies for the extra 'push' that will allow the scale up and industrialization of these assays necessary for the screening of large small molecule libraries and subsequent drug discovery and development will be presented.

DISCLOSURE Nothing to disclose.

O.3.1.4.004

Development of an Anopheles vector and tools to study *Plasmodium cynomolgi*, a surrogate for *P. vivax*

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INTRODUCTION Malaria is endemic to several countries in Southeast Asia with the exception of Singapore. However, this status quo of Singapore should not be taken for granted as high exposure to travelers from malaria-endemic countries puts Singapore under continuous risk to increased prevalence of the infectious disease. *Plasmodium vivax* is the most clinically prevalent agent of malaria in Southeast Asia and is also the *Plasmodium* species that gives relapses of the disease if inappropriate chemotherapies are administered. *Plasmodium vivax* has dormant forms known as 'hypnozoites' that are believed to give rise to relapses and can only be eliminated by the 8-aminoquinolines but this drug class is contraindicated in glucose-6-phosphate dehydrogenase-deficient patients. In order to discover the next generation of drugs against hypnozoites, high throughput drug screening assays are necessary for *P. vivax* or *P. cynomolgi*, a surrogate for the former. *Anopheles epiroticus*, a member of *An. sundaicus* complex, is a predominant malaria vector in the region and is endogenous to Singapore. Although *An. stephensi* and *An. gambiae* are the common *Anopheles* spp. used in laboratories for malaria studies, local regulatory authorities of Singapore have imposed sanctions on their import. Therefore we explored the possibility of developing *An. epiroticus* as a malaria vector in the laboratory to produce sporozoites for *in vitro* culture of liverstages and to investigate host-parasite interactions.

METHODS AND MATERIALS Wild-type *An. epiroticus* was adapted to laboratory environment and a robust colony was established. Membrane feeding protocols were adapted to infect the mosquitoes. Using green fluorescent protein-expressing rodent malaria parasites, the mosquitoes were evaluated for their vectorial capacity. The mosquitoes were also fed on *P. cynomolgi*-infected monkeys and parasite loads were assessed by mercurochrome-staining of mosquito midguts and sporozoite counts.

RESULTS *An. epiroticus* can be adapted for rearing in the insectary and can be infected by multiple *P. berghei, P. yoelii* and *P. cynomolgi*. Sporozoites produced are infectious *in vitro* and *in vivo*. Infection prevalence can be increased by selection of susceptible progenies generation after generation.

CONCLUSIONS With a supply of *P. cynomolgi* sporozoites, more tools for *P. cynomolgi* to dissect its biology can be developed as its liverstages can be explored and drug screening assays can be established.

DISCLOSURE Nothing to disclose.

O.3.1.4.005

Confirmed *Plasmodium vivax* resistance to chloroquine in Central Vietnam

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BACKGROUND *Plasmodium vivax* resistance to chloroquine (PvCQR) is currently reported in almost all vivax endemic countries. In Vietnam, despite a single published report of PvCQR in the early 2000s, *P. vivax* was still considered sensitive to CQ. Between May 2009 and December 2011, a 2-year cohort study was conducted in Central Vietnam to assess the recommended radical cure regimen based on a 10-day course Primaquine (0.5 mg/kg/day) together with 3 days CQ (25 mg/kg). We hereby report the results of the first 28-day follow-up estimating the cumulative risk of *P. vivax* recurrences together with the corresponding CQ blood concentrations among other endpoints.

RESULTS Out of 260 recruited *P. vivax* patients, 240 completed treatment and were followed up to day 28 according to the WHO guidelines. Eight patients (3.45%) had a *P. vivax* recurrent infection, at day 14 ($n = 2$), day 21 ($n = 1$) and day 28 ($n = 5$). Chloroquine blood concentrations, available in 3/8 recurrent infections (day 14,21,28) were above the minimal inhibitory concentration (>100 ng/ml whole blood) in all of them. Fever and parasitaemia (both sexual and asexual stages) were cleared by day 3. Anemia was common at day 0 (35.8%) especially in children below 10 (50%) and hemoglobin (Hb) recovery at day 28 was significant among anemic patients (median change d28-d0 = +1.7 g/dl; IQR[+0.7; +3.2]).

CONCLUSION This report confirms for the first time *P. vivax* CQ resistance in Central Vietnam, and calls for further studies using standardized protocols for accurately monitoring the extend and evolution of PvCQR in Vietnam. These results, together with the mounting evidence of artemisinin resistance in Central Vietnam, further highlight the increasing threat of antimalarial drug resistance on malaria elimination in Vietnam.

DISCLOSURE Nothing to disclose.

3.1.5. Malaria transmission: from the field to the bench

O.3.1.5.002

Where to start malaria elimination: core or fringes?

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INTRODUCTION Malaria and some other tropical diseases are currently targeted for elimination and eventually eradication. In many areas where diseases have been eliminated it is concluded that it would have been more efficient to focus efforts earlier in the places with the highest disease burden and transmission. These areas remained a threat after transmission was interrupted elsewhere, leading to the need to maintain potentially expensive surveillance activities in peripheral areas after the disease has been eliminated from them.

METHODS We use a mathematical model to compare the implications of prioritisation choices in reducing overall burden and costs. We consider the implications of various assumptions of the relationships between burden, risk of importation, and the required durations of the elimination program to transmission potential.

RESULTS We show that:

1 When the duration of the elimination program is independent of the transmission potential, burden is always reduced most by targeting high transmission areas first.
2 The optimal ordering to reduce costs depends on the actual transmission levels.
3 In general, when overall transmission potential is low and the surveillance cost per secondary case is low compared to the cost per imported case, targeting the higher transmission area first is favoured.

CONCLUSION In the current global health climate, many prioritisation decisions are made *ad hoc*, without consideration of whether there might be technically optimal ways of organising a program. This theoretical analysis provides guiding principles on optimal ordering of different settings for malaria elimination.

DISCLOSURE Nothing to disclose.

O.3.1.5.003

Comparative transmission-stage dynamics of *Plasmodium vivax* and *P. falciparum*

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Knowledge of *Plasmodium vivax* and *P. falciparum* transmission dynamics is important to design and monitor transmission-blocking interventions aiming at reducing the burden of malaria. To investigate the contribution of *P. vivax* relapses or new infections to the gametocyte reservoir a cohort study was carried out in Papua New Guinea. Because *P. falciparum* is sympatric and has a prevalence of 23% in the study area, the effect of mixed-species infections on gametocyte production could be analyzed.

504 children were randomized to two treatment arms receiving blood-stage clearing drugs plus either Primaquine (PQ) or placebo and were actively and passively followed for 8 months. All blood samples positive for *P. vivax* or *P. falciparum* by qPCR were genotyped and tested for gametocyte carriage and density by qRT-PCR targeting *pvs25* or *pfs25* transcripts.

PQ-treated children had a 75% lower risk of carrying *P. vivax* gametocytes compared to Placebo recipients. This corresponded well with the observed PQ effect on *P. vivax* parasite positivity. Gametocyte positivity and density in *P. vivax* positive children did not differ between the treatment arms suggesting that relapses do not differ from new infections with respect to gametocyte production. The time to first *P. vivax* gametocyte detection in the PQ arm was 125 days post-treatment in contrast to 91 days in the placebo arm ($P = 0.008$). Gametocytes were observed by qRT-PCR in 38% of *P. vivax* blood-stage positive samples compared to 25% of *P. falciparum* infections ($P < 0.001$). A higher proportion of *P. falciparum* gametocyte

carriers was observed in the first *P. falciparum* infections after PQ treatment compared to placebo ($P = 0.02$).

We conclude that *P. vivax* relapses and new infections produce gametocytes at similar rates, and that relapses contribute equally to transmission. This highlights the importance of eliminating hypnozoites to control *P. vivax*. Reduction of the burden of *P. vivax* infection by PQ seemed to increase *P. falciparum* gametocyte positivity in the first infections after treatment. This could indicate competitive interactions between both species within the same host: absence of one infecting parasite species increases the infectivity to mosquitoes of the other. Yet, the precise effect of mixed-species infection on transmission success remains to be investigated.

DISCLOSURE Nothing to disclose.

O.3.1.5.004

Impact of intensified malaria control on the epidemiology and transmission of malaria in two areas of Papua New Guinea

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A renewed emphasis on malaria control in Papua New Guinea (PNG) has resulted in a significant overall reduction in the prevalence and incidence of malaria. However the reduction observed at the national/provincial level masks substantial heterogeneity of transmission at the local district and village level. Reduced transmission may also delay the acquisition of clinical immunity and lead to an upward shift in the peak age of malaria infection and clinical illness. To investigate this, repeated community cross-sectional surveys and longitudinal child cohorts were undertaken in two hyper-/holo-endemic areas of PNG combining sensitive molecular diagnosis of infections with demographic, immunological and GPS data. The PCR prevalence of *P. falciparum* (Pf) and *P. vivax* (Pv) in surveyed communities in East Sepik decreased from 55% (2005) to 7% (2013) and 36% to 4% respectively. In Madang, Pf prevalence declined from 39% (2006) to 18% (2010) and Pv from 32% to 13%. In the recent surveys the vast majority of infections were asymptomatic and sub-microscopic, with a trend towards an upward shift in the age-specific burden of symptomatic malaria in 2013. There is substantial heterogeneity in transmission with cluster analysis identifying Pf and Pv specific hotspots and key determinants are being investigated. In 1–5 year old children, the prevalence of Pf and Pv infections at enrolment has more than halved from 50% (2006) to 14% (2013) and 53–14%, respectively. The prevalence of clinical malaria episodes has also declined from 21% to 5%. In 5–12 year-old children, the prevalence of Pf infections at enrolment has markedly declined from 67% (2004) to 16% (2013), while the prevalence of clinical Pf episodes has remained relatively constant, from 2.4% to 1.7%. Conversely, although prevalence of Pv infections in this age group has declined from 34% to 24%, the prevalence of clinical episodes increased from 0.1% to 1.5%. Full and detailed analysis of cohort data is ongoing and will be presented. In conclusion, preliminary data confirms both a decline in the prevalence of Pf and Pv infections, a corresponding delay in the acquisition of clinical immunity and an increase in the heterogeneity of transmission. A detailed understanding of the increasingly complex epidemiology of malaria in PNG is critical to identify and implement targeted control strategies to ensure the ongoing success of malaria control in PNG and make progress towards elimination.

DISCLOSURE Nothing to disclose.

O.3.1.5.005

Malaria prevalence and mosquito establishment in Nouakchott, Mauritania

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Recently, the prevalence of malaria has dramatically increased in Nouakchott, the capital city of Mauritania. Numerous factors, such as exceptional rainfalls, the 'Aftout Essahli' hydraulic project that supplies safe potable water to Nouakchott from the Senegal River, and various human practices, have contributed to this situation by creating *Culicidae* fauna, particularly those involved in mosquito-borne diseases.. The objectives of this study were to (i) collect and identify *Culicidae* fauna in the city, (ii) identify and characterize mosquitoes' larval development sites, and (iii) further consolidate the evidence for local malaria transmission within the city. From January 2012 to December 2014, regular monitoring of the *Culicidea* fauna was carried out in the Ksar, Dar Naim, Tevragh Zeina, Arafat, and Teyarett districts of Nouakchott and malaria incidence was checked monthly among febrile patients presenting spontaneously at Teyarett Health Centre in 2012 and 2013. Of 55 potential mosquito habitats, both artificial and natural water collections were productive for *Anopheles gambiae* s.l, *Culex* sp., *Aedes aegypti,* and *Aedes* (*Ochlerotatus*) *caspius*. These consisted of water discharge from public standpipes, household drinking-water tanks, and rainwater puddles. *Anopheles* mosquitoes were present throughout the year reaching the maximum of abundance in October, corresponding to the peak of the transmission season. Multivariate regression analyses showed that salinity up to 0.1 g/l and shaded areas were protective factors against high larval density, and a pH up to 7.61 was a risk factor for high larval density in anopheline larval habitats. While no *Aedes* mosquito was found in 2013, their emergence was reported in September 2014. Moreover, the number of laboratory-confirmed *Plasmodium vivax* cases has increased steadily in 2012 and 2013, reaching more than 2,000 cases in 2013 at the district of Teyarett. The present data strongly support the establishment of malaria in Nouakchott, where environmental and human factors favour the establishment of mosquito larval and adult populations. Our

results highlight the need for more detailed studies to assess both mosquito (larvae and adults) biology and ecology and the risk of vector-borne disease transmission.
KEYWORDS *Anopheles gambiae* s.l.; *Aedes* sp.; habitats; larvae; Nouakchott; standpipes; emergence, malaria.
DISCLOSURE Nothing to disclose.

3.1.6. Answering key questions on malaria drug delivery – the importance of diagnostics

O.3.1.6.002
Impact of malaria rapid diagnostic tests on patient care: results from the ACT consortium

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Malaria rapid diagnostic tests (RDTs) are intended to have a beneficial impact on management of suspected malaria, including that patients with confirmed malaria receive artemisinin-based combination therapy (ACT) and patients without malaria receive non-antimalarial treatment. The ACT Consortium includes several studies designed to test operational strategies for ACT and RDT implementation in various settings, providing an opportunity to draw on data from multiple projects that have introduced RDTs across a range of clinical, social, and epidemiological contexts, and in public, private retail, and community health service sectors. To assess the impact of RDTs on patient treatment and satisfaction at the consultation, data were examined from nine studies comparing scenarios where RDTs were made available to control scenarios where RDTs were not made available. Where RDTs were introduced, the proportion of patients tested ranged from 39% to 99%; figures were similar for children under 5 years and for older patients. Prescription of ACT was less common in nearly all RDT scenarios (range 8–64% vs. 15–99% in scenarios without RDTs), driven mostly by reduced prescription for RDT-negative patients (range 3–45% vs. 18–98% for RDT-positive patients). An exception to this pattern was seen in public facilities in a high-transmission setting, where RDTs were irregularly available in the control arm. The impact of RDTs on prescription of systemic antibiotics varied, ranging from 15–73% in scenarios without RDTs and 21–75% in scenarios with RDTs available, and was slightly higher for RDT-negative patients (range 29–78% vs. 13–65% for RDT-positive patients). There was no clear pattern observed for prescription of other treatments, polypharmacy, or patient satisfaction. This ongoing analysis aims to understand factors associated with variation in case management outcomes in order to offer more tailored guidance for RDT introduction in other areas.
DISCLOSURE Nothing to disclose.

O.3.1.6.003
Effects of introducing malaria rapid diagnostic tests in drug shops: findings from the evaluation of a cluster randomised trial in Uganda

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WHO recommends universal access to malaria diagnosis, encompassing all treatment providers, including the private sector. Rapid diagnostic tests (mRDTs) provide a feasible means of confirming malaria diagnosis in drug shops. As yet, there is limited evidence of the impact of diagnostic testing on antimalarial drug sales and referral practices by drug shops in Africa. A cluster-randomised trial to evaluate the impact and cost-effectiveness of using mRDTs, compared with presumptive treatment, undertaken in 65 registered drug shops in Mukono District, Uganda in 2010–12, was one of the first investigations of the impact of introducing mRDTs in the private retail sector. Analysis of treatment data routinely recorded by drug shop vendors (DSVs) during the trial found that use of mRDTs in drug shops was feasible and highly acceptable to both providers and to their customers; a finding confirmed by household interviews in a random sample of patients. Adherence to mRDT results by DSVs was high with over 95% of treatment decisions consistent with mRDT test result, reducing sales of ACTs by 40% compared to drug shops using presumptive diagnosis. Validation of DSV treatment decisions by expert microscopy, demonstrated that use of mRDTs substantially improved the targeting of ACTs to patients with malaria parasites (72.9% of ACT treatments in drug shops using mRDTs were correctly targeted vs. 33.7% in drug shops using presumptive diagnosis, $P < 0.001$). A series of qualitative and economic evaluations amongst drug shop vendors, patients and local health staff, conducted alongside the trial, revealed how pre-existing social and economic relationships between DSVs and their clients, and between DSVs and the wider health system, shaped the response of drug vendors to the intervention and may have contributed to the high adherence to mRDT test results. Perceived increases in the professionalization of DSVs and as trusted providers also contributed to the popularity of the intervention. Nonetheless, potential for other unintended, including less desirous, consequences was also revealed. A synthesis of the insights generated by this early ground breaking intervention trial in the retail sector will be presented, drawing on evidence from across the epidemiological, ethnographic and economic investigations conducted as part of this study, to illustrate and discuss the potential benefits and pitfalls of introducing mRDTs into drug shops.
DISCLOSURE Nothing to disclose.

O.3.1.6.004
Improving appropriate use of quality-assured RDTs in the private sector: baseline and midterm evaluation results from Uganda

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Coverage of fever case management interventions remains low across sub-Saharan Africa, including Uganda. While many care-

givers seek treatment for symptoms of fever in the private sector, private sector outlets may not have adequate fever diagnostics, training, waste management, and first line quality assured treatments to ensure appropriate case management.

The Malaria Consortium together with FIND, PSI and WHO are implementing a project creating a private sector market for quality assured RDTs in malaria endemic countries from April 2013 to date targeting the private sector. Accredited outlet types including drug shops, pharmacies and clinics have been established, and participating members received training on integrated case management for febrile illnesses, supportive supervision, quality assured malaria rapid diagnostic test kits, and waste management services.

Baseline and follow-up population-based household and exit client surveys were conducted in 2013 and 2014 to assess changes in case management in the implementation district - Wakiso. Treatment-seeking behavior for fever was assessed using standard methods. Key results include overall change in appropriate case management by private providers; changes in coverage across relative household socioeconomic status; and changes in case management of those who reportedly received treatment in the private sector. Implications for scaling up case management coverage through strengthening services provided by private sector providers focusing on the different outlet type will be discussed.

DISCLOSURE Nothing to disclose.

O.3.1.6.005

Factors impacting malaria rapid diagnostic test performance

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INTRODUCTION WHO endorses the use of malaria rapid diagnostic tests (RDT), which have high sensitivity, specificity and accuracy considered equal to alternate diagnostic methods in the field. However this is contingent on whether healthcare workers properly, consistently perform the tests, and recognize errors as they occur.

METHODS To ensure a variety of factors could be identified, data from nine implementation studies from multiple countries and regions were aggregated. In each study, healthcare workers received training on processing RDTs and integrated an automated RDT reader into their point-of-care case management. Users were aware that high-resolution images of all RDTs would be captured. User errors relate to procedure (e.g. incorrect volume or placement of blood sample or buffer solution, delayed reading) and interpretation (e.g. not recognizing invalid test results, disregarding faint test lines, interpreting the incorrect RDT). Descriptive statistics of the prevalence of each error type was calculated for each study. A random-effects meta-analysis was used to estimate the average proportion of errors across studies.

RESULTS There were over 150 healthcare workers, who conducted a minimum of 30 malaria RDTs across the 9 studies, with a total of 31 705 RDTs processed. Overall, the estimated proportion of all errors was 10.72% (95% CI: 9.67, 12.05). The most frequent errors were: too much blood added, analysis outside the recommended time period, or incorrect RDT. The proportion of errors significantly varied between studies. Three RDT brands were used across the nine studies. The RDT brand was significantly associated with the prevalence of errors where the control line not visible and a red background. In a subset of studies were healthcare workers were able to receive feedback, a decreased proportion of human processing errors were observed over the study period.

CONCLUSIONS Even with healthcare workers aware that RDT processing was being remotely monitored, there was a significant amount of processing and interpreting errors. The accuracy of RDTs can be jeopardized by these errors. Being able to intervene, provide additional training, and provide quality control assurances would help increase the accuracy of malaria testing in the field.

DISCLOSURE Fio Corporation provided some financial support for this project but had no impact on the study results.

3.1.7. Drug resistance in malaria

O.3.1.7.002

New medicines for malaria eradication – 7 years on

T. N. Wells

Medicines for Malaria Venture, Geneva, Switzerland

It has been 7 years since the initial call by WHO and the Bill and Melinda Gates Foundation for an agenda which would lead to the eventual eradication of malaria. There have been significant advances, but the discovery and development of new medicines is still a work in progress.

Over the last 7 years, we have seen the launch of five fixed-dose artemisinin combination therapies, which have treated hundreds of millions of children; the prequalification of artesunate as a treatment for severe malaria; and the use of medicines to protect children in the Sahel region (seasonal malaria chemoprotection).

The new medicines that are being developed are to overcome two issues with current medication. First, to simplify therapy, possibly with a single dose cure; and second, activity against all resistant strains of parasite. Increased investment, increased access to new technologies, and a high degree of cooperation between partners has led to an unprecedented number of new molecules entering clinical development. MMV and our partners have currently five new molecules being studied in humans: the endoperoxide OZ439, the PfATP4 sodium channel inhibitor KAE609, the DHODH inhibitor DSM265, the cyclic amine transporter inhibitor KAF156, and the PI 4-kinase inhibitor MMV048. In addition there are a wide range of new molecules with a potential to start human studies over the next 5 years. These molecules are active against all the currently known resistant strains of parasite, including the artemisinin-resistant strains from the Mekong subregion. They have pharmacokinetics which support their use as part of a single dose cure. In addition, some have good activity in transmission blocking, which could lead them to be primaquine sparing, and some have activity against liver schizonts, which would support chemoprotection. However, no new scaffolds have been found with anti-relapse activity, and for the moment this is being shouldered by tafenoquine, which is now in pivotal phase III studies.

For the future, the challenge will be to keep up the momentum, but also to identify new molecules. A single dose cure implies pushing these new medicines to their limits, and if they are to be used in asymptomatic subjects we will need 'vaccine' levels of safety.

There is bound to be a high degree of attrition. The talk will highlight the challenges of the next 5 years in the discovery and development of new medicines.

DISCLOSURE TW is an employee of Medicines for Malaria Venture, a Swiss charity dedicated to the discovery, development and delivery of new medicines against Malaria, which has been involved in the design and development of these projects.

O.3.1.7.003

Efficacy, safety and pharmacokinetics of KAF156 in adult patients with acute, uncomplicated *P. falciparum* or *vivax* malaria: a proof-of-concept, open label study

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KAF156 is the first in a new class of antimalarial (imidazolopiperazines) with a novel mechanism of action demonstrating *in vitro* potency against *P. falciparum* and blood stage *P. vivax*. This proof-of-concept, open-label, multicenter study assessed efficacy, safety, tolerability and pharmacokinetics after single and multiple dosing. Comprising 2 parts, a total of 43 adult Asian male patients with uncomplicated monoinfection malaria were enrolled. Part 1 was a 3-day (400 mg/day) repeated dose study in two cohorts:

1 Cohort 1 (n = 11, *P. vivax*).
2 Cohort 2 (n = 10, *P. falciparum*).

Standard-of-care pharmacotherapy was given on Day 5, followup was to Day 11. Part 2 (n = 22) was a single dose (800 mg) study in patients with uncomplicated *P. falciparum* with follow-up after 28 days. All patients in Part 1 completed the study except for one who was withdrawn due to mixed infection. In Part 2, 13/22 patients completed: 1 withdrew on Day 1 due to vomiting, 7 discontinued due to recrudescence, 1 due to new malaria infection. All patients achieved parasite clearance within 36 h in Cohort 1, 66.1 h in Cohort 2, and 67.9 h in Part 2 (withdrawn patient excluded). Median parasite clearance time was 23.6 h and 45.0 h in Cohort 1 and 2; 48.8 h in Part 2. The WWARN parasite clearance estimator slope half-life was lower in *P. vivax* patients (1.86) than *P. falciparum* patients (3.51 Cohort 2; 3.48 Part 2). Median fever clearance time was 14.1 and 6.1 h in Cohorts 1 and 2; 4.2 h in Part 2. PCR-corrected 28-day cure rate was 67% in Part 2. Overall, PK between patients with *P. vivax* and *P. falciparum* infection was similar. Mean T1/2 was ~39 h in Cohort 1, ~40.8 h in Cohort 2 and ~48.7 h in Part 2. No deaths or SAEs were reported. The total incidence of adverse events (AEs) was 61.9% in Part 1 (sinus bradycardia the commonest AE) and 100% in Part 2 (sinus bradycardia [63.6%], thrombocytopenia [59.1%], hypokalemia [50.0%], anemia [31.8%], the top three AEs). KAF156 is a new chemical entity with good clinical potential as an antimalarial, predictable PK, and a tolerable safety profile.

DISCLOSURE Ruobing Li, Baldur Magnusson, Xiaolei Xun, Rong Zhao, Thierry T. Diagana, Peter Pertel, and F. Joel Leong, are all Novartis employees.

O.3.1.7.004

Artemisinin-based combination therapy efficacy in Kisumu, Western Kenya: selection of parasite subpopulations of *Plasmodium falciparum* with attenuated response to ACTs

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Genetically determined artemisinin resistance in *Plasmodium falciparum* has been described in Southeast Asia where parasite subpopulations can be segregated into artemisinin sensitive and resistant groups. In a recent study, we described genetically determined response to artemisinin treatment in parasites from western Kenya. In the current study, we investigated if there are specific parasite subpopulations that are selected for after patients with uncomplicated malaria are treated with ACTs. Subjects with uncomplicated malaria were recruited into the study, randomized to receive either artemether lumefantrine or artesunate mefloquine. Blood samples were collected at hours 0, 4, 8, 12 and 6-h thereafter until parasites were cleared. The changes in parasite genetics at hour 0 were compared to those collected in subsequent time-points starting at hour 24. Analysis was carried out using microsatellite (MS). Drug resistance profiles were analyzed at *pfmdr1* codons 86 and 184 by sequencing. K13 polymorphism analysis is underway. Parasites collected at each time-point were grouped as a population. Expected heterozygosity (H_e), the variance in allele size and the number of alleles at each locus in each population was measured. Each of the locus analyzed had multiple alleles; ARA2 was the least polymorphic whereas Polyα was the most polymorphic. Of the 12 MS, three (ARA2, TA1, TA40) were selected for based on the reduction of H_e at subsequent time-points compared to hour 0. In each of these three loci, one of the alleles increased in frequency in subsequent parasite populations. The skewed frequency of certain alleles at these three loci is indicative of selection of specific parasite subpopulations. Although TA42 and TA81 loci were not selected for, they carried two of the alleles which had the largest increment in frequency from hour 0 parasite population to subsequent populations (35- and 20-fold respectively). ARA2, TA1 and TA40 are found in chromosome 11, 6 and 10 respectively. These are regions of interest warranting further analysis of SNPs within the genome because they may be associated with selection of parasites by ACTs in western Kenya.

DISCLOSURE Nothing to disclose.

O.3.1.7.005

Plasmodium falciparum multiplication rates in recurrent parasitaemias

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INTRODUCTION Recurrent *Plasmodium falciparum* parasitaemia after treatment may be caused by recrudescence or reinfection. During active follow-up recurrences may be discovered when still asymptomatic. The questions addressed here are: at what rate recurrent parasites multiply in recrudescences or reinfections, and what factors may determine parasite multiplication rates (PMR).
METHODS A database was compiled from 42 trials which treated uncomplicated malaria with various drugs (97 study arms) during 2002–2005 in 13 Sub-Saharan African countries, and followed recurrent asymptomatic parasitaemia until symptomatic or day 28.

Linear mixed models were used for reinfections and recrudescences to evaluate the PMR. The PMR was calculated by using the slope of the parasitaemia model as a function of the days of assessment of recurrent parasitaemia both for individual treatments and overall for recrudescences and reinfections.
RESULTS Overall, 8728 patients were assessed and 1355 were parasitological recurrences amounting to 3097 measurements between Day 7 and Day 28, of which 1958 (63%) and 1139 (37%) being from patients with a recrudescent and a reinfection, respectively. 839 (62%) recurrences were genotyped as recrudescences and 516 (38%) as reinfections. The PMR for recrudescences [2.09 (95% CI 2.00 – 2.38)] was lower than reinfections [2.54 (2.41 – 2.96)]. The PMRs of recrudescences ranged from 4.23 (artemether-lumefantrine, AL) to 1.58 (chloroquine CQ), and that of reinfections from 4.77 (sulphadoxine-pyrimethamine, SP) (followed by AL with 3.98) to 2.25 (CQ). The PMRs of recrudescences classed as LCF and LPF were 2.05 and 3.02 respectively; for reinfections, the respective PMRs were 3.56 and 4.77 – these differences were not statistically significant.
DISCUSSION Parasites exposed to CQ (probably due to its long t1/2) have the lowest PMRs, while the highest PMRs were found after AL and SP. These recurrent PMRs are are consistent with challenge trials in Gambian subjects (2.4 per cycle) and much lower than those obtained in naïve volunteers (very similar to the estimated *in vitro* PMR of 9.4), indicating a clear additional effect of natural responses and lingering drug levels.
DISCLOSURE Nothing to disclose.

3.1.8. Insecticide resistance

O.3.1.8.002

Malaria vector control at a crossroads: public health entomology and the drive to elimination

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Vector control has been at the core of successful malaria control. However, a dearth of field-oriented vector biologists threatens to undermine global reductions in malaria burden. Skilled cadres are needed to manage insecticide resistance, to maintain coverage with current interventions, to develop new paradigms for tackling 'residual' transmission and to target interventions as transmission becomes increasingly heterogeneous. Recognising this human resource crisis, in September 2013, WHO Global Malaria Programme issued guidance for capacity building in entomology and vector control, including recommendations for countries and implementing partners. Ministries were urged to develop long-range strategic plans for building human resources for public health entomology and vector control (including skills in epidemiology, geographic information systems, operational research and programme management) and to put in place the requisite professional posts and career opportunities. Capacity building and national ownership in all partner projects and a clear exit strategy to sustain human and technical resources after project completion were emphasised. Implementing partners were urged to support global and regional efforts to enhance public health entomology capacity. While the challenges inherent in such capacity building are great, so too are the opportunities to establish the next generation of public health entomologists that will enable programmes to continue on the path to malaria elimination.
DISCLOSURE Nothing to disclose.

O.3.1.8.003

Anopheles arabiensis is not successfully controlled by indoor residual spraying in Northwest Tanzania: implication for malaria vector control in the area

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High coverage of insecticidal bednets (LLINs/ITNs) and Indoor residual spraying (IRS) in parts of East Africa has been associated with a drastic reduction in the abundance of *Anopheles gambiae s.s.* the primary vector in the area. This led to an apparent shift in *An. gambiae s.l.* sibling species ratio toward the more zoophilic and more exophilic *An. arabiensis* which is less likely be killed by IRS and ITN. The impact of IRS with bendiocarb on the relative abundance of *An. gambiae s.s.* and *An. arabiensis* was evaluated in North West part of Tanzania during a community randomised trial.

Pre intervention, *An. arabiensis* represented 18.6% (95% CI: 13.9–24.6) and *An. gambiae s.s.* 81.4% (95% CI: 75.5–86.1) of the population of *An. gambiae s.l.* collected with indoor light traps, while *An. arabiensis* accounted for 3.8% and *An. gambiae s.s.* 96.2% of the population found resting indoor. Sporozoite

rate was 1.4% (95% CI: 1.1–2.0) and only *An. gambiae s.s.* were found positive. After IRS, density of *An. gambiae s.s* was reduced by 75% ($P = 0.046$) and *An. arabiensis* by 25% ($P = 0.745$). In the IRS villages sporozoite rate in *An. gambiae s.s.* was 1.8% and 0% for *An. arabiensis*. There was a significant difference in the gambiae s.s./arabiensis species ratio with *An. arabiensis* constituting 11.3% the control arm alone compared to 26.1% in the IRS arm (OR: 2.8 (95% CI: 1.1–6.8) $P = 0.027$).

Indoor Residual Spraying was more effective in controlling *An. gambiae* than *An. arabiensis* in North West Tanzania. *An. arabiensis* in this area is a secondary vector and appeared to contribute little to malaria transmission. The focus of control should remain on *An. gambiae s.s.* the main vector in this area while more specific vector control tools for *An. arabiensis* could be investigated.

DISCLOSURE Nothing to disclose.

O.3.1.8.004

Insecticide susceptibility of *Anopheles gambiae* s.l. in sentinel sites in the Democratic Republic of Congo

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In its national strategic plan for malaria control, DRC has distributed around 14.5 million long-lasting insecticidal nets (LLINs) in the period 2006–2010. Although they have been very effective in certain areas, there are challenges to their use including the loss of physical integrity and the loss of insecticidal effect. The aim of this study, conducted in 2013, was to evaluate the susceptibility of *Anopheles gambiae* s.l. to insecticides of four classes used in public health in DRC. The study was conducted in 2013 in 4 sentinel sites (Kapolowe, Lodja, Tshikaji, and Kabondo), 3 years after a mass distribution of LLINs by the National Malaria Control Program. Adult *An. gambiae*, reared from field-collected larvae, were tested in WHO susceptibility tests. The insecticides used in the tests were fenitrothion (1%), bendiocarb (1%), deltamethrin (0.05%), permethrin (0.75%), and DDT (4%). Mosquitoes from all sites were susceptible to fenitrothion and bendiocarb; however, resistance to DDT was detected in all sites. The susceptibility of mosquitoes to deltamethrin, by site, was: Kapolowe (95%), Kabondo (100%), Tshikaji (92%), and Lodja (96%). The susceptibility of mosquitoes to permethrin was: Kapolowe (39%), Kabondo (27%), Tshikaji (45%), and Lodja (49%). As the susceptibility of mosquitoes differed between sites, it is necessary to elaborate a resistance management strategy, with the aim of maintaining effectiveness of interventions. The resistance of *An. gambiae* s.l. to pyrethroids, the only family of insecticide approved for use in LLINs, is a worrying problem that threatens the immense efforts by the country to prevent deaths from malaria.

DISCLOSURE Nothing to disclose.

O.3.1.8.005

Micro-encapsulated pirimiphos-methyl shows high insecticidal efficacy against pyrethroid-resistant malaria vectors

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BACKGROUND Due to increasing resistance in *Anopheles gambiae* sensu lato mosquitoes to dichlorodiphenyl trichloroethane (DDT) and pyrethroids, alternative insecticide formulations for IRS with long-lasting residual activity are required to sustain the gains obtained in most malaria-endemic countries.

METHODS Three experimental capsule suspension (CS) formulations of the organophosphate pirimiphos-methyl were evaluated together with Actellic 50 EC, an emulsifiable concentrate (EC) of pirimiphos-methyl, and the pyrethroid ICON 10 CS, a lambda-cyhalothrin CS formulation, in an experimental hut trial. The formulations were tested on two types of surfaces: mud and cement.

RESULTS One of the CS formulations of pirimiphos-methyl, CS BM, outperformed all other formulations tested. On cement, the residual activity of pirimiphos-methyl CS BM measured using cone tests was similar to that of lambda-cyhalothrin and for both treatments., The mortality of susceptible Kisumu laboratory strain was not significantly below the WHO pre-set threshold of 80% for 30 weeks after spraying. Residual activity was shorter on mud surfaces, mortality falling below 80% on both pirimiphos-methyl CS BM and lambda-cyhalothrin treated surfaces at 25 weeks post-treatment.

CONCLUSION CS formulations of pirimiphos-methyl are promising alternatives for IRS, as they demonstrate prolonged insecticidal effect and residual activity against malaria mosquitoes.

DISCLOSURE Nothing to disclose.

3.1.9. Towards malaria vaccines

O.3.1.9.002

Novel approaches for the identification and profiling of new *Plasmodium falciparum* antigens as promising blood-stage candidates for inclusion in a malaria subunit vaccine

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The development of an effective malaria vaccine is recognized as one of the most promising approaches for preventing infections and reducing transmission. Since the *P. falciparum* genome was sequenced and annotated, reverse vaccinology represents the most attractive strategy to identify novel malaria vaccine candidates.

On the basis of available genome-wide transcriptomic and proteomic data, we have selected uncharacterized ORFs to evalu-

ate their potential as vaccine candidate antigens. For the characterization of selected antigens we have developed a rapid and efficient cell-based approach for monoclonal antibody (mAb) production:

1 Generation of mammalian cell lines expressing high levels of target antigen as transmembrane proteins.
2 Living-cell immunization of mice.
3 Generation of hybridoma cell lines.

This strategy has led us to the identification of the Cysteine-Rich Protective Antigen (CyRPA) as promising blood-stage malaria vaccine candidate: (i) generated α-CyRPA mAbs showed parasite *in vitro* growth-inhibitory activity due to inhibition of merozoite invasion; (ii) passive immunization experiments in *P. falciparum* infected NOD-scid $IL2R\gamma^{null}$ mice engrafted with human erythrocytes demonstrated the *in vivo* growth-inhibitory activity.

To investigate whether growth inhibitory α-CyRPA Abs can be induced by active immunization with the recombinant protein, CyRPA was recombinantly expressed as secreted protein in mammalian cells (i), purified from culture supernatant (ii) and employed for mice immunization (iii). Monoclonal antibodies against rec_CyRPA have been raised and have shown growth-inhibitory activity both *in vitro* and *in vivo*.

Taken together these results show that our strategy of immunization offers a rapid and efficient approach for the screening and characterization of predicted proteins. Using this approach, we are currently profiling additional parasite proteins and their combinations to assess their potential as vaccine components.

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DISCLOSURE Nothing to disclose.

O.3.1.9.003

Safety and immunogenicity of novel candidate blood-stage malaria vaccine P27A with Alhydrogel® or GLA-SE as adjuvant in healthy malaria non-exposed European and malaria exposed African adults aged 18–45 years

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INTRODUCTION The development of an efficient vaccine would present an essential complementary tool for control and elimination of malaria. P27A is a peptide from the asexual stage targeted by human antibodies inhibiting parasite growth in an antibody-dependent cellular (ADCI) assay. A synthetic peptide-of 104 amino acids based on the P27A sequence is thought to induce protective antibody responses.

METHODS AND MATERIALS The currently ongoing combined Phase Ia/Ib trial in Lausanne, Switzerland and Bagamoyo, Tanzania is designed to evaluate the safety and tolerability of P27A given in combination with Alhydrogel or Glucopyranosyl Lipid Adjuvant-Stable Emulsion (GLA-SE) as adjuvant in two populations, in non-immune Swiss adults and semi-immune Tanzanian ones. The vaccine is tested in healthy adults aged 18 – 45 years recruited in Lausanne (n = 16) and in healthy African adults with previous exposure to the parasite (n = 40). Humoral and cellular immune responses are assessed in all volunteers using shared protocol.

RESULTS Preliminary safety results suggest that administration of 10 or 50 mg P27A with Alhydrogel or with GLA-SE (2.5 or 5 mg) in healthy European and African adults is safe. In Swiss volunteers, three injections of P27A in Alhydrogel or GLA-SE elicited specific antibody titers of 1/3200 (range 1/200 to 1/12800) and 1/51200 (range 1/3200 to 1/204800), respectively. All volunteers seroconverted to positive P27A antibody titers after the third injection in the Alhydrogel group and already after the second injection in the GLA-SE group.

CONCLUSION These data show that the P27A vaccine candidate with either adjuvant is safe and induces marked humoral immune response. Waiting for final analysis of this parallel phase Ia/Ib trial, these data support further evaluation of this candidate vaccine.

DISCLOSURE Nothing to disclose.

O.3.1.9.004

PfSPZ vaccine: from concept to focal elimination of *Plasmodium falciparum*

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The concept of a malaria vaccine based on whole *Plasmodium falciparum* (Pf) sporozoites (SPZ) was first demonstrated in 1970s, but never translated into a vaccine, because it was considered impossible to do so. Sanaria has developed the capacity to manufacture aseptic, purified, cryopreserved PfSPZ in compliance with current Good Manufacturing Practices. PfSPZ Vaccine comprises radiation-attenuated PfSPZ. PfSPZ Challenge (used for controlled human malaria infection) and PfSPZ-CVac (PfSPZ Challenge co-administered with an antimalarial), comprise non-attenuated PfSPZ. These PfSPZ have now demonstrated:

1 Infectivity to volunteers, including 100% of volunteers infected 3200 PfSPZ administered by direct venous inoculation (DVI) in Germany, Spain, Gabon and Tanzania.
2 56/69 (81%) malaria naïve volunteers protected after administration of 3–5 doses of PfSPZ Vaccine at different doses administered intravenously (IV) or by DVI (13/15 with 3 doses).
3 Protection against a strain of Pf different from that in PfSPZ Vaccine (heterologous protection).
4 Over 50% protection for 6 months in a malaria endemic setting (Mali) against natural populations of Pf (heterogeneous protection) with PfSPZ Vaccine administered by DVI.
5 100% protection at 10 weeks in malaria naïve volunteers administered 3 doses of PfSPZ-CVac by DVI.

These results are the springboard for the next phase of Sanaria's Clinical Development Plan (CDP), which will optimize dose regimens for all ages and test the vaccine in groups with HIV or other co-infections, in women of childbearing age and against *P. vivax*. To reach pivotal Phase 3 studies that will support licensure and elimination campaigns post licensure, Sanaria and its partners have established the International PfSPZ Consortium, which includes public and private sectors institutions from Africa, Europe and the US.

DISCLOSURE Nothing to disclose.

O.3.1.9.005

Assessment of FMP2.1/AS01B, an asexual blood-stage malaria vaccine, in a phase I/II a clinical trial using blood-stage controlled human malaria infection

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INTRODUCTION This trial examined FMP2.1/AS01B, a blood-stage *Plasmodium falciparum* vaccine based on AMA1, which had previously shown some evidence of strain-specific efficacy in a Phase IIb field study. The primary endpoint of this study was to assess whether the *in vivo* parasite multiplication rate (PMR) was reduced in vaccinees compared to controls, following blood-stage controlled human malaria infection (CHMI) with homologous 3D7 parasites. This model was chosen because it should enable the efficacy of a blood-stage vaccine to be more accurately assessed than with mosquito-bite CHMI, whereby the liver-to-blood inoculum is not accurately known.
MATERIALS AND METHODS Fifteen healthy, malaria-naïve volunteers aged 18 – 45 were enrolled to receive FMP2.1/AS01B at days 0, 28 and 56. Twelve volunteers completed vaccination; three withdrew before the final vaccination. Data on adverse events were collected throughout the trial. CHMI was carried out 2 weeks after the third vaccination in the remaining vaccinees and 15 malaria-naïve control volunteers. Each volunteer was inoculated intravenously with 690 blood-stage parasites and seen twice daily, with bloods taken for thick film and quantitative PCR (qPCR). Diagnosis was made with a qPCR result of ≥500 parasites/mL and a positive thick film or symptoms consistent with malaria infection and volunteers were then treated.
RESULTS The vaccine was immunogenic eliciting both AMA1-specific T cell and antibody responses. The median anti-AMA1 serum IgG response in vaccinees at the time of CHMI was 97 μg/ml (range 45–159 μg/ml). Purified IgG from vaccinees demonstrated functional activity against malaria parasites in an *in vitro* assay of growth inhibition activity (GIA) with a median level of 59% (range 39–87%) at 10 mg/ml and 20% (range 6–39%) at 2.5 mg/ml purified IgG on the day of CHMI.

All volunteers commenced treatment 7 – 10 days after CHMI. The mean PMR, modelled from qPCR data, was 10.32 (95% CI 8.97 – 11.67) in vaccinees and 10.31 (95% CI 9.00 – 11.62) in controls, demonstrating no significant difference.
CONCLUSION FMP2.1/AS01B did not demonstrate any efficacy in this trial, presumably due to inadequate induction of functional antibodies following vaccination. Levels of *in vitro* GIA <40% using 2.5 mg/ml purified IgG are not sufficient to impact on *in vivo* PMR. The blood-stage CHMI model, however, was robust and highly suitable for proof-of-concept analysis of future blood-stage vaccine candidates.
DISCLOSURE Nothing to disclose.

3.1.11. Tuberculosis: current challenges

O.3.1.11.002

Prevalence and clinical relevance of helminth and tuberculosis co-infections in urban Dar es Salaam, Tanzania

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BACKGROUND Helminth infections may negatively affect the immune response in humans against *Mycobacterium tuberculosis* and may favour progression from tuberculous infection to tuberculosis (TB) disease. We aimed to study the associations between TB and helminth infection in a high TB burden setting.
METHODS From an ongoing TB cohort study in Dar es Salaam (TB-DAR), we included; smear-positive adults (>18 years) TB patients and controls without TB from the households who were recruited in the Temeke District, Dar es Salaam, Tanzania, between November 2013 and March 2015. GeneXpert MTB/RIF ruled out TB in controls. Triple Kato-Katz, double Baermann technique, urine filtration and circulating cathodic antigen (CCA) diagnosed helminth. Anemia was defined as haemoglobin (hb) levels <11 g/dl. Descriptive statistics and logistic regression were used.
RESULTS We recruited 334 TB patients and 226 household contact controls. The median age was similar for TB patients [33.6 years, Inter Quartile Range (IQR) 26.6–42.3] and controls (32.6, IQR 26.1–42.6, *P*-value = 0.6). The proportion of men in TB patients was 232 (69.5%) and controls 111 (51.3%). TB/HIV co-infection was 68 (20.4%). The prevalence of any helminth infection was similar in TB patients (30.5%, 95% Confidence Interval [95% CI]: 25.6–35.8) and controls (27%, 95% CI: 21.3–33.3%), *P* = 0.3. *Strongyloides stercolaris* was the commonest species (17.7% in TB patients vs. 14.6% in controls), followed by *Ancylostoma duodenale* (9.9% vs. 8.4%) and *Schistosoma mansoni* (8.4% vs. 5.8%).

In TB patients, TB/helminth co-infection was lower in HIV-infected compared to HIV-negative patients (11% vs. 24.5%, *P* = 0.005), compared to TB patients without helminth infection. In multiple logistic regression models, adjusted for age, sex, HIV and BMI, anaemia was not associated with any helminth infection (aOR 1.40, 95% CI: 0.82–2.41, *P* -value=0.2). However, TB patients co-infected with *S. mansoni* tended to have anaemia compared to TB patients without *S. mansoni* (aOR 2.28, 95% CI 0.98–5.31, *P* = 0.057), and had lower median hb levels (11.2 g/dl vs. 12.1 g/dl, *P* = 0.011) among HIV-negative TB patients.
CONCLUSION Helminth infections are common among TB patients in urban Dar es Salaam, but less in HIV patients possibly due to periodic de-worming at HIV treatment clinics. Clinical management of gastrointestinal helminths should be considered for TB patients in certain settings to address the triple burden of TB, HIV and helminths.
DISCLOSURE Nothing to disclose.

O.3.1.11.003

Spatio-temporal distribution of *Mycobacterium tuberculosis* complex strains from Ghana

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INTRODUCTION *Mycobacterium tuberculosis* complex (MTBC) has two species adapted to humans even though there are occasional cross-species infections especially with *M. bovis*. *M. tuberculosis* sensu stricto (Mtbss) is perceived to have competitive advantage over *M. africanum (*Mafric) and may gradually out-compete Mafric. Our objective was to analyze the distribution of these species among TB cases over 8-year period.
METHODOLOGY Mycobacterial isolates obtained from sputum were confirmed as MTBC by IS*6110* PCR and further characterized by spoligotyping and LSPs (RDs 9, 4, 12,702,711) assays. The distribution of the species and lineages isolated was stratified both in space and in time for analyses.
RESULTS Among 1926 Mtbc isolates obtained from 2007–2014, 1516 (78.7%), 400 (20.8%) and 10 (0.8%) were identified as Mtbss, Mafric and *M. bovis* respectively. The proportion of Mafric in the same period were 22.2%, 15.4%,10.7%, 23.1%, 11.5%, 24.6%, 23.0% and 18.5% respectively. *M. bovis* was isolated in 2012 to 2014 as 1.0%, 0.4% and 2.0% respectively when Northern Ghana (NG) was included in the Study. Comparing the isolates from 2012 to 2014, we found *M. bovis* to be significantly higher in NG (2.6% of 151) than Southern Ghana (SG; 0.5% of1164) ($P = 0.020$). Among the Mafric isolates, 58.7% and 41.3% of the SG as compared to 48.1% and 51.9% of the NG isolates were lineage 5 and lineage 6 respectively. The most dominant spoligotype of Mtbss in SG was SIT 61 (42.9%) as compared to SIT 53 (28.7%) in NG. Lineage 6 spoligotype SIT 181 and 326 were the most prevalent in south where as SIT 181 (6.7%) for the north.
CONCLUSION *M. africanum* contributes significantly to TB in Ghana as its prevalence over the years remains fairly constant.
FUNDING This work was supported by the Wellcome Trust Fellowship number 097134/Z/11.
DISCLOSURE Nothing to disclose.

O.3.1.11.004

Identification of potential tuberculosis vaccine antigens by integrating population genomics and immunology

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One of the major problems in global tuberculosis (TB) control is the lack of an efficacious vaccine. Unlike most other pathogens, the majority of known human T cell epitopes in *Mycobacterium tuberculosis* are evolutionary conserved, suggesting that immune recognition of these epitopes benefits the pathogen rather than the host. Focusing on variable regions of the pathogen genome might thus represent a way to identify novel vaccine antigens against TB. Here we analysed 216 whole genome sequences representative of the global diversity of *M. tuberculosis* and computationally predicted human T cell epitopes in variable genes. We then synthesized 52 peptides representing both wild type and mutant sequence variants of 25 candidate epitopes, and used those to stimulate whole-blood from 88 patients with active TB in The Gambia. On average, these variable epitopes induced a significant IFN-g response in 11 (13%) subjects, and 59 (67%) subjects responded to at least on peptide, demonstrating that these variable epitopes are immunogenic. Comparing wild type to mutant variant of each epitope, we found that naturally-occurring sequence variation significantly altered the IFN-g response to 17 (69%) of the 25 candidate epitopes. Whether these changes in host response reflect immune evasion, bacterial adaptation to different human genotypes, or a combination of both, remains to be determined. The findings reported here highlight a group of novel *M. tuberculosis* T cell antigens that harbour variable epitopes. Future work will tell whether these antigens are associated with protection from active TB disease.
DISCLOSURE Nothing to disclose.

O.3.1.11.005

The effect of diabetes mellitus on the pharmacokinetics of tuberculosis drugs in Tanzanian patients

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INTRODUCTION Diabetes mellitus (DM) is a well-known risk factor for tuberculosis (TB). With the current global increase in type 2 DM, more attention is needed on optimum treatment of TB in TB-DM patients. Pharmacokinetic profiles of TB drugs in Asian and American TB-DM patients have been described, but such data are lacking in Africa. We performed a pharmacokinetic study in Tanzanian patients.
METHODS Forty adult Tanzanian TB patients (20 TB only, 20 TB and Diabetes) who were in the intensive phase of TB treatment for at least 2 weeks were recruited at a Tanzanian out-patient TB clinic. Plasma concentrations were determined in venous blood samples taken just before and at 1, 2, 3, 4, 6, 8, 10, 24 h after observed drug intake to estimate pharmacokinetic parameters of isoniazid, rifampicin, pyrazinamide and ethambutol using validated HPLC methods.
RESULTS The geometric mean exposures ($AUC_{0\text{-}24}$) of rifampicin and isoniazid (in h*mg/L) were significantly lower in TBDM patients (29.3 rifampicin, 5.4 isoniazid) than TB only patients (39.9 rifampicin, 10.6 isoniazid). C_{max} (mg/l) of isoniazid was also lower in TBDM patients (1.6 vs. 2.8, $P = 0.01$). 73.7% vs. 55% of patients had C_{max} of isoniazid below reference range in the TBDM group as compared to the TB only group, and for rifampicin, the proportions were 43.4% against 35%. In a multiple linear regression analysis, age, bodyweight, or BMI did not affect the association between DM and the PK parameters. All PK parameters for pyrazinamide and ethambutol were not significantly different between the groups.
CONCLUSION Exposure to isoniazid and rifampicin is reduced in Tanzanian diabetic patients with TB. These effects are most likely explained by the diabetes disease. Increasing the doses of these drugs in treating TBDM patients may be considered in view of accumulating evidence that exposure to TB drugs is related to response.
DISCLOSURE Nothing to disclose.

3.1.12. The struggle with MDR-TB

O.3.1.12.002

Towards first in human clinical trial with the novel drug candidate PBTZ169

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WHO recommends a 'short-course' tuberculosis (TB) therapy that includes 6 months treatment with rifampicin and isoniazid, in combination with 2 additional drugs for 2 months. A current goal of TB clinical research is to shorten existing therapy to as little as 2 months, in order to substantially diminish the risks of treatment failure, relapse of the disease and increased prevalence of drug-resistant bacteria associated with TB sufferers who fail to comply with the current therapy. The past decade has seen intensive efforts to discover and develop new drugs to treat both drug susceptible (DS)-TB, multidrug resistant (MDR)-TB and extensive drug resistant (XDR)-TB. New combination regimens are also being devised and tested in clinical trials (http://www.newtbdrugs.org).

Amongst new agents in development, PBTZ 169 is a novel, highly potent drug candidate for the treatment of TB that targets the DprE1 subunit of the essential flavoprotein decaprenylphosphoryl-β-D-ribose 2′-epimerase (DprE). This enzyme produces the sole source of D-arabinose required for the key *Mycobacterium tuberculosis* cell wall components arabinogalactan and lipoarabinomannan. PBTZ 169 serves as a suicide substrate for the reduced form of DprE1. The drug candidate is devoid of genotoxic effects, is well tolerated in preclinical species and no risk of Drug-Drug Interaction could be anticipated as PBTZ169 does not inhibit a large panel of cytochromes (CYP) at up to 20 μM and also does not induce CYP1A2, CYP2B6 and CYP3A4 in human hepatocytes. The drug consistently shows efficacy at the daily dose of 25 mg/kg p.o. (5 days per week) in the murine model of TB, equivalent to isoniazid and has additive effects in that model, when combined with isoniazid, rifampicin, moxifloxacin, PA-824, clofazimine or SQ109. It also has synergistic effects with bedaquiline (TMC-207). Other TB drug combinations are currently under assessment. A First In Human Phase I study in Healthy Volunteers is planned in order to assess the Safety, Tolerability, ADME behaviour and potential bactericidal activity of the drug candidate PBTZ169 after oral administration.

The research and development underpinning PBTZ 169 is provided by the FP7 programme « More Medicines for Tuberculosis (MM4 TB) » with support from the European Commission and EPFL.

DISCLOSURE Nothing to disclose.

O.3.1.12.003

Novel molecular approaches to assessing the burden of drug-resistant tuberculosis

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INTRODUCTION To achieve the goals of WHO's 'END TB' strategy of zero deaths, disease and suffering due to tuberculosis (TB) by 2035, it will be essential to address the global burden of drug-resistant TB. The Global Project on Anti-TB Drug Resistance Surveillance, hosted by WHO, has provided technical support to countries since 1994 to estimate the burden of drug resistance among TB patients. This is the oldest and largest project on antimicrobial drug resistance in the world. In recent years, molecular technologies have been increasingly incorporated into the surveillance of drug-resistant TB, either alone or as screening tools used in combination with conventional culture-based methods for drug susceptibility testing.

METHODS Novel molecular approaches used in national anti-TB drug resistance surveys over the past 3 years were reviewed and evaluated.

RESULTS The use of Xpert MTB/RIF as a screening tool in national surveys has:

1 Increased numbers of eligible patients with drug susceptibility testing results and therefore reduced the risk of bias (Namibia, Pakistan).
2 Reduced workload for laboratories with minimal impact on routine activities (Senegal).
3 Allowed surveys to be conducted in countries where nationally representative data were previously not available (Democratic Republic of Congo, Papua New Guinea).

Additionally, the use of sequencing technologies in six countries in Asia and Eastern Europe has allowed the expansion of surveillance activities to anti-TB drugs which are not currently tested within standard surveys (pyrazinamide and fluoroquinolones in particular). This has provided the first nationally representative data from high TB burden countries for drugs that may form part of new TB treatment regimens. These data will be used to assess the feasibility of introducing new regimens in different settings.

CONCLUSIONS Recent surveys of TB patients in different countries have demonstrated the added value of molecular technologies for detecting drug resistance. Molecular technologies, including sequencing-based technologies, will play an increasingly important role in addressing the drug-resistant TB burden as we move towards achieving the 'zero TB' goal by 2035.

DISCLOSURE Nothing to disclose.

O.3.1.12.004

Pyrazinamide resistance in *Mycobacterium tuberculosis* develops after resistance to rifampicin and is increasingly common as strains become resistant to additional antibiotics

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Multidrug resistant (MDR) and extensively drug resistant (XDR) strains of *Mycobacterium tuberculosis* constitute a major world health concern because they are not cured by standardized first-line treatment regimens recommended by World Health Organi-

zation (WHO). Among the differents drugs used to fight tuberculosis, pyrazinamide (PZA) is a key pillar of chemotherapy because of its sterilizing action against semi-dormant bacilli. However, phenotypic susceptibility remains a challenge. This study sought to determine the timing of *pnc*A mutations conferring PZA resistance (PZA-R), relative to the appearance of mutations conferring resistance to isoniazid (INH) and rifampicin (RMP).

Phenotypic susceptibility to INH and RMP was performed on 202 strains with the proportion method using Löwenstein-Jensen media. The Hain GenoType MTBDR*plus* was performed on 101 strains from Paris to identify mutations conferring resistance to RMP and INH, thus defining a strain as MDR, while the Multiplex Real-Time PCR Melting Curve Assay was used to identify these mutations in 171 strains from Shangai. To determine which of the MDR strains qualified as XDR, PCR amplification and sequencing was performed on the *gyr*A/B and *rrs* genes to identify mutations associated with fluoroquinolone (FQ) and aminoglycoside (AG) resistance respectively. Mutations conferring PZA-R were identified by PCR amplification and sequencing of the entire *pnc*A gene.

Mutations in *pnc*A gene conferring PZA-R were present in 0.7% (1/134) of INH-S strains, 3% (2/76) of INH-R non-MDR strains, 25% (10/34) of MDR strains, 55% (12/22) of MDR strains with FQ-R and 100% (3/3) of MDR strains with AG-R.

The results show that PZA-R is rare in non-MDR strains, including those with isolated INH-R, but the percentage of strains with PZA-R increases progressively as strains accumulate mutations conferring resistance to other antibiotics. These observations suggest that PZA-R generally occurs after a strain has developed resistance to both RMP and INH.

DISCLOSURE Nothing to disclose.

O.3.1.12.005

Impact of the *M. tuberculosis* genetic background on the acquisition of drug resistance-conferring mutations

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The extent of genetic diversity in *M.tuberculosis* (Mtb) is more pronounced than was traditionally believed, and can be classified into seven different geographically distributed lineages. The average inter lineage genetic distance is approximately 2000 single nucleotide polymorphisms (SNPs). The impact of this diversity on the baseline metabolism is still unknown. One of these lineages; the Beijing lineage has repeatedly been associated with drug resistant tuberculosis (DR-TB). The reason for this association is still not clear. To evaluate the influence of genetic background on the acquisition of specific Isoniazid (INH) resistance-conferring mutations, and to explore whether the Beijing lineage is better adapted to the potential physiological effects than other phylogenetical distant lineages, associations between lineage and INH-DR were sought. We performed Lüria-Delbruck fluctuation assay (LDFA), and found lineage-specific differences in the baseline INH-resistance acquisition rate, with Beijing showing a higher rate compared to the other lineages. Lineage specific INH-associated mutations were also explored. In addition, since Beijing intra lineage diversity shows a phylogeographical structure and epidemiological studies have evidenced differences on the Beijing-DR association depending on the strain geographical origin, we further explored the impact of intra lineage diversity on the basal INH-DR mutation rate performing LDFA of a collection of clinical Beijing strains globally distributed.Overall, our findings support a role of Mtb lineage diversity in the emergence of global drug resistance and consequently on the specific evolution of drug-resistance within each lineage.

DISCLOSURE Nothing to disclose.

3.1.13. Malaria control

O.3.1.13.001

Seasonal malaria chemoprevention combined with micronutrient supplementation delivered through community preschools: findings from a cluster randomized trial in Mali

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Early childhood is a time of rapid growth and development and public health interventions during this period could yield substantial benefits across several developmental areas: physical, cognitive and linguistic. Iron is important in brain function, and interventions that reduce iron-deficiency and anemia may improve cognitive function and learning. A randomized trial was undertaken to examine the combined impact of two newly-recommended interventions in early childhood: seasonal malaria chemoprevention and home fortification with micronutrient powders. Though each intervention has been shown to improve malaria morbidity, anemia and/or physical growth, the benefits for cognitive and linguistic development are not known. The combined effect of these two interventions has not previously been examined.

A cluster-randomized controlled trial was conducted in 60 rural communities with community-based pre-schools in southern Mali. Children aged less than 5 years living in the 30 intervention communities received two rounds of seasonal malaria chemoprevention in Oct and Nov 2013, followed by daily supplementation of micronutrients for four months from January-April 2014. Delivery of the two interventions at community-level was organized by pre-school management committees. The combined impact of the interventions was evaluated in May 2014 through cross-sectional surveys to compare malaria infection, nutritional indices and cognitive performance in children aged 3 and 5 years living in intervention and control communities.

Parental interviews found that 64% of children had received two monthly malaria treatments and 80% had received the micronutrient powders, with high community acceptability and compliance to both interventions. A significant reduction in malaria infection was observed six months after the last treatment in intervention compared to control communities (3y olds: 21% vs. 45%, $P < 0.001$; 5y olds: 32% vs. 55%, $P < 0.001$). No difference was observed in hemoglobin concentration, nutritional indices (height-for-age, weight-for-age), or cognitive function.

In conclusion, despite high compliance and a significant reduction in malaria infection, the results suggest no overall effect of combining malaria chemoprevention and micronutrient supplementation on anaemia. Implications for the local aetiology of anaemia, interventions required, and the optimal timing of seasonal malaria chemoprevention and micronutrient supplementation will be discussed.
DISCLOSURE Nothing to disclose.

O.3.1.13.002

Malaria control in hyperendemic settings - lessons learned from a Médecins Sans Frontières malaria intervention in Guéckédou, the Republic of Guinea

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BACKGROUND In 2010 Médecins Sans Frontières Switzerland (MSF) in collaboration with the Ministry of Health implemented a multi-component malaria intervention in Guéckédou Prefecture, Guinea. The intervention included both curative and preventive components with the objective of reducing malaria related morbidity and mortality. The end of the intervention in 2014 coincided with the declaration of Ebola in the region. The study aim was to quantify changes in malaria epidemiology over time in the intervention area (IA) compared to a non-intervention area (NIA).
METHODS AND MATERIALS Five cross-sectional surveys using cluster based sampling and stratified by area were conducted in Guéckédou. The surveys were repeated every six months, corresponding with the dry and rainy seasons, in order to measure the prevalence of rapid diagnostic test (RDT) diagnosed *Plasmodium falciparum* infections in the population.
RESULTS 35,123 individuals participated in the surveys, 25% were children under 5. At baseline 60.8% and 64.5% of all participants and 70.6% and 78.8% of children under 5 in the IA and NIA respectively were RDT positive. In the IA there was an overall 10.9% decrease in RDT malaria prevalence and a 23.9% decrease in children under 5 ($P < 0.001$ & $P < 0.001$). Any changes in RDT malaria prevalence for either group in the NIA were not significant ($P = 0.112$ & $P = 0.168$).

Regarding symptomatic infections, there was an 8.2% decrease in the IA ($P = 0.007$) while the change in the NIA was not significant ($P = 0.995$). There was no change in the proportion of individuals in either area with an asymptomatic malaria infection ($P = 0.859$ & $P = 0.424$). The proportion of asymptomatic infections by age group after 2.5 years of intervention was 26.8% in children under 5, 40.2% in children 5–14 years of age and 32.9% in individuals 15+.
CONCLUSIONS The multi-component malaria intervention implemented by MSF was successful in decreasing malaria prevalence in the IA. However, many challenges remain to control malaria in hyperendemic areas where many currently available control strategies are difficult to implement. A lesson learned from our intervention is that future malaria control activities in similar areas should place more emphasis on reducing asymptomatic infections in children under 15 years of age. For Guéckédou in particular, any gains that were made during our intervention are likely to have been lost due to reduced malaria activities resulting from the Ebola epidemic.
DISCLOSURE Nothing to disclose.

O.3.1.13.003

Dynamic changes in prevalence and incidence of malaria after intensifying control across Papua New Guinea

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INTRODUCTION *Plasmodium falciparum* and *P. vivax* have in the past both contributed to high malaria endemicity in Papua New Guinea (PNG). In the 1960s to 1980s, it was mainly indoor residual spraying of insecticides that led to a reduction in malaria prevalence but rebounds occurred after the cessation of the program. Malaria control efforts were intensified again with the free provision of long lasting insecticidal nets (LLIN) since 2005 and the introduction of artemisinin-based combination therapy (ACT) in 2012. The effects of the recent control efforts on population parasite prevalence and incidence of clinical episodes were investigated.
METHODS Three country-wide malaria surveys were carried out in 2008/09, 2010/11 and 2013/14. In randomly sampled villages, coverage with malaria control interventions was assessed and prevalence of infection was determined in all age groups by light microscopy. In sentinel health facilities, trends in clinical episodes were followed over time. The pooled datasets include observations from approximately 6000 households, 25 000 community members and 20,000 fever patients.
RESULTS Population prevalence of infection decreased from 12% in 2008/09 to below 2% in 2013/14. Reductions were observed in *P. falciparum* and *P. vivax* infections. In sentinel health facilities, malaria cases dropped following the first LLIN distribution, most prominently cases of *P. falciparum*, but reductions were not sustained everywhere. A shift from *P. falciparum*-dominance towards *P. vivax*-dominance in clinical cases was observed in some sites. LLINs were the primary driver of observed reductions but their effect may be hampered by the behaviour of local *Anopheles* vectors.
CONCLUSIONS Scaling up LLIN coverage has led to a reduction in the malaria burden across PNG but effects vary between sites. Understanding such variations and underlying determinants of transmission will be key to further progress in malaria control in PNG.
DISCLOSURE Nothing to disclose.

O.3.1.13.004

Impact of IRS on malaria burden when combined with LLIN in Ethiopia: modelling the 2015–2017 malaria national strategy

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BACKGROUND The Ethiopian malaria strategy is stratified on transmission level with full coverage of long lasting insecticidal nets (LLINs) in all malarious *woredas* (sub-districts), supplemented in some woredas by indoor residual spraying (IRS) using carbamate. Simultaneous LLIN and IRS deployment is

planned only in epidemic-prone woredas and those with high transmission. Fine scale simulation of multiple scenarios can help to assess the likely impact of such approaches, especially where local data are limited.
MATERIAL AND METHODS We simulated malaria transmission, prevalence and burden for each of these woredas using the OpenMalaria platform. Transmission levels were derived from recent annual parasite incidence and parasite prevalence data. National estimates of access to healthcare, historical intervention coverage and malaria seasonality were used to parameterize the simulations further. The national strategic plan for 2015–2017 was simulated accounting for variable levels of effective LLIN usage, access to healthcare and pyrethroid resistance.
RESULTS The predicted incremental benefit of IRS decreases with levels of effective usage of LLINs and of pyrethroid resistance. Changes in mosquito biting behaviour, prevalence of *Plasmodium vivax* and LLIN deployment delays would contribute to a higher impact of IRS.
CONCLUSION The simulations of the different scenarios indicate the expected impact of the interventions in Ethiopia and can be used during decision making process, for example in cost effectiveness analysis. They can also help to understand what would happen when interventions are deployed if all factors influencing malaria transmission intensity could be controlled. Deviations from the predictions could be used to identify where implementation differs from what was anticipated in the plan and hence where additional efforts are required.
DISCLOSURE Nothing to disclose.

O.3.1.13.005

Development of Aim: action and investment to defeat malaria 2016–2030

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Since 2000, united action in the fight against malaria has made a tremendous impact. Malaria infection rates have been cut in half and 4.3 million lives have been saved. Fifty-five countries are on track to reach the World Health Assembly target of a 75% reduction in their malaria burden by 2015. The benefits and economic returns from investing in the reduction and elimination of malaria are unprecedented - for every dollar spent, up to sixty dollars' worth of benefits can be gained. These returns can create healthier, more equitable societies, and enable countries to attract international investors, trade and tourism, all of which can drive transformative growth and sustainable development. The end of the Millennium Development Goals era and the consequent Sustainable Development Goals call for more multi-sectoral and encompassing approaches. Additionally, funding for malaria needs to be increased significantly to reach 2030 targets prevent resurgence, as has happened many times in the past.

The Roll Back Malaria Partnership called for a next generation document to follow its Global Malaria Action Plan (GMAP), through the organisation of global, regional and country level consultations with malaria stakeholders and other sectors. Over 1400 people from over 90 countries contributed to the document.

As a companion to the WHO's Global Technical Strategy for malaria, AIM positions malaria as a wider issue for development and for economic and health security. AIM builds the case for investment in malaria and thus provides the global malaria community with a powerful advocacy tool. It also provides direction for action to mobilize resources; improve policy and governance; foster collaboration between countries and between sectors; increase the quality, availability and use of data and evidence; and strengthen and integrate malaria into health systems. It underscores how future progress will be contingent on new products and innovations, and calls upon us all to keep people at the center of the response. Working in partnership with affected communities will increase the demand for malaria services wherever they are needed, and will allow the voices of the poorest to ring out loudly in the global call for a malaria-free world.
DISCLOSURE Nothing to disclose.

O.3.1.13.006

Malaria epidemiological profile: use of evidence to improve efficiency, effectiveness, equity and economy of malaria control in Tanzania

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Over the last decade, substantial decreases in malaria transmission and deaths have been reported in Tanzania. This large public health gain was due to massive investments in malaria control through scaling up preventive and curative interventions.

Between 2000 and 2010, there was an overall reduction of more than 50% in the parasite prevalence in children aged 2–10 years across Tanzania. The proportion of population living in areas of intense transmission declined from 11.6% to only 2.3%, while the population living in malaria-free and extremely low transmission areas increased from 7% to 25%. However, the dramatic decline in malaria burden has not been observed in all settings. Some areas In the Southern and North-Western regions of the country saw little or no improvements. In addition to the broad geographical heterogeneity of malaria transmission, particular population segments remain disproportionately affected even in areas with good overall control effect. People with very low income have a ten-fold higher risk of being infected, and housing and educational levels for example are major determinants of the disease burden. In additional, children living in rural areas are affected three-times more than the ones living in urban areas.

In addition to this heterogeneity of risk, there are increasing concerns about the sustainability of current funding level for malaria control and therefore a call for more efficient and effective control measures that take into account the transmission heterogeneity, while concurrently improving equity in the delivery of services.

The National Malaria Control programme in Tanzania is contemplating, within its overall strategic plan, to assess the factors affecting malaria transmission diversity. In a second step, epidemiological stratification complemented by high-quality evidence on operational, socioeconomic and vulnerability factors, will guide the country in selecting and implementing targeted control intervention packages for different transmission settings and high-risk populations.
DISCLOSURE Nothing to disclose.

3.2.1. The development of new treatments for helminth infections

INV.3.2.1.001

Alternative drug regimens and mass drug administration strategies for lymphatic filariasis and onchocerciasis elimination programmes

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The DOLF project ('Death to Onchocerciasis and Lymphatic Filariasis', supported by the Bill & Melinda Gates Foundation) comprises an ambitious set of applied field research projects that share the common goal of optimizing mass drug administration (MDA) to improve chances for elimination of lymphatic filariasis (LF) and onchocerciasis. DOLF is conducting 11 studies (4 clinical trials and 7 community-based MDA studies) in 7 countries in Africa and Asia. Early results from a community MDA study in the Republic of the Congo suggest that semiannual MDA with albendazole alone can be used to eliminate LF in areas of Central Africa where co-endemicity with loiasis rules out conventional treatment with albendazole plus ivermectin. In addition, exciting results from a pilot study in Papua New Guinea suggest that a triple drug regimen (diethylcarbamazine/albendazole/ivermectin) is safe and more effective for clearing *W. bancrofti* microfilaremia than the conventional MDA regimen of DEC/Alb. Full clinical trials of the triple drug treatment are now underway in Papua New Guinea and in Côte d'Ivoire. Although LF elimination programmes have distributed more than 5 billion MDA treatments since 2000, the impact of MDA on soil transmitted helminth (STH) infections has not been well documented. DOLF is studying this and comparing the impact of annual and semiannual MDA on STH in different endemic settings. Early results have shown that community MDA for LF has a dramatic effect on hookworm prevalence rates with more modest effects on *Ascaris* and *Trichuris* and that MDA reduces infection intensities for all three species. These studies have shown that community-wide MDA has a major impact on STH, and they suggest that it may be possible to achieve local elimination of hookworm infections by MDA alone in some settings. However, resurgence of STH infections is likely after MDA is discontinued unless it is followed by a maintenance program.

DISCLOSURE Nothing to disclose.

INV.3.2.1.002

Towards the future: the development of new macrofilaricide treatments

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INTRODUCTION The development of a macrofiliaricidal treatment has been identified by DNDi as a priority to improve patient care, reduce the number of rounds of Mass Drug Administration required to break transmission, provide treatment in areas with *Loa loa* co-infection and accelerate progress towards the elimination of Lymphatic Filariasis and Onchocerciasis.

DNDi's strategy consists of three components: repurposing of drugs from human health applications through a programme of active screening of drug compounds; identification of drugs from animal health applications and determination of their suitability for development as a macrofilaricide for human use; and the assessment of new candidates to be brought into the drug development pipeline from pharmaceutical, biotechnology, and academic partners.

METHODS AND MATERIALS Compounds accessed from pharmaceutical companies were initially tested in vitro against Onchocerca *lienalis* microfilariae and *O.gutturosa* adult worms. Active compounds were then evaluated in animal models, either in jirds or mice naturally infected with *Litomosoides* sigmodontis.

RESULTS Approximately 14 000 compounds were screened in vitro, of which 450 were found to be active. Around 100 compounds were evaluated in vivo, of which emodepside, oxfendazole and anti-Wolbachia compounds, were of particular interest and are under consideration for clinical development.

Emodepside was found to have a macrofilaricidal effect in vivo compared to untreated control groups, with comparable efficacious exposures in different *Litmosoides* rodent models and consistent 80% reduction in numbers of the adult worm.

Emodepside is commercialized by Bayer under license from Astellas as an anthelmintic veterinary drug for cats and dogs in combination with praziquantel (Profender®) and in combination with toltrazuril (Procox®).

DNDi has an agreement with Bayer to develop emodepside for the treatment of onchocerciasis; it is currently undergoing preclinical development and will enter the clinical phase in 2015.

CONCLUSIONS Filariasis exacts a huge burden on poor communities. With several candidates destined for clinical development, DNDi aims to offer new tools to treat patients and accelerate disease elimination in the next decade.

DISCLOSURE DNDi would like to acknowledge the financial support from the Bill and Melinda Gates Foundation (BMGF), United States Agency for International Development (USAID) and Federal Ministry of Education and Research (BMBF) through KfW / GERMANY and part of the EDCTP2 programme supported by the European Union.

O.3.2.1.004

Tribendimidine is an efficacious and safe drug against *Opisthorchis viverrini*: results of a randomized controlled trial in southern Lao PDR

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BACKGROUND Infection with the liver fluke *Opisthorchis viverrini* is a major public health problem in Thailand and Lao People's Democratic Republic (Lao PDR). Today, praziquantel (PZQ) is the only drug with a satisfactory efficacy. Hence, there is a pressing need for alternative treatments. Tribendimidine (TBD) was identified as a potential alternative drug.

METHODS We conducted an open-label, phase IIb, randomized controlled clinical trial in *O. viverrini* infected patients who received either a single dose of TBD (200 mg children 8–14 years; 400 mg individuals ≥15 years) or a PZQ treatment (75 mg/kg BW in two doses). We assessed the cure rate (CR), egg reduction rate (ERR) and the adverse events (AEs). The trial

was carried out in the district of Pathumphone, Champasack province, southern Lao PDR where *O. viverrini* is highly prevalent.
RESULTS 607 persons with a confirmed *O. viverrini* infection were randomly assigned to TBD (300 patients) and PZQ (307 patients) treatment. 295 patients in the TBD and 253 patients in the PZQ group were available at the follow-up survey. The available case analysis showed that a single oral dose of TBD cured 93.6% of *O. viverrini* infected patients with an ERR of 99.3%. In children (8–14 years) and adults (≥15 years) the CR was 100% and 92.6%, respectively. PZQ treatment yielded a CR of 96.8% with an ERR of 99.6%. There was no statistically significant difference between the treatment groups
(c2 = 3.13, *P*-value = 0.077). Overall, AEs were diagnosed in 32.5% (96/295) of the patients in the TBD and in 64.8% (164/253) of patients in the PZQ treatment group. Patients with PZQ treatment had an almost four-fold risk of AEs compared to TBD treated patients (OR = 3.8; 95%, CI: 2.6–5.5; *P*-value < 0.001).
CONCLUSIONS Our findings suggest that the efficacy of a single dose of TBD against *O. viverrini* is comparable to a PZQ treatment (75 mg/kg BW divided) but has significantly fewer and less severe AEs. Next steps must be undertaken to make TBD accessible in Lao PDR and other *Opisthorchis* endemic areas.
DISCLOSURE Nothing to disclose.

O.3.2.1.005
A phase I relative bioavailability study in healthy volunteers after administration of the pediatric formulation of the active enantiomer of praziquantel (L-PZQ)

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INTRODUCTION Praziquantel (PZQ) was developed in the 1970s by Bayer and Merck to treat schistosomiasis. PZQ tablets are donated by Merck to endemic countries, but are not palatable to young children. A new pediatric oral disintegrating tablet (ODT) for the active L-enantiomer of praziquantel (L-PZQ) is being developed. The ODT L-PZQ formulation and the reference racemate PZQ (Cysticide) formulation have been administered to healthy male volunteers in a randomized cross-over relative bioavailability study under controlled conditions.
METHODS After screening, 36 subjects were included in the study and 34 subjects finished all 5 treatment periods. Single oral doses dispersed in water (L-PZQ) or as tablets (rac-PZQ) were given with a wash-out of 7 days in between. Treatments were resp. L-PZQ at an oral dose of 10, 20 or 30 mg/kg under fed conditions, of 20 mg/kg under fasting conditions and of 40 mg/kg PZQ (Cysticide) under fed conditions. L-PZQ ODT was also administered directly in the mouth. Safety and tolerability were measured by recoding of adverse events (AEs), vital signs, ECGs and laboratory investigations for hematology, biochemistry and urinalysis. Overall palatability of the formulations was evaluated using a questionnaire. Plasma samples were taken at pre-specified timepoints up to 24 h. Plasma levels of L- and D-PZQ were measured with a validated enantioselective LC-MS/MS method (LOQ of 5 ng/ml) and PK parameters as C_{max} and area under the curve (AUC) were calculated.
RESULTS L-PZQ showed low numbers of treatment emergent AEs. No new type of AE were observed. No consistent abnormalities in the laboratory investigations or ECGs were identified and palatability was good. After administration of L-PZQ no conversion to the D-PZQ enantiomer was seen. C_{max} and AUC parameters after administration of 10, 20 and 30 mg/kg of L-PZQ were greater than dose proportional.
A clear food effect was identified. Exposure to L-PZQ administered as Cysticide tablets was higher than after administration of equivalent doses of L-PZQ as ODT. Administration directly in the mouth led to the same exposure as dispersion in water.
CONCLUSIONS L-PZQ showed a good safety profile and good palatability. The lower exposure of L-PZQ after administration of L-PZQ ODT compared to administration of equivalent amounts as cysticide tablets might indicate the need for higher L-PZQ ODT dosages to be administered to achieve therapeutic effects.
DISCLOSURE This work was supported by Merck KGaA and by grants from the Bill & Melinda Gates Foundation and the Global Health Innovative Technology Fund.

3.2.2. Ebola and other emerging infectious diseases

O.3.2.2.002
Mobile suitcase laboratory for rapid detection of Ebola virus at low resource settings

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INTRODUCTION The current outbreak of Ebola has killed over 10 000 people in Guinea, Sierra Leone and Liberia. Early identification and isolation of the infected Ebola cases are the most important control measures. Detection of the Ebola virus by using the rapid antigen lateral flow tests is an easy to be applied at the point-of-care. Nevertheless, the results must be confirmed by additional laboratory tests. Laboratory diagnosis mainly depends on Ebola RNA detection by reverse transcription real-time polymerase chain reaction (RT-PCR), which is available in central laboratories and has a turnaround time of more than 3 h. For decentralized low resource settings, there is a need for a simple molecular point-of-need test.
MATERIALS AND METHODS In this study, a mobile suitcase laboratory (62 × 49 × 30 cm) containing all reagents and equipment for the detection of Ebola RNA was developed. Moreover, it was operated by a solar power battery. All reagents were cold-chain independent in order to ease the use at poor resource settings. RNA extraction was performed by a magnetic bead based method, in which a simple fast lysis protocol was applied. In one reaction tube, the reverse transcription step as well as the DNA amplification and detection by the recombinase polymerase amplification (RPA) assay was achieved.
RESULTS Using spiked plasma samples, as few as 15 Ebola RNA copies were detected in less than 30 min, while samples containing Crimean-Congo-Hemorrhagic-Fever, Yellow Fever, Lassa, Marburg, Rift Valley Fever, Dengue, Chikungunya and Zika viruses and *Plasmodium falciparum* were negative.
CONCLUSION The mobile suitcase laboratory is ideal for rapid sensitive and specific detection of Ebola virus especially at low resource settings. Currently, two mobile suitcase laboratories are being used in Guinea.

DISCLOSURE The study was funded by the Welcome Trust. All authors except Oliver Nentwich and Olaf Piepenburg have no financial interests in RPA technology. Oliver Nentwich and Olaf Piepenburg are employed by TwistDx and have commercial interest in the use of the RPA technology. This does not alter the authors' adherence to all the scientific policies on sharing data and materials.

O.3.2.2.003

Artesunate-amodiaquine is associated with reduced Ebola mortality

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BACKGROUND Malaria treatment is recommended for all suspected cases of Ebola virus disease (EVD), either presumptively or based on malaria diagnosis. In Foya Ebola Treatment Center (ETC), Lofa County, Liberia, the first-line anti-malarial, artemether-lumefantrine (AL), ran out for a 2-week period in August 2014; during this time patients received artesunate-amodiaquine (ASAQ), which includes amodiaquine, a compound with anti-Ebola virus activity *in vitro*.
METHODS With standardized line-list data we estimated the relative risk of mortality in confirmed EVD patients prescribed ASAQ compared to either AL or no anti-malarial therapy, using unadjusted and adjusted regression models.
RESULTS Between 5 June—21 October 2014, 382 patients with confirmed EVD were admitted to the Foya ETC, with 194 prescribed AL and 71 prescribed ASAQ at admission. Patients prescribed ASAQ were similar to those prescribed AL or no anti-malarial therapy. Sixty-four percent (125/194) of patients prescribed AL died, compared to 51% (36/71) for ASAQ. In adjusted analyses, ASAQ prescription reduced mortality risk by 31% (risk ratio 0.69, 95% confidence interval, 0.54–0.89) compared to AL, with a stronger effect in individuals without malaria. Age, cycle threshold value at admission, total number of ETC inpatients on the day of patient admission, and IV rehydration were associated with risk of dying in the adjusted model.
CONCLUSIONS Artesunate-amodiaquine may provide substantial protection against EVD mortality compared to AL. While more pre-clinical and clinical research is needed to understand these biologically plausible findings, health policy makers should consider recommending ASAQ for all EVD patients regardless of malaria status.
DISCLOSURE Nothing to disclose.

O.3.2.2.004

The velocity of Ebola virus disease spread in the West African epidemic

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INTRODUCTION A variety of risk factors have contributed to the human-to-human spread of Ebola virus disease (EVD) in the ongoing West African epidemic including caring for the infected, involvement in funeral preparations of infected corpses, and healthcare infrastructure. At the population level, mobile populations, porous borders, and commercial air travel patterns have influenced the frequency and breadth of EBV transmission. However, little is known about the speed and pattern of EVD spread in the current epidemic. The goal of our analysis was to calculate the velocity of spread of EVD in Guinea, Liberia, and Sierra Leone.
METHODS AND MATERIALS Publically available data from the World Health Organization (WHO) were used for this analysis, which we restricted to confirmed cases of EVD. Using a surface trend analysis, the speed and direction of EVD diffusion was calculated for each district. Surface trend is a spatial interpolation method used to estimate continuous surfaces from point data. The response variable was time from first confirmed EVD case (week of 06 to 12 January 2014) for each coordinate, and the continuous surface of time to infection was estimated by regressing it against X and Y coordinates.
RESULTS The average speed of EVD spread across Guinea, Liberia, and Sierra Leone was 13.8 km/week, and varied from 1.9 km/week to 69.6 km/week. There was a radial pattern of diffusion from the initial EVD-affected districts that bordered Guinea and Liberia. Other spatial patterns of spread were present, which could likely be explained by the translocation of infected individuals.
CONCLUSIONS Understanding the movement of EVD is useful for identifying the timing and placement of treatment and containment efforts. These methods can be applied prospectively and also to other infectious diseases, to understand the broad pattern of spatial and temporal spread.
DISCLOSURE Nothing to disclose.

O.3.2.2.005

Biodiversity, Bushmeat and Monkeypox in the Democratic Republic of the Congo: another viral threat upon larger cities?

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INTRODUCTION While the world is watching the 25th unprecedented known outbreak of Ebola virus disease other silent epidemics are on-going. In the decade preceding the victory of WHO on smallpox (1970–80) – the prevalence of a similar eruptive skin disease, also caused by an Orthopoxvirus, started to increase in the heart of Africa. The Monkeypox (MKPX) virus, a smallpox-like virus endemic to the African region, emerged in 1970 in human populations and - to the contrary of smallpox - seems to have several zoonotic reservoirs. Ecological studies of candidate reservoir have repeatedly pointed towards squirrels as potentials reservoir hosts but the range of hosts is much wider and the ecological relationships between them poorly studied, nor are the routes of human contamination.
METHODS AND MATERIALS The Biodiversity Monitoring Centre (CSB) at the University of Kisangani has been contributing to the search of Monkeypox reservoirs providing ecological data and samples from a series of remote locations and reserves in the Orientale Province. Biopsies of a selection of specimens (200) were shipped to the University of Antwerpen and screened by PCR targetting two Orthopoxvirus markers

namely FP3 and HA genes. Animal sequences were then compared to sequences of human MKPX available in Genbank.
RESULTS DNA evidence of Monkeypox virus was found in 4 localities, and in 10 species, including rodents (*Funisciurus*, *Cricetomys*, and 4 other species), a primate (*Galagoides*) and a carnivore (*Nandinia*). Squirrels of the *Funisciurus* genus accounted for 61% of the positive specimens. All sequences grouped with the Central African clade MKPX published sequences; homology between human and animal sequences ranged from 97 to 100%.
CONCLUSION The dramatic increase in prevalence in MKPX in the last 3 decades has been associated to the cessation of smallpox vaccination and decreasing immunity against Orthopoxvirus and reported in populations relying on bushmeat for survival. The strong relationship between the animal and human strains show an active circulation of the virus among wildlife and humans, and illustrates how wide the host range is. Looking at those results through the lens of viral emergence and public health risk, there is an urgent need to consider this viral threat. Knowing that 270 tons of bushmeat is estimated to transit through Roissy (Paris) airport a year, what comes out of Africa has become more than ever in the past the global concern of a global village.
DISCLOSURE Nothing to disclose.

3.2.3. Leishmaniasis

O.3.2.3.001

Effectiveness, safety profile of new treatments and long term outcome for Kala-azar at public health facilities in Bihar, India

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INTRODUCTION Phase III trials had demonstrated excellent efficacy with single dose Ambisome (SDA) and combination regimens of miltefosine plus paromomycin (M+P) and Ambisome plus miltefosine (A+M) for kala-azar (KA) in India. The expert committee had recommended the use of these regimens in the KA elimination programme. There was a need to generate pharmacovigilance data and see the feasibility of using these treatments within the health facilities in this region to provide evidence for the adoption of these regimens by the national programme.
METHODS This was an open label, prospective, non-randomised, non-comparative, multicentric trial conducted at public health facilities. The study was conducted from Aug 2012 to Oct 2014 at 02 districts (Vaishali and Saran) in Bihar and at a kala-azar referral hospital in Patna. Ethical clearance was obtained from the Institutional Ethical Committees concerned.

In Vaishali district, patients were treated with SDA (10 mg/kg) at the district hospital and A+M (single dose Ambisome 5 mg/kg + miltefosine 7 days) at 5 primary healthcare centres (PHC). In Saran District, patients received M+P for 10 days at district hospital and 3 PHC. The patients were diagnosed and treated by staff of health facilities. The outcome of treatment was assessed at the end of treatment, at 6 and 12 month follow up (FU).

RESULTS 1761 patients were treated in the study and 1576 patients were followed up for 6 months (185 patients ongoing). The cure rates at 6 months were 93.3% (95% CI 91.56–95.03) for SDA (n = 748), 90.0% (CI 86.77–93.23) for A+M (n = 298) and 97.5% (CI 96.05–98.95) for M+P arm (n = 432). During 12 month FU (n = 629) there were additional relapses, 4 in SDA (n = 242) and 5 in A+M (n = 162), 4 patients developed PKDL in M+P (n = 225) and 1 in SDA. Five SAE occurred in SDA arm, 2 considered related and 3 non-related to Ambisome, all of them resolved. Full sample size with 6 month FU and available 12 month FU data will be presented at the time of conference.
CONCLUSION The new treatment regimens showed excellent outcome and safety profile to be used within the programme. Extension of the FU beyond the standard 6 months yielded additional relapses and PKDL cases and this supports the need for monitoring long term outcome within the programme. Considering the cold chain need in deploying Ambisome, the use of M+P should be the second option in the elimination strategy. Cohort event monitoring at sentinel sites should be implemented for all regimens used in India.
DISCLOSURE Nothing to disclose.

O.3.2.3.002

IgG1 as a potential biomarker of post-chemotherapeutic relapse in visceral leishmaniasis, and adaptation to a rapid diagnostic test

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BRIEF INTRODUCTION Visceral leishmaniasis (VL), caused by protozoa of the *Leishmania donovani* complex, is a widespread parasitic disease of great public health importance; without effective chemotherapy symptomatic VL is usually fatal. Distinction of asymptomatic carriage from progressive disease and the prediction of relapse following treatment are hampered by the lack of prognostic biomarkers for use at point of care.
METHODS AND MATERIALS IgG subclass antibody levels were determined by ELISA against whole cell *Leishmania* lysate using serum samples from Indian and Sudanese patients with differing clinical status of VL, which included pre-treatment active VL, post-treatment deemed cured, post-treatment relapsed, seropositive endemic healthy controls (EHCs) and seronegative EHCs. Additionally, a prototype immunochromatographic rapid diagnostic test (RDT) to detect IgG1 was tested.
RESULTS *L. donovani* antigen-specific IgG1 levels were significantly elevated in relapsed versus cured VL patients ($P < 0.0001$).

Using paired Indian VL sera, IgG1 levels had not decreased significantly at day 30 after the start of treatment ($P = 0.8304$), consistent with the known IgG1 half-life, but were dramatically decreased by 6 months compared to day 0 ($P = 0.0032$) or day 15 ($P < 0.0001$) after start of treatment. Similarly, Sudanese sera taken soon after treatment did not show a significant change in the IgG1 levels ($P = 0.3939$).

The prototype RDT detected IgG1 levels in 94.3% of active pre-treatment (n = 89), 100% of day 30 (n = 20) samples from cured patients, and 100% of relapsed (n = 20). In general agree-

ment with the ELISA data, 80% of the day 180 (n = 20) samples from cured patients were negative by this test. Specificity with healthy or other disease controls was 87.3% (n = 55).
CONCLUSIONS Six months after treatment of active VL, elevated levels of specific IgG1 were associated with treatment failure and relapse, but not with cure. A prototype lateral flow RDT was successfully developed to detect anti-VL IgG1 levels as a promising point-of care biomarker of post-chemotherapeutic relapse.
DISCLOSURE Nothing to disclose.

O.3.2.3.003

Portable HECT-CL thermotherapy for *L. tropica cutaneous leishmaniasis* in Aleppo, Syria during 2014

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The Syrian war has escalated Cutaneous Leishmaniasis (CL) from endemic to epidemic status over much of northern Syria. We evaluated a 7-day portable thermotherapy (TT) treatment for CL called the Handheld Exothermic Crystallization Treatment for CL (HECT-CL), the first time HECT-CL was used in the Mideast. HECT-CL has previously proven a safe and efficacious CL treatment in Peru and Pakistan trials.

Study period was from May 10 to September 30, 2014; study site was a clinic in eastern Aleppo. CL diagnosis in real time was clinical, although microscopists later confirmed CL positive Giemsa smears. *Improvement* of CL lesions after HECT-CL treatment was defined as less erythema, smaller lesions, and re-epithelialization. *Cure* of CL lesions after HECT-CL treatment was defined as complete re-epithelialization. Patient treatment and follow-up obstacles included bombings, ISIL expansion, interruption of electricity, water, and communications, and refugee migrations.

230 patients were identified for HECT-CL treatment; 74 were excluded because of active migration. Of 156 patients entered, only 136 were able to complete more than 6 days of HECT-CL and evaluated on Day 7, 93 were further evaluated between Days 8 and 21, and 24 were evaluated between Days 21 and 63 (the optimal follow-up date to evaluate for *L. tropica* cure or failure). Patients (20) who received less than 7 days (1–6 days) HECT-CL treatment did not show improvement within that time period. Forty-seven (47%) percent (9/19) of patients who received 7 days of HECT-CL treatment and had their last follow-up on that date showed improvement or cure of their CL lesions. Fifty-four (54%) percent (32/59) of patients who received 7 days of HECT-CL treatment and had their last follow-up between Days 8–14 showed improvement or cure of their CL lesions. Seventy-nine (79%) percent (27/34) of patients who received 7 days of HECT-CL treatment and had their last follow-up between Days 15–21 showed improvement or cure of their CL lesions. Ninety-six (96%) percent (23/24) of patients who received 7 days of HECT-CL treatment and had their last follow-up between Days 21–63 showed improvement or cure of their CL lesions.

HECT-CL is a low-cost ($2), low-tech, non-invasive, safe, and efficacious treatment for CL, which appears to work by stimulating an *in vivo* vaccine response. With the proper logistical scale-up, HECT-CL has the potential to cover much more of the Syrian CL epidemic as a community-based treatment.

DISCLOSURE Support for this study was provided by a grant from the Mulago Foundation to Social Vaccine Strategies, New Orleans.

O.3.2.3.004

Post kala-azar dermal leishmaniasis treated with liposomal amphotericin B (AmBisome)

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INTRODUCTION Post-kala-azar dermal leishmaniasis (PKDL), a cutaneous sequela of visceral leishmaniasis (VL), develops in approximately 10% of treated VL patients in the Indian subcontinent and may act as a reservoir of disease. Current evidence for treatment is limited; only long and toxic treatments currently exist for a condition that is more a public health rather than an individual health problem. We describe the characteristics and outcome of PKDL treated with liposomal amphotericin B (AmBisome®) in MSF-supported facilities in India and Bangladesh.
METHODS We administered intravenous liposomal amphotericin B 30 mg/kg body weight in divided doses over 3 weeks on an ambulatory basis to patients with PKDL. To assess the treatment response, trained physicians regularly scored the severity of lesions and took medical photographs at baseline and at 12 months' follow-up. The main end-points were safety of treatment, with an emphasis on development of hypokalaemia, and efficacy at 12 months' follow-up. Following safety concerns in Bangladesh, we introduced a lower dose of 15 mg/kg, given in 5 doses of 3 mg/kg over 3 weeks.
RESULT 223 patients initiated treatment with the 30 mg/kg regimen, 110 in Bangladesh and 113 in India. In India, of 50 patients who completed 12 months' follow-up, 42 (84%) cases showed substantial or compete cure, with excellent tolerance and safety. In Bangladesh, of 63 patients who completed 12 months' follow-up, 59 (93%) showed substantial or complete cure; however, 6.5% developed severe hypokalaemia. No patients in either group developed rhabdomyolosis or further sequelae. In Bangladesh, 221 patients were subsequently treated with the 15 mg/kg regimen; 6-month follow-up results are available for 42. Of these, 33 (79%) showed substantial or complete cure. The safety profile was excellent with no severe hypokalaemia. We expect many more results to be available by early June.
CONCLUSIONS Short-course liposomal amphotericin B treatment regimens for PKDL appeared to be effective and may be considered as an option for the treatment of PKDL patients in India when biochemical monitoring is available. However, levels of hypokalaemia seen in Bangladeshi patients meant that a lower dosage regimen is necessary, which appears to be safe and effective.
DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

O.3.2.3.005

Mimotope-based vaccines of *Leishmania infantum* antigens and their protective efficacy against visceral leishmaniasis

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BACKGROUND The development of cost-effective prophylactic strategies to prevent leishmaniasis has become a high-priority. The present study has used the phage display technology to identify new immunogens, which were evaluated as vaccines in the murine model of visceral leishmaniasis (VL). Epitope-based immunogens, represented by phage-fused peptides that mimic Leishmania infantum antigens, were selected according to their affinity to antibodies from asymptomatic and symptomatic VL dogs′ sera.
METHODOLOGY Twenty phage clones were selected after three selection cycles, and were evaluated by means of *in vitro* assays of the immune stimulation of spleen cells derived from naive and chronically infected with *L. infantum* BALB/c mice. Clones that were able to induce specific Th1 immune response, represented by high levels of IFN-γ and low levels of IL-4 were selected, and based on their selectivity and specificity, two clones, namely B10 and C01, were further employed in the vaccination protocols. BALB/c mice vaccinated with clones plus saponin showed both a high and specific production of IFN-γ, IL-12, and GM-CSF after in vitro stimulation with individual clones or *L. infantum* extracts. Additionally, these animals, when compared to control groups (saline, saponin, wild-type phage plus saponin, or non-relevant phage clone plus saponin), showed significant reductions in the parasite burden in the liver, spleen, bone marrow, and paws′ draining lymph nodes. Protection was associated with an IL-12-dependent production of IFN-γ, mainly by CD8+ T cells, against parasite proteins. These animals also presented decreased parasite-mediated IL-4 and IL-10 responses, and increased levels of parasite-specific IgG2a antibodies.
CONCLUSIONS/SIGNIFICANCE This study describes two phage clones that mimic *L. infantum* antigens, which were directly used as immunogens in vaccines and presented Th1-type immune responses, and that significantly reduced the parasite burden. This is the first study that describes phage-displayed peptides as successful immunogens in vaccine formulations against VL.
DISCLOSURE Nothing to disclose.

O.3.2.3.006

Innovative approaches to visceral leishmaniasis: 18F-FDG PET/CT as a diagnostic tool and treatment with a single dose of liposomal amphotericin B

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INTRODUCTION Visceral leishmaniasis (VL) represents the most severe form oh human leishmanial infection, leading to death if untreated. Italy is an endemic country for leishmaniasis and an increasing number of autochthonous VL cases has recently been reported in Bologna Province, Northern Italy [1].
METHODS AND MATERIALS A retrospective data analysis was performed on all patients (pts) diagnosed with VL who underwent 18F- FDG PET/CT (PET/CT) in our centre between May 2008 and March 2015. PET/CT was performed to clarify the cause of FUO, VL was subsequently diagnosed in all pts by microbiological methods (serology and molecular tests). Data about the treatment were also collected.
RESULTS All 15 pts were male and mean age was 60 years old. All pts presented with fever of unknown origin (FUO) accompanied by aspecific symptoms. PET/CT showed splenic involvement in 14/15 pts (93%). The FDG uptake in the spleen was measured and two different patterns were established: diffuse splenic uptake (8 pts, mean SUVmax: 7.2, mean hepatic SUV: 3.4), and focal splenic uptake (6 pts, mean SUVmax: 13, mean hepatic SUV: 3.4). The only patient who did not show any splenic uptake was the only one with HIV infection. 6/15 pts (40%) also presented other areas of increased 18F-FDG uptake: difuse bone marrow uptake was observed in three patients (mean SUVmax: 4.2), and high 18F-FDG uptake in multiple lymph nodes in two pts. 13/15 pts (87%) were successfully treated with a single dose of intravenous liposomal amphotericina B (10 mg/kg bodyweight), which was well tolerated with no adverse events, as previously described [2]. None of the 11 pts who have had the follow-up visit at 6 months after the treatment showed relapse of the infection.
CONCLUSIONS In this retrospective study we observed splenic 18F-FDG uptake in 93% of pts with confirmed VL, showing two different patterns (diffuse or focal). In an endemic area as Italy, these findings should induce the suspicion of VL in pts presenting with FUO. Therefore, we suggest to rule out VL before of invasive investigation on spleen (biopsy or splenectomy). Our data also confirmed that treatment of VL with a single dose of liposomal amphotericin B is safe and effective.
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DISCLOSURE Nothing to disclose.

3.2.4. Visceral leishmaniasis – from patient to public health needs: the role of R&D in disease elimination and control

INV.3.2.4.001
Treatment of visceral leishmaniasis

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Visceral leishmaniasis (VL) is the most severe form of leishmaniasis, and is fatal, if untreated. Most cases (90%) occur in India, Bangladesh, Sudan, South Sudan, Ethiopia and Brazil. Clinical features include fever, splenomegaly, lymphadenopathy. Response to various antileishmanial drugs varies in different geographical regions. In the Indian subcontinent there is significant decline to the response to sodium stibogluconate and it is no longer used in India, Nepal and Bangladesh. Oral miltefosine has been used for the treatment of VL in the Kala-azar Elimination Programme of the three countries mentioned above. However, Response to miltefosine varies in the three countries of the Indian Subcontinent. In India 94% patients were cured with miltefosine in a phase 3 trial, it declined to 90% in a subsequent study a decade later. Definitive cure rates from Nepal and Bangladesh are not satisfactory. Single dose AmBisome (10 mg/kg) has performed very well and cure rates of 95.7% and 97% were achieved in studies from India and Bangladesh, respectively. In the subsequent study a combination of AmBisome with miltefosine or paromomycin, and that of miltefosine and paromomycin returned a cure rate of >97% in India. In East African countries Sudan, South Sudan and Ethiopia, sodium stibogluconate with paromomycin is the treatment of choice. In Europe amBisome is the preferred treatment. Thus, for VL different treatment has to used in different endemic regions.

DISCLOSURE Nothing to disclose.

INV.3.2.4.004
Opportunities in visceral leishmaniasis: analysis of large, pooled data sets

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Pooled analyses combine data from many studies to answer specific scientific questions not accessible in any of the smaller individual studies. Currently, the overall outcomes from each of the studies are compared, but the heterogeneity of study and analytical designs makes direct comparison difficult. Alternatively, Individual Participant Data (IPD) files can be harmonized and analysed as a single much larger group, allowing detailed analysis of this merged larger pool. At present, only a small fraction of systematic reviews and meta-analyses employ pooled analysis of these IPD. However, the additional statistical power and increasing interest in data sharing are likely to stimulate more frequent use of IPD meta-analyses to review therapeutic techniques.

At the outset of this work, it was not clear that an IPD based analysis of clinical trial data from visceral leishmaniasis (VL) would be feasible as a better approach to evaluate the treatments of VL. To assess the potential value for developing a platform to collate and analyze VL clinical trial data, we conducted a systematic review to identify the number of published or unpublished clinical trials that could provide IPD and to categorize the consistency of the trial designs.

We conducted a systematic search of both published and unpublished studies since 1980. 140 published VL clinical trials were identified and these had enrolled a total of 25 876 patients, 1379 additional patients were enrolled in unpublished trials, and 9802 patents are targeted currently for enrolment into active trials. Once all trials are completed a total of 37 057 patients' data will be available for analysis. These trials used a limited number of drugs and were dominated by only few different dose regimes. The results suggest that overall outcomes of treatment with different drugs and dose regimens could be compared in IPD pooled meta-analyses, with hundreds or possibly thousands of patients per arm.

The WorldWide Antimalarial Resistance Network (WWARN) has developed an IPD-based approach for pooled analyses of clinical trials of antimalarial medicines. The WWARN platform could be adapted for analyses of VL-IPD files. The number of VL trials identified in this review and the relatively limited diversity of drugs and regimens tested in the most recent years provide good evidence that establishing an IPD based VL data sharing platform would be feasible and valuable to explore factors affecting VL drug efficacy.

DISCLOSURE Nothing to disclose.

3.2.5. Diagnosis and management of cutaneous leishmaniasis in travellers

INV.3.2.5.002
Comparison of Leishmania species typing results in 17 European clinical laboratories

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INTRODUCTION Many typing technologies are currently available for identification of the infecting species in leishmaniasis patients. The study group for clinical parasitology of ESCMID (European Society of Clinical Microbiology and Infectious Diseases) together with the LeishMan network (a European consortium for harmonisation of diagnosis and treatment of leishmaniasis) conducted a comparative study across 17 European clinical laboratories. The aim was to assess whether the various methods produce the same typing outcome.

METHODS AND MATERIALS A panel of 21 DNA samples isolated from *Leishmania* strains belonging to 14 different species was randomized and sent blindly to 17 clinical laboratories in Belgium, France, Germany, Israel, Italy, The Netherlands, Portugal, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. Both Old and New World *Leishmania* species were included, as most laboratories deal primarily with imported cases whereby the origin of infection is often unknown. The 17 laboratories were asked to apply their routinely used species typing method, and report the obtained result. The study was funded by ESCMID.
RESULTS Sixteen laboratories used a total of 5 genome targets for typing: the internal transcribed spacer of the ribosomal DNA array, the mini-exon, kinetoplast DNA, the heat-shock protein 70 gene, and a repetitive DNA sequence. These were analysed using restriction fragment length polymorphisms or sequencing. The 17th laboratory used multilocus sequence typing. Different levels of identification were achieved: some defined only the *Leishmania* subgenus, others the species complex, yet others typed to the actual species. Even laboratories using the same method reported different levels of identification. In total 9% of typing results were incorrect, whereby 6% classified a strain in the wrong species complex, while the remaining 3% identified the correct complex but the wrong species within the complex. Sequence analysis of the heat-shock protein 70 gene produced the most accurate and precise typing.
CONCLUSIONS The study shows there is considerable room for improvement and standardization of *Leishmania* species typing in Europe. All participants will evaluate their current methodology in the light of these results to achieve the best possible parasite identification for leishmaniasis patients. Recommendations for diagnostic laboratories from the LeishMan network and the ESCMID study group for clinical parasitology will be formulated.
DISCLOSURE Nothing to disclose.

INV.3.2.5.003

Worldwide diversity of leishmaniasis: harmonized collection of data and isolates by the European "LeishMan" network: the LeishMan Network

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BACKGROUND Leishmaniasis displays a challenging geographic, clinical and parasitological diversity.
METHODS Analysis of a database collecting observations from patients with parasitologically confirmed leishmaniasis in 11 centers from 6 European countries, 2012–2015.
RESULTS Of 203 patients with leishmaniasis, 59% were males, 97% travelers, mostly tourists. Most patients were followed in the hospital (n = 136, 67%) by ID physicians (n = 92, 53%) or dermatologists (n = 42, 24%); 170 episodes were cutaneous (CL, 84%), 15 were visceral (VL, 7%), 9 were mucosal (ML, 5%). Infection was acquired in the Americas for 63 patients (33%), Africa for 54 (29%), Europe for 42 (22%), Asia and Middle East for 26 (14%). Infections had been acquired in 43 different countries i.e., 51% of the 85 Leishmania-endemic countries according to WHO. Immunocompromised status was markedly more frequent in VL (11, 73%) than in CL or ML (8, 4%). In localized CL, lesions (median number: 2) were mostly ulcers (n = 91, 60%) or papulo-nodules (n = 28, 19%). In CL and ML, the most widely used sample and diagnosis technique were punch biopsy (112 patients, 78%) and PCR (112 patients, 66%), respectively. Healing or sustained cure following first-line therapy was obtained in 103/170 CL (82%), 6/9 ML (75%), and 6/12 VL (50%). No disease-related death was recorded but severe complications occurred, including lymphohistiocytic hemophagocytosis and blindness following uveitis in diffuse CL. There was a great heterogeneity in treatment approaches, especially in CL. In tegumentary leishmaniasis, local treatment was prescribed in 69 patients (53%). Amphotericin B and pentamidine were the most frequently used treatments in VL (33% each). Most frequent infecting species were *L. braziliensis* and other species belonging to the Vianna subgenus (n = 34), *L. major* (n = 21), *L. tropica* (n = 21) in CL; *L. donovani* (n = 7) and *L. infantum* (n = 3) in VL.
CONCLUSIONS The emergence and consolidation of the LeishMan network has enabled the harmonized collection of data and isolates from patients infected in more than half of *Leishmania*-endemic countries in <4 years. This prospective analysis enables a wide epidemiological surveillance across most reported clinical forms and species. The growing role of PCR for diagnosis and of local treatment for CL are marked trends in the management of patients.
DISCLOSURE Nothing to disclose

INV.3.2.5.004

Visceral leishmaniasis in London: identifying immunosuppression as a risk factor

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Visceral leishmaniasis (VL) is a parasitic protozoon infection caused by the Leishmania species and transmitted by sandflies. Patients acquire VL in five main tropical areas and the Mediterranean basin, and clinicians from non-endemic regions regularly see infected patients. We describe the population presenting with VL to the Hospital for Tropical Diseases (HTD), London in a 13-year period and identify risk factors for developing VL[1].
METHODS AND PRINCIPAL FINDINGS A retrospective study of imported VL to the HTD, London, including patients diagnosed and/or managed at the HTD between January 2000 and July 2013. Twenty-eight patients were treated for VL at the HTD. The median age at VL diagnosis was 44 years (range 4–87 years). Most patients were British and acquired their infection in the Mediterranean basin. The median time from first symptom to diagnosis was six months (range of 1–12 months) and diagnosis

included microscopic visualisation of leishmania amastigotes, positive serological tests (DAT and k39 antibody) or identification of leishmania DNA. Nineteen patients had immunosuppression (7 HIV, 6 auto-immune disease, 2 haematological malignancies, 2 diabetes, 2 alcohol excess) and the numbers with autoimmune disease has increased. Immunosuppressed patients had significantly lower cure and higher relapse rates.

The rise of VL in patients with immunosuppression secondary to autoimmune disease on immune-modulatory drugs presents new diagnostic and therapeutic challenges. VL should be a differential diagnosis in immunosuppressed patients with pyrexia of unknown origin returning from travel in leishmania endemic areas.

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DISCLOSURE Nothing to disclose.

INV.3.2.5.005

Recommendations for management for cutaneous and mucosal leishmaniasis: case studies and discussion

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INTRODUCTION Imported cases of leishmaniasis have recently become more frequent in Europe due to increased travel to risk areas. Standardized species identification and treatment protocols are warranted to provide the patients with the best possible treatment.

The sensitivity to anti-leishmanial drugs varies according to the Leishmania species. The wide availability of PCR genotyping tools allows a rapid determination of species as a precondition for species-specific treatment.

METHODS Treatment guidelines can now be species based and this is replacing previous guidelines based on geographical exposure. We have established a European expert group 'LeishMan' (Leishmaniasis Management), a group of experts of 13 institutions from 8 European countries. This group is collaborating on clinical and parasitological research.

RESULTS AND CONCLUSION Recommendations from this group comprise an evidence based review of the species based treatment data on CL. Based on practical examples of patients practical treatment recommendations for imported CL and mucosal leishmaniasis in Europe will be discussed. For the involved species the first and second choice of treatment will be presented.

In addition, the experience of the group in the management of patients with immunosuppression and cutaneous leishmaniasis will be presented: 16 patients treated with a TNF alpha blocker had species specific treatment and all responded well to treatment, but in most of them TNF alpha blockers were discontinued.

DISCLOSURE Nothing to disclose.

3.2.6. Dengue control

INV.3.2.6.001

DengueTools: innovative strategies and tools for the prevention and control of dengue

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With estimated 390 million infections annually and 2.5 billion people at risk, dengue is a major emerging disease threat and an escalating public health problem worldwide. Effective vector control remains elusive, and surveillance in dengue endemic countries remains suboptimal at best. We lack understanding of individual or combined roles of viral, entomological, ecological, environmental and climate factors that influence dengue transmission dynamics and their respective outbreak predictive capability and the most cost-effective approach for surveillance and early warning systems. To address those gaps we have set up a comprehensive, early warning, laboratory-based sentinel disease surveillance system in Sri Lanka that has predictive capability for epidemic dengue.

Furthermore, children are the most vulnerable group for dengue. We desperately need simple, cost-effective and scalable control strategies to protect children from dengue. Our DengueTools consortium hypothesized that insecticide treated school uniforms may be a target for school-based intervention to reduce the incidence of dengue in school children. We will report on our preliminary results.

Lastly, DengueTools examines gaps in understanding the risk of introduction of dengue to non-infected areas, including Europe. We currently have insufficient data on the magnitude and trends of importation and virus evolution over time and by geographic origin. We also only have a poor understanding of vector density, preferred breeding sites, and vectorial capacity of *Aedes* in temperate climates that are needed for predictive models under changing climate conditions. We will collect clinical and virological data in travellers returning to Europe from dengue endemic countries, explore the effectiveness of vector control programs against *Aedes albopictus* in Southern France, and develop predictive risk models and maps the the introduction and establishment of dengue in Europe under different future climate scenarios in Europe.

DengueTools is a global consortium of 14 partners, funded by the European commission 7th framework. We have 12 work packages around 3 main research areas.

DISCLOSURE Principal Investigator of DengueTools. No other conflict of interests since January 2011.

INV.3.2.6.002

Global dispersion patterns and outbreak risks of Dengue

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Dengue, a mosquito-borne viral disease, is rapidly becoming a global health threat due to climate change, globalisation, urbanisation, and population growth. The estimates of the global burden of disease of dengue has recently been updated to show much higher estimates than previous studies. The future burden is likely to expand due to human activities unless effective control measures are put in place. Dengue vectors take advantage of urbanisation, particularly urban heat islands and changes in environment and human populations densities. Global mobility is responsible for the global dispersion of dengue virus and vectors.

The introduction of dengue to Europe is highly correlated to international flight network traffic flows. Further, climate change is associated with changes in seasonal weather patterns with potential subsequent impacts on the suitability and temporal and spatial distribution of vectors. Within this context of multiple factors that contribute to the increasing geographic range and intensity of transmission of dengue, prediction and early identification of outbreak risk areas are critically important.

Understanding dengue occurrence and outbreaks is complex. We use disease data from international surveillance registers, and meteorological and climate data from online databases. Population and data on global mobility were obtained from IATA registers, and estimates of introduction to dengue in Europe are derived. We used mathematical and statistical methods to describe relationships, timing, and geographic areas of dengue risk in the past, present, and future using a formula for dengue relative vectorial capacity.

Modeled global drivers of dengue can predict historic and current risk of dengue outbreaks, and future risk indices indicate further risk of expansion and prolonged transmission seasons in Europe. Information, like this, can guide preventive strategies and actions to control dengue. However, we also acknowledge data scarcity and difficulties in projecting future disease burdens of dengue given that the virus can change, vectors can adapt, and interventions such as vaccine development can radically alter the future disease burden.

DISCLOSURE Nothing to disclose.

INV.3.2.6.003

Dengue transmission dynamics: the role of asymptomatic infections

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Dengue is a self-limiting, systemic infection caused by RNA viruses transmitted by *Aedes* mosquitoes. Close to 400-million dengue virus (DENV) infections are estimated to occur each year throughout the tropics, of which about 75% are clinically inapparent. Symptomatic DENV infections cover a wide range of disease manifestations from mild febrile illness to severe and fatal disease. People with mildly symptomatic and clinically inapparent DENV infections are generally assumed to inefficiently infect mosquitoes and, therefore, to contribute non-significantly to DENV transmission. We used cluster sampling around index cases to identify 182 people with natural, active DENV infections in real-time and quantify human-to-mosquito transmission across the full spectrum of disease manifestations, including 14 people with strictly asymptomatic infections and 42 viremic people prior to the onset of symptoms. We found that despite their lower average level of plasma viremia, the contribution of asymptomatic people to mosquito infection is similar to those with symptomatic infections, due to their higher relative infectiousness. At a given level of viremia, people with asymptomatic and presymptomatic DENV infections are markedly more infectious to mosquitoes than when a person's infection is symptomatic. Because DENV infected people with mild or undetectable symptoms may be exposed to more mosquitoes than sick people through their undisrupted daily routine and they represent the majority of DENV infections, our data indicate that mild and inapparent infections contribute significantly more to DENV transmission than previously recognized. This finding fundamentally changes the current paradigm of dengue epidemiology, which is based on people with apparent illness.

DISCLOSURE Nothing to disclose.

INV.3.2.6.004

Dengue vaccine development: lessons learnt from asymptomatic infections

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Several vaccine candidates for dengue are currently in pre-clinical or clinical development, the most advanced of which recently finished phase III efficacy trials. Although these studies have shown that populations can be protected from dengue disease, they have also raised numerous other issues. First, the neutralizing antibody conferred only partial protection against dengue infection. The second problem is viral interference, which is a common key issue among all tetravalent live attenuated vaccine. Booster immunization is required but must be delayed for at least four months due to sterilizing immunity developed from first immunization.

In the DENFREE consortium, we discovered two important information which leads to a new concept of dengue vaccine. First, we identified highly potent, broadly neutralizing antibodies. The X-ray structures of four of these antibodies in complex with the envelope glycoprotein E from dengue virus, revealed that the recognition determinants are at a serotype-invariant site at the E-dimer interface, including the exposed main chain of the E fusion loop and the two conserved glycan chains. This 'E-dimer-dependent epitope' is also the binding site for the viral glycoprotein prM during virus maturation in the secretory pathway of the infected cell, explaining its conservation across serotypes and highlighting an Achilles' heel of the virus with respect to antibody neutralization.

Secondly, we observed a significant number of genes corresponding to CD8+ T cell activation overexpressed in asymptomatic individuals, in comparison with symptomatic donors. An important protective role for CD8+ T cells during primary DENV infection was also identified in a mouse model. More strikingly, a detailed analysis of HLA-restricted T-cell responses in donors from hyperendemic area even reinforces the protective role of CD8+ T cells during DENV infection. It appears that, whereas serotype-specific responses are a hallmark of primary infection, there is a shift towards a response against conserved epitopes following secondary infection, without any difference in the avidity or functionality in CD8+ T cells among serotype-specific or conserved responses.

These findings will be instrumental for devising novel immunogens to protect simultaneously against all four serotypes of dengue virus as a monovalent dengue vaccine.

DISCLOSURE Nothing to disclose.

INV.3.2.6.005

Dengue control in the IDAMS consortium

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Dengue Control in the IDAMS consortium. Around half of the world's population live in areas at risk for dengue transmission. While dengue has reached unprecedented levels, new and more effective disease control measures are urgently needed.

The IDAMS consortium (www.idams.eu; 2011–2016) focuses on the following areas of disease control and prevention for dengue:

1 Secondary prevention on the individual level: We will evaluate potential risk factors or warning signs in order to identify patients at high risk of developing severe disease, thus facilitating triage during outbreaks. In an ongoing multicenter observational study we are recruiting patients across south-east Asia and Latin America who are potentially infected with dengue virus to empirically validate important clinical signs and symptoms, as well as evaluate virological and immunological markers.
2 Secondary prevention on the population level: Better methods for early detection of dengue outbreaks are urgently needed worldwide. Based on an initial series of systematic reviews in key topics, we defined priority areas for the development of a dengue surveillance and response system. A prospective-retrospective study in selected countries across south-east Asia and Latin America is ongoing. In addition, a number of widely-used vector control approaches will be evaluated in a cluster-randomized trial.
3 Primary prevention and control using mapping and modelling techniques: We aim to define the current extent of dengue disease globally and assess the risk of future spread to previously uninfected regions. Updated global risk maps and burden estimates for dengue were already generated. Potential changes to the distribution of the global dengue risk will be evaluated for the future (2020, 2050, 2080) under scenarios of climate and demographic change.

Maps of the history of spread of each of the four distinct dengue viruses have been produced. We also conducted an expert conference on dengue in Africa as the burden of dengue in Africa is currently unknown.

Finally, we will present the results of our mapping of Aedes vectors, which is the subject of a separate presentation.

DISCLOSURE Nothing to disclose.

INV.3.2.6.006

The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*

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Dengue and chikungunya are increasing global public health concerns due to their rapid geographical spread and increasing disease burden. Knowledge of the contemporary distribution of their shared vectors, *Aedes aegypti* and *Ae. albopictus* remains incomplete and is complicated by an ongoing range expansion fuelled by increased global trade and travel. Mapping the global distribution of these vectors and the geographical determinants of their ranges is essential for public health planning. Here we compile the largest contemporary database for both species and pair it with relevant environmental variables predicting their global distribution. We show *Aedes* distributions to be the widest ever recorded; now extensive in all continents, including North America and Europe. These maps will help define the spatial limits of current autochthonous transmission of dengue and chikungunya viruses. It is only with this kind of rigorous entomological baseline that we can hope to project future health impacts of these viruses.

DISCLOSURE Nothing to disclose.

3.2.7. Geospatial health

O.3.2.7.002

Malaria incidence and temperature show a steady and correlated increase between 2003 till 2014 in Lubumbashi, Democratic Republic of Congo: a spatio-temporal analysis

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BACKGROUND Malaria is holoendemic with seasonal variation in Lubumbashi, Democratic Republic of Congo (DRC). The malaria burden is influenced by meteorological features as temperature, humidity and rainfall and host factors as immunity, population density. We assessed during from 2003–2014 the meteorological variables and reported malaria burden in the public and private health sector.

METHODS Monthly and annual malaria incidence rates (MIR) per 1000 were drawn from case numbers recorded weekly at primary health care in all 9 health districts (HD) of Lubumbashi city, and reported from 2003 to 2014. We computed malaria predicted cases in each health zone monthly and yearly to get the standardised incidence ratios (SRI) for the studied period. Negative binomial regression were used to evaluate the association between meteorological variables and malaria cases per year.

RESULTS From 2003 till 2012, MIR has steadily increased, from 90/10000/year to 180/10000/year. Analysing separately the 9 HD, MIR was four times higher in the wealthiest HD compared to 8 others. For each degree Celsius increase of temperature, there was an increase of 4.2% of yearly MIR ratio ($P < 0.001$). The utilisation rate evolved from 0.206 contacts/person year in 2003 to 0.237/person year in 2012. After a LLIN mass campaign in Lubumbashi city in 2012, we didn't notice any trend in malaria cases.

CONCLUSION While worldwide, the world is observing a malaria decline, we observe in Lubumbashi a steady increase of malaria incidence rates correlated with a temperature increase. Access to care remained stable throughout the observed period. Only during the last 2 years, due to a LLIN mass campaign, this trend was halted. Climate change may have a counter-current effect in combating malaria in this geographic area.

DISCLOSURE Nothing to disclose.

O.3.2.7.003

A fine-scale geospatial analysis of factors associated with monkeypox transmission, Tshuapa District, Democratic Republic of the Congo, 2013

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Monkeypox virus is a zoonotic pathogen causing severe febrile rash illness and occasional mortality. The disease has an undetermined wildlife host and is mainly restricted to forested areas of Central Africa. Communities affected by monkeypox are often small and isolated, which complicates investigation of fine-scale spatial patterns of disease. In October 2013, the Ministry of Health in Democratic Republic of Congo (DRC) and Centers for Disease Control and Prevention were notified of a 6-fold increase of monkeypox cases over the previous 3 years in the Bokungu health zone, Tshuapa District, DRC. During an ensuing epidemiological investigation, geographic information from 11 cases households was collected and combined with remotely-sensed data for spatial analysis. The locations of all human structures were digitized from 0.5-meter panchromatic satellite imagery allowing for density analyses to be performed. A 50-meter resolution multispectral landsat composite image was classified into 5 land cover categories. The land-cover composition of the area surrounding case households were compared with other inhabited structures in the area at several distances. The analysis showed that the land cover contained in a 500-meter ring around case households differed significantly from households not reporting cases. Additional analysis found that 55.5% of case households were located in areas statistically delineated as areas of y high population density. Results indicate that even in remote forest communities, there is often a large-degree of heterogeneity in structural density and surrounding landscape. Suspect monkeypox cases were more likely to live in more crowded areas with a greater percentage of disturbed habitat than were residents of the area in general. These characteristics could influence monkeypox transmission either by increasing opportunities for zoonotic introduction or via increased inter-human contacts in areas of high population density.

DISCLOSURE The findings and conclusions in this presentation have not been formally disseminated by the agency and should not be construed to represent any agency determination or policy.

O.3.2.7.004

Bayesian risk profiling and model-based prediction of soil-transmitted helminth infections among schoolchildren from Côte d'Ivoire

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BACKGROUND Soil transmitted helminthiases (STH) rank first among neglected tropical diseases and occur mostly in disadvantaged communities. STH infection is associated with poor hygiene and sanitation conditions and its distribution be favoured by environmental and climatic factors. The aim of this study was to predict and map the spatial distribution of STH infection among school-aged children within a Bayesian statistical framework for the whole country of Côte d'Ivoire.

METHODS From November 2011 to February 2012, a national cross-sectional parasitological survey was conducted among schoolchildren in 92 localities. Helminth infection status was determined from microscopic examination of duplicate Kato-Katz thick smears from a single stool sample per child. Various proxies of environmental and socioeconomic factors, known to favour helminthiases, were considered as potential explanatory variables for building predictive geostatistical models of infection risk. Then, we modelled the infection risk within a standard Bayesian geostatistical framework and used Markov chain Monte Carlo (MCMC) simulations algorithms to estimate model parameters.

RESULTS Complete parasitological data were available for 5246 children. Hookworm was the predominant STH species encountered (17.2%) and was present all over the country. The Bayesian modelling fitted for hookworm infection in relation with socioeconomics, demographics, and environmental exposures selected rural setting as the main risk factor. Moderate-to-high risk areas (≥20% prevalence) were predicted for north-eastern (i.e. Boukani, Goftogo, Bélier and N'Zi regions) and north-western (i.e. Kabadougou, Worodougou, Banfing, and Haut Sassandra regions) parts of the country. Low risk areas (<5% prevalence) of hookworm infection were predicted for the extreme north and south-eastern parts of the country.

CONCLUSION Hookworm infection is the main STH infection among schoolchildren in Côte d'Ivoire, and occurs more pronouncedly in rural settings. These findings may assist in planning and guiding the efforts of the established national control programme.

DISCLOSURE Nothing to disclose.

O.3.2.7.005

Mapping and modelling the geographical distribution and environmental limits of podoconiosis in Ethiopia

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INTRODUCTION Ethiopia is assumed to have the highest burden of podoconiosis globally, but the geographical distribution and environmental limits and correlates are yet to be fully investigated. In this paper we use data from a nationwide survey to address these issues.

METHODS AND MATERIALS Our analyses are based on data arising from the integrated mapping of podoconiosis and lymphatic filariasis (LF) conducted in 2013, supplemented by data from an earlier mapping of LF in western Ethiopia in 2008–2010. The integrated mapping used *woreda* (district) health offices' reports of podoconiosis and LF to guide selection of survey sites. A suite of environmental and climatic data and boosted regression tree (BRT) modelling was used to investigate environmental limits and predict the probability of podoconiosis occurrence.
RESULTS Data were available for 141 238 individuals from 1442 communities in 775 districts from all nine regional states and two city administrations of Ethiopia. In 41.9% of surveyed districts no cases of podoconiosis were identified, with all districts in Affar, Dire Dawa, Somali and Gambella regional states lacking the disease. The disease was most common, with lymphoedema positivity rate exceeding 5%, in the central highlands of Ethiopia, in Amhara, Oromia and Southern Nations, Nationalities and Peoples regional states. BRT modelling indicated that the probability of podoconiosis occurrence increased with increasing altitude, precipitation and silt fraction of soil and decreased with population density and clay content of the soil. Based on the BRT model, we estimate that in 2010, 34.9 [95% confidence interval (CI): 20.2–51.7] million people (i.e. 43.8%; 95% CI: 25.3–64.8% of Ethiopia's national population) lived in areas environmentally suitable for the occurrence of podoconiosis.
CONCLUSIONS Podoconiosis is more widespread in Ethiopia than previously estimated, but occurs in distinct geographical regions that are tied to identifiable environmental factors. The resultant maps can be used to guide programme planning and implementation and estimate disease burden in Ethiopia. This work provides a framework with which the geographical limits of podoconiosis could be delineated at a continental scale.
DISCLOSURE Nothing to disclose.

3.2.8. Leprosy elimination

O.3.2.8.003

Global elimination of leprosy by 2020: are we on track?

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Annually more than 200 000 new leprosy cases are registered. This number has been fairly stable in the past 8 years. WHO has set a target to eliminate leprosy globally by 2020.The aim of this study is to investigate whether this is feasible given the current control strategy. We focus on three endemic countries, India, Brazil and Indonesia, which together account for nearly 80% of all leprosy cases.

We used the existing individual-based model SIMCOLEP to predict future trends of leprosy incidence given the current control strategy in each country. SIMCOLEP simulates life histories of individuals, structured in households, and the natural history of infection with *M. leprae*. Current control consists of passive case detection, some active case detection, and multidrug therapy (MDT). Also, BCG vaccination of infants against tuberculosis is known to be effective against leprosy. Predictions of leprosy incidence were made for each country as a whole and for one high-endemic region in each country: Chhattisgarh (India), Para (Brazil) and Madura (Indonesia). Data for model quantification came from the *National Leprosy Elimination Program* (*NLEP*, India), *SINAN* database (Brazil) and the *Netherlands Leprosy Relief* (Indonesia).

Our projections of future leprosy incidence all show a downward trend. In 2020, the country-level leprosy incidence has decreased to 6, 7 and 4 per 100 000 in India, Brazil and Indonesia, respectively, meeting the elimination target of less than 10 per 100 000. However, elimination may not be achieved in the high-endemic regions. The leprosy incidence in 2020 is predicted to be 17, 19 and 24 per 100 000 in Chhattisgarh, Para and Madura, respectively.

Although it seems that country-level elimination will be reached by 2020, leprosy is likely to remain a problem in the high endemic regions, which account for most of the cases in a country. We therefore conclude that elimination may only be reached by 2020 with additional control measures.
DISCLOSURE Nothing to disclose.

O.3.2.8.004

Cambodia retrospective contact tracing project: innovation in contact tracing to improve early diagnosis of leprosy

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INTRODUCTION The Retrospective Contact-Tracing Project (RCTP) pilots a new method of contact-tracing (CT) by tracing former leprosy patients (FLPs) and screening their contacts. The primary aim is to diagnose leprosy early, and consequently, reduce the number of patients with disability and reduce transmission (which should be seen by fewer cases among children). The secondary aim of the RCTP is to provide evidence to support retrospective CT as a leprosy elimination strategy in low-endemic settings.
METHODS The RCTP approach entails 'drives' comprising high intensity tracing of FLPs and screening their contacts over 1–3 days in select districts. A central database is used to trace FLPs diagnosed between 2001–2010. Data collected during the drives measures the effectiveness to detect cases early and feasibility to conduct the approach and includes the name, age, gender, screening result of FLP contacts. To measure the impact on early case detection, as compared to routine practice, national data on leprosy incidence pre and post-drive are compared with drive yield and the proportion of MB/PB. To determine optimal timing to conduct retrospective CT, individual data analysis measures risk of contacts compared to duration of exposure and time since FLP diagnosis.
RESULTS Since 2011, drives have been implemented in 67 of 77 districts in Cambodia; finding 608 cases. 568 were found earlier enough to avoid disability, including 71 children. Over 2000 examinations were led. This May drives will be finished in all districts.
CONCLUSIONS Preliminary results show drives are effective in connecting FLP contacts to experts in leprosy diagnosis and in finding cases early to avoid disability. Data analysis in June will define the proportion of FLPs retrieved, contacts present and screened during the drives, to establish feasibility. Analysis will also reveal the impact, as comparted to routine practice, as well as, the optimal timing after FLP diagnosis to conduct retrospective CT, thereby defining the ideal drive frequency to target leprosy elimination. Roll-out of a new, Cycle 2 will be extended for 2–3 years to measure the indirect effect of the RCTP on leprosy incidence. If the drives are repeated it may reveal to be a steady approach to take Cambodia towards

elimination. Analysis will determine the effect of repeated drives, in select districts, on the overall trend of the new case detection rate, compared to districts which received only one drive.
DISCLOSURE The Novartis Foundation supports the Cambodia Retrospective Contact Tracing Project (RCTP).

O.3.2.8.005
Leprosy alert response network and surveillance system (LEARNS): Iloilo implementation

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INTRODUCTION The Philippines eliminated leprosy as a public health problem in 1998. Despite this, subnational areas of hyperendemicity still exist and the Philippines reports 1000–3000 new cases per year. The majority of these cases are multibacillary leprosy highlighting the need for early diagnosis and detection. A public private partnership including persons affected by leprosy developed the Leprosy Alert Response Network and Surveillance System (LEARNS) in 2013.
METHODS LEARNS is a mobile phone-based leprosy teleconsultation system focused on improving communication among health care providers and specialists to minimize delays in diagnosis and treatment. The provider sends an image of the skin lesion and standardized de-identified patient information through a mobile phone. LEARNS also accepts short-message service (SMS) when providers have no camera. The LEARNS training takes two days, and includes a clinical refresher on leprosy

(case detection methods/identification of leprosy lesions) and training on the LEARNS system. Providers are then registered into the database. The Iloilo province in Region 6 was selected as a pilot site for LEARNS.
RESULTS LEARNS was implemented in Iloilo City and 19 (of 42) municipalities in Iloilo in May 2014. These 19 provinces were selected as they had the nine new leprosy cases in 2013.[5] Iloilo trained 26 medical doctors, 22 nurses and 8 midwives. These providers then trained an additional 1,978 health workers, 858 *barangay* officials, 492 community health members and leaders. Of the eight leprosy cases five (63%) were from LEARNS in 2014. LEARNS maintenance cost is minimal consisting of local telecommunication charges of sending an image or message. LEARNS employs the health care provider's own phone and thus no mobile devices were provided through the program. Qualitative feedback obtained from providers who have used LEARNS is the following:

1. Ease of use.
2. The raised awareness for leprosy.
3. The confidence gained in clinical diagnosis by having a specialist answer immediately through LEARNS.

CONCLUSIONS Case detection in the implementation period rendered 8 cases versus 9 in 2013, but the implementation period was only 7 months. LEARNS can work within and complements leprosy control and monitoring initiatives, and it empowers and increases capacity of peripheral health care providers.

DISCLOSURE Novartis and Novartis Foundation provide support for the Leprosy Task Force activities in the Philippines.

3.2.9. Helminth infections - burden and impact

INV.3.2.9.001
Helminth infections - burden and impact

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The move to quantify disease impact of different health states comes from the greater implementation of health economics in evaluation of disease control initiatives. It springs from the efforts of policymakers to improve the efficiency of health care investments and health care delivery in all settings, including less-developed countries. Health metrics based on health-adjusted life years have become standard units for comparing the disease burden and treatment benefits of individual health conditions. The Disability-Adjusted Life Year (DALY) and the Quality-Adjusted Life Year (QALY) are the most frequently used in cost-effect analyses in national and global health policy discussions for allocation of health care resources. While sometimes useful, both the DALY and QALY metrics have significant limitations in their ability to capture the full health impact of helminth infections and other 'neglected tropical diseases' (NTDs). An adequate description of disease severity is essential for proper ranking of disease states. Our standard screening diagnostics are often poorly sensitive for 'light' infections, which are nevertheless pathogenic. For many helminth infections, a proper cataloging of the milder, infection-attributable sub-clinical morbidities has not been done, and because of a lack of cohort studies, risk for longitudinal progression to more severe health states is unknown, even by experts. This has led to the false impression that 'the majority of helminth infections are asymptomatic', which is not the case, but which often translates to a public indifference to their impact on community health. Gaps in current knowledge of disease burden are identified, particularly for the recent GBD 2010/2013 assessments, and interim approaches to disease burden assessment will be discussed.
DISCLOSURE Nothing to disclose.

O.3.2.9.003
The impact of soil transmitted helminth on malaria clinical presentation and treatment outcome: a case control study among children in Bagamoyo district, coastal region of Tanzania

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BACKGROUND Epidemiological evidence is mostly lacking and little is known and invested on how the two common parasites

Plasmodium and soil transmitted helminth interact. There are contradictory findings in different studies. This study investigated the impact of soil transmitted helminth (STH) on clinical malaria presentation and treatment outcome.

Method and materials: A matched case control study with a semi longitudinal follow up according to WHO antimalarial surveillance guideline was done among children aged 2 months to 9 years inclusively living in western rural areas of Bagamoyo, coastal region of Tanzania. Cases were children with uncomplicated and severe malaria enrolled from the health facilities while controls were children with asymptomatic *Plasmodium* parasitemia enrolled from the same community.

RESULTS In simple conditional regression analysis there was a tendency for a protective effect of helminth on the development of clinical malaria [OR = 0.6, 95% CI of 0.3 – 1.3] which was more marked for *E. vermicularis* species [OR = 0.2, 95% CI of 0.0 – 0.9]. On the contrary, hookworm species tended to be associated with clinical malaria [OR = 3.0, 95% CI of 0.9 – 9.5]. In multiple conditional regression analysis, the overall protective effect was lower for all helminth infection [OR = 0.8, 95% CI of 0.3 – 1.9] but remained significantly protective for *E. vermicularis* species [OR = 0.1, 95% CI of 0.0 – 1.0] and borderline significant for hookworm species [OR = 3.6, 95% CI of 0.9 – 14.3]. Using ordinal logistic regression, there was a 50% protective effect with overall helminth [OR = 0.5, 95% CI of 0.3 – 0.9]. On the contrary, hookworm species was highly predictive of uncomplicated and severe malaria [OR = 7.8, 95% (CI of 1.8 – 33.9) and 49.7 (95% CI of 1.9 – 1298.9) respectively]. Generally, children infected with STH had higher geometric mean time to first clearance of parasitemia.

CONCLUSION The findings of a protective effect of *E. vermicularis* and an enhancing effect of hookworms may explain the contradictory results found in the literature about impact of helminths on clinical malaria. More insight should be gained on possible mechanisms for these opposite effects. These results should not deter at this stage deworming programs but rather foster implementation of integrated control program for these two common parasites to speed up the momentum of moving from morbidity and transmission control to elimination.

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O.3.2.9.004

Factors driving co-occurrence of *Schistosoma mansoni* and *S. haematobium* at the micro-geographical level

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INTRODUCTION Several studies have shown that the two major human *Schistosoma* species, *S. mansoni* and *S. haematobium*, co-exist in the same individuals at the micro-geographical level. However, the drivers of this co-occurrence are still largely unknown. Here, we studied whether co-exposure and/or host immune responses might explain this phenomenon.

METHODS AND MATERIALS A multidisciplinary study was conducted in two neighboring rural communities in northern Senegal, where *S. mansoni* and *S. haematobium* are co-endemic (n = 857). Kato-Katz and urine filtration were used for microscopic detection of the respective *Schistosoma* species. Households were located using handheld differential global positioning system in the largest community (n = 599), and the Kulldorff's scan statistic was used to detect spatial clusters of infection. *Schistosoma*-specific cytokine responses (IL-10, IL-5, IFN-γ, TNF-α, and IL-2) were assessed in 72 h whole blood culture supernatants (n = 200), and analyzed by the multivariate technique nonmetric multidimensional scaling (nMDS).

RESULTS Classical epidemiological analyses showed that the two parasites were more likely to co-occur in the same individuals ($P < 0.001$). Moreover, co-infected subjects had significantly higher infection levels than their mono-infected counterparts ($P < 0.001$; adjusted for age and gender). In contrast, micro-geographical analyses revealed a very focal spatial distribution with *S. mansoni* clustering in one ($P = 0.002$) and *S. haematobium* infections in another section ($P = 0.023$) of the community. nMDS analysis of the cytokine data indicated that the characteristic modified Th2 response was most pronounced in co-infected subjects.

CONCLUSIONS The divergent geographical distribution of *S. mansoni* and *S. haematobium* in this community could not explain why the two infections cluster in the same individuals. This implies that co-infection is not driven by co-exposure, but by within-host interactions. Cytokine profiles suggested that co-occurrence of the two species may be due to host immunological factors and/or parasite-induced immunomodulation. However, other factors may also play a role. More research is needed to further unravel which direct and/or indirect interactions between *Schistosoma* species in the human host drive the co-occurrence of *S. mansoni* and *S. haematobium*.

DISCLOSURE Nothing to disclose.

O.3.2.9.005

Impact of preventive chemotherapy on burden of disease due to helminthiasis: the lesson from Zanzibar

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INTRODUCTION In Zanzibar neglected tropical diseases (NTDs) like soil-transmitted helminthiasis (STH), schistosomiasis (SCH) and lymphatic filariasis (LF) were serious public health problems only a few years ago. Large scale preventive chemotherapy (PC) with albendazole/mebendazole, praziquantel, ivermectin, for morbidity and transmission control has been pioneered by the Zanzibar Ministry of Health with support from international partners since the early 80s.

METHODS The Public Health Laboratory Ivo de Carneri located in Pemba Island, is a WHO Collaborating Centre to assess, monitor and evaluate national strategies for NTDs surveillance and control. Baseline parasitological, nutritional and clinical surveys were carried out before beginning control activities, and are regularly performed to assess the impact of the intervention.

RESULTS Severe morbidity due to NTDs has been virtually eliminated. Hookworm heavy infections have declined to 1%

and moderate infections reduced from 15 to 4% despite the overall STH prevalence remaining high (32-81%). Treatment with benzimidazoles every six months has prevented blood loss due to hookworm infection of about 180 ml blood/child /year. Visual haematuria has been lowered from 15% to 1.5% and national prevalence of urinary SCH is now <5% with remaining defined hotspots. Urogenital tract pathology assessed by ultrasound has been lowered from 40 to 20% in adult males. SCH is now targeted for elimination through collaboration with several international partners. LF morbidity (hydrocele, lymphoedema and acute adenolymphangitis) is negligible and microfilaraemia has been lowered to <1% after 6 rounds of albendazole + ivermectin treatment. However, a transmission assessment survey carried out in 2012 has shown that LF transmission is still ongoing. As side benefit of PC, scabies has almost disappeared and strongyloidiasis is at low level (7%) compared to baseline data (41%).
CONCLUSIONS Despite the partial efficacy of drugs and the high transmission, the PC intervention in Zanzibar has reduced the burden of disease as well as the related cost for patient management through the health system and income loss, at an average cost of 0.3 US$/person/year. Research is ongoing to explore drug combinations to be used, should drug resistance occur. Other interventions like WASH, and vector control for SCH and LF, should be integrated to eliminate NTDs, but PC alone has improved the health and development of thousands of poor people.
DISCLOSURE Nothing to disclose.

3.2.10. Ebola - vaccination

INV.3.2.10.002

Safety and immunogenicity of the Chimpanzee-Adenovirus vectored Ebola vaccine: the Lausanne phase I/IIa clinical trial

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INTRODUCTION The largest recorded Ebola outbreak is ongoing, and there have been more than 27 000 reported cases and 11'000 deaths in 3 countries in West Africa. The World Health Organization (WHO) has declared the current outbreak as an international health emergency and led to accelerated efforts to test vaccine candidates in Phase I to III trials. Current efforts to develop a vaccine are focused on the single viral glycoprotein (GP) encoded by the virus. Candidates in which viral GP is expressed in either chimpanzee adenovirus or vesicular stomatitis virus (VSV) vector have shown promise in non-human primate models of Ebolavirus disease and in initial clinical trials. Following a request by WHO, a Phase I/IIa clinical trial of the monovalent Ebola (Zaire) vaccine ChAd3-EBO-Z was conducted in healthy adults in Lausanne, Switzerland.

Methods and materials: A randomized, double-blind, placebo-controlled, trial to asses safety and immunogenicity of ChAd3-EBO-Z vaccine was conducted in Lausanne from the 24th of October 2014 to the 22nd of June 2015. 120 healthy adult volunteers were assigned to three arms, 2.5×10^{10} vp dose, 5×10^{10} vp dose, or placebo (ratio 2:2:1). Volunteers who were potentially to be deployed in epidemic areas were assigned to vaccine doses only. Vaccinations were administered from October 31st to December 12th. Safety and immunogenicity were assessed up to 6 months post vaccination.
RESULTS No vaccine-related SAE was observed in any of the 120 volunteers. In the 102 non-deployed volunteers, local AEs were observed in 75% of 5×10^{10}, 78.6% of 2.5×10^{10} and 25% of volunteers receiving placebo. Headache was the most frequent systemic AE [65%, 69% and 30% respectively] followed by fatigue/malaise [65%, 64%, 30%] and musculo-articular pain [57%, 43%, 25%]. Fever occurred during the 24 h post injection in 30% of vaccinees [32%, 29%, 5%]. Geometric mean concentrations (GMC) of IgG antibodies against Ebola glycoprotein peaked on day 28 with respective response rates of 96%, 96% and 5%. The majority of vaccines developed GP-specific CD4+ or CD8+ responses.
CONCLUSIONS ChAd3-EBO-Z appears to be safe and well tolerated, although mild to moderate systemic AEs were frequent. A single dose was immunogenic in almost all vaccinees. There were no significant differences between 5×10^{10} vp dose and 2.5×10^{10} vp dose in terms of safety and immunogenicity outcomes. Antibody responses were at the lower range of responses seen in protected macaques.
DISCLOSURE FR, IDR, WRB are employees of GSK. The others authors have reported no conflict of interest.

O.3.2.10.003.LB

Malaria prevalence decreased following mass drug administration of malaria chemoprevention during the Ebola outbreak, Monrovia, Liberia, 2014

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INTRODUCTION In 2014, Médecins Sans Frontières implemented a mass drug administration (MDA) of Artesunate/Amodiaquine (ASAQ) malaria chemoprevention to reduce admissions for fever to Ebola-treatment-centres (ETC) and malaria-associated morbidity in Monrovia, Liberia. To inform future MDAs targeting the reduction of malaria, we estimated the number of malaria cases prevented.
METHODS We systematically included every 200th household in the distribution area (target population 551 971) to monitor two rounds of ASAQ-MDA, one month apart. We collected information on age, self-reported adherence and self-reported malaria in the previous month for all household members (HM) after both rounds. We calculated prevalence differences (PD) and 95% confidence intervals (95% CIs) of malaria prevalence before the first (r1) and the second round (r2), stratified by

adherence and age-group. We extrapolated the differences to the target population.
RESULTS Of 1229 HM, 4.2% reported malaria prior to r1, and 1.5% prior to r2 (PD = 2.7%; 95% CI 1.4–4.0%; $P < 0.0001$), suggesting that 14,821 (95% CI 4801–24 840) malaria cases were averted in the target population. Reported malaria among children <=5 years of age completing a full course of ASAQ in r1, was 9.7% before r1 and 1.1% after r1 (PD = 8.6%; 95% CI 2.2–15.0%; $P = 0.009$); among children not completing the course 3.8% and 1.3%, respectively (PD = 2.5%; 95% CI −2.3 to 7.3%; $P = 0.3112$). Among HM >5 years old completing treatment, 5.8% reported malaria before r1 and 1.6% after r1 (PD = 4.2%; 95% CI 1.9–6.5%; $P = 0.0004$); among those not completing treatment 2.0% and 1.8%, respectively (PD = 0.2%; 96% CI −1.4 to 1.9; $P = 0.8168$).
CONCLUSIONS Self-reported malaria decreased significantly after the first round of ASAQ-MDA among individuals reporting to complete the full course. Further research into the extent to which MDAs are independently associated with the reduction in malaria prevalence and ETC admissions for fever is needed.
DISCLOSURE Nothing to disclose.

3.2.11. Evaluating therapeutic interventions against Ebola: challenges and lessons learned

INV.3.2.11.002
The Ebola field reality for conducting clinical trials

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When MSF decided to host clinical phase II trials with experimental interventions in the midst of an uncontrolled Ebola outbreak, it posed several types of operational challenges.

Ensuring trial engagement of geographically spread communities that have little Ebola knowledge and are mistrusting 'white people's' actions was not always feasible considering the short time frame. Additionally community leaders and Ebola survivors advised not to be too explicit with the communities.

In the Ebola treatment centers, turnaround time to receive results of diagnostic Poly Chain Reaction Assay (PCR) of up to 12 h caused delays in initiation of experimental treatments that would likely be more effective when viral load is still low. As overall case fatality rates remained around 50%, introducing concurrent controls and denying one group of patients potentially life-saving treatments was perceived as ethically unacceptable. Reassuring patients, giving clear information and obtaining informed consent by staff in full personal protective equipment (PPE) was challenging.

Admission rates are variable and so is the clinical status of patients, making it difficult to ensure continuous standard of care of equal quality. The need for (PPE) reduces the time spend at patient's bed side. Any additional intervention or monitoring has impact on the clinical staff's work load and security. Long treatment duration implies longer length of stay. Intravenous infusion or transfusion therapy and more frequent blood sampling increase risks for staff and patients. Pharmacovigilance is time consuming and it is difficult to make the distinction between adverse events and Ebola virus disease symptoms. The introduction of biochemistry laboratory tests lead to unexpected difficulties both technically at laboratory level and in the interpretation of results and management of alterations. The rotation of supervising staff demanded coordination, continuous training and briefing on roles responsibilities. As the trials were single-arm studies and the endpoint survival in a context of high mortality, blinding of staff and communities was not possible. Patient's medical confidentiality is difficult to respect and wild interpretation of trial results was difficult to avoid.

Trial preparation and implementation require continuous evaluation of field reality to confront protocol and standard procedures with feasibility and engage in adaptations both to the trial protocol and the field procedures.
DISCLOSURE Nothing to disclose.

INV.3.2.11.004
Emergency evaluation of convalescent plasma for Ebola virus disease in Guinea

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BACKGROUND Evaluation of convalescent plasma (CP) for the treatment of Ebola Virus Disease (EVD) has been prioritized by the WHO in the current epidemic.
METHODS The Ebola_Tx trial is designed to assess the feasibility, safety and efficacy of convalescent plasma (CP) against EVD in Conakry, Guinea. Pathogen-reduced CP is administered as two units (200–250 ml each) given consecutively on the same day, from two different donors. Survival 14 days after intervention is the primary outcome measure. The survival of patients treated with CP + supportive care will be compared to that of patients receiving supportive care alone, in an open-label, non-randomised comparative study. A 20% lower case fatality rate in patients treated with CP will be considered proof of clinical efficacy. All consecutive eligible and consenting patients of any age (including pregnant women) with confirmed EVD will be enrolled; exclusion criteria are limited to contra-indications for CP or patients very close to death. Available ABO compatible plasma is given, within 48 h after diagnosis, and patients with no compatible plasma available will be enrolled as concurrent controls. The control group will be complemented with historical controls if needed. A minimum of 130 patients will be treated with CP.

Secondary outcomes include
1 30 day all-cause mortality.
2 Transfusion-related serious adverse reactions.
3 Change in viral load and association with titres of neutralising antibodies in the donor plasma.
4 Safety risks in health workers administering CP.
5 Risk factors for mortality.

RESULTS The first plasma collection started on February 9, 2015 and the first CP administration was done February 19, 2015. As of April 7, a total of 94 donors have presented for plasma donation, of which 81 have donated at least once. Qualified plasma (no transfusion transmissible infections detected) was obtained for 69. A total of 83 patients have been enrolled, of which 81 received CP. Of these, 9 additionally received favipiravir via another trial, leaving 72 patients for inclusion in primary analysis. The main analysis will be done after 130 CP-treated patients have reached day 14 (planned early June).
CONCLUSIONS This is the largest trial ever conducted on convalescent blood products against EVD. If found to be effective, this intervention can then be scaled-up, as the trial will provide the information required to mobilize local partners.
DISCLOSURE Nothing to disclose.

INV.3.2.11.006
Favipiravir in patients with Ebola virus disease

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BACKGROUND The JIKI trial (Inserm C1463) assesses the benefits of high-dose favipiravir in reducing mortality and decreasing Ebola virus (EBOV) viral load in patients with Ebola virus disease (EVD).
METHODS JIKI is a phase II trial conducted in 4 Ebola care units run by MSF and ALIMA, Croix Rouge Française and French Army Health Service in Guinea. Inclusion criteria are: positive EBOV RT-PCR (Altona, crossing cycle threshold [CT] for positivity≤40), age ≥1 year, ability to take oral drugs, and informed consent. Participants are prescribed oral favipiravir (adults: 6000 mg Day [D]0 [H0 2400 mg, H8 2400 mg, H16 1200 mg], and then 1200 mg bid from D1 to 9). The primary endpoint is mortality. Comparator for mortality among participants was the 3-month pre-trial figure in the same centers, as recorded in the MSF/EMLab database.
RESULTS From December 17, 2014 through January 20, 2015, 80 patients received favipiravir in addition to basic standard of care, including 69 adults and adolescents ≥14 years (women 64%, mean age 38 years, median duration of illness 5 days). The baseline CT (BCT) was<20 in 42% and ≥20 in 58%; the baseline creatinine was ≥110 μM/l in 60% (BCT< 20: 79%; BCT ≥20: 36%), including ≥300/μM/L in 27% (BCT< 20: 43%; BCT ≥20: 10%); baseline ASAT level was ≥1000 IU in 38% (BCT< 20: 77%; BCT ≥20: 17%); and baseline Creatine Kinase level ≥4000 IU in 18% (BCT< 20: 24%; BCT ≥20: 8%). Among patients with baseline CT above 20, 51% reached undetectability within 4 days, and the mean gain in CT at day 4 was +12 Overall, 48% of participants died (BCT< 20: 85%; BCT ≥20: 15%). The pre-trial mortality was 58% overall, 85% in patients with BCT< 20 and 30% in patients with BCT ≥20. Mortality was 100% and 7% in patients with impaired renal function and BCT <20 or ≥20, respectively. The drug was easily administered and well tolerated.
CONCLUSIONS In this non comparative proof of concept trial, most patients with CT<20 had renal function impairment and died, with no indication that favipiravir monotherapy could improve survival. Early results in patients with CT ≥20 suggest a lower mortality rate compared to pre-trial figures in the same settings. These intermediate data encourage continued testing of favipiravir with particular attention to identifying patients earlier in disease course, and to explore other therapeutic options, including combinations, in patients who present at advanced stages.
DISCLOSURE Nothing to declare.

3.2.12. Mycetoma: addressing the unbearable treatment gap

INV.3.2.12.001
Global overview of mycetoma and treatment gaps

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Mycetoma is a common but neglected health problem, endemic in many tropical and subtropical regions and characterized by devastating deformities, disability and high morbidity. It affects the poorest populations in the most remote areas, typically adult male labourers between 20 and 40 years old who work outdoors, causing serious negative socio-economic impact on patients, families, communities and health authorities. Mycetoma has been officially recognised as a neglected condition by the WHO since 2013. However it is not in their priority list of neglected diseases as yet resulting in limited funding and focus on the disease. As a consequence of this lack of attention, there are massive knowledge gaps in various aspects of the disease. Chronic infection of subcutaneous tissues affects mainly, although not exclusively, the foot, and it is thought that infection may be due to thorn pricks - people are often barefoot in endemic countries - but its true incidence, prevalence, route of infection, susceptibility and resistance are not well characterized. There are no control or prevention programmes, and worldwide measurements of the extent of mycetoma are unavailable and in need of development. The research and advocacy community for mycetoma is limited, there are just a handful of organisations involved in the treatment of the disease, and even fewer are trying to find a cure. Despite advocacy and scientific work from the Mycetoma Research Centre (MRC), the disease has not received any attention from funders and pharma for past decade. DNDi is lending its support in advocacy as well as R&D, with the launch of an RCT for a potential therapy E1224. There is a range of R&D needs and opportunities. In the short-term, there needs to be clinical proof of concept for E1224, existing libraries need to be screened for promising compounds and an ecological study needs to be conducted. In the medium term, the clinical proof of concept for isavuconazole and voriconazole need to be demonstrated and the global epidemiology studied. In the long term, R&D efforts need to focus on the search for a new chemical entity, a clinical combination option, a proof of concept test for biomarkers and a global collection of strains for typing and resistance.
DISCLOSURE Nothing to disclose.

INV.3.2.12.002
Clinical aspects, diagnosis, and treatment of mycetoma

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Mycetoma is a debilitating disease which progresses relatively silently, causing little pain, but resulting in devastating deformities, disability and high morbidity. The lack of pain and health education can delay people seeking treatment, however once the disease has reached the later stages treatment options are much more limited. Reversal of symptoms is rare and, if left untreated, a chronic situation gradually develops often resulting in the need for multiple amputations with the concomitant risk of potentially fatal complications.

Mycetoma is caused by bacteria (actinomycetoma) and fungi (eumycetoma). Actinomycetoma is prevalent in Middle and South America and responds reasonably well to treatment with antibiotics, while eumycetoma is mainly endemic in Africa. Most commonly, the affected parts become very swollen and disfigured over time.

There has been limited research carried out on mycetoma, and current treatments are neither safe, nor affordable, with a 25–35% efficacy rate. For eumycetoma, the treatment requires extensive and destructive surgery and prolonged antifungal treatment. The currently available antifungals, ketoconazole and itraconazole, are proving to be ineffective and have serious side effects; what is more, the FDA and EMA have restricted the use

of ketoconazole due to its toxicity. Treatment with itraconazole lasts twelve months, at a cost of approximately 30 USD per month, making it too expensive for patients and health authorities in endemic areas, resulting in high drop-out rate from treatment. Treatment outcomes are generally disappointing, characterized by low cure rate and high amputation rates. More research is needed on how this disease occurs and on new treatments that are safe, effective and affordable.
DISCLOSURE Nothing to disclose.

INV.3.2.12.003
New concepts in diagnosis for eumycetoma

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Eumycetoma can be caused by a large variety of different fungal species. Accurate identification of these causative agents is a priority for treatment. Currently, histology and culture are the only identification tools in use in endemic settings, but these techniques are not able to identify the causative agent to the species level and are time-consuming. So-far only molecular identification tools were able to identify the causative agent to the species level, but these techniques were not well suited to be used in the endemic setting since expensive equipment was needed and DNA isolation was only possible from in vitro grown cultures not directly from eumycetoma grains. Three different DNA isolation techniques were tested for their suitability to isolate DNA directly from eumycetoma biopsies. It appeared that only bead-beating the grains with metal beads followed by the Qiagen DNAeasy Plant mini kit was able to isolate enough DNA directly from grains for downstream DNA amplification techniques. To identify the eumycetoma causative agents to the species level, three different isothermal DNA amplification techniques were developed: Rolling Circle Amplification (RCA), loop-mediated isothermal amplification (LAMP) and Recombinase polymerase amplification (RPA). RCA assays were developed to identify Falciformispora senegalensis, F. tompkinsii, Madurella fahalii, M. mycetomatis, M. pseudomycetomatis, M. tropicana, Medicopsis romeroi, and Trematosphaeria grisea and 62 isolates were successfully identified with 100% specificity and no cross reactivity or false results. LAMP and RPA were developed for M. mycetomatis only and identified all M. mycetomatis isolates with 100% specificity and no cross reactivity. For LAMP unspecific amplification was noted when high concentrations of DNA were used. When the three techniques were compare for their performance in the identification of *M. mycetomatis* identification, it appeared that RPA and LAMP had shortest turnaround times combined with sufficient sensitivity and specificity. RPA appeared the easiest method to perform, with the risk of contamination being lower than that of LAMP.
DISCLOSURE Nothing to disclose.

INV.3.2.12.004
Potential R&D pathways for new treatment of Eumycetoma

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Eumycetoma is a difficult and challenging disease to treat. To date the available therapies are limited to the antifungals, ketoconazole and itraconazole, which are expensive and are proving to be ineffective with serious side effects. This results in amputation, often repeated, and sometimes death. There is an urgent need for new antifungal agents that are safe, effective and appropriate for use in rural settings. Azoles are currently the only drug class found to be effective against the disease. Recent evidence has shown that fosravuconazole (E1224), a potent orally available triazole currently under development for Chagas disease, could be an effective and affordable option for the treatment of fungal mycetoma. Fosravuconazole is a prodrug that is rapidly converted to ravuconazole, shown to have potent in vitro activity against Madurella mycetomatis, one of the causative agents of eumycetoma. It has favourable pharmacokinetic properties and low toxicity. DNDi plans to carry out a randomized controlled trial to study the efficacy of fosravuconazole compared to the current treatment, itraconazole in moderate mycetoma lesions. This will be a double-blinded, randomised, monocentre superiority study with an interim analysis at three months, with a primary objective of seeing superiority of fosravuconazole over itraconazole at 12 months follow-up. The study will be conducted with the WHO Collaborating Centre on Mycetoma in Khartoum.
DISCLOSURE Nothing to disclose.

3.2.14. Progress and challenges for the elimination of gambiense sleeping sickness

INV.3.2.14.002
The role of National Control Programmes in HAT elimination and integration into primary healthcare

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Human African Trypanosomiasis (HAT), also known as sleeping sickness, is a vector-borne parasitic disease, transmitted to humans by the bite of an infected tsetse fly. HAT is found in sub-Saharan Africa within the geographical limits of distribution of the vector. Two sub-species of Trypanosoma cause the disease in humans:
1 *Trypanosoma brucei gambiense*, which causes gambiense HAT, endemic in West and Central Africa (chronic form, at least 95% of all cases).
2 *Trypanosoma brucei rhodesiense*, which causes rhodesiense HAT, present in East and Southern Africa (acute form, less than 5% of current cases).

WHO has targeted elimination of HAT as a public health problem by 2020. Democratic Republic of the Congo (DRC) has reported at least 80 % of all HAT cases for the last 5 years, but there has been a large drop reported since the beginning of the millennium, from 16 975 in 2000 to 3026 in 2014. When active screening stops the number of cases tends to increase, however between 2000 and 2014 the number of mobile teams responsible for active screening was reduced from 43 to 30 in the DRC. The cost effectiveness of active screening as currently implemented

decreases significantly as the number of cases decreases; highlighting the need to better integrate activities to fight HAT into the primary healthcare (PHC) system.

A sustainable surveillance system needs to be implemented in order to assure, evaluate, maintain and monitor the elimination of the disease. It will be difficult to justify active screening as the number of cases reaches zero. Passive screening by PHC facilities will have to play an important role in capturing any risk of reemergence of the disease. At this point, when a suspected case is confirmed, the entire population in the village concerned will be actively screened. To better integrate activities, there is a need for a well-functioning PHC system that has trained health workers, is technically supported and properly equipped, and has adequate supplies of lab and medical consumables, reagents and drugs. Integrating the activities of the HAT national control programme into PHC is important for guaranteeing surveillance where the number of cases is very low and active screening is no longer justified, and for helping to increase the coverage of at-risk populations in screening activities. Here we analyse the critical role of National control programmes for a better and more sustainable integration of HAT activities into the PHC system.

DISCLOSURE Nothing to disclose.

INV.3.2.14.004

A new dawn for sleeping sickness - the development of oral treatments

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The number of cases of Human African Trypanosomiasis (HAT) has decreased significantly over the last few years due to improved diagnosis, vector and case control. Nifurtimox-Eflornithine Combination Therapy (NECT) is currently first line treatment for gambiense HAT in all endemic countries, and a vast improvement over previous treatments. However, NECT is only effective against stage 2 of the disease, and requires hospitalisation during administration of the required 14 injections of eflornithine over 7 days and 10 days of oral treatment with nifurtimox. There is a need for treatments that can be easily administered at village level which are effective against both stages of the disease, in order for WHO elimination targets to be met.

The first two oral treatments for HAT are currently undergoing clinical development. Fexinidazole, the result of compound mining efforts, is undergoing evaluation in a pivotal Phase II/III study to assess its safety and efficacy compared to NECT when treating stage 2 disease. Complementary studies are underway in adult patients with early second stage/first stage disease, and in children aged 6–14 years. An oxaborole compound, SCYX-7158 (also known AN5568), discovered by Anacor Pharmaceuticals, is the first new chemical entity to arise out of DNDi's lead optimization programme. Pre-clinical studies showed preliminary evidence that SCYX-7158 was safe and efficacious to treat stage 2 of the disease, as it is able to cross the blood-brain barrier. The longer than expected half-life in healthy human volunteers necessitated additional animal studies, but results supported continued evaluation of single ascending doses. Clinical safety profiling showed there were no identifiable issues of concern with doses up to and exceeding the therapeutic dose. Follow up of these subjects is complete and results will be reported in the meeting. With its long half-life, SCYX-7158 has the potential to be a single-dose treatment for HAT.

DISCLOSURE Nothing to disclose.

3.2.15. Helminth infections – diagnosis

O.3.2.15.001

Is PCR the next gold standard for the diagnosis of *Schistosoma* in stool? A comparison with microscopy in Senegal and Kenya

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INTRODUCTION The current reference test for the detection of *S. mansoni* in endemic areas is stool microscopy based on one or more Kato-Katz stool smears. However, stool microscopy has several shortcomings that greatly affect the efficacy of current schistosomiasis control programs. A highly specific multiplex real-time PCR targeting the *Schistosoma* internal transcriber-spacer-2 sequence (ITS2) was developed by our group a few years ago, but so far this PCR has been applied mostly on urine samples. Here, we performed more in-depth evaluation of the ITS2 PCR as an alternative method to standard microscopy for the detection and quantification of *Schistosoma* spp. in stool samples.

METHODS AND MATERIALS Microscopy and PCR were performed in a Senegalese community (n = 197) in an area with high *S. mansoni* transmission and co-occurrence of *S. haematobium*, and in Kenyan schoolchildren (n = 760) from an area with comparatively low *S. mansoni* transmission.

RESULTS Despite the differences in *Schistosoma* endemicity the PCR performed very similarly in both areas; 13–15% more infections were detected by PCR when comparing to microscopy of a single stool sample. Even when 2–3 stool samples were used for microscopy, PCR on one stool sample detected more infections, especially in people with light-intensity infections and in children from low-risk schools. The low prevalence of soil-transmitted helminthiasis in both populations was confirmed by an additional multiplex PCR.

CONCLUSIONS The ITS2-based PCR was more sensitive than standard microscopy in detecting *Schistosoma* spp. This would be particularly useful for *S. mansoni* detection in low transmission areas, and post-control settings, and as such improve schistosomiasis control programs, epidemiological research, and quality control of microscopy. Moreover, it can be complemented with other (multiplex real-time) PCRs to detect a wider range of helminths and thus enhance effectiveness of current integrated control and elimination strategies for neglected tropical diseases.

DISCLOSURE Nothing to disclose.

O.3.2.15.002

Sensitivity of Strongyloides IgG antibody detection by ELISA among immunocompromised patients

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INTRODUCTION Strongyloidiasis can be fatal in immunocompromised patients. It is essential to detect and treat carriers before the onset of hyperinfection. Diagnosis of infection is hampered by the suboptimal sensitivity of fecal-based tests. Serological methods are more sensitive. However, studies evaluating the sensitivity of serological tests are usually performed among immunocompetent populations. The aim of this study is to evaluate the sensitivity of an ELISA among immunocompromised patients.
METHODS AND MATERIALS In a prospective study conducted in Bolivia among patients at high risk of hyperinfection (patients with cancer, HIV, rheumatic or hematologic diseases), 88 patients with parasitologically proven *S. stercoralis* infection were selected for this study. Strongyloides IgG antibody titers were measured by enzyme-linked immunosorbent assay (Bordier Affinity Products; reported sensitivity: 88–90%).
RESULTS Out of 88 patients with positive stool exams for strongyloidiasis, 41 were HIV positive, eight had a rheumatologic disease, 28 had cancer and eleven suffered from a hematological disease. Among these patients, 20/88 (22.7%) had a negative serology (sensitivity 77.3%).

Among HIV positive patients with a CD4 count less than 300, 64.5% (20/31) had a positive serology. Of all those with a CD4 count over 300 (HIV positive or negative), 84.2% (48/57) had a positive serology. This difference is statistically significant ($P = 0.035$). Only one HIV positive patient with a CD4 count over 300 had a negative serological result (1/10).
CONCLUSIONS The sensitivity of serology to detect *Strongyloides* infection was only 77.3% among a population of patients with various degrees of immunosuppression, who are at increased risk of complications. The sensitivity is even lower among HIV positive patients with low CD4 counts. Empirical treatment of strongyloidiasis in immunocompromised patients should be considered in areas of high endemicity.
DISCLOSURE Nothing to disclose.

O.3.2.15.003

Innovative diagnostic tools to control cystic echinococcosis

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INTRODUCTION Cystic echinococcosis (CE) is a widespread parasitic zoonosis, caused by the larval stages (hydatid cysts) of a tapeworm of the *Taeniidae* family, namely *Echinococcus granulosus*. The life cycle of *E. granulosus* includes canids as definitive hosts and a wide range of domestic and wild mammals and humans as intermediate hosts. Disability-adjusted life years (DALYs) resulting from human CE have been calculated as high as 1 million, similar to dengue, Chagas disease and trypanosomiasis. The aim of this study was to develop and standardize innovative diagnostic tools for the control of *E. granulosus* in endemic areas such as southern Italy.

Methods and materials: Fifty faecal samples collected from farm dogs infected by *E. granulosus* were used for the study. Each sample was examined by five different protocols using FLOTAC and the following flotation solutions: sodium chloride (specific gravity, s.g. = 1200), zinc sulphate (s.g. = 1350), zinc chloride (s.g. = 1450), Breza solution 1 (s.g. = 1300) and Breza solution 2 (s.g. = 1400). Moreover, four different protocols of DNA extraction were compared and standardized for the diagnosis of *E. granulosus*: (i) QIAamp Tissue Kit (Qiagen) from eggs, (ii) QIAamp Stool (Qiagen) from eggs, (iii) QIAamp Stool (Qiagen) from faeces, (iv) Wizard Magnetic Purification System for Food (Promega) from faeces. DNA extraction was followed by PCR amplification and sequencing of mitochondrial cytochrome C oxidase subunit 1.
RESULTS The FLOTAC technique with zinc sulphate solution (s.g.1350) resulted the best copromicroscopic method for faecal egg counts of *Taeniidae* eggs. Noteworthy, the FLOTAC device was also very useful recovering *Taeniidae* eggs to be used for DNA extraction. Indeed, the best kit for DNA extraction resulted the QIAamp Stool that provided the highest number of positive samples, i.e. 47/50 (94.0%; 95% Confidence Interval = 82.5–98.4%). The three negative samples had very low faecal egg counts (2 eggs per gram of faeces).
CONCLUSION The best method for the diagnosis of *E. granulosus* in dogs resulted the combination of FLOTAC (with zinc sulphate) and QIAamp Stool (Qiagen) using the floated eggs.

These techniques could be very useful for the control of *E. granulosus* in animals and humans in endemic areas as the Campania region of southern Italy.
DISCLOSURE Nothing to disclose.

O.3.2.15.004

An ultra-sensitive urine-based assay targeting the circulating anodic antigen (CAA) for diagnosis of urogenital and intestinal schistosomiasis in low-endemic areas

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The recent renewed interest in mapping, intensified control and elimination of schistosomiasis has put the need for highly accurate diagnostic assays high on the agenda. The well-studied schistosome antigen detection assays CCA- and CAA-ELISA have been converted into a Point-of-Care rapid test (POC-CCA) and an ultra-sensitive UCP lateral flow based strip assay (UCP-CAA), respectively. The simple field applicable POC-CCA test may replace the Kato-Katz testing for prevalence mapping of community-level *S. mansoni* infections using a single drop of urine and evaluate quickly (within days) the efficacy of treatment. However, this test shows variable sensitivity in the diagnosis of *S. haematobium*.

The recently developed UCP-CAA assay detects antigen in serum or urine of all schistosome species at sub-pg levels, a sensitivity allowing detection of single worm infections. The assay has been adapted to a robust, dry-reagent based test, and is currently used in several low-resource settings in Africa. In combination with optimized sampling schedules involving pooled urines this would allow rapid identification of foci of low prevalence/intensity *S. haematobium* and *S. mansoni* infections.

Recent studies using the 2 ml urine dry reagent UCP-CAA format performed in low prevalence (<2%), *S. haematobium* settings (near elimination) show an over 10-fold increase in the prevalence of active schistosome infections. Similar results have been shown for *S. japonicum* settings in China and *S. mansoni* settings in Brasil and Africa.

The UCP-CAA strip assay therefore is a valuable highly sensitive diagnostic tool, applicable for screening and case finding in very low prevalence areas, including pre-elimination settings.
DISCLOSURE Nothing to disclose.

O.3.2.15.005

Comparison of different diagnostic procedures, including mini-FLOTAC and multiplex real-time PCR, for the diagnosis of soil transmitted helminths and protozoa in stool samples from Ende, Indonesia

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INTRODUCTION The newly developed mini-FLOTAC (MF) is a low cost and easy to perform quantitative coproscopic method based on the flotation capacity of parasitic eggs and cysts. The aim of this study is to evaluate the diagnostic performance of MF as an epidemiological tool for population-based screening by examining formalin fixed stool samples and comparing the outcome with other coproscopic procedures, using PCR as the reference standard.
METHODS Stool samples (n = 64) were collected at Flores Island, Indonesia, in a community known for its high parasite prevalence. Microscopic examination of Kato-smears (KS) was done instantly, while aliquots either mixed with formalin or ethanol were transported to a centralized laboratory for further examination by microscopy and PCR, respectively. Besides MF, microscopic analysis included direct smear (DS), and formalin-ether concentration (FEC). Multiplex real-time PCRs for the detection of six helminth species and four protozoa were performed on spin column isolated DNA, preceded by removal of the ethanol and a bead-beating procedure.
RESULTS Based on PCR findings the most prevalent infection was hookworm (64%), followed by *Ascaris lumbricoides* (63%) and *Trichuris trichiura* (58%). Of all microscopy techniques, the highest number of helminth positive cases were seen with KS, namely 48%, 63% and 47% for these three species respectively. MF performed relatively poorly, in particular for the detection of hookworm eggs (6%), while 48% and 39% of the samples were positive at the MF for the two other helminth species. No positive *Strongyloides stercoralis*, *Schistosoma*, *Entamoeba histolytica* or *Cryptosporidium* cases were detected with any of the used diagnostic techniques, with the exception of a single *Cryptosporidium* PCR positive sample. DNA of *Dientamoeba fragilis* and of *Giardia lamblia* could be detected in 48.4% and 12.5% of the samples, respectively. The mini-FLOTAC device was found to be impractical for the detection of protozoa.
CONCLUSION Although the mini-FLOTAC may still be an adequate and easy to use device for the detection of helminth eggs in the field, we found the detection rates to be surprisingly low when used retrospectively on formalin fixed samples, in particular for the detection of hookworm. Our findings confirm real-time PCR, despite requiring advanced laboratory technology, to be a powerful technique for high-throughput detection and quantification of multiple intestinal parasites.
DISCLOSURE Nothing to disclose.

O.3.2.15.006

Nanobody®-based sandwich enzyme-linked immunosorbent assay for the detection of *Toxocara canis* excretory-secretory proteins

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INTRODUCTION Human Toxocariasis (HT) is a neglected disease resulting from tissue invasion of L_2 larva from *Toxocara canis*. The only laboratory diagnostic tool currently available is a serological test detecting IgG against the excretory secretory proteins of the parasite (TES). This method is unable to distinguish between current and past infections. We developed a sandwich enzyme-linked immunosorbent assay (ELISA) taking advantage of the inherent features of specific single variable domain fragments of camelids (nanobodies®).
METHODS AND MATERIALS An alpaca was immunized with 125 μg of TES 5 times in intervals of 7 days. One week after the last immunization, peripheral blood was extracted and nanobody® sequences were amplified through reverse-transcription polymerase chain reaction (RT-PCR) from blood lymphocytes. Selection of binders was performed by biopanning based on phage display. A sandwich ELISA was set up with a capturing nanobody® cloned in pHEN6c vector and a detection nanobody® in vector pBAD17 containing an AviTag™ for *in vivo* biotinylation. Cross-reactivity was tested with excretory antigens of *Ascaris lumbricoides* and *A. suum*. Immunocapturing with paramagnetic beads was used to isolate the specific fraction of TES recognized in the sandwich ELISA.
RESULTS Nanobody® sequences were present in $3x10^8$ transformants. 84% of them contained a plasmid encoding 20 different nanobody sequences. The combination 1TCE39 and 1TCE52 had the best Optical Density (OD) signal in sandwich ELISA with no cross-reactivity with *A. lumbricoides* or *A. suum*. The detection limit using ELISA sandwich format in negative samples spiked with TES was 40 ng/ml. Immunocapturing demonstrated that the epitopes recognised by the sandwich ELISA are located in the 120 kDa fraction of TES.
CONCLUSIONS Tests to diagnose active HT are currently not available, hampering the estimation of the real prevalence of the disease and its control. Nanobody®-based sandwich ELISA provides an innovative approach to detect TES of *T. canis* in clinical samples.
DISCLOSURE This project is funded by the Research Foundation Flanders (FWO).

3.2.16. R&D for Trypanosomiasis, African and South-American

O.3.2.16.001

A new diagnostic algorithm for *Trypanosoma brucei gambiense* human African trypanosomiasis (HAT) case detection in a low prevalence setting in North Western Uganda

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HAT is caused by 2 trypanosome sub-species; the chronic *Trypanosoma brucei gambiense* and acute *T. b. rhodesiense*. Both

forms exist in Uganda, the former occurring in 7 districts in the North West, putting more than 2 million people at risk. The global incidence of HAT is declining; in Uganda only 20 *T. b. gambiense* cases were reported in 2012, down from about 200 recorded in 2008. Detection of *gambiense* HAT cases and relies on screening large numbers of at-risk individuals, which is usually done through active screening of the entire population. However, costs rise greatly as incidence declines. Here we determine the feasibility of eliminating *T. b. gambiense* HAT through passive screening, using a new diagnostic strategy that combines the use of Rapid Diagnostic Tests (RDTs), fluorescence microscopy and Loop mediated isothermal Amplification (LAMP) to identify cases in a region of low prevalence. We characterized health care facilities in the 7 endemic districts and generated a map that was used to rationalize the distribution of diagnostic capacity. Consequently, 200 RDT sites, 9 microscopy and 3 LAMP centres were established across the districts. The entry point to this algorithm is presentation with symptoms suggestive of HAT. A referral system where RDT positive individuals are sent to the nearest microscopy centre (median distance: 11.4 km) for parasitology tests was established. RDT positive suspects in which trypanosomes cannot be demonstrated are sampled and tested at the LAMP centres; positive results from LAMP increase suspicion and warrant scheduled parasitological re-checks until their status is confirmed. Data transfer from all sites by mobile phone and an online application are used to monitor the use of tests in all the participating facilities. Over 400 clinicians and technicians were trained to recognize symptoms and diagnose HAT. Out of 11 157 symptomatic individuals screened by RDT within 20 months, 320 were positive and 10 were eventually confirmed as cases by microscopy. Four of the confirmed cases were detected after re-examination prompted by positive LAMP results. Our results to date indicate that this strategy would be appropriate to accelerate HAT elimination in low-prevalence settings by upgrading existing infrastructure, while limiting the costs associated with large scale mobile screening of entire populations. This model could be deployed in other areas of Africa with a low incidence of *gambiense* HAT.

DISCLOSURE Nothing to disclose.

O.3.2.16.002

Development of a rapid diagnostic test for active case detection in sleeping sickness control: *recHAT* Sero-Strip

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BACKGROUND With the elimination of human African trypanosomiasis (HAT) in focus for 2020, highly accurate diagnostics are needed. In the past, large scale use of the card agglutination test for trypanosomiasis (CATT) followed by proper therapy has allowed to drastically reduce the prevalence of *Trypanosoma brucei gambiense* HAT. However, the need for a cold chain and electricity is a limiting factor in deploying CATT in very remote areas. An immunochromatographic test that fully complies with the ASSURED (affordable, sensitive, specific, user-friendly, rapid, equipment-free and deliverable) criteria and that is based on recombinant antigens may overcome the shortcomings of CATT.

METHODS *T. b. gambiense* antigens were expressed in *E. coli* and incorporated in an immunochromatographic test format: the *recHAT* Sero-Strip.

Tests kit (with 25 strips in tubes) contains all necessary materials to perform the test on finger-prick blood. The recHAT Sero-Strip was tested on sera from 134 *T. b. gambiense* sleeping sickness patients and 359 endemic controls (the results were compared with parasitology as gold standard method). A real-time stability study was performed at 30, 37, 40 and 45°C. Another real-time stability study testing of open tubes in high humidity atmosphere is ongoing at the time of the abstract writing.

RESULTS *recHAT* Sero-Strip is available in bulk with about 10 kg and 50 L for 3000 tests including all necessary accessories to run the test. Sensitivity was 97% (95% CI: 92.6–98.8%) and specificity was 96% (95% CI: 92.9–97.2%). The *recHAT* Sero-Strip is stable for 2 months at 45°C and for 3 months at 40°C. The strips remain valid at least for 2 months after opening in high humidity atmosphere (ongoing).

CONCLUSION *recHAT* Sero-Strip is a new RDT for *T. b. gambiense* sleeping sickness that can be deployed for active screening in remote areas under conditions where CATT cannot be performed. *recHAT* Sero-Strip complies with the ASSURED criteria and might thus play a role in achieving HAT elimination by 2020.

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DISCLOSURE Nothing to disclose.

O.3.2.16.003

Migration between Côte d'Ivoire and bordering countries and Human African Trypanosomiasis

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Human African Trypanosomiasis (HAT) - also known as sleeping sickness - is a tsetse fly transmitted parasitic disease that remains endemic in zones of Côte d'Ivoire but with decreasing detected numbers of cases in the past years. This largely rural disease is of increasing concern among migrants coming from bordering countries and also of seasonal workers from within Côte d'Ivoire from non-endemic zones. Seasonal workers usually work in cocoa cash crop areas, where they can be exposed in the fields or due to poor housing conditions. Our previous study highlighted their increased risk of infection and poor access to appropriate diagnostic and treatment. Out of 805 seasonal migrants tested (440 from abroad and 366 from within Côte d'Ivoire), 8 (1%) and 4 (0.5%) were sero- and parasitology-positive, respectively. In contrast, among the local sedentary tested population (n = 329) these prevalences were lower with 0.6% and 0%, respectively.

The seasonal workers from abroad commonly come from Burkina Faso. They develop HAT after the harvest season and back in Burkina Faso (or another neighboring country). In surveys conducted together with the National Control program against sleeping sickness and the WHO reference center for

sleeping sickness in Bobo-Dioulasso, Burkina-Faso, it was found that a case of HAT infected in Côte d'Ivoire was detected in Burkina Faso, raising concerns of possible of reactivation of former foci of HAT in the country since the vector is still present. So far, no recent autochthone case of HAT was detected in Burkina Faso. In non-endemic HAT zones of West Africa, physicians are not aware about HAT - and doctors rarely ask about previous travels of patients. Late - if at all - diagnosis of HAT patients renders treatment very problematic. We should consider more prominently in sociological aspects in studies to better understand the epidemiology of maintenance and resurgence of sleeping sickness in endemic foci in cash-crop areas. Mobility of people is one aspect. This in view of successful elimination of sleeping sickness in Africa - as advocated by the WHO - and thus not to miss important linkages and subsequent control/elimination options.

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DISCLOSURE Nothing to disclose.

O.3.2.16.004

Research and development landscape in Chagas disease

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Chagas disease (CD) is one of the world's most neglected diseases, with estimates of 5.6 million people infected and 70 million in the at-risk population. Available treatments for CD are limited and new, safer and simpler therapeutic alternatives are needed.

After decades of negligible progress, the last few years have witnessed a significant change in the landscape of research and drug development (R&D) in CD. Recent scientific advances have occurred in multiple areas and impacted all phases of R&D.

The current global portfolio includes novel classes of compounds under evaluation, with a range of new collaborations between product development partnership, academia and industry. Innovative *in vitro* and *in vivo* models have been developed and are now part of the regular profiling of new compounds.

Consensus on the design of proof-of-concept (PoC) trials, in particular the definition of target population and outcome measures for clinical studies in chronic CD provided a roadmap and new impetus for development. The PoC evaluation of ergosterol biosynthesis inhibitors (posaconazole and E1224) generated key new information in CD, prompting changes in the existing screening cascades, new decision-gates for drug discovery and lead optimisation, as well as new hypotheses for testing in clinical investigations in CD.

A lot remains to be done. Continued work is needed for a better understanding of pharmacokinetic-pharmacodynamics relationships in CD and the relevance of the various *T. cruzi* strains to human disease. Sustained efforts are also required for the evaluation of biological markers of early therapeutic response for CD.

At the same time, adult and pediatric clinical trials in chronic CD have provided clear efficacy and safety information on benznidazole, supporting the clinical assessment of alternative treatment regimens (reduced doses and treatment duration), in monotherapy and combination with existing azoles. Most importantly, however, these results provide additional evidence-base for the immediate scaling up of diagnosis and treatment with current therapeutic tools for CD.

DISCLOSURE Nothing to disclose.

O.3.2.16.005

High frequency of *Trypanosoma cruzi* polyclonal infections detected by molecular characterization of natural parasite populations in Chagas disease patients enrolled in clinical trials with antiparasitic drugs

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T. cruzi natural populations are composed of multiple clones from six discrete typing units (DTUs). The clinical, epidemiologic and therapeutic relevance of existing genetic diversity remains unknown. Genetic polymorphism of parasite populations was analysed before and after treatment with different anti-parasitic drugs [E1224 and benznidazole (BZN)] and placebo in a DNDi-sponsored phase II randomized, multicenter, safety and efficacy study in adult patients with chronic CD in Bolivia (DNDi-CH-E1224-001; NCT01489228).

METHODS AND MATERIALS 231 positive DNA samples from baseline and follow-up were used as template for PCR targeted to *T. cruzi* satellite DNA (SatDNA) and the variable regions of kinetoplastid DNA (vkDNA). SatDNA PCR products were purified, sequenced and aligned using ClustalX. RFLP-PCR profiles were obtained after digestion of purified vkDNA amplicons with 1U of HinfI/MspI/RsaI restriction enzymes, 10% PAGE and Sybr Gold staining. Genetic distances among baseline and follow-up minicircle signatures for each patient were estimated using the Jaccard's coefficient (JC).

RESULTS At baseline, 31% of samples showed SatDNA type II sequences (present in DTUs II/III) and 69% type I/II hybrid (present in DTUs V/VI); whereas 12 months after treatment, 12.8% of samples showed SatDNA type II and 87.2% type I/II hybrid sequences. SatDNA type I sequences (present in DTUs I/IV) were not found. After treatment, a change in the predominant SatDNA sequences was observed in both treated and placebo groups. Mean JC of minicircle signatures for placebo and the three E1224 arms (high, single and low dose) were 0.44 (0.00, 0.77), 0.47 (0.11, 0.75), 0.46 (0.30, 0.80), and 0.43 (0.31, 0.60), respectively; whereas it was 0.82 for the single refractory case of the BZN-treated group.

DISCUSSION Our findings indicate that the genetic composition of *T. cruzi* bloodstream populations during follow-up reflects the natural fluctuation of multiclonal parasite populations in chronic Chagas disease. This is the first report documenting the molecular characterization of *T. cruzi* populations after treatment and during natural infection of Chagas disease patients.

DISCLOSURE Nothing to disclose.

O.3.2.16.006

Immunogenicity and efficacy of a subunit therapeutic vaccine against Chagas disease

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Chagas disease, caused by the protozoal parasite *Trypanosoma cruzi*, is a neglected tropical disease characterized by chronic cardiac disease in approximately 30% of infected individuals. Tc24 is a 24 kilodalton calcium binding flagellar antigen that significantly reduces parasitemia, increases survival, and reduces cardiac pathology in *T. cruzi* infected mice when delivered therapeutically as a DNA vaccine. As DNA vaccines have limited success translating to clinical use, our goal is to develop a recombinant protein based vaccine that induces antigen specific interferon gamma (IFNγ) producing T cells and IgG2a antibody, reduces parasite burdens, increases survival, and reduces cardiac pathology when delivered therapeutically. Naïve BALB/c mice were vaccinated twice with recombinant Tc24 protein adsorbed to Alhydrogel®, Alhydrogel® +CpG, or E6020 adjuvant in a stable emulsion (E6020 SE). Antigen specific IFNγ production and IgG2a was measured in splenocytes and serum, respectively. Vaccine formulations containing Tc24 protein combined with E6020 SE, or Tc24 protein adsorbed to Alhydrogel® +CpG induced antigen specific IFNγ production and anti-Tc24 IgG2a antibodies at levels greater than antigen or adjuvant only controls, and Tc24 protein adsorbed to Alhydrogel®. BALB/c mice infected with 5000 *T. cruzi* H1 blood form parasites were vaccinated 7 and 14 days after infection with Tc24 protein combined with E6020 SE. Parasitemia was measured twice weekly and survival was monitored daily. Parasitemia was significantly reduced ($P > 0.05$) in vaccinated mice compared to unvaccinated mice by 18 days of infection. By 35 days of infection, 80% of vaccinated mice survived while only 40% of unvaccinated mice survived. To evaluate chronic disease, outbred ICR mice were infected with a sublethal dose of 500 *T. cruzi* H1 blood form parasites and monitored by electrocardiogram (ECG) and echocardiography. By 70 days of infection, 20% of mice showed conduction deficits by ECG, including atrial fibrillation, ectopic activity and conduction block. By 180 days of infection, heart failure was detectable on echocardiography. These results indicate that a candidate vaccine containing Tc24 protein and E6020 SE induces antigen specific IFNγ production and IgG2a, reduces parasitemia and increases survival in a mouse model of acute Chagas disease. Future studies will evaluate the effects of therapeutic vaccination on the progression of chronic cardiac disease in a mouse model.

DISCLOSURE Nothing to disclose.

3.2.17. Schistosomiasis

O.3.2.17.001

Rapid clearance of schistosomal circulating cathodic antigen (CCA) after treatment shown by urine strip tests - importance for monitoring treatment efficacy and re-infection

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Schistosomiasis elimination has reached agendas in many public health sectors; however, reaching this goal remains a substantial challenge. In order to assess the progress of interventions and monitor treatment efficacy, accurate, feasible and affordable diagnostic tools are an absolute requirement. Detection of *Schistosoma mansoni* by circulating cathodic antigen (CCA) in urine is an attractive option as this measure describes active worm infection noninvasively. In order to interpret treatment efficacy and re-infections, knowledge about clearance of this antigen is necessary. This study aims to investigate whether systemic antigen clearance is reflected in decreasing CCA levels in urine after only 24 h in response to both a single and two treatments with praziquantel.

The study was designed as a series of cross-sectional sample collections from 426 individuals nested in a two-arm randomised single blinded longitudinal clinical trial cohort matched by gender and age (ClinicalTrials.gov Identifier: NCT00215267). One arm was baseline treatment only, whereas the other arm received a second treatment at 2 weeks. Samples from baseline (urine+stool), baseline+24 h (urine), 2 weeks (urine), 2 weeks+24 h (urine), 9 weeks (urine+stool) and 2 years (urine+stool) were analysed. CCA levels in urine were determined by carbon-conjugated monoclonal antibody lateral flow strip assay and *S. mansoni* and soil-transmitted helminths eggs per gram (EPG) by Kato-Katz (six slides).

Significant correlations between CCA levels and *S. mansoni* EPG at baseline, 9 weeks and 2 years regardless of treatment arm were observed. Both tests showed significantly lower levels at 9 weeks in the two treatments group compared to those only receiving one treatment. Furthermore, presence of hookworm was found not to be a confounder for CCA specificity. At baseline mean CCA scores were significantly reduced 24 h after treatment ($P < 0.001$). Again, at 2 weeks CCA scores were significantly lowered ($P < 0.001$) 24 h after the second treatment in contrast to the one treatment arm ($P = 0.568$).

In conclusion, CCA clearance in response to treatment is measurable in urine already after 24 h. This is imperative when monitoring treatment efficacy as well as assessing re-infection proportions, because this antigen detecting assay provides information on the presence of actively feeding stages of *S. mansoni*, which conventional faecal microscopy methods do not accurately reflect.

DISCLOSURE This study was funded by the Commission of the European Community's Science and Technology for Development Programme [INCO-DEV Contract No: 517733 (MUSTSchistUKEMA)]. The funders had no role in study design, data collection and analysis.

O.3.2.17.002

A 5-year progress report from SCORE, the Schistosomiasis Consortium for Operational Research and Evaluation

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INTRODUCTION SCORE, the Schistosomiasis Consortium for Operational Research and Evaluation, is researching multiple practical aspects of schistosomiasis control to find evidence-based answers to programmatic questions that confront NTD control managers.
METHODS SCORE is performing (i) ongoing randomized trials of school- versus community-based drug delivery in Niger, Cote d'Ivoire, Kenya, Tanzania, and Mozambique in areas with moderate to high prevalence of *Schistosoma haematobium* or *S. mansoni*; (ii) trials to compare the performance of a point-of-contact urine antigen-detection assay (POC-CCA) for *S. mansoni* infection versus standard egg counting in 7 different countries; (iii) comparison trials of supplementary interventions (snail control, behaviour change, water and sanitation) to move toward local elimination in Zanzibar and Burundi; iv) the SCORE Rapid Answers Project, which uses systematic reviews and meta-analysis, combined with calibrated mathematical models of transmission, in aid of policy development.
RESULTS Preliminary 4- and 5-year results from partner countries indicate significantly better control of infection using annual versus biennial schedules, both for moderate- and high-prevalence areas. The optimal venue of delivery (school- versus community-based) depends on location and school-enrolment. POC-CCA offers a more sensitive means of detection of light intensity *S. mansoni* infections in areas doing multi-year MDA programs. The results of 'MDA-plus' strategies for local elimination are pending. Calibrated projections of program outcomes indicate that both school-age and adult treatments will be needed to approach local elimination targets in typical transmission settings.
CONCLUSION Achieving the goals of the 2012 London Declaration will prove challenging. For optimal results, implementation of anti-schistosomiasis MDA needs to be well-planned, well-delivered, and well-monitored. Benefits must be much more widely disseminated and promoted to effect the worldwide policy goal of *Schistosoma*-related disease elimination.
DISCLOSURE SCORE is funded by the University of Georgia (USA) Research Foundation through a grant from the Bill & Melinda Gates Foundation.

O.3.2.17.003

Transmission dynamics of *Opisthorchis viverrini*, *Schistosoma mekongi* and other helminth infections in two communities of Khong Islands, Southern Lao PDR

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BACKGROUND *Opisthorchis viverrini* and *Schistosoma mekongi* are trematode infections of public health importance in the lower Mekong Basin. Studies simultaneously focusing on human and animal hosts are lacking. We assessed *O. viverrini* and *S. mekongi* infection and their risk factors in humans, animal reservoir and intermediate hosts on two endemic Mekong islands in the Khong district, Champasak province, Southern Lao PDR, using an EcoHealth approach.
METHODS Cross-sectional studies were conducted in Don Khone and Don Som Mekong island in Khong district. Human infection status and risk factors were obtained from Kato-Katz examination and interviews. *Bythinia* and *Neotricula aperta* snails were collected and examined on the presence of *O. viverrini* and *S. mekongi* cercariae, respectively. Cyprinoid fish were collected in the villages' water bodies and digested to detect *O. viverrini* metacercariae. Fecal samples of dogs, cats, pigs and buffalos were examined using concentration technique.
RESULTS Prevalence of *O. viverrini,* hookworm, *S. mekongi, Trichuris trichiura*, *Ascaris lumbricoides* and *Taenia* spp. were 60.7%, 44.1%, 22.2%, 4.1%, 0.6% and 0.1%, respectively. Heavy infections were observed in humans for *O. viverrini* (4.2%), *S. mekongi* (3.6%) and hookworm (1.8%) infections. In total, 0.3% of *Bythinia* snails and 0.01% of *N. aperta* snails were infected with *O. viverrini* and *S. mekongi*, respectively. *O. viverrini* metacercariae were found in 26.9% of examined cyprinoid fish. They were most prevalence in *Hampala macrolepidota, Cyclocheilichthys apogon* and *Puntius brevis*. Cats (53.1%) and dogs (25.0%) were highly infected with *O. viverrini*. Dogs were found infected with *S. mekongi* (14.7%). Availability of a latrine at home was a protective factor and having observed cats or dogs eating raw fish was a risk factor for *O. viverrini* infection. Children below 10 years of age had the highest infection prevalence for *S. mekongi* (29.0%). Children of older age groups and adults until the age of 36 years had a significantly lower risk for a *S. mekongi* infection.
CONCLUSIONS *O. viverrini* and *S. mekongi* are highly prevalent on Mekong islands in Southern Lao PDR. Cats and dogs act contribute to *O. viverrini* transmission. Dogs must be considered reservoir hosts for *S. mekongi*. Sustainable control approaches must address human and animal risk factors.
DISCLOSURE Nothing to disclose.

O.3.2.17.004

Assessment of the safety and efficacy of oral Moxidectin, Synriam®, Synriam®-Praziquantel combination versus Praziquantel in schoolchildren infected with *Schistosoma haematobium* and *Schistosoma mansoni*

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INTRODUCTION Millions of people are affected by schistosomiasis. Despite the huge burden of the disease, its treatment relies on one drug only, praziquantel. Synriam is a combination of piperaquine 150 mg and arterolane 750 mg, a synthetic artemisinin derivative, which has been proven to have antischistosomal properties in laboratory studies. This antimalarial is now registered in different African countries. Moxidectin, a veterinary drug currently developed for onchocerciasis demonstrated efficacy in a Phase 3 clinical trial in *Onchocerca volvulus* patients against *Schistosoma mansoni* co-infections.

METHODS AND MATERIALS We conducted two parallel randomized single-blinded exploratory studies in *Schistosoma mansoni* and *S. haematobium* infected school-aged children in Côte d'Ivoire. We enrolled 120 school-children (12–14 years old) in each study. At baseline each child was asked to provide two stool samples (for the *S. mansoni* trial) or two urine samples (for the *S. haematobium* trial) and one finger prick for malaria screening. Samples were examined according to WHO standard procedures and supplementary diagnostic methods (microhematuria test, Baermann and CCA test) for the diagnosis of schistosomes, other intestinal parasites (*Trichuris trichiura, Ascaris lumbricoides, Strongyloides stercoralis* and hookworm) and malaria parasites. The four arms of treatment were:
1 Moxidectin (8 ml).
2 Synriam for three consecutive days.
3 Synriam® for three consecutive days plus praziquantel (40 mg/kg).
4 Praziquantel (40 mg/kg).

Adverse events were monitored at several time points post-treatment. The children were asked to provide another two stool/urine samples for follow-up 21 and 50/80 days after treatment.
RESULTS AND CONCLUSIONS Cure and egg reduction rates of the different treatments will be presented. I will show how the treatments were tolerated by the children. Our results are of great importance as we will have elucidated the antischistosomal activity of two novel treatments, which will be widely used across Africa in geographical settings where malaria or onchocerciasis overlap with schistososomiasis.
DISCLOSURE Nothing to disclose.

O.3.2.17.005

Mapping freshwater snails in Angola: distribution, identity and molecular diversity of medically important taxa

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INTRODUCTION This study was designed to determine the presence and identity of potential intermediate snail hosts of schistosomiasis in Bengo, Luanda, Kwanza Norte and Malanje Provinces in NW Angola. This is an area where infection with Schistosoma haematobium, causing urogenital schistosomiasis, is common but little is known about transmission of the disease. Angola has had a varied past with regards to disease control and is revitalising efforts to combat Neglected Tropical Diseases.
METHODS Snails were sampled from 60 water contact points taking note of the habitat and water chemistry. In total nine mollusc genera were identified using morphological characteristics; *Lymnaea, Melanoides, Lanistes, Gyraulus, Lentorbis, Succinea, Physa, Biomphalaria,* and *Bulinus*. Of greatest importance was the discovery of *Bulinus globosus, Bulinus canescens, Bulinus angolensis, Bulinus crystallinus* and *Biomphalaria salinarum* in what is believed to be their type locations. Many of the habitats had been visited in 1957 by Dr C.A. Wright and his collections were available for comparison. Any specimens of *Bulinus, Biomphalaria* or *Lymnaea* were screened for trematode infections. Furthermore, miracidia were hatched from eggs from urine samples provided by children from Icáu Wando, Bengo Province. Cercariae and miracidia were captured for molecular analysis. A partial cytochrome oxidase 1 (COX1) fragment was amplified from each specimen and resulting sequences were used for phylogenetic analyses.
RESULTS All snails were identified using shell morphology and a subset from each site (and all species), was used for molecular identification. These data showed two distinct areas where either *B. globosus* or *B. angolensis* are found. *B. globosus* COX1 differs from specimens from other countries. *Schistosoma haematobium* specimens were collected from *B. globosus* from two locations: Cabungo, Bengo ($n = 20$) and Calandula, Malanje ($n = 5$). *Schistosoma haematobium* was identified as group 1 and therefore corresponds to the mainland African type.
CONCLUSIONS This study is a good start in the characterisation of snails and schistosomes from this region and highlighted a need to map the rest of the country. Important type-locality specimens for *Bulinus globosus* and *Biomphalaria salinarum* have been characterised; including some data from snails collected in 1957. The molecular phylogeny generated from the samples suggests that considerable variation exists in *B. globosus*, which is a major host for *S. haematobium*.
DISCLOSURE Nothing to disclose.

O.3.2.17.006

Serum hyaluronic acid as a non-invasive tool to diagnose schistosomal periportal fibrosis in *Schistosoma mansoni* endemic areas of Ethiopia

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BACKGROUND Among parasitic infections, Schistosoma mansoni induced infection is the most prevalent worldwide with a significant public health and economic outcome. Morbidity and mortality associated with *S. mansoni* is mainly the result of periportal fibrosis (PPF) which can be diagnosed using ultrasonography. As ultrasound equipment is not readily available in *S. mansoni* endemic areas, serum markers like hyaluronic acid (HA) have been used as an alternative means of diagnosing PPF.
METHODS A cross sectional study was conducted from November 15–25, 2011, with the aim of determining the importance of serum HA as a marker for schistosomal PPF in patients found in *S. mansoni* endemic areas situated in Northeastern Ethiopia. The study involved 55 individuals from Kemise town and surrounding *S. mansoni* endemic villages, and 20 controls from *S. mansoni* non-endemic area (Addis Ababa). PPF was determined using portable ultrasound equipment and graded according to the 'Niamey protocol'. Serum HA concentration was determined using commercially available ELISA kit.
RESULTS The mean concentration of HA in the sera of the cases was significantly higher than the controls ($P < 0.001$). The concentration of HA also increased significantly as the pattern of PPF became severe while serum HA concentration positively correlated with PPF scores ($\mu g = 0.6438$, $P < 0.001$). An HA concentration of 27.9 μg/liter of serum differentiated moderate cases of PPF from advanced cases with a sensitivity, specificity, positive predictive value and negative predictive value of 85.71%, 75.61%, 60.5 %, 93.9%, respectively ($P < 0.001$).

CONCLUSION In conclusion, serum HA concentrations could be used as an alternative, noninvasive potential marker for schistosomal PPF and to assess its severity in patients found in *S. mansoni* endemic areas.
DISCLOSURE Nothing to disclose.

3.2.18. Buruli and other NTDs

O.3.2.18.001

The role of molecular diagnostics in the clinical management and control of Buruli ulcer disease and leprosy - two neglected mycobacterial diseases

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Buruli ulcer disease (BUD) caused by *Mycobacterium ulcerans* and leprosy (*Mycobacterium leprae*) - two neglected mycobacterial diseases - mainly affect impoverished inhabitants of resource poor settings and are leading causes of permanent disabilities. In the absence of proven strategies for prevention of infection, disease control is based on early case detection and treatment. Current WHO recommendations in particular call for the development of decentralized diagnostic point-of-care (POC) tests for BUD, and leading experts in the field of leprosy suggest deployment of diagnostic tools to identify early and subclinical disease as well as transmitters of leprosy among patients and their contacts. In response to current requirements this study evaluated a range of molecular tools suitable for application in BUD and leprosy control which were developed in cooperation with partners in Ghana and Togo.

A dry-reagent-based (DRB) loop mediated amplification (LAMP) assay (a technology which does not require sophisticated instrumentation) enables decentralized POC laboratory confirmation of BUD. A 16S rRNA based viability assay (also available in a DRB format) identifies viable *M. ulcerans* in clinical samples, thus constitutes an alternative for classical cultures and allows monitoring of treatment outcome. RLEP qPCR identifies *M. leprae* DNA in nasal swab samples from leprosy patients and their contacts, and a RNA-based assay detecting viable *M. leprae* provides a valuable tool for identification of transmitters of leprosy. Results of a pilot study conducted in Togo suggested that 37.5% of patients harboring viable *M. leprae* infected contact persons, and vice versa 5% of the contacts were found to be carriers of *M. leprae*. The molecular assays are 100% pathogen specific, analytical sensitivities are high (0.01 to 3 genome equivalents), and the clinical sensitivities are between 75–95%.

In conclusion, a range of 100% specific and highly sensitive molecular assays is available for application in BUD and leprosy control. The assays address the current needs for decentralized diagnosis and monitoring of treatment outcome for BUD, as well as control of transmission of leprosy. However, large-scale evaluation trials in endemic areas are required to investigate their feasibility under field conditions.
DISCLOSURE Nothing to disclose.

O.3.2.18.002

On the way to point-of-care diagnostics for Buruli ulcer: an antigen capture approach

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Buruli ulcer (BU) is a chronic and disfiguring skin disease caused by infection with *Mycobacterium ulcerans*. Since mechanisms of transmission remain elusive, the current strategy to control BU relies on early case detection and antibiotic treatment. Due to limited access to treatment centres and laboratory services the diagnosis of BU in remote areas of West and Central Africa, which are most affected by the disease, is primarily based on clinical findings. However, there is broad differential diagnosis not only for non-specific early stages of the disease but also for ulcerative lesions. Thus laboratory reconfirmation of clinical diagnosis is crucial to ensure appropriate treatment. A simple and rapid diagnostic test that can be implemented in rural health care facilities is therefore urgently needed.

We have shown that antigenic cross-reactivities between different mycobacterial species as well as immune responses against *M. ulcerans* antigens frequently observed in exposed, but healthy individuals living in BU endemic areas, complicate the development of a specific serological test. Therefore, we are now focusing on the direct detection of *M. ulcerans* antigens within BU lesions. For identification of suitable proteins that could be used as targets in diagnostic test formats, we have analysed an *M. ulcerans* whole protein lysate by 2D gel electrophoresis.

The previously uncharacterized cell wall-associated protein MUL_3720 best met the predefined criteria of being highly expressed by *M. ulcerans* and not having orthologs in other prevalent pathogenic mycobacteria. We generated a panel of high affinity antibodies against this antigen and developed a sandwich-ELISA format with a sensitivity rate comparable to that of microscopic detection of acid fast bacilli in smears from clinical specimens. Currently, the application of the developed immunological reagents is tested in a lateral flow assay platform in a partnership between SwissTPH, the Foundation for Innovative New Diagnostics (FIND) and Alere.

Preliminary results show that this approach has great potential to be developed into a field-compatible confirmatory test for *M. ulcerans* infection.

This project is supported by the Stop Buruli Initiative funded by the UBS-Optimus Foundation and the Swiss Development Cooperation (SDC) through FIND.
DISCLOSURE Nothing to disclose.

O.3.2.18.003

Performance of a clinical score for the diagnosis of *Mycobacterium ulcerans* infection in Akonolinga, Cameroon

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Access to laboratory diagnosis can be a challenge for individuals suspected of Buruli ulcer (BU). Our objective was to establish a clinical score to assist clinicians working in resource-limited settings for BU diagnosis.

Between 2011 and 2013, all individuals presenting at Akonolinga District Hospital, Cameroon, with a skin lesion suspect of new BU were consecutively enrolled after consent. Clinical data and laboratory results were collected prospectively. Results of the laboratory tests (ZN, PCR, culture) were included into a latent class model, based on which patients were categorized into a high, respectively low BU probability. Variables associated with a high BU probability ($P < 0.20$) were included in a multivariate model and those still associated with BU with an OR >1.5 or <0.67 after adjustment were included in the score. Sensitivity, specificity and predictive values were calculated for each score value, and final cutoff was chosen based on predefined thresholds.

Out of the 325 patients with an ulcerative lesion included in the latent class model, 51 (15.7%) had a high probability of BU. The following variables were included in the Buruli score: characteristic smell (+3 points), yellow color (+2), female sex (+2), undermining (+1), green color (+1), lesion hyposensitivity (+1), pain at rest (−1), size >5 cm (−1), locoregional adenopathy (−2), age above 20 and below 40 years (−3), and age above 40 (−5). The score had an area under the ROC of 0.86 (95CI 0.82–0.89). The cut-off to reasonably exclude BU was set at scores below 0 (NPV 96.5% 95CI 93.0–98.6). The treatment threshold was set at a cut-off superior or equal to 4 (PPV 69.0%, 95CI 49.2–84.7). Patients with scores between 0 and 3 had an intermediate probability of BU and would need to be tested further by PCR. Applying this algorithm to the study patients would have correctly classified 94% (299/318), with PCR done in only 28% (90/318) of them.

We propose a decisional algorithm based on a clinical score to assess the probability of BU infection. Applying the algorithm to the patients included in the study would have resulted in almost four times less PCR performed. The score still requires further validation and standardization before it can be recommended for wide use.

DISCLOSURE Nothing to disclose.

O.3.2.18.004

Antibody-mediated neutralisation of the exotoxin mycolactone prevents cells from undergoing apoptosis

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Mycolactone, the macrolide exotoxin produced by *Mycobacterium ulcerans*, causes extensive tissue destruction by inducing Bim-dependent apoptosis. In this study, we aimed at the production of anti-mycolactone antibodies that could neutralize the cytotoxic activities of mycolactone.

By applying the B cell hybridoma technology, we were able to generate a series of monoclonal antibodies (mAbs) with specificity for mycolactone from spleen cells of mice immunized with a synthetic mycolactone-protein conjugate. L929 fibroblasts were used as a model system to investigate whether these antibodies can inhibit the biological effects of mycolactone.

By measuring the metabolic activity of L929 fibroblasts, we found that the cytotoxic activity of mycolactone can be completely neutralized by the mAbs. In addition, we demonstrated that the triggering of the molecular pathway underlying mycolactone-mediated apoptosis was also blocked by the mAbs.

Based on these findings, the *in vivo* functionality of the produced anti-mycolactone mAbs will now be evaluated by performing passive immunisation experiments in infected mice. Furthermore, in active immunisation experiments, we will investigate whether immunisation with mycolactone-protein conjugates protects mice infected with *M. ulcerans* from developing the necrotizing pathology characteristic of Buruli ulcer.

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DISCLOSURE Nothing to disclose.

O.3.2.18.005

Sero-epidemiology of Buruli ulcer in the Offin river valley of Ghana

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BACKGROUND Transmission of *Mycobacterium ulcerans* (MU), the causative agent of the necrotizing skin disease Buruli ulcer (BU), is unclear. While sero-epidemiological studies have revealed a late onset of serological response in healthy children living in BU endemic areas against the MU 18KD small heat shock protein (shsp), the stability of the anti-MU antibody titers is not known. We present a comprehensive longitudinal study aimed at investigating the stability of antibodies developed against MU and comparing the age-dependent emergence of the anti-shsp response with antibody responses against other pathogens (i.e. *Schistosoma mansoni*, *Plasmodium falciparum* and *Strongyloides stercoralis*).

METHODS AND MATERIALS We sampled whole blood from 1,352 individuals who were randomly selected as representatives of all age groups within a surveyed population of 13 communities along the Offin river in Ghana. We then followed up after 6, 12 and 18 months by randomly sampling one-third of the sero-cohort at each time point. Subsequently, we determined plasma IgG titres against the MU shsp by enzyme-linked immunosorbent assay and Western blot analysis. Additionally, we profiled serological response of our sero-cohort to *P. falciparum* AMA-1 antigen, *S. mansoni* adult worm and egg antigens, as well as *S. stercoralis* adult worm antigen.

RESULTS At baseline, we observed an overall 18% prevalence of the anti-shsp response within our cohort with the onset of sero-conversion at age 4. Similarly, we observed a late onset of sero-conversion (at age 7) for both egg and adult worm antigens of *S. mansoni*. On the contrary, the onset of serological responses to both *P. falciparum* and *S. stercoralis* antigens was earlier (ages 1 to 2). 98%, 96.7% and 92.4% of those followed up after 6, 12 and 18 months respectively maintained their positive anti-shsp sero-status.

CONCLUSIONS Our data indicate that exposure to MU intensifies in children >4 years of age, coinciding with moving further away from their homes and having more intense environmental contact, including exposure to water bodies at the periphery of their villages. Comparisons to age response patterns against *S. mansoni*, *P. falciparum* and *S. stercoralis* speak against an involvement of vectors or environmental reservoirs localized within households in BU transmission.

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DISCLOSURE Nothing to disclose.

O.3.2.18.006

Parasitic skin diseases and dermatomycoses in rural Amazonia are associated with poverty

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In countries of the global south parasitic skin diseases and dermatomycoses are associated with considerable morbidity and may lead to social exclusion. Although these diseases are widespread, little is known about their epidemiological determinants.

A cross-sectional study was performed in Liberdade, a rural district in the Brazilian Amazonian region. Using a door-to-door-survey the inhabitants were examined for the presence of parasitic skin diseases (tungiasis, cutaneous larva migrans, scabies and pediculosis capitis) and dermatomycoses (tinea infections and pytiriasis versicolor). Sociodemographic, economic, environmental and behavioural risk factors were collected using standardized interviews. Risk factors were assessed using bivariate and multivariate regression analysis.

At the time of the study Liberdade was inhabited by 1123 individuals.

993 individuals (89.8% of the residents) were included in the study; 397 (40%) had at least one type of infectious dermatosis. Pediculosis capitis was the most common dermatosis (20.1%), followed by the foot mycosis (17.1%). Pityriasis versicolor, tinea corporis and tinea capitis had in total a prevalence of 7.8%. The ectoparasitoses cutaneous larva migrans, scabies and tungiasis altogether only had a prevalence of 2.1%.

Long hair was the most important independent risk factor for pediculosis capitis (adjusted OR 5.3; 95% CI: 2.5–11.3). Age 5–9 years (OR 9.4; 95% CI: 3.9–22.9) and female sex (OR 2.9; 95% CI: 2.1–4.1) were other significant risk factors. The prevalence of foot mycoses increased with increasing age (≥60 years: OR 60.4; 95% CI: 16.1–227.1); whereas pityriasis versicolor and tinea corporis were most common among 15 to 19 year–olds (OR 3.2; 95% CI: 1.4–7.9). Poverty-associated factors, such as low quality of housing, low household income, food shortages in the past 12 months, unsafe drinking water, absence of waste collection and crowding all showed a significant association with the presence of infectious dermatoses.

The results indicate that infectious dermatoses are highly prevalent in rural Amazonia and present a public health problem. In addition to age and sex, poverty-associated factors were identified as risk factors. The close link with poverty indicates that attempts to eliminate this group of diseases without adressing poverty will not be successful.

DISCLOSURE Nothing to disclose.

3.3.1. The globalization of Chagas diseases: an emerging disease in Europe

INV.3.3.1.002

Chronic Chagas disease: to treat or not to treat?

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Chagas disease (CD) is a major neglected disease. Even if the World Health Organization indicates that the specific antiparasitic treatment for all chronic-phase *Trypanosoma cruzi (T. cruzi)*-infected individuals should be recommended, there is a controversy based on several theories that have not been proved, like the autoimmune origin of chronic tissue injuries and the absence of the parasite in tissues. Current evidence highlights the importance of the parasite persistence on the pathogenesis of CD and in the development of the disease. There are several studies that support the inflammatory immune response in CD, which is triggered and sustained by the parasite itself, and is directly related to parasite burden. Other pathogenic mechanisms as microvascular disorders or autonomic nervous system derangements are ancillary and have also been related to the parasite persistence in tissues.

In this context specific treatment against *T. cruzi* is a key issue. However, the only drugs available to treat Chagas disease (nifurtimox and benznidazole) are limited in terms of efficacy and safety. Moreover, in chronic adult patients, the decline of the conventional serology over the years (10–15 years) is the only evidence of the therapeutic efficacy after anti-parasitic treatment: there is a lack of early biomarkers of therapeutic response to assess the treatment efficacy which is important for the follow-up of treated patients. Besides, there are no biomarkers to predict which patients will develop heart or digestive complications (35–40%).

There are several studies that show that anti-parasitic treatment slow the progression of disease, through eradication or through the decrease in the parasite burden; and that vertical transmission is less effective in women that have received specific treatment before pregnancy. Moreover recent clinical trials show an efficacy of 80% of benznidazole 12 months after treatment, measured by serial PCRs during the follow-up.

All these factors together tend to favour the antiparasitic treatment for all chronic patients. Unfortunately, less than one per cent of *T. cruzi*-infected has had access to treatment today.

CONCLUSIONS The persistence of the *T. cruzi* in tissues is a key feature for the pathogenesis of CD. Etiological treatment should now be recommended for all adult chronic CD patients. There is a need to scale-up the access to treatment.

DISCLOSURE Nothing to disclose.

3.3.2. Dual burden of communicable and non-communicable disease in low and high income countries

O.3.3.2.002

Longitudinal evolution of diabetes during tuberculosis in Dar es Salaam, Tanzania

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INTRODUCTION Diabetes mellitus (DM) increases the risk of active tuberculosis (TB) and adverse TB outcome. TB, as an infectious disease, leads to transient hyperglycemia. The best algorithm for DM screening among TB patients has to be established. We analyzed the longitudinal evolution of the three

recommended DM screening tests among new TB patients over 5 months follow-up in Dar es Salaam, Tanzania.
METHODS AND MATERIALS Longitudinal case-control study between July 2012 and June 2014. Consecutively recruited adults with new active TB diagnosed by the national TB program were included. Healthy volunteers, free of acute infection and without past history of TB, were enrolled in the same recruitment area. Screening for HIV and DM [fasting capillary glucose (FCG), 2-h capillary glucose (2 h-CG) and glycated hemoglobin (HbA1c; Roche Cobas Integra)] were performed at enrolment and DM screening was repeated after at least five months of TB treatment. The association between TB and DM was assessed using logistic regression.
RESULTS Overall, 539 TB patients and 496 healthy controls were included. At enrolment, DM prevalence was significantly higher in TB cases compared to controls using any DM diagnostic test [FCG>7 mM: 5.3 vs. 1% ($P = 0.002$); 2-h CG>11 mM: 6.8 vs. 3.1% ($P = 0.006$); HbA1c>6.5%: 9.3 vs. 2.2% ($P < 0.001$)] irrespective of HIV status. A significant association between newly diagnosed DM and TB was no longer found after 5 months of TB treatment with any of the screening tests [enrolment versus follow up (OR (95% CI): FCG 4.7 (1.1–20.7) vs. 1.7 (0.3–11); 2-h CG 1.42 (0.6–3.7)] vs. 0.5 (0.1–1.7); HbA1c 3.9 (1.5-10) vs. 1.2 (0.4–3.6)]. DM and pre-DM diagnosed at enrolment with FCG and 2-h CG were associated with adverse TB outcome, OR (95% CI) 2.3 (1–4.9) and 2.3 (1.2–4.3), respectively. Among TB cases, the positive predictive value (PPV) of DM diagnosis at enrolment for persisting DM at follow-up was 71, 61 and 42% for FCG, 2-h CG and HbA1c, respectively.
CONCLUSIONS All three DM screening tests lead to the detection of transient hyperglycemia at TB diagnosis. The prevalence of DM after 5 months of TB treatment approached that of the healthy controls. FCG screening at enrolment captures TB patients at risk of adverse outcome and gives the opportunity to manage hyperglycemia, but screening should be repeated after TB treatment to confirm DM. HbA1c was not useful at TB diagnosis as it did not detect patients at risk of adverse TB outcome and had the smallest PPV.
DISCLOSURE Nothing to disclose.

O.3.3.2.003

The illness experiences on the double burden of disease: a case of diabetes in the context of malaria in Southeastern Tanzania

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BACKGROUND Tanzania is experiencing a double burden of disease, from the emerging non-communicable diseases alongside the persisting infectious diseases. However, information on the illness experiences in the co-existence of these conditions is limited. The study used Kleinmans' illness conceptions to assess the illness experiences of diabetes in a context of predominating malaria condition in rural settings.
METHODS To explore the shared illness experiences, we conducted 17 focus group discussions with adult members of the community, diabetes patients and either neighbors or relatives of diabetes patients. To gain in-depth understanding of the individual illness experiences we conducted 41 in-depth interviews with malaria or diabetes patients and family members of diabetes patients. The analysis followed grounded theory principles relating Kleinman's illness conceptual underpinnings as deductive framework.
RESULTS Both malaria and diabetes were perceived as fatal illnesses. Unlike malaria, diabetes was perceived as relatively new and persisting life threatening disease. Illness experiences with diabetes were shaped with multitude of sufferings based on the persistence and severity of the illness. Uncertainty and perpetual fear of present and future life characterized diabetes patients and their families' illness experiences. Increased susceptibility to malaria and other illnesses, undetermined health conditions, functional incapability, loss of consciousness, memory, and sexual desires were common health consequences experienced by diabetes patients. Both direct and indirect costs of illness were expressed as pushing individuals and their families further into poverty and were more pronounced for diabetes. Limited social life and being conscious about what to eat and drink were other reported illness experiences on diabetes.
CONCLUSION Malaria and diabetes are distressing illnesses however, the magnitude of which is more on diabetes. Strategies involving families and communities in support of social, emotional, and psychological well-being of the patients could be useful into improving illness experiences and quality of life for chronically ill.
DISCLOSURE Nothing to disclose.

O.3.3.2.004

Glycated nail proteins as a biomarker of diabetes

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BACKGROUND Diabetes prevalence is rising dramatically in developing countries. This implies a need for affordable and robust diagnostics. Nail clippings contain 85% of proteins (keratins) which are prone to glycation. We have explored the possibilities to assess glycation of nail keratins as a tool for diabetes diagnosis and monitoring.
METHODS Fructosamine was assessed in clippings from 116 healthy subjects and 112 diabetics using a modified photometric nitro blue tetrazolium-based assay. A group of 51 patients who underwent cataract surgery (34 diabetics and 17 non-diabetics) were also enrolled to this study. Following lens extraction (cataract surgery), fructosamine was analyzed in lens and nail fragments. Following a cutting of the nail plate into superficial and deep layers, differential analysis of fructosamine was performed.
RESULTS Glycated nail proteins discriminated well diabetics (median: 4.07 μmol/g nail, $P < 0.0001$) and non - diabetics (1.75 μmol/g nail). ROC analysis showed an AUC of 0.848 (specificity 93.1%; sensitivity 68.9%). The marker was found useful in the monitoring of diabetes retinopathy and nephropathy. A marked correlation was found between nail and lens glycated proteins ($R^2 = 0.55$, $P < 0.001$). Furthermore, differential analysis of material originating from deep and superficial nail layers yielded a higher fructosamine level in deeper layers (median 3.6 μmol/g nails, $P < 0.05$) than in superficial layers (median 1.12 μmol/g nails). The nails could be

stored at elevated temperatures for months without quality loss, which implies a major pre-analytical advantage.
CONCLUSION Assaying glycated nail proteins is an affordable and simple alternative for diagnosing diabetes in remote areas. Glycation of nail proteins occurs in the deep layer of finger nails, which is in close contact with blood vessels and interstitial fluid. Nail protein glycation can be regarded as a non-invasive marker for diabetic glycation-associated target organ damage. The method requires only a simple photometer and cheap reagents which are stable and can be home made, making the method very suitable for developing countries.
DISCLOSURE Nothing to disclose.

O.3.3.2.005

Heterogeneity of obesity-asthma association disentangled by latent class analysis

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INTRODUCTION Asthma is not a single disease but a complex mixture of heterogeneous phenotypes with presumably different etiologies. Obesity, a well-known risk factor for asthma, might have distinct effect on different asthma phenotypes.
METHODS Latent class analysis (LCA) was conducted to cluster 1217 ever self-reported asthmatics in the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA). Information on asthma attacks in the last 12 months, current asthma medication, asthma symptoms reported in the last 12 months or repeatedly from baseline (1991) to the second follow-up (2010–2011), presence of atopic sensitisation and age of asthma onset were used. Taking non-asthmatics as reference, association of obesity to each LCA-derived asthma class was analyzed by mixed logistic regression using different obesity measures i.e. body mass index (BMI), percent body fat (PBF), waist hip ratio (WHR), waist height ratio (WHtR) as well as waist circumference (WC) and adjusting for potential confounders and area of study.
RESULTS The LCA identified four asthma classes: a persistent severe asthma class (n = 91); moderately severe asthma class (n = 236); mild allergic asthma class (n = 302) and mild non-allergic asthma class (n = 430). None of the obesity measures was associated with mild asthma classes. Most of the obesity measures tested showed positive associations to the severe or moderately severe asthma classes (for the severe asthma class: OR_{BMI} = 1.31 [1.08, 1.58]; OR_{PBF} = 1.65 [1.23, 2.21]; OR_{WHtR} = 1.38 [1.12, 1.70]; OR_{WC} = 1.37 [1.09, 1.72] for 1 SD increase). PBF showed the strongest association with the severe asthma class and this effect remained significant after adjustment for BMI (OR = 1.63 [1.01, 2.63] for 1 SD increase in PBF). When the same analysis was restricted to those who have been stably overweight i.e. BMI ≥25 kg/m^2 from baseline to the second follow-up, the association of PBF to the severe asthma class increased (OR = 2.55 [1.23, 5.32] for 1 SD increase in PBF).
CONCLUSIONS Association with obesity is heterogeneous across different asthma phenotypes. Chronic exposure to high PBF is associated with higher risk of severe asthma.
DISCLOSURE Nothing to disclose.

3.3.3. NCDs with particular relevance to mental health

O.3.3.3.002

Depression in people living with HIV/AIDS in Fitche Hospital, Central Ethiopia: a cross-sectional study

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BACKGROUND Depression is one of the commonest psychiatric disorders with a prevalence ranging from 5 to 10% in the general population and about 60% among people living with HIV/AIDS. Depression and HIV are related and negatively impacting the life of people living with HIV/AIDS.
OBJECTIVE The objective of this study was to identify the factors associated with depression among people living with HIV/AIDS attending an anti-retro viral therapy (ART) clinic at Fitche hospital.
METHODS This was a cross-sectional study conducted in Fitche Hospital from February 15 to March 15/2012 among people living with HIV/AIDS. The Center for Epidemiologic Studies Depression Tool (CES-D) was used to collect the data from 390 people living with HIV/AIDS (PLWHA). Both bivariate and multivariate logistic regression analyses were done and variables with $P < 0.25$ in bivariate logistic regression analysis were entered to multivariate logistic regression analysis and statistical significance was declared at $P \leq 0.05$ in multivariate logistic regression.
RESULTS The prevalence of depression was 299 (76.7%) ranging from mild to moderate (33.6%) to major depression (43.1%) with the highest proportion observed among food insecure individuals 287 (79.3%). Being female [(Adjusted Odds Ratio (AOR) = 1.951 (1.055–3.608)], food insecurity [AOR = 3.809 (1.535–9.452)], non-ownership of livestock [2.257 (1.179–4.320)] and opportunistic infections [AOR = 5.119 (1.302–20.135)] were significantly associated with depression.
CONCLUSION Depression is prevalent in the study population. Social disparities are important factors of depression among PLWHA. Integration of mental health care services with HIV/AIDS-related health care services at all levels is needed.
DISCLOSURE The authors have no any conflict of interest.

O.3.3.3.003

Mental health problems of undocumented migrants in the Netherlands: a qualitative exploration of help-seeking behaviour and experiences with primary care

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OBJECTIVE To explore health-seeking behaviour and experiences of undocumented migrants (UMs) in general practice in relation to mental health problems.
DESIGN Qualitative study using semistructured interviews and thematic analysis.
PARTICIPANTS 15 UMs in the Netherlands, varying in age, gender, country of origin and education; inclusion until theoretical saturation was reached.
SETTING 4 cities in the Netherlands.
RESULTS UMs consider mental health problems to be directly related to their precarious living conditions. For support, they

refer to friends and religion first, the general practitioner (GP) is their last resort. Barriers for seeking help include taboo on mental health problems, lack of knowledge of and trust in GPs competencies regarding mental health and general barriers in accessing healthcare as an UM (lack of knowledge of the right to access healthcare, fear of prosecution, financial constraints and practical difficulties). Once access has been gained, satisfaction with care is high. This is primarily due to the attitude of the GPs and the effectiveness of the treatment. Reasons for dissatisfaction with GP care are an experienced lack of time, lack of personal attention and absence of physical examination. Expectations of the GP vary, medication for mental health problems is not necessarily seen as a good practice.
CONCLUSIONS UMs often see their precarious living conditions as an important determinant of their mental health; they do not easily seek help for mental health problems and various barriers hamper access to healthcare for them. Rather than for medication, UMs are looking for encouragement and support from their GP. We recommend that barriers experienced in seeking professional care are tackled at an institutional level as well as at the level of GP.
DISCLOSURE Nothing to disclose.

O.3.3.3.004

The effect of vitamin B1 on anxiety associated with premenstrual syndrome in young women in Iran

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BACKGROUND AND AIM Premenstrual syndrome (PMS) is a cyclical disorder observed in late luteal phase and presenting with behavioral changes that can affect interpersonal relationships and normal daily activity. Anxiety is also common complaint.
ANXIETY Is an unpleasant state of inner turmoil, often accompanied by nervous behavior, such as pacing back and forth, somatic complaints and rumination. It is the subjectively unpleasant feelings of dread over anticipated events, such as the feeling of imminent death. Anxiety is not the same as fear, which is a response to a real or perceived immediate threat; whereas anxiety is the expectation of future threat. Anxiety is a feeling of fear, worry, and uneasiness, usually generalized and unfocused as an overreaction to a situation that is only subjectively seen as menacing. It is often accompanied by muscular tension, restlessness, fatigue and problems in concentration. Anxiety can be appropriate, but when experienced regularly the individual may suffer from an anxiety disorder.

The aim of this study is to investigate the determine effect of vitamin B1 on anxiety associated with PMS and severity anxiety in the Academy students, whom do not have considerable information about menstruation.
MATERIALS AND METHODS In this double-blind placebo-controlled clinical trial, 80 students with sleep disorder related to PMS residing at dormitories of Jahrom University were divided randomly into two groups, vitamin B1 and placebo. The severity of the symptoms of PMS in two cycles, before the intervention and during the intervention, was recorded by the students. PMS was detected with 'Premenstrual Syndrome Scale'.

The data were collected using an information collection form, PMS provisional diagnosis form, daily status record form, Beck Depression Inventory. The data were analyzed using descriptive and inferential statistics.

RESULTS There was no significant difference among the studied variables in terms of confounding variables. The comparison of vitamin B1 group before the intervention with that after the intervention showed that vitamin B1 reduced anxiety (96%) significantly ($P < 0.0001$).
CONCLUSION It seems that vitamin B1 is effective in recovery of mental and physical symptoms of PMS such as anxiety. Therefore, this vitamin can be used to reach a major goal of midwifery, that is, reduction of symptom severity of PMS - specially anxiety - without any side effects.
KEYWORDS Premenstrual syndrome, anxiety, vitamin B1.
DISCLOSURE Nothing to disclose.

O.3.3.3.005

A qualitative study of the social response to patients and caretakers of mental health disorders in a rural community of Maharashtra, India

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INTRODUCTION The WHO definition of health underlines the importance of the social component and it becomes even more pivotal in the field of mental health. Societal beliefs, attitudes and responses influence patients affected by these disorders and their care takers and also decide the trajectory of mental illness and recovery. In a favourable environment, recovery and reintegration are better facilitated whereas in an unsupported social environment, recovery can be hindered owing to stigma and discriminatory attitudes and practices. The present study aimed to qualitatively explore the social response of the community(stigma and support) towards people affected by mental health disorders and their families in a rural community of Maharashtra, India both from the perspectives of the community, the patients or their care takers.
METHODS A total of 20 in-depth interviews were taken of the patients affected by Common Mental Disorders (CMD), Severe Mental Disorders (SMD) and Epilepsy [composite tool prepared from Explanatory Model Interview Catalogue, McGill Illness Narrative and Cultural Formulation Interview] and care takers and 2 Focus group discussions were conducted with the community members using a FGD guide. All interviews were tape recorded, translated verbatim and analysed through thematic analysis in MAX-QDA 11 software.
RESULTS The community exhibited a mixed response towards people affected by these disorders and their families with more respondents empathetically stressing collective help for them and expressing aversion to discriminatory practices contradicting the negative views of others. They also elaborated on the consequences that negative attitudes and practices will have over the patients and their help seeking behaviour. The patients and their care takers supplemented this with description of their lived experience of the social response to the illness. However, there were a few responses elaborating on the stigmatising attitudes of the community.
CONCLUSION It was concluded through the study that the community members (study area) display an empathetic attitude towards the people and their families. This can be utilised in ensuring optimal uptake of health services addressing the needs of patients and also can be used to form support groups in the community for the families of the patients.
DISCLOSURE Nothing to disclose.

3.3.4. Global faces of challenges with diabetes and hypertension

O.3.3.4.001

A community based model for care and control of type 2 diabetes in rural Western India

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INTRODUCTION Type 2 Diabetes Mellitus (T2DM) has assumed epidemic proportions in India with an estimated patient load of 65 million. Whilst urban areas are reasonably well covered by medical services, public health structures to cope with T2DM are poorly developed or virtually nonexistent in rural areas estimated to have a burden of 3–7.5% of affected population. The use of Community Health Workers (CHWs) placed in rural areas in tackling T2DM is also unexplored even within the National Rural Health Mission.
DESIGN OF MODEL The efficacy of a community based model based on self reporting and self care aided by awareness and accessibility to local clinics and investigation services was tested in a community of 14 000 in rural Pune district of Maharashtra. Six trained CHWs under field supervisors and two clinicians delivered services through rotated clinics in the area. CHWs undertook awareness and screening of blood glucose in high risk individuals and referred them to clinics for confirmation, investigations, treatment and follow ups for glycemic control and complications related to cardiovascular system, retinopathy and other eye problems, renal and peripheral nerve involvement. Lifestyle changes viz. nutrition and physical activity were constantly stressed to patients, carers and community. Investigations were outsourced to reputed institutions in Pune for local action. A detailed health information system was developed for clinical records using MS ACCESS software version 10.
RESULTS Using conventional quality ensured drugs, a 3 year follow up of 219 Type 2 Diabetes Mellitus patients showed acceptable glycemic, lipid and renal values of 63%, 90% and 86% respectively. Hypertension control was achieved in 65% of patients. Favorable outcomes were recorded in patients who were compliant for follow-up, medication and lifestyle changes. Hypoglycemia, patient occupation travel obligations and socioeconomic status emerged as major factors for patient compliance. The latter also had a significant role in determining participation in investigations.
CONCLUSION The model demonstrates an important role of CHWs in T2DM care and control. Their involvement in this setting helped in achieving acceptable levels of glycemic control with basic medication. The sustenance of this control, the link to tertiary care for severe complications and the financial burden to the community over time are factors which will modify the success of such models.
DISCLOSURE Nothing to disclose.

O.3.3.4.002

Environmental tobacco smoke exposure and diabetes in adult never-smokers

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INTRODUCTION Active smoking has been linked to type 2 diabetes mellitus (T2DM) but only few recent studies have shown environmental tobacco smoke (ETS) to be associated with DM in never-smokers. We assessed the association between long term ETS exposure and DM and explored effect modifications of this association in our sample.
METHODS We analysed 6392 participants of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA). We used mixed logistic regression models to assess the cross-sectional association between ETS and DM. Selected variables were tested for effect modification and several sensitivity analyses were performed, mostly treating participants' study area as a random effect.
RESULTS The prevalence of DM and ETS in the sample was 5.5% and 47% respectively. There were 2779 never-smokers with 4% diabetes prevalence. Exposure to ETS increased risk of DM in never-smokers by 50% [95% confidence interval (CI): 1.00, 2.26], and we observed a positive dose-response relationship between ETS exposure level and DM in never-smokers. Associations were strengthened (more than three-folds) by older age ($OR_{interaction} = 5.20$, $P = 0.05$) and chronic obstructive pulmonary disease ($OR_{int} = 3.84$, $P = 0.015$) and were stronger in post-menopausal, obese, hypertriglyceridaemic and physically inactive participants. A history of early childhood infections did not significantly modify the association between ETS and DM in never-smokers ($P > 0.5$), but this association was stronger among those who did not report any childhood infection [OR: 1.53 (0.99, 2.37)] compared to those who reported a childhood infection [OR: 1.31 (0.41, 2.37)]. Estimates of association were robust across all sensitivity analyses. ETS had no substantial associations in current and ex-smokers in our study.
CONCLUSIONS We found a positive association between ETS exposure and DM in never smokers. Additional longitudinal studies involving biomarkers are needed to further explore underlying mechanisms and susceptibilities.
DISCLOSURE Nothing to disclose.

O.3.3.4.003

Are we treating the right people- are we treating the people right? Analysis of patients attending the Diabetes Clinic at Kamuzu Central Hospital, Lilongwe, Malawi

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INTRODUCTION Diabetes Mellitus (DM) prevalence in Malawi, one of the poorest countries globally exceeds the world's average (5.26% vs. 4%) exemplifying double burden

of diseases and posing a challenge to health system and society (1).

METHODS AND MATERIALS We describe demographic characteristics, health status, knowledge, attitude and practice and quality of life (QoL) in patients with diagnosed DM attending the Diabetes Clinic (DC) at Kamuzu Central Hospital in Lilongwe, Malawi from April to May 2014.

RESULTS We recruited a random sample of 271 (30% males) of a total of 1056 registered patients. Mean age and body mass index were 53.4 years and 30 kg/m^2 respectively. 52% had achieved secondary level of education, 16% were formally employed and 11% were retired. Clinically, 77% were classified as type 2 and 23 % as type 1 DM. Mean fasting blood sugar was 166 mg/dl and mean glycated Haemoglobin was 7.1%, about 33.5 % below 6.5%. Most patients (73%) were on oral anti diabetic therapy. Hypertension was the commonest comorbidity detected (61%); it was poorly controlled, followed by chronic kidney disease, peripheral neuropathy (24%) and diabetes retinopathy (20%). Of note 65% of males complained of erectile dysfunction.

Knowledge about the name of the disease depended on level of education but was generally poor as a reflection of absence of structured patient's education / treatment literacy programs.

Perceived QoL was fair.

CONCLUSION DC is predominantly utilised by relatively well off, overweight female patients, some of whom may not have DM but impaired glucose tolerance test. Glycaemic control was good for the majority. The worst off patients may not reach the DC. The group of patients with more complications requires more attention. Constraint resources and potential under provision of diabetic care hampered diagnosis and treatment of complication. This needs to be addressed.

REFERENCE

1. International Diabetes Federation. Diabetes Atlas, 6th edition. 2013.

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O.3.3.4.004

Complications of diabetes and hypertension at a referral hospital in Zimbabwe

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INTRODUCTION The relationship between admission, in-hospital mortality and complications related to hypertension and diabetes in Zimbabwe is not well documented. We examined complications, length of stay (LOS) and mortality among diabetic and hypertensive in-patients at Harare Central Hospital, a public hospital catering predominantly to lower socioeconomic groups.

MATERIALS AND METHODS A retrospective analysis was undertaken of medical records of patients with vascular complications (n = 500), admitted to Harare Central Hospital (HCH) between January 2012 and December 2013. Data regarding in-hospital medical complications, including congestive heart failure (CCF), stroke, renal failure, diabetic complications together with LOS, cost and cause of death were prospectively registered. Data were analysed to determine the complications and cause of deaths for hypertensive and diabetic patients.

RESULTS Of 500 admitted patients, the most frequent diagnoses were hypertension (44%), diabetes (8%), diabetes and hypertension (7%), cardiomyopathy (6%) and gastritis and gastroenteritis (5%). Among diabetic patients, the most common comorbidities were HIV (21%), anaemia (21%), pneumonia (16%) and septicaemia (16%); for hypertensive patients, HIV (18%), pneumonia (11%), cardiomyopathy (8%) and anaemia (7%) were the most common. In-hospital mortality was 36%, with the main causes of death among diabetic patients being stroke (28%), renal failure (14%), and diabetic ketoacidosis (13%), and among hypertensive patients, stroke (47%), CCF (26%) and renal failure (14%). A longer length of stay was significantly associated with diabetes, hypertension and comorbidity ($P < 0.05$). Total admission expense for the patients was US $126, 304, with patients with renal failure, stroke, CCF, and diabetic complications together comprising 95% of admission costs.

CONCLUSIONS Complications related to diabetes and hypertension increase in-hospital mortality and the cost of hospital admission for patients from low-income groups. Public health interventions for prevention, early diagnosis and treatment of chronic diseases like hypertension and diabetes are urgently required to reduce morbidity and mortality.

DISCLOSURE Nothing to disclose.

O.3.3.4.005

Prevalence of hypertension and associated risk factors among diabetes patients in urban Dar es Salaam, Tanzania: a case for integrated care

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BACKGROUND Tanzania is in an epidemiologic transition with an increase in chronic non-communicable diseases (NCDs) such as hypertension (HTN) and diabetes mellitus (DM). Little is known about DM and comorbidities in sub-Saharan Africa. Tanzania has a well-developed system of diabetes clinics which offers the unique opportunity to systematically screen patients with DM for HTN and associated risk factors.

METHODS The study was conducted in eight large diabetes llinics in the three districts of Dar es Salaam during two months between February 17th and April 18th 2014. All DM patients aged 18 years and above attending these clinics had a clinical examination, a measurement of blood pressure (BP) and capillary glycaemia. Additionally, clients were counselled for HIV testing. Hypertension was defined as BP ≥140/90 mmHg based on the eighth Joint National Committee (JNC). We used descriptive statistics and logistic regression models to identify risk factors for hypertension adjusted for sex, body mass index (BMI), type of DM, history of TB, and hyperglycaemia (glycaemia >11.1 mM); presented as adjusted Odds Ratios (aORs).

RESULTS A total of 1,164 DM patients were seen, with a median age of 54 years (interquartile range [IQR] 44–63); 709 (60.9%) were females, and 1,076 (92.6%) had type II DM. The median BMI was 25.9 kg/m^2 (IQR 22.6–29.6). Of 890 DM patients tested for HIV, 22 (2.5%) patients were HIV-infected, and 62 (7%) had a history of previous tuberculosis. The median systolic blood pressure was 130 mm/Hg (IQR 120–145), and the

diastolic blood pressure 80 mm/Hg (IQR 75–90). The prevalence of HTN (>140/90 mmHg) was 23% (95% confidence interval [95% CI] 20.6–25.6), and was significantly higher among type II DM patients compared to type I (24.2% vs. 9.3%, $P = 0.002$). Only 177 (15.2%) DM patients had BP equal-to or lower than 120/80 mmHg. Hypertension was associated with older age above 50 years (aOR 1.7, 95% CI 1.2–2.3, $P = 0.001$) and increased BMI (aOR 1.06, 95% CI 1.03–1.08, $P < 0.0001$).
CONCLUSIONS The results show a high prevalence of HTN among DM patients, which was associated with increasing age and BMI. DM Clinics offer the opportunity to screen and treat NCDs. A comprehensive health care package is needed for DM patients addressing this changing epidemiological profile in Tanzania which calls for integrated care of chronic diseases under-one-roof.
DISCLOSURE Nothing to disclose.

O.3.3.4.006
Tackling NCDs and risk factors in Kyrgyzstan: the impact of community action for health in Kyrgyzstan

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INTRODUCTION When local people assessed the burden of diseases in their community in rural Kyrgyzstan they rated hypertension, iodine deficiency and substance abuse (alcohol and smoking) high on the health agenda. Over the past 12 years the above mentioned noncommunicable diseases (NCDs) and risk factors were tackled through specific health actions and intensive health promotion using Community Action for Health countrywide in more than 1′600 villages covering a population of 3.3 million people. This study shows the impact of this approach on morbidity, mortality and behavior change in the local communities.
METHODS Annual household surveys with questionnaires and individual screening were conducted over the past 12 years by community members. In the first 10 years, a large sample of 10,000 to 30,000 people was used. From 2012 onwards, representative cluster surveys were conducted. The data were entered and analyzed by the Republican Center for Health Promotion in Kyrgyzstan and cross-checked with the National Center for Disease Surveillance.
RESULTS Screening of hypertension increased the awareness and compliance of treatment and contributed to a decrease in cardio-vascular mortality of 5 % over 2 years. The consumption of iodized salt in the communities increased 8 to 28 % in the different oblasts, resulting in decrease of goiter prevalence in school children from 55% in 2004 to 10% in 2008. Higher awareness of alcohol related problems led to changes driven by the community deciding that alcohol should not be offered at public events such as funerals etc.; and this resulted in a 10-20% reduction of alcohol consumption. One hundred anonymous alcoholic groups were established and more than 1,000 persons were fully rehabilitated. Less incidents of domestic violence in families and communities were reported. Health actions on smoking increased the awareness on tobacco related knowledge and behavior. A decrease in family members (65% in 2011 – 60% in 2013) and friends (29% in 2011 – 17% in 2013) of the respondents smoking was seen.
CONCLUSION Health actions, developed with and implemented through the community can successfully tackle NCDs and risk factors. Implemented on a large scale they can contribute to reduce national mortality and morbidity rates.
DISCLOSURE Nothing to disclose.

3.3.5. HIV and comorbidities

INV.3.3.5.001
HIV-associated malignancies in the current era: notes from the epicentre in Sub-Saharan Africa

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Dr. Satish Gopal is Director of the Cancer Program at UNC Project-Malawi, and Principal Investigator of the Malawi Cancer Consortium. In this talk, he will briefly review the changing epidemiology and clinical features of HIV-associated malignancies in the current antiretroviral therapy era, with a particular focus on sub-Saharan Africa. In this part of the world, HIV-associated malignancies are principal causes of cancer morbidity and mortality overall, and exact an enormous burden in countries with often extremely limited capacity for cancer prevention, diagnosis, treatment, and palliation. By reviewing relevant literature from sub-Saharan Africa as well as ongoing work in Malawi specifically, possible approaches to address cancer in the region by building on progress against HIV will be proposed.
DISCLOSURE Dr. Gopal has received fellowship research funding from Bristol-Myers Squibb and has served on the Novartis Breast Cancer Advisory Group for Southern Africa.

O.3.3.5.002
Assessing the global coverage of antiretroviral and cotrimoxazole prophylactic therapies among HIV/TB co-infected patients

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INTRODUCTION Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS) and Tuberculosis (TB) are among the foremost diseases of poverty and leading causes of deaths globally. Patients with advanced HIV infection are vulnerable to opportunistic infections such as *Pneumocystic jirovecii pneumonia* but this particular infection can be prevented with the use of prophylactic cotrimoxazole. Monitoring the level of progress of treatment coverage is essential in attaining the Millennium Development Goal (MDG) 6. This study seeks to evaluate the progress made in the treatment and care of people living with HIV who are also co-infected with tuberculosis (TB) globally.
METHODS AND MATERIALS Data were obtained from the World Health Organization (WHO) Global Tuberculosis Report 2014. Percentages of HIV positive TB patients who are on antiretroviral therapy (ART) and those on cotrimoxazole prophylaxis therapy (CPT) in Africa, the Americas, Eastern Mediterranean, Europe, South- East Asia, Western Pacific regions and globally were analysed. The data obtained and analysed were that of 2005, 2010 and 2013 using a one-way independent analysis of variance (ANOVA).
RESULTS Globally, the percentages of HIV positive TB patients who are on ART increased from 35% (2005) to 46% (2010) and 70% (2013). However, the percentages of those on CPT increased progressive from 77% (2005) to 81% (2010) and 85%

(2013). Among the six WHO regions evaluated, ART percentage use increased from 34% (2005) to 61% (2013); while CPT percentage use increased from 35% (2005) to 66% (2013). The data was analysed with a one-way independent ANOVA to compare the treatment coverage in 2005, 2010 and 2013. The ART coverage result was significant, $F(2, 15) = 3.76$, $P = 0.0475$. CPT coverage was also significant, $F(2, 15) = 4.53$, $P = 0.0289$.

CONCLUSIONS There has been a progressive increase in the coverage of ART and CPT among HIV/TB co-infected individuals in the six WHO regions. This significant coverage will help in reducing progression to advanced stages of HIV/AIDS, development of resistant TB, incidence of opportunistic infections such as *Pneumocystic jirovecii pneumonia* and subsequently lead to better quality of life. These progressive treatment coverages are very pivotal in achieving the global goals of WHO, the MDGs and the post- 2015 global development agenda.

DISCLOSURE Nothing to disclose.

O.3.3.5.003

Influence of TB lineage on drug resistance and HIV comorbidity in Ghana

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BACKGROUND The two most important factors greatly hampering the control of TB are HIV pandemic and drug resistant strains.

METHOD Standard genotypic classification into main lineages circulating in Ghana (MTBss and Mafric) were done in a stepwise manner: Species classification by TaqMan-based SNP-typing, large sequence polymorphisms (RD 9, 711 and 702) typing, while spoligotyping was used for sub-lineage determination. Associations between the different phylogenetic lineages of MTBC and epidemiological variables were assessed using univariate and multivariate logistic regression.

RESULTS We genotyped 1305 isolates; 927 (71.0%) belonged to Lineage 4 (Euro-American), 164 (12.6%) to Lineage 5 (*M. africanum* West Africa I) and 120 (9.2%) to Lineage 6 (*M. africanum* West Africa II). Sixteen isolates (1.2%) belonged to Lineage 1 (includes EAI), 53 (4.1%) to Lineage 2 (includes 'Beijing'), 14 (1.1%) to Lineage 3 (includes CAS) with the remaining 11 (0.8%) isolates identified as *M. bovis*. Compared with our previous study, this study saw a significant increase in the proportion of Lineage 6 (*M. africanum* West Africa II) isolates from 19 /613(3.1%) to 120/1305 (9.2%) $P = 0.000$. Stratifying by lineage, we found *M. africanum* West Africa II more likely to be found among HIV positive TB patients (adjusted odds ratio (adjOR) = 2.4; 95% confidence interval (CI): 1.4–3.9) $P < 0.000$) and associated with isoniazid resistance adjusted odds ratio (adjOR) = 4.3; 95% CI: 1.6–17.9 $P = 0.01$). Further analysis showed no significant association between MTBC lineage and patient age, gender, prior BCG vaccination, or bacterial burden estimated by the degree of sputum smear positivity.

CONCLUSION Our findings confirm the importance of *M. africanum* in West Africa. This is particularly worrying for a region unique to *M. africanum* with high prevalence of HIV comorbidity and high isoniazid resistance.

DISCLOSURE Nothing to disclose.

O.3.3.5.004

Metabolic disorders among adult patients on anti-retroviral therapy in rural Southern Africa - a cross-sectional multi-center study in rural Lesotho

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BACKGROUND HIV infection as well as anti-retroviral therapy (ART) may predispose for impaired glucose metabolism and dyslipidemia. However, data on metabolic disorders among persons on ART in rural African settings are still limited. This cross-sectional survey assesses prevalence of and risk factors for metabolic disorders among adult patients on first-line ART in Lesotho, Southern Africa.

METHODS Data derive from the study *Comorbidities and Virologic Outcome among Patients on ART in rural Lesotho (CART-1, NCT02126696)*. Patients aged ≥ 16 years on first-line ART ≥6 months were enrolled. Screening for diabetes mellitus (DM) and impaired fasting glucose (IFG) was done with random blood-sugar measurement (RBS). In case of RBS ≥5.6 mM, glycosylated hemoglobin (HbA1c) was measured. Definitions of IFG and DM were HbA1c 6.0–6.4% and ≥6.5% respectively. HbA1c and lipid-panels for screening for an elevated LDL/HDL cholesterol ratio were measured using Roche Cobas 101 point-of care technology. Risk factors were assessed using univariate logistic regression for clinical and socio-demographic patient characteristics. Variables showing significant association in univariate analysis were subsequently tested in a multivariate logistic regression reporting adjusted odds-ratios (aOR).

RESULTS Lipid-panels and RBS/HbA1c-values were available from 1165 patients (66.1% female). Median age was 44 years (interquartile-range: 35–54). Overall DM prevalence was 0.94% (95% CI: 0.47–1.7), prevalence of IFG was 1.6% (0.9–2.5) with no significant difference between genders. In multivariate analysis higher age (aOR: 1.05, 95% CI: 1.02–1.09), higher wealth quintile (1.9, 1.3–2.6), being employed (1.6, 1.1–2.5) and abdominal obesity (2.9, 1.3–6.7) were significantly associated with presentation of IFG or DM. Prevalence of LDL/HDL–ratio ≥3.0 was 14.2% (95% CI: 10.9–18.0) among men and 9.6% (7.6–11.9) among women. Women (aOR: 0.59, 95% CI: 0.38–0.95), patients with viral suppression (0.53, 0.30–0.95) and patients on efavirenz (versus nevirapine: 0.46, 0.27–0.79) were less likely and patients with a higher wealth quintile (1.27, 1.11–1.45) more likely to have a LDL/HDL-ratio ≥3.0.

CONCLUSION Prevalence of IFG or DM was low in this rural cohort on first-line ART. But more than one out of ten had an elevated HDL/LDL cholesterol ratio. Men, patients on nevirapine and wealthier persons were at particular risk and may be prioritized for screening in case of limited access to lipid-panel testing.

DISCLOSURE Nothing to disclose.

O.3.3.5.005

Female genital schistosomiasis and human immunodeficiency virus infection: a systematic literature review

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INTRODUCTION Schistosomiasis affects more than 200 000 000 persons worldwide, 90% living in Sub-Saharan Africa. Female Genital Schistosomiasis (FGS) is a frequent, yet neglected, manifestation of the infection with *S. haematobium*. Prevalence of FGS in different Sub-Saharan countries can vary from 33% to 75%. FGS is associated with substantial morbidity in the lower and upper female genital tract of girls and women and is associated with pain and bleeding during sexual intercourse.

African women are particularly vulnerable to Human Immunodeficiency Virus (HIV) infection and female genital schistosomiasis (FGS) could be an important risk factor for its acquisition.

This study aimed to examine the published literature on the association of FGS and HIV infection.

METHODS AND MATERIALS We searched the usual medical databases for published grey and peer-reviewed articles using the key words: HIV, AIDS, schistosomiasis, *Schistosoma haematobium* and bilharzia. Articles mentioning schistosomiasis and HIV were retained for analysis. In addition, identified articles were screened for references on the topic of interest and if relevant were included in the review. The references were listed and then grouped according to the research question.

RESULTS A number of epidemiological studies supported FGS being a risk factor for HIV infection: Kjetland et al (2006) found in Zimbabwe an HIV prevalence of 41% (29/70) in women with laboratory proven genital schistosomiasis compared to an HIV prevalence of 26% (96/375) in a schistosomal ova negative control group (OR 2.1; 95% confidence interval (CI), 1.2–3.5; $P = 0.008$). Down et al (2011) showed that FGS was associated with HIV infection (OR = 4.0, 95% CI = 1.2–13.5). Ndeffo Mbah et al (2013) has shown in a study covering several African countries that each infection wit*h S. haematobium* per 100 women was associated with a 2.9% (95% CI: 0.2–5.8%) relative increase in HIV prevalence. Other aspects of the interaction of these two infections will be further reported.

CONCLUSIONS Increasing evidence is available supporting the hypothesis that schistosomiasis, in particular *S. haematobium* infection, is linked with a higher risk of HIV infection. Knowing that schistosomiasis is one of the top ten most important diseases in the world and in particular in sub-Saharan Africa, schistosomiasis treatment could be important in preventing HIV infections.

DISCLOSURE Nothing to disclose.

3.4.1. Environmental health problems from different global perspectives

O.3.4.1.001

Challenging the global health threat of air pollution

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According to the Global Burden of Disease 2010, ambient air pollution belongs to the top ranking causes of morbidity and mortality in the world. Whereas air quality improved in most high income countries (HIC) in the past 30 years, heavily polluted cities in low to middle income countries (LMIC) have seen opposite trends as monitoring efforts, health research and policy making lag substantially behind the public health needs. In light of the dominant role of this environmental exposure and the well-proven ability to abate air pollution, the global health community need to tackle these challenges. Five key pillars need to be developed and sustained by local experts to globalize the clean air agenda in line with the WHO Guidelines:

1 Air pollution measurements need to be part of sustained and standardized monitoring networks, providing good quality data that are freely accessible for air quality modelers, health researchers, risk assessors, policy makers and the public alike.
2 Local expertise in epidemiologic research methods linking air quality data with health registry data to evaluate acute effects of air pollution needs to be developed through international research collaborations.
3 Compared to high income countries, air pollution in LMICs may consist in different mixtures of pollutants and originate from rather different sources. Moreover, local populations may have poorly comparable co-morbidities and susceptibility patterns. Therefore, research findings from HICs may not be generalizable globally. LMIC's need local research capacity to understand and communicate the role of air pollution for public health.
4 Results from epidemiological studies, local data on health status, and information about air quality need to be combined to provide estimates of the local public health burden attributable to air pollution as well as the benefits of clean air policy scenaria.
5 Expertise in the development and implementation of local air quality management plans need to be shared through international collaborations and globally adopted best available emission standards.

The Global Health research community has a vital role in fostering all five pillars locally and internationally to promote evidence based environmental policy making to protect public health. Examples and successes stories will be discussed in the five domains and put in context of research needs in LMICs.

DISCLOSURE Nothing to disclose.

O.3.4.1.002

Integrating environmental home-based interventions to improve the quality of household air, drinking water and hygiene in rural Peru: community-randomised controlled trial

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INTRODUCTION Diarrhoea and acute lower respiratory infections are leading causes of ill child health. Low-cost interventions have proved effective in reducing child diarrhoea and pneumonia. An integrated package provides opportunities for synergism. We conducted a community-randomised controlled trial in 51 rural communities in Peru to evaluate an environmental home-based intervention package (IHIP) reducing acute respiratory infections and diarrhoeal disease in children under 36 months of age.
METHODS Six months prior to the start of the interventions, ie. a ventilated improved cookstove (ICS), a kitchen sink with a water faucet and solar disinfection of drinking water (SODIS) method were developed and installed together with beneficiaries of the intervention arm. To reduce potential impact of non-blinding bias, the control arm received a comparison intervention comprising a psychomotor early child development intervention focusing on the mother-child daily playing interaction with age and stage-appropriate toys. Diarrhoea and respiratory (weekly) surveillance was done at home during a 12-month period and ECD assessments at baseline and end-of-study.
RESULTS We randomised 51 communities and enrolled 534 children. Baseline characteristics were balanced between study arms. The rate of diarrhoeal episodes in children in the intervention was 2.8 episodes per child per year as compared to 3.1 episodes in the control arm. The relative rate was 0.78 (95% CI: 0.58–1.05). Similarly, care takers in the intervention group reported fewer days of diarrhoea (mean 4.9 vs. 6.4 days per year; OR: 0.71, 95% CI: 0.47–1.06). No effect on acute lower respiratory infections was observed. The home-based ECD intervention effectively improved child development in all age-specific developmental milestones tested. Compared to the IHIP intervention arm we observed the biggest difference in child fine motor skills (62% vs. 39% scoring above the mean of the age specific group, OR: 2·6, 95% CI: 1·7–3·9). An evaluation 24 months post study end revealed not only a 90% user rate of ICS and kitchen sinks but also a 27% auto-dissemination beyond study homes.
CONCLUSION We found evidence that integrated home-based strategies can improve child health and development outcomes and are sustainable if addressing household needs. The findings of this study support two Peruvian national programmes on clean cooking and early child development focusing newly on household based implementation.
DISCLOSURE Nothing to disclose.

O.3.4.1.003

The impact of hormonally active pesticides on the health of vulnerable communities in South Africa

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INTRODUCTION Dichlorodiphenyltrichloroethane (DDT) is used for malaria control and many current agricultural pesticides are hormonally active. A study investigating reproductive health effects of DDT on male vector control workers and one that investigated the effect of agricultural pesticide exposure on pubertal growth of boys in South Africa is described.
METHODS AND MATERIALS The DDT study was a cross-sectional study of 60 workers from 3 camps situated near the Malaria Control Center (MCC). Tests included a questionnaire, a physical examination, blood reproductive hormones, semen quality and serum DDT metabolites. The agricultural study was a cross-sectional study of 269 boys including 176 boys residing on farms and 93 not residing on farms. Tests included a questionnaire, clinical assessment of sexual maturity development according to Tanner Stage, anthropometric measurements including height, weight and BMI of boys, and reproductive hormones in blood.
RESULTS In the DDT study, associations between DDT exposure measures (years worked at MCC and DDT metabolites) and reproductive outcomes were weak and inconsistent. The strongest association was a linear regression relationship between baseline estradiol and p'p' DDT (= 1.14 ± 0.33 pg/ml/mg/g lipid, $P = 0.001$, $R^2 = 0.31$, $n = 46$; adjusted for age and sex hormone binding globulin). In the agricultural study, farm boys were shorter (Regression coefficient (RC) = −3.42 cm; 95% confidence interval(CI): −6.38 to −0.45 cm); lighter (RC = −2.26 kg; CI: −4.44 to −0.75 kg); had lower serum lutenizing hormone (RC = −0.28 IU/l; CI: −0.48 to −0.08 IU/l); and had higher serum oestradiol (RC = 8.07 pM; CI: 2.34 – 13.81 pM) and follicle stimulating hormone (RC = 0.63 IU/L; CI: 0.19 – 1.08 U/l).
CONCLUSIONS In the DDT study, an overall anti-androgenic mechanism best explains the results, but with a number of inconsistencies. The agricultural study provides evidence that environmental exposure to pesticides is associated with adverse reproductive and developmental effects in boys.
DISCLOSURE Nothing to disclose.

O.3.4.1.004

Assessment of drinking water quality based on chemical and microbiological parameters in rural Bangladesh

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INTRODUCTION Public health in Bangladesh is at risk due to increased urbanization, industrialization and associated environmental pollutions. Children are more vulnerable than the adults living in such polluted environment because of their low preventive capacity to pollutants. The water, sanitation and hygiene (WASH) program of Bangladesh Rural Advancement Committee (BRAC) has been providing interventions in 250 rural sub-districts since 2006 with the aim of improving health of the rural poor. The aim of the present study is to assess quality of drinking water in terms of chemical and microbiological water parameters.

METHODS AND MATERIALS Arsenic of drinking water at sources (tubewell) was tested using arsenic test kit in 24 sub-districts of Bangladesh. A portable pH meter was used to test water pH. Results of arsenic test kit and pH meter were validated in the laboratory. For laboratory test, we collected 293 water samples from 12 out of 24 sub-districts. Other chemical parameters such as iron, manganese and salinity were tested in the laboratory. A total of 160 water samples were collected to test fecal coliform in drinking water at source and point-of-use from the nearby sub-districts of Dhaka so that water samples could be sent to laboratory within 12 h after collection.
RESULTS Drinking water at sample sites was found slightly alkaline (7.4 ± 0.4). Manganese concentration varied from 0.1 to 5.5 mg/l with a mean value of 0.3 mg/l. Excess chloride concentration in drinking water was found in coastal sub-districts. Both field and laboratory test results showed that arsenic in groundwater exceeded Bangladesh standard (0.05 mg/l) in *Shibchar*. About 57.5% and 7.5% of water samples collected from tubewells (sources) and consumption points were found free from fecal contamination implying that a large proportion of households' drinking water became contaminated in-between stages. Out of the total sample sites, majority of the households (67%) had poor quality water for drinking based on water quality index (WQI) value.
CONCLUSIONS The existing gap in drinking water quality at source and point-of-use implies fecal contamination in-between stages. Hygienic management of drinking water sources and monitoring of human activities surrounding those sources are imperative to improve water quality. Building awareness about water pollution and hygienic management of drinking water at each point from source to consumption can be beneficial to health.
DISCLOSURE Nothing to disclose.

O.3.4.1.005

Environmental contamination and effect on domestic animals in relation to rubber plantation activities in Eastern Thailand

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Rubber is an important commercial crop in Thailand. Intensive use of land for cultivation, application of chemical fertilizers and herbicides, and disposal of waste water upon processing rubber sheets may pollute the environment. This study aims to assess the environmental impact on health related to rubber plantation activities in Eastern Thailand. Water samples, i.e., drinking and utility water, collected from households located in rubber plantation areas, including waste water from rubber sheet processing, were assessed for physical, biological and chemical contamination. Soil samples collected from rubber plantations were evaluated for microorganisms and selected heavy metal level. Chemical fertilizers used in rubber plant cultivation and other chemicals used in rubber plantation processing were also recorded. In addition, blood samples of domestic dogs living in this area were evaluated for heavy metal residues. In total, 82 water samples from 109 visited rubber plantations were collected. Biological and chemical contaminants in ground water and water from natural reservoirs used in households were evaluated. Ground water samples demonstrated *E. coli* contamination over standard level (29%). They were also contaminated with *Salmonella spp* (1.9%). Chemical contaminations found were iron (11.5%), manganese (11.5%), magnesium (3.9%), nitrate (3.1%), and ammonia (13.5%). Water from natural reservoirs was contaminated with *E. coli* (8.7%) and *Salmonella spp*. (4.4%) while chemicals detected were iron (60.9%) and ammonia (56.5%). Waste water was found to be highly contaminated with *Salmonella* spp. (87.5%). Concentration of selected heavy metals such as lead, manganese, nickel and cadmium in water and soil did not exceed the reference values. However, blood samples from domestic dogs found high concentration level of manganese (100%), nickel (76.9%) and cadmium (54.5%). Chemical fertilizers and herbicides were periodically used in rubber plantations where improper self protection and low awareness on chemical contamination in labour workers were recognized. Environmental contaminations were detected in rubber plantation areas. The quality of water in some rubber plantations was not appropriate for drinking or other domestic usage. Education regarding chemical use, self protection and sanitation targeting rubber workers and owners should be implemented together with periodically follow-up on environmental impact assessment.
DISCLOSURE Nothing to disclose.

O.3.4.1.006

Endocrine disruptors and women reproductive health: the case of bisphenol-A and breast cancer

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Breast cancer is a world-wide leading cancer of women. Indeed, each year, over a million women worldwide are diagnosed with breast cancer, accounting for 25% of all female cancers. Across the environmental contaminants, particularly, endocrine disrupting chemicals (EDCs) have been emphasized for over a decade due to their risks of increasing cancers in reproductive systems. The estrogen-mimic bisphenol A (BPA) as an EDC is a synthetic phenolic compound which people is exposed to frequently via different exposure routes and raising concerns about potential effects on breast tissue and breast cancer risk. There are few epidemiological studies about association between urinary BPA concentration and breast cancer. Therefore, we focused on the effects of BPA exposure on type of breast cancer (benign and malignant) and performed biomonitoring of BPA in breast cancer patients and controls ($N = 45$). This case-control study included patients with malignant breast mass ($N = 15$), benign breast mass ($N = 15$) and women with normal breast (controls, $N = 15$). Mean age of the 45 participants was 44.3 ± 11.5 years, with a range of 19 to 71 years. The effect of urinary concentration of BPA on breast cancer was tested using multinomial logistic regression models.

Overall, results have shown a strong positive association between urinary concentration of BPA and both benign and malignant breast masses [OR = 2.14 (CI: 1.04–4.42) and OR = 2.27 (CI: 1.09–4.72) respectively], although other included covariates were only significantly associated with increased risk of benign breast mass. BPA exposure was associated with breast

cancer but, given inconsistencies with previous findings for other study populations, results should be interpreted with caution. Future independent replication and follow up studies are needed to confirm or disprove these findings. If the results of this research would be confirmed in future prospective studies, reducing BPA exposure may play a role in the prevention and reduce of breast cancer incidence.
DISCLOSURE Nothing to disclose.

3.4.2. Resistant bacteria and viruses in a mobile world

O.3.4.2.002

Detection of hospital acquired infections and antibiotic selection in neonatal ICU in El-Husain University Hospital

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Although nosocomial infection is not a recent problem, It continues to be a major world wide public health problem especially between the neonates in the NICU.
AIM The aim of this study was to estimate the incidence of nosocomial infections in the NICU in EL-Husain University Hospital, identification of the causative organisms and their antibiotic susceptibility pattern, studying the various factors influencing hospital acquired infections in neonatal intensive care unit.
MATERIAL AND METHODS This study was conducted on 300 NICU patients randomly selected from NICU in EL-Husain University Hospital. Infections appeared after 48 h of admission were the subject of this study.

For every neonate, personal and family history were taken from the mother and clinical examination was performed.

Nasal, throat, and umbilical swabs were taken from every neonate once admitted to the NICU and another swabs were also taken if any symptoms or signs denoting presence of infection appeared. The later samples were taken according to the site of infection. If bacteraemia, a blood sample was taken.
RESULTS Results of the study showed that the incidence of NIs was 20% where the incidence was significantly higher in VLBW neonates when compared with LBW and NBW groups. The mortality rate with NIs was twice of that without NIs.
CONCLUSION The study showed that invasive procedures played an important role as a risk factors of NIs in the NICU including venous catheter placement, IV fluid, and ventilator. Also, very low birth weight and prolonged hospital stay constitute very important risk factors. Neonates in NICU are at high risk for development of nosocomial infection. Nosocomial infection surveillance in NICU must be done periodically to put a new policy depending on the scientific collective data.
KEYWORDS nosocomial infection, neonatal intensive care unit.
DISCLOSURE Nothing to disclose.

O.3.4.2.003

Possible nosocomial transmission as a cause of secondary infection and healing delay of Buruli ulcer wounds

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INTRODUCTION We identified secondary infection of Buruli ulcer (BU) wounds as a cause of wound healing delay. To gain understanding into possible routes of infection, we characterised *Staphylococcus aureus* isolates from patient lesions and the environment of two Ghanaian health centres.
METHODS AND MATERIALS Hundred and five *Staphylococcus aureus* isolates were isolated from wounds (97, 92.3%) and the hospital environment (8, 7.6%) by microbiological culture and characterised by the spa gene, *mecA* and the Panton-Valentine leukocidin (*PVL*) followed by spa sequencing. Antibiotic susceptibility of the isolates to commonly prescribed antibiotics was performed by Kirby-Bauer disc diffusion method.
RESULTS Spa typing and sequencing of the gene from 91 isolates identified 29 different spa types; t355 (ST152), t186 (ST88), and t346 with 7 (7.6%) isolates each dominating. While many distinct strains were isolated from both health centers, health center clustering was also identified. Among the clustered strains were isolates from three different lesions of one patient, which had the same spa type (t2500). Also identified was a group of related strains from one health center isolated from samples taken on the same day from the hand of a health care worker and three patients dressed consecutively by this worker. Twenty four (22.8%) isolates were identified as MRSA by typing of the mecA gene and this correlated with phenotypic results, however the gene was also detected in 7 isolates showing susceptible phenotypic results and could be considered borderline resistant strains. PVL was identified in 67(63.8%) of the isolates, 20 (29.8%) of which were MRSA. Frequencies of resistance to selected antibiotics were: Erythromycin 56 (55.4%), Tetracycline 62 (61.3%), Amikacin 13 (12.8%), Rifampicin 46 (45.5%) and Streptomycin 32 (31.6%).
CONCLUSION Our findings indicate that nosocomial transmission contributes to BU wound infection and calls for training in aseptic training to prevent the occurrence of epidemics of nosocomial MRSA.
ACKNOWLEDGEMENTS This project was supported by the Stop Buruli Initiative funded by the UBS-Optimus Foundation.
DISCLOSURE Nothing to disclose.

O.3.4.2.004

Device-associated infections at El-Salam Hospital in Cairo

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BACKGROUND Device-associated infections (DAIs), particularly ventilator-associated pneumonia (VAP), venous catheter-related bloodstream infection (CABSI), and catheter-associated urinary tract infection (CAUTI) pose the greatest threat to hospitalized patients.
OBJECTIVES To identify the most common organisms and major invasive medical devices (CAUTI, VAP, and CABSI) related to nosocomial infection at El-Salam hospital.

This study was conducted on 200 patients during the period from March to October 2010. Patients were 108 males (54%) and 92 females (46%) with mean age of 50.6 (± 13.5) years. Cases were selected and device-related nosocomial infections typed according to the definitions provided by the Nosocomial Infections Surveillance System .

This study revealed that catheter-associated urinary tract infections (CAUTI) were the most prevalent (114 cases), followed by ventilator-associated pneumonia (VAP) with 49 cases, and lastly venous catheter-associated bloodstream infections (CABSI) with 37 cases.

In the present study, the organisms isolated were; *E. coli* (76), *Staph. aureus* (21), *Coagulase -ve staph.* (21), *Kl. pneumoniae* (21), *Enterococci spp.* (17), *Pseudomonas aeruginosa* (11), *Proteus vulgaris* (6), *β-hemolytic strept.* (4), *St. pneumonia* (4), *N. meningitides* (3), *Hemophilus influenza* (3), *Sph. paucomobilis* (2), *Yers. enterocolitica* (2), and *Citrobacter freundii* (2). The isolated pathogens were identified by standard techniques.

The results of this study revealed that *E. coli* was the most common organism causing CAUTI (54.4% CAUTI cases), followed by *Kl. pneumonia* (9.6%) and *Coagulase -ve staph.* (6.1%). The commonest organism causing VAP was *Staph. aureus* (16.3%) of VAP cases), followed by *Kl. pneumonia* (14.3%) and *E. coli* (12.2%). The commonest organism causing CABSI was *Coagulase -ve staph.* (38% of CABSI cases), followed by *Staph. aureus* (16.2%) and *Pseudomonas aeurginosa* (8.1%).

The most effective antibiotic against isolated organisms in general was Augmentin. The second was Ofloxacin. A pattern of resistance to a wide range antibiotics was observed in the isolated strains (Gram positive and Gram negative) which might be attributed to misuse and overuse of antibiotics.

Results of the study show the lack of adherence to proper infection control practices and the absence of guidelines for antibiotic usage at the site of the study.

CONCLUSION Device-related infections constitute a major source of morbidity and mortality in hospitalized patients. The continued occurrence of device-related infections despite infection control measures indicates the need of assessment of each potential preventive measure to ascertain its efficacy.

DISCLOSURE Nothing to disclose.

O.3.4.2.005

Analysis of prescription behaviour and structural barriers for rational use of antibiotics at a tertiary hospital in Malawi

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INTRODUCTION Antibiotic resistance is of growing global concern. The high burden of infectious diseases coupled with constraints in resources makes developing countries more vulnerable. Patterns of hospital-based prescription and consumption of antibiotics constitute one important factor for potential resistance development.

This study examines determinants of antibiotic prescription in relation to pharmaceutical supply and demand chains, planning and monitoring processes, and prescription behaviors among clinicians of the Medical and Pediatric Department at Kamuzu Central Hospital (KCH) in Lilongwe, Malawi.

METHODS The study employed a cross-sectional mixed methods research design. In total, twenty-six clinicians and the head pharmacist were interviewed. Participatory observation was applied from admission to therapeutic decision-making. Registers, clinical guidelines, diagnosis records, drug ordering forms, stock cards and 835 prescription cards were investigated. Data was collected from May 2014-April 2014.

RESULTS We found insufficient processes for internal supply chain management, as well as unclear documentation of diagnoses and prescribed doses of antibiotics. The pharmacy relies on poor data for procurement, and drugs ordered through the system frequently do not match the demand. Finally, diagnostic support through laboratory test was limited. Prescription behavior followed a pragmatic approach that prescribes what is available and not necessarily based on the guidelines or skepticism towards outdated guidelines. Antibiotics accounted for 62% of all prescriptions and 31% of the total hospital medicine expenditure. Among outpatients, amoxicillin was the most consumed antibiotic.

CONCLUSION Despite a high proportion of infectious diseases among inpatients and outpatients, rational use of antibiotics is compromised from multiple angles: high workload, presumptive treatment, inconsistent supply and erratic procurement systems amongst others. The results demonstrate the tight linkage between health systems organization and the emergence of wider antibiotic resistance. Structural changes are needed to ensure effective antibiotic care today and to save it for future patients.

DISCLOSURE Nothing to disclose.

3.4.3. Management of protozoal and helminthic pathogens in travellers

O.3.4.3.002

Asymptomatic carriage of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in travelers returning from Southern Asia: trends over time

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INTRODUCTION Numerous recent studies have identified international travel as a risk factor for colonization and infection with extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*. High colonization rates have been reported, especially for travellers returning from South and Southeast Asia. Besides destination, several other risk factors have been identified: travellers' diarrhoea, use of antibiotics, length of stay, visiting friends and relatives and eating ice cream and pastry. Even though increasing colonization rates in the community over the past years have been shown for all continents, there are no data on temporal changes in colonization rates in travellers.

METHODS AND MATERIALS Data from three different studies carried out between 2009 and 2013 in Finland, the Netherlands and Switzerland were pooled and analysed. All studies investigated colonization rates with ESBL-producing *Enterobacteriaceae* and associated risk factors in travellers returning from different countries in South Asia.

RESULTS Data on 271 travellers were available for this analysis. In travellers returning from Southern Asia, the travel-associated colonization incidence increased significantly from 53.5% in 2009 (95% CI 38.9–67.5) to 69.5% in 2013 (95% CI

62.3–75.8%, $P < 0.05$). Focusing on travellers who had visited India during their trip, the colonization incidence increased from 57.9% (95% CI 42.2–72.1) to 86.1% (95% CI 76.3–92.3, $P < 0.001$).

CONCLUSIONS Within less than 5 years, the colonization incidence with ESBL-producing *Enterobacteriaceae* in travellers returning from Southern Asia has increased considerably. Similar developments might be expected for other travel destinations as well, suggesting a further increase in the influx of multidrug resistant bacteria into low-endemicity settings through international travel.

DISCLOSURE Nothing to disclose.

O.3.4.3.003

Surveillance for enteropathogenic bacteria, protozoa and helminths in travellers returning from the tropics

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Diarrhoea is one of the most common clinical conditions associated with travelling to tropical regions. Bacteria but also protozoa are usually the causative agents. However, the significance of intestinal protozoa such as *Blastocystis hominis* or *Dientamoeba fragilis* is still under discussion and remains to be determined. The aim of this study was to assess whether multiplex PCR methods are able to reduce the percentage of unresolved cases and to analyse a possible association between symptoms and the detection of *Blastocystis hominis*.

Datasets of 565 patients that presented at the outpatient department of the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany between 2006 and 2010 were investigated. All patients underwent stool examinations for screening purposes or because of diarrhoea. After concentration methods for intestinal parasites microscopy was done. In addition, two real-time multiplex-PCR assays were performed targeting *Entamoeba histolytica*, *Entamoeba dispar*, *Giardia duodenalis* and *Cryptosporidium* spp., or *Salmonella* spp., *Shigella*/EIEC spp., *Campylobacter jejuni* and *Yersinia*.

A total 368 patients presented with diarrhoea and associated symptoms such as meteorism, cramps, nausea, vomiting and/or fever. 36% ($n = 135$) tested positive for bacteria or parasites, of which 58 % ($n = 79$) had a known enteropathogenic potential. Stool microscopy and bacterial culture identified 14% ($n = 55$) of all cases. In patients without diarrhoea ($n = 196$), 41% ($n = 80$) were positive for the investigated bacteria and protozoa, but only 9% ($n = 19$) of these cases harboured agents of pathogenic potential. Association with clinical symptoms was found for infections with *Shigella* spp./EIEC spp. (RR = 1.4, 95% CI: 1.2–1.7, $P = 0.012$) and *Campylobacter jejuni* (RR = 1.4, 95% CI: 1.2–1.7, n.s.), but not with *Blastocystis hominis* or *Giardia duodenalis*. *Blastocystis hominis* was even more frequent in asymptomatic [$n = 36$ (18%)] than in symptomatic [$n = 23$ (6.3%), RR = 0.5, 95% CI: 0.4–0.7, $P < 0.0001$] travellers. *Dientamoeba fragilis* was rare [($n = 4$) in asymptomatic ($n = 5$) in symptomatic].

The use of PCR markedly increases the detection of intestinal pathogens But only in one third of all patients a potential infectious cause could be identified. This study does not support *Blastocystis hominis* as a causative agent for acute or prolonged diarrhoea.

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DISCLOSURE Nothing to disclose.

O.3.4.3.004

Validating parasitological tests – not an easy task

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INTRODUCTION Diagnostic laboratories are increasingly faced with demands of documentation of the reliability of test results. Obtaining information on basic performance parameters such as reproducibility and factors contributing to inaccuracy should be a simple matter for well-established methods such as microscopy for malaria and faecal parasites. However, in our work on becoming accredited according to DN/EN ISO 15189 we encountered a striking lack of standards for acceptable performances.

Here we have focused on two analyses: detection and identification of parasites in faecal samples and estimation of parasitaemia in blood with *Plasmodium falciparum*. For both analyses we used techniques that have been golden standards for decades.

METHODS AND MATERIALS We used samples provided by UK NEQAS as part of an ongoing quality assurance programme. For blood parasitology the sample format is blood film on glass slides. For faecal parasitology the samples are formalin fixed suspensions of human faeces, fixed smears and others, depending on the parasites. Formalin fixed suspensions are stained with an iodine-stained wet-mount preparation and with modified a Ziehl-Neelsen stain when *Cryptosporidium* species, *Isospora belli,* or *Cyclospora cayetanensis* may be suspected.

Our reported results were compared to expected findings. In order to estimate inter-observer variation 32 trained microscopists examined five Giemsa-stained thin blood smears, with varying numbers of *P. falciparum*.

RESULTS Despite intensive literature search we did not find evidence-based recommendations for acceptable levels of reproducibility of parasitological analyses. Neither did we find systematic analyses of factors contributing to inaccuracy.

Our reported results of faecal and blood examination showed excellent performance when compared to the expected findings. However, the variation in estimating parasitaemia of *P. falciparum* between observers was surprisingly high.

CONCLUSIONS Despite a high inter-observer variation in estimation of parasitaemia, our reported results of external quality assurance samples showed excellent performance. The acceptable levels of variation in quality control material are often based on expert evaluation with an option of changes when many participating laboratories deviate from acceptable intervals. If all laboratories reach average observations that are close to the expected values the true inter-observer variation is never estimated. Further documentation is needed.

DISCLOSURE Nothing to disclose.

O.3.4.3.005

Nitroimidazole-resistant *Giardia intestinalis* in European travellers and migrants

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INTRODUCTION Persistence of *Giardia intestinalis* after treatment with nitroimidazoles represents a common problem in travel clinics. This study is aimed to describe the epidemiological characteristics of a population attending tropical disease units with giardiasis and to estimate the prevalence of refractory *G.intestinalis*.
METHODS A prospective observational study was conducted in three tropical disease units in Barcelona from 2012–2013 including patients with giardiasis confirmed microbiologically. Polymerase chain reaction (PCR) technique was performed in faecal samples to determine the genotype of *Giardia*. Risk factors associated with refractory giardiasis were evaluated.
RESULTS 77 patients were included in the study, 41 (53.3%) were male and 22 (29%) were < 18 years-old. Twenty-eight (%) were migrants, including 7 visiting friends & relatives, 41 (%) were European travellers who had gone to endemic countries and 8(%) had not previously travelled. Forty-eight percent of infections were acquired in Asia, 26% in Africa, 14.3% in Latin-America (LA) and 11.7% in Europe. Eighty-one percent of European travellers acquired the disease in Asia, and 54.6% of migrants in Latin America ($P < 0.001$). Sixty-eight percent and 60% of patients had consumed raw food or drank occasionally tap water, respectively. Around a third of patients had been working with children and 4% had a previous episode of *Giardia*. Eight patients (10.53%) were asymptomatic, 7 of them migrants ($P = 0.018$).

All patients were treated with nitroimidazoles. In 71 patients with completed follow-up, 14 (19.7%) had persistence of *G. intestinalis* which was more frequent when the infection had been acquired in Asia (28.6%) compared to Africa (16.7%), America (9.1%) or Europe (0%).

Thirteen patients with *Giardia* persistence received quinacrine and all of them but one patient who had not completed the treatment due to adverse effects, were cured after this treatment.

In 73 patients, PCR at baseline was undertaken showing the genotype A in 18 (24.7%) samples, B in 31 (42.5%) samples, and 1 sample had a mixed genotype (A/B). The finding of a particular genotype was not associated with the persistence of giardiasis.
CONCLUSIONS Almost 20% of patients presented persistence of giardiasis after nitroimidazole therapy and this fact was not associated with a particular genotype. Nearly all refractory cases were cured after receiving quinacrine.
DISCLOSURE Nothing to disclose.

3.5.1. Research priorities in obstetrics and reproductive health

O.3.5.1.002

Addressing hidden barriers to institutional deliveries - a key intervention for reducing maternal mortality in rural Zambia

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BACKGROUND In Zambia, the majority of rural women deliver at home without skilled birth attendants, leading to a maternal mortality rate (MMR) of 591/100 000 live births; among highest worldwide. 60% Zambians live below the poverty line. Institutional delivery by skilled birth attendants is considered most important strategy to reduce MMR. Institutional deliveries are low (48%) despite high single antenatal attendance (93%). An important barrier to institutional delivery identified was demands by health providers requesting women to bring delivery supplies and mother/baby clothes. The aim of this study was to determine the effect of provision of non-financial incentives on institutional deliveries in rural Monze district, Zambia.
METHODOLOGY A 1-year community intervention trial was conducted (Jan- Dec 2014) supported by UNICEF and WHO. Two comparable rural regions in Monze separated by a central urban region, intervention-arm expectant women who chose delivering at health facility received a mother-baby delivery-pack at health facility at delivery containing basic hygienic delivery supplies as non-financial incentives accompanied by health education; the control arm continued with routine health services. The primary outcome measure was the number of institutional deliveries in the two arms over 1 year, as well as comparing institutional deliveries before (2012 and 2013) and after (2014) the intervention.
RESULTS There was a 43% increase in institutional deliveries in the intervention arm in 2014 ($n = 2396$) compared to 2013 ($n = 1674$; $P < 0.000$) and 2012 ($n = 1680$; $P < 0.000$), while in the control arm the numbers of deliveries did not significantly change over the 3 years (2012 $n = 1182$; 2013 $n = 1322$; 2014 $n = 1182$; $P > 0.103$). The secondary outcome measures showed better birth preparedness, postnatal and under five attendance in the intervention arm compared to the control arm.
CONCLUSION The mother-baby delivery pack provides a high-impact, low-cost, easier-to-replicate and scale-up intervention using existing health systems. The pack was developed responding to hidden barriers to institutional deliveries identified and expressed by the end users in the community through a cross-sectional survey conducted prior to the study. The study results provide scientific evidence for policy makers to design effective interventions to overcome reversible barriers hindering utilisation of health facilities by pregnant-women, a key intervention for reducing MMR.
DISCLOSURE Nothing to disclose.

O.3.5.1.003

Related factors of inter-community of women with gestational diabetes in postpartum diabetes screening

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INTRODUCTION Patients with gestational diabetes are more susceptible to diabetes type 2 in the future. Post partum diabetes screening creates an invaluable opportunity for prevention or delay of diabetes type 2 and its irreversible complications. This study aimed at determining the factors relating to one′s referrals for post partum diabetes screening among women with gestational diabetes.
METHODS AND MATERIALS In this cross-sectional study, 150 women with gestational diabetes history at least six month after their delivery referring to Health and Treatment Centers in Kermanshah were chosen. Data collection was carried out using self-developed questionnaires performed via interviews. Demographic and reproductive questionnaires along with diabetes characteristics and the quality of health care provision ones were used collecting data. Data analysis was performed using *t*-test and χ^2statistical tests.
FINDINGS 48/7% of the samples (73 women) with GDM completed postpartum glucose screening. Among the individual factors, relationships were spotted among level of education ($P < 0/001$), number of children ($P < 0/001$), income level, ($P < 0/002$), insurance coverage and its type ($P < 0/001$), fetus weight ($P < 0/001$), gestational health care ($P < 0/001$). For the disease factors, the following were proved to be significantly related: age of diabetes onset ($P < 0/002$), insulin administration during pregnancy ($P < 0/001$), family history of diabetes ($P < 0/001$), and history of hospitalization ($P < 0/002$). The following features of health care services were also found to be correlated with the rate of referrals for screening: dissemination of information regarding post partum diabetes screening during pregnancy, delivery, and discharge from hospital; receiving an order for blood glucose screening during post partum visit, and phone-mediated follow ups ($P < 0/001$).
CONCLUSION Regarding the low rate of referral for postpartum glucose screening, it is necessary to remove the obstacles in light of determining the contributing factors, and through adequate diagnosis of diabetes type 2, its complications can be reduced.
DISCLOSURE Nothing to disclose.

O.3.5.1.004

A national programme of freely-available ambulance transportation for women in labour halves maternal mortality in Ethiopia: an operational analysis from Tigray Region

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INTRODUCTION One of the challenges for maternal health services across Africa is physically getting women to health facilities for delivery at the appropriate time. A lack of transportation has often been cited as a major obstacle. The Ethiopian Federal Ministry of Health implemented a national programme of freely available ambulance transportation in every District from 2012, and this operational analysis investigated the effects of the ambulance programme on maternal mortality.
METHODS Maternal mortality was measured in a survey of six randomly selected districts in Tigray Region over a 1-year period in 2012/13. For the same time period, data from ambulance log books from the same six Districts were captured and ambulance trips associated with deliveries extracted. Data on month, distance to health facility and mobile network coverage at local area level were included.
RESULTS The survey identified 51 maternal deaths and 19 179 live births, corresponding to an overall maternal mortality ratio (MMR) of 266 per 100 000 live births. Districts using ambulances for at least 25% of deliveries had an MMR of 116 per 100 000 compared with 407 per 100 000 elsewhere. Distance from home to facility, the availability of a mobile telephone network and utilisation of ambulances were all independently associated with maternal mortality. When all these factors competed in a multivariable model at local area level, only utilisation of ambulances persisted as a significant factor, with a maternal mortality rate ratio of 0.51. One maternal death was estimated to have been averted for every 5000 ambulance-kilometres driven.
CONCLUSIONS Freely available ambulance transport in Ethiopia was associated with significant reductions in maternal mortality, although this was a strategy requiring substantial investment. Similar results could probably be achieved elsewhere given sufficient investment in vehicles and operational infrastructure.
ACKNOWLEDGEMENTS The Tigray Regional Health Bureau funded this operational assessment, including the maternal mortality survey and capturing the ambulance data. A collaboration grant from the Swedish Research Council facilitated analysis.
DISCLOSURE Hagos Godefay is the Head of Tigray Regional Bureau and Kesetebirhan Admasu is the Minister of Health, Federal Democratic Republic of Ethiopia.

O.3.5.1.005

Maternal body mass index and adverse pregnancy outcomes: a Ghanaian cohort study

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INTRODUCTION Worldwide, overweight and obesity are an increasing problem. Studies conducted in high-income countries suggest an association between maternal BMI and complications during pregnancy, delivery and postpartum period for both mother and offspring. Yet, results from studies performed in high-income countries may not be directly applicable to the context of low- and middle-income countries (LMICs).

The objective of this study was to examine the association between maternal weight at less than 17 weeks gestation and maternal and infant outcomes of pregnancy, delivery and post-partum period in a cohort of pregnant Ghanaian women.

METHODS A prospective cohort study of 1,010 women in Accra, Ghana (2012 – 2014). Women were classified as overweight (BMI 25–30) and obese (BMI ≥30), and their obstetric and infant outcomes analysed using multivariate logistic regression.
RESULTS 824 women, average 28 years (SD 5.1), were included in the analysis; 313 (31.3%) were overweight and 169 (16.9%) obese. Obese women had a two-fold increased risk for caesarean sections (RR 2.20, 95% CI 1.21–4.02), and more than a six-fold higher risk for pregnancy induced hypertension (RR 6.17, 95% CI 2.90–13.13) and chronic hypertension (RR 6.00, 95% CI 1.40–25.76). Infants of overweight and obese women were more likely to be macrosomic (RR 2.37, 95% CI 1.13–4.97).
CONCLUSION The global obesity epidemic has reached women in LMICs with important adverse consequences for maternal and infant health. Antenatal care in LMICs will need to anticipate this potential expansion of complications, including the development of guidelines for optimal maternity care for overweight and obese pregnant women.
DISCLOSURE Nothing to disclose.

3.5.2. Child health

O.3.5.2.002

Promoting mother-child interaction - improving early child development through a psychomotor stimulation intervention in rural Peru: secondary outcomes of a cluster randomised trial

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BACKGROUND Early childhood stimulation can improve child health and -development, alleviate adverse effects of poverty and impact on well-being of future generations. Within a community-randomised trial we implemented two home-based interventions, whereby each intervention served as an active control for the other. One group received an early child development (ECD) intervention and the other an integrated environmental household intervention package (IHIP) improving household air-, drinking water quality and hygiene.
METHODS An ECD intervention, adapted from the National Wawa Wasi Programme, was implemented in 25 communities. We enrolled children aged 6–35 months and their caretaker in 50 communities randomised into ECD- and IHIP-communities. In ECD-communities, trained fieldworkers instructed mothers to stimulate and interact with their children, to create safe playing environments and to use standard programme toys. IHIP-communities received a ventilated improved cookstove, a kitchen sink with running water and a safe drinking water- and hygiene promotion. At baseline and after 12 months of follow-up, all children were evaluated on age-specific developmental milestones in seven domains including motor proficiency, personal/social development, essential relational skills and communication.
FINDINGS At baseline, ECD- and IHIP-children performed similar in all domains. After 12 months of follow-up the proportion of children scoring above the mean of the age specific group was in all domains statistically significant higher in the ECD-group (range: 12–23%-points higher than IHIP-group). We observed the biggest difference in fine motor skills (62% vs. 39% scoring above the mean, odds ratio (OR): 2.6, 95% CI: 1·7–3.9).
INTERPRETATION The home-based ECD effectively improved child development in all investigated domains. Home-based strategies might be promising to improve development outcomes in rural Peruvian children as an important component of poverty alleviation programmes.
DISCLOSURE Nothing to disclose.

O.3.5.2.003

Paediatric anti-retroviral therapy in a rural setting: comparisons of mortality pre- and post-initiation of early paediatric ART and Option B+

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BACKGROUND In 2013 the WHO changed two inclusion criteria for anti-retroviral therapy (ART) in their HIV guidelines. Pregnant women (Option B+) and all children ≤5 years should initiate ART, regardless of their clinical or immunological status. Mozambique adopted the protocol and in July 2013 the new guidelines were implemented in Cabo Delgado Province. This analysis compares the mortality rate of HIV+ children on ART before and after implementation of these guidelines in Cabo Delgado.
METHODS Retrospective analysis of data collected from health centers between January 2009 and January 2015, in the rural districts of Chiure and Ancuabe, Mozambique. All children on ART under the age of 13 years were included in the analysis. STATA version 13.1 was used to compare the data before and after July 2013. Wilcoxon rank-sum was used to compare medians. For the bivariate analysis either Chi-square test or Fishers exact test was used.
RESULTS 480 children were included. The child-mortality rate decreased significantly after July 2013, in both districts: from 16.7 % to 7.4% (OR 2.51 $P < 0.002$). Loss-to-follow-up was 3.6% before and 1.3% after July 2013 (OR 2.8 $P = 0.14$). Age at starting ART remained unchanged at 1.8 years ($P = 0.46$). CD4 count at ART initiation increased from 549 cells/µl to 827 cells/µl after the guideline was implemented ($P = 0.001$).
CONCLUSION The results suggest that the changes in the national ART guideline for pregnant women (option B+) and children (early initiation of ART) are associated with a decrease in mortality rate in HIV+ children under ART. The baseline CD4 count increased significantly after July 2013. Starting children on ART with a higher immunological status could have impacted on the improved mortality rate. Our findings on LTFU and the average age that children start ART merit further investigation into clinical practice in the districts.
DISCLOSURE Nothing to disclose.

O.3.5.2.004

Geographic disparities in bednet ownership and usage: an analysis of Burkina Faso 2010 Demographic and Health Survey data

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INTRODUCTION Insecticide-treated nets (ITNs) are one of the most important keys strategies for malaria control. However, ITN coverage varies among regions in the same country, and such variations may seriously limit the potential impact of nets. Understanding the important gap between bednet ownership and use will help program managers target particularly vulnerable populations. The aim of this study was to map, at the district level, e.g. where national programmes are being applied, disparities of ownership and usage of bednets in Burkina Faso and to subsequently explore the influence of sociodemographic factors in bednet usage among owning households.
METHODS AND MATERIALS The Burkina Faso 2010 Demographic and Health Survey (DHS) data were used to derive the district level estimates. The DHS provided extensive information on individuals, as well as the geographic coordinates of household clusters using a stratified two-stage cluster sampling.
RESULTS Bednet ownership varied across the districts ranging from 34 % to almost 99 % in some regions. Regions in the North and the Central Plateau had considerably high percentages, with the districts including Zorgho, Yako and Ouahigouya having rates of bed ownership of more than 96%. The proportion of the population living in a household with 1 bednet for each 2 household members (universal coverage) was 14 % (9 5% CI: 13–15%), ranging from 4% to59 % across the districts. ITN use in Burkina Faso ranged from 15% to 80% within geographically-defined districts. The majority of regions (70%) had a use level under 40%. Where ITN ownerships were high, ITN use was also high. The presence of children under 5 years (U5) and pregnant women (PG) in the household increased the odds of bednet use (U5: OR = 2.09, (95 % CI: 1.94–2.25); PG: OR = 1.83, (95 % CI: 1.56–2.15). Living in urban areas (OR = 1.37, (95% CI: 1.12–1.67), and in wealthier households were strongly associated with bednet use.
CONCLUSIONS A high bednet usage was observed among households of more than 6 people in comparison to households of more than 8 people. To our knowledge, this is the first study to demonstrate the geographical variation of bednet ownership and usage indicators within districts in Burkina Faso at a scale that is smaller than what is currently available. We emphasise the advantages of estimating coverage rates at the district level.
DISCLOSURE Nothing to disclose.

O.3.5.2.005

Monitoring the protective effect and the effectiveness of seasonal malaria chemoprevention in Niger

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INTRODUCTION Seasonal malaria chemoprevention (SMC) is a preventive strategy consisting of intermittent administration of sulphadoxine-pyrimethamine (SP) and amodiaquine (AQ) to children living in areas of highly seasonal transmission. Since 2013, SMC has been used in children 3–59 months old in Niger during 4 distribution rounds at 28-day intervals. A cross-sectional survey conducted in Magaria district estimated the coverage of each round from 85–94%.
METHODS Individual data were collected on all fever cases in children <5 years in 4 sentinel sites in Magaria district as part of routine monitoring during the 5 months of SMC. In multivariate analyses we calculated the odds ratios (ORs) for malaria, defined as fever and positive histidine-rich protein II rapid diagnostic test (RDT) in children that received the SMC versus children that did not. We conducted stratified analysis on distribution round and time since the last SMC. We used a method traditionally used for vaccine effectiveness estimates, the screening method, to estimate the effectiveness of SMC (SMC_E).
RESULTS Children receiving SMC had a 26% reduced odds of malaria (OR = 0.74, 95% CI 0.61–0.88) compared to those not getting SMC. The protective effect was highest during the first two SMC rounds: ORs 0.22 (95%CI 0.12–0.40) and 0.15 (95% CI 0.09–0.23) and absent during the last SMC round OR 0.85 (95%CI 0.54–1.31). ORs during the first 21 days after an SMC distribution and during the last 7 days were 0.39 (95%CI 0.30–0.49) and 2.28 (95%CI 1.69–3.08). We estimated global SMC_E at 63%. SMC_E decreased with each subsequent round (94%, 80%, 59%, 16%). SMC_E during the 21 days post-distribution averaged 74%, dropping to 31% during the 7 days before the next round.
CONCLUSIONS Our results suggest that SMC is effective in Niger. However, the protective effect and SMC_E seems to wane through the distribution rounds, possibly due to increasing exposure to malaria over time, but perhaps to use of RDTs that remains positive after parasite clearance. As data on resistance to SP and AQ are lacking, resistance could contribute to the declining effectiveness. As the protective effect seems to be absent during the last 7 days of each cycle, narrowing the interval could be beneficial, especially during peak malaria transmission periods. Data from additional years and locations, in addition to the use of *Plasmodium* lactate dehydrogenase RDTs will improve the interpretation and generalizability of these results.
DISCLOSURE Nothing to disclose.

3.5.4. Sexual and reproductive health

O.3.5.4.002

Sexuality education is associated with increased disclosure and treatment seeking after violence experiences of young women 15–24: results from a multi-country-survey including Eastern DRC, Rwanda, and Burundi

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INTRODUCTION In the post-conflict regions of Eastern DRC, Burundi, and Rwanda in Central Africa, high rates of violence against women continue to be observed. Different government and non-governmental organizations (NGOs) have been implementing strategies to respond to the widespread violence against women. This paper analyzes the effectiveness of comprehensive sexuality education on tolerance, disclosure, and help-seeking after sexual violence among women 15–24 years old.

METHODS A multi-stage cluster survey was conducted including 866 women in DRC, 745 women in Burundi and 773 in Rwanda. The survey instrument addressed socio-economic and behavioral questions; having received sexuality education, which included topics around gender, rights, and violence (comprehensive sexuality education); experience of sexual violence, defined as forced sexual intercourse; high tolerance of violence, defined as agreeing strongly to the statements 'There are times when a woman deserves to be beaten', 'It is alright for a man to beat his wife if she is unfaithful', 'A man can hit his wife if she refuses to have sex with him'. Disclosure of violence was defined as talking to someone about the experience of violence; help-seeking as having used health services after sexual violence. Multi-level logistic regression analysis was conducted using STATA V.13.
RESULTS In the past 12 months 52.2% of young women in DRC, 29% in Burundi, and 43.3% in Rwanda had received comprehensive sexuality education. In the same time period, 16.3% of young women in DRC, 11.3% in Burundi and 15.4% in Rwanda had experienced sexual violence. In Rwanda, 70.1% of the women disclosed sexual violence, in DRC 50.4% and in Burundi 53.1%. Less than 10% sought professional help. In Burundi young women who received comprehensive sexuality education had a lower tolerance of violence (Coef. −0.63, CI −1.08, −0.17), and disclosure of sexual violence was more common in DRC and Rwanda (DRC Coef. 1.00, CI 0.35, 1.64; RW Coef. 0.72, CI 0.07, 1.37). In Rwanda, going to see a healthcare provider offering GBV services was also correlated with exposure to comprehensive sexuality education (RW 2.10, CI 1.29, 2.91).
CONCLUSION Comprehensive sexuality education for young people may have the potential to decrease the social acceptability of sexual violence and to increase disclosure and help seeking after experiencing violence.
DISCLOSURE Nothing to disclose.

O.3.5.4.003

'I try to avoid the boys!' Adolescents' sexuality representation in Rwanda, a mixed method analysis

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Adolescents' sexuality is a source of concern not only to parents, but adolescent health care providers as well as policy makers worldwide. This study explores the views and opinions of adolescents on sexuality.

Data collection was conducted in the context of the Next Generation Programme with the aim of obtaining an in-depth perspective of the sexual and reproductive health of adolescents (15–19 years). From April to July 2014, a random sample of 789 adolescents from 6 districts were interviewed using questionnaires. In addition, informal talks and interviews were conducted with 16 girls and boys thereafter. The mixed method analysis approach supports a complementary understanding of adolescent sexuality.

Adolescents usually lived with their parents or a relative (91%), went to school (54%) and visited a religious service at least once a week (71%). Some disclosed that they were in a relationship (20%) and reported ever having had sexual intercourse (11%) with the median age of sexual debut of 17 years. More than half of the adolescents (63%) had received some sexual education, either at school, health and youth centers or at religious services.

Discussing love and intimate relations yielded manifold representation of sexuality along notions of time (childhood, adolescence, and adulthood). Sexuality during adolescents had negative connotations, expressed by fear of pregnancy and HIV infection. The childhood was represented through innocently 'playing sex', the imagined future was also positive envisioned with procreation embedded in marriage as a socially accepted way of expressing sexuality.

In the representation of adolescent sexuality, social values and public health norms become highly visible. Instead of creating an environment of fear around adolescent sexuality, policy makers and service providers in particular should pay attention to what adolescents perceive as 'friendly' health services.
DISCLOSURE Nothing to disclose.

O.3.5.4.004

Linking capitals and entitlements in health promotion

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INTRODUCTION Health promotion research has recently received criticism for mainly focusing on individuals' behavior. These perspectives do not explain how and why healthy behaviors may change over time and how they are embedded in a broader social, political and economic context. Moreover, health promotion is criticized for its focus on behavioral choices relevant to different health risks. This objectification of the individual does not take into account contextual factors as well as the political environment in which actors act and by which they are shaped.
METHODS In health promotion many studies focus only on social capital such as social networks or the role of parents or peers, however, other resources such as cultural resources are also of great importance. Drawing on Pierre Bourdieu's practice theory, we examined whether and how female adolescents aged 15–19 years mobilized social (i.e. social networks), economic (i.e. cash, savings), cultural (i.e. knowledge and skills) as well as symbolic capital (i.e. social reputation) in Dar es Salaam and Mtwara, Tanzania, in order to deal with teenage pregnancy. A cross-sectional survey was conducted with 1250 girls who had never been pregnant or were pregnant adolescents and young mothers.
RESULTS Findings showed that the majority of the female adolescents, especially pregnant girls and young mothers, very actively mobilized social, cultural and economic support to avoid pregnancy or deal with it successfully. However, only girls that maintained symbolic capital in form of social reputation and acceptance within their socio-cultural environment were able to get the needed support. In addition, findings emphasized the role of cultural capital such as health promotion skills provided by mass media (radio, television, and magazines).
CONCLUSION It is argued that modern health promotion research should consider Bourdieu's practice theory by focusing on the role of social, economic, cultural and symbolic resources that are available to people for maintaining and promoting their health. However, in line with Thomas Abel and colleagues we propose that modern health promotion should not only take into account the interplay of health related capitals but also of capabilities. Combining Amartya Sen's capability approach with the practice theory of Pierre Bourdieu would allow for further highlighting people's capabilities in health promotion.
DISCLOSURE Nothing to disclose.

O.3.5.4.005.LB

Adolescents and youth taking control of their HIV treatment through the web-based peer support platform: the case of Mombasa, Kenya (ELIMIKA Project)

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INTRODUCTION Adolescents and youths (A-Y) are arguably the most dynamic and challenging group among populations living with HIV. A number of studies have demonstrated that adherence to antiretroviral therapy (ART) among A-Y is low. In addition, a review of the literature reveals limited evidence of effective and creative strategies to improve access and adherence to ART among A-Y. The aim of this study is to develop and test a secured digital peer support platform in improving access to health information that will lead to increased adherence to ART among A-Y receiving treatment in two clinics in Mombasa, Kenya.

METHODS Cross-sectional design is used to generate baseline data on adherence by extracting the information from A-Y medical records from two clinics. Qualitative approach including focus group discussion (FGDs) with A-Y and in depth-interviews with health care providers (HCPs) is used to collect data/information for designing the intervention and content of the web platform.

90 HIV positive young people (15–24 years old) are enrolled to test the digital platform. Pre- and post-intervention comparison of usability and short term psycho-social outcomes is carried out using on-line questionnaires. The intervention's effectiveness in improving adherence among A-Y will be estimated by comparing post intervention adherence with the baseline data.

RESULTS To define the content of the digital peer support system and features to be included, three FGDs with A-Y and three in-depth interviews with HCPs were held in January 2015. The findings demonstrated that the most common challenges A-Y face in regards to adherence to ART are fear of disclosure, stigma, peer pressure, problems of combining school schedule and dose timing. Positive living with HIV, prevention of sexually transmitted infections and family planning were suggested as key topics in which information is needed. Further, as suggested by the participants, the platform has to contain open public discussion, educational videos, privacy chat and possibility to ask questions to health care professionals, ensure privacy and confidentiality.

CONCLUSIONS Based on these findings, a secured web platform administered by peer volunteers was designed and started to function in April 2015. The mid-term evaluation of usability and assessment of short-term psycho-social outcomes are planned to be performed in July 2015 through FGDs and on-line questionnaires administrated to the participating A-Y.

DISCLOSURE Nothing to disclose.

3.6.1. Gut microbiota and its interaction with nutrition and diseases

O.3.6.1.002

Polyclonal intestinal colonization with ESBL-producing *Enterobacteriaceae* upon traveling to the Indian subcontinent

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Expansion and dissemination of extended-spectrum cephalosporin-resistant *Enterobacteriaceae* (ESC-R-Ent) is a worldwide problem enhanced by international traveling. Traveling to countries with high prevalence of ESC-R-Ent increases the risk of importation of epidemic clones which can then spread in new geographic regions. Moreover, colonization of the human gut by ESC-R-Ent is a relevant and known factor that can promote the development of infections. However, key factors and colonization dynamics by these organisms are still unknown. In this work, we aimed to assess the clonal diversity of ESC-R-Ent colonizing the gut of humans travelling to high prevalence areas.

Twenty-five Swiss volunteers travelling to the Indian subcontinent underwent screening before and after travelling. An aliquot of native stools were enriched in LB broth with a cefuroxime disc. Enrichments were plated in BLSE, ChromID ESBL, and an in house made Drigalski plate containing imipenem and cloxacillin. Species identification was obtained using the MALDI-TOF. For ten randomly selected volunteers, at least 5 *Enterobacteriaceae* colonies per plate were recovered. Double disk synergism test was performed for each isolate and clonal relatedness was assessed using the rep-PCR and MLST. The Check-Points CT103 XL microarray and PCR/DNA sequencing were implemented to detect ESBL-, plasmid-mediated AmpC-, and carbapenemase-producing *Enterobacteriaceae*.

Only one volunteer was colonized prior to traveling, whereas 95% were colonized upon return. For the sub-group of 10 volunteers, 46 ESBL producers were identified, the majority being *E. coli* ($n = 45$) and only one *K. pneumoniae*. Among these isolates, rep-PCR identified 29 different clones. Remarkably, clonal diversity within each volunteer varied between 2 and 6 clones. Nevertheless, β-lactamase diversity was low: only CTX-M-Group 1 types (including CTX-M-15) were found, which are endemic in this region.

It seems that in the initial steps of intestinal colonization by ESC-R-Ent (probably via the food chain) there is a polyclonal acquisition, being *E. coli* the most relevant species. This phenomenon was never observed and could have important implications for both microbiologists and ID specialists. In the near future, we will analyze the plasmid background of the different ESC-R Ent and we will monitor the volunteers over time to better understand the course and dynamic evolution of gut colonization due to these life-threatening pathogens.

DISCLOSURE Nothing to disclose.

O.3.6.1.003

Molecular risk assessment of Shiga toxin-producing *E. coli* O157: H7

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INTRODUCTION In this study, we analyzed *E. coli* O157:H7 genotypes that act as potential risk for human illness from food sources of animal origin and use these genotypes as potential indicators of clinical outcome of infection in human.
OBJECTIVES (1) Determine the genetic diversity in frequencies of distribution of different genotypes among *E. coli* O157:H7 strains recovered from food and human clinical sources using a combination of molecular subtyping methods and access if human clinical strains were overrepresented by specific genotypes of *E. coli* O157:H7. (2) Determine the potential correlation of these genotypes in clusters with severe clinical symptoms.
METHODS A diverse collection of human (n = 100) and food (n = 70) *E. coli* O157:H7 isolates from Belgium displaying different PFGE patterns was characterized by conducting different molecular assays that have previously demonstrated non random distribution of *E. coli* O157:H7 genotypes among clinical and non-clinical isolates. Genotypic characterization included lineage-specific polymorphism assay, Shiga-toxin-encoding bacteriophage insertion site assay, clade typing, *Tir* (*255A* and *T*), and variant analysis of Shiga toxin 2, and antiterminator *Q* genes. Genetic clustering was performed using MCMC model, implemented in Structure software package.
RESULTS AND CONCLUSION Our results supported the epidemiological evidence of existence of clinically significant microbial genetic factors that are overrepresented among *E. coli* O157:H7 clinical isolates and are important determinants of human infection risk. Furthermore, clusters 1 and 3 were observed to be more frequent isolated from bloody diarrhea and haemolytic uremic syndrome, respectively. Our results may contribute to monitoring of risk genotypes with high virulence/transmission potential.
DISCLOSURE Nothing to disclose.

O.3.6.1.004

Campylobacter surpassed *Salmonella*: an analysis of Swiss surveillance data, 1988–2013

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INTRODUCTION *Campylobacter* spp. and *Salmonella* spp. are foodborne pathogens of human and veterinary public health importance in Switzerland. Clinical isolates of *Campylobacter* and *Salmonella* from humans are notifiable for diagnostic laboratories in Switzerland. While *Campylobacter* case notifications increased between 1988 and 2013, *Salmonella* case notifications decreased during this time period.
METHODS We descriptively analysed notification data of the years 1988 to 2013 for these two gastrointestinal, bacterial pathogens. Notification rates were calculated using data on the yearly average resident population in Switzerland.
RESULTS Notified campylobacteriosis cases more than doubled – from 3127 to 7499 cases – between 1988 and 2013. Contrary, *Salmonella* case notifications decreased during the same time period from 4291 to 1267 cases. Since 1995, *Campylobacter* is more frequently reported than *Salmonella*. Both pathogens are most frequently reported during summer months, but *Campylobacter* additionally shows a very distinct peak during the winter festive season. While the notification rate of campylobacteriosis decreased from 105.3 to 102.3 cases / 100'000 population in the youngest age group (<5 years) between 1988 and 2013, the notification rate increased more than 7-fold in the oldest age group (85+) from 11.7 to 92.2 cases/100 000 population.
CONCLUSION The observed inverse trends in case notifications for *Campylobacter* and *Salmonella* indicate a true increase in campylobacteriosis incidence and a true decrease in salmonellosis incidence. Changes in case detection rates or in notification compliance are unlikely to lead to inverse trends of these two pathogens.

Legal microbiological criteria for foodstuffs have been implemented for *Salmonella* control in the early nineties of the last century and appear to be effective. For *Campylobacter* in poultry, process hygiene criteria for slaughterhouses will be introduced in 2016. The impact of those criteria on human campylobacteriosis cases is currently unknown and needs to be evaluated after implementation.
DISCLOSURE Nothing to disclose.

O.3.6.1.005

Medical consultations due to acute gastroenteritis in Swiss primary care: results from the sentinel surveillance network 'Sentinella'

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INTRODUCTION Population-based studies in European countries estimated an acute gastroenteritis (AG) incidence of 0.5 to 1.0 episodes per person-year. This high disease burden leads to considerable health system use, health care costs and socio-economic impact. We assessed the frequency of medical consultations at the primary care level, course of disease, days of work lost and physicians' diagnostic and treatment approaches using the Swiss Sentinel Surveillance Network 'Sentinella'.
METHODS AND MATERIALS During the study period (January to December 2014), 163 primary care physicians participated in the 'Sentinella' network covering entire Switzerland. The weekly number of consultations due to AG and basic patient characteristics were reported. For a subsample of patients, additional information like the number of patients' visits, signs and symptoms, general condition, stool diagnostic, prescribed symptomatic and antibiotic treatment, days of work lost and risk exposures were reported.
RESULTS On average, each physician reported 0.5 cases of AG per week. In total, 3867 cases were reported during the study period. Consultation frequency was influenced by age, but not by sex. Median age of patients was 19 years for males (range < 1–94)

and 22 for females (<1–97). Out of 2235 cases with additional information, 78% consulted the physician once, 17% twice, 3% three and 1% four times. Physicians classified the patients' general condition with a median score of 7 on a scale from 1 (poor) to 10 (good). 83% of patients with salaried employment were on sick leave, the median duration was 4 days. The majority of cases (91%) received symptomatic treatment. Antibiotic treatment was prescribed for 9% of patients and was more frequent in older age groups. 3% of all patients were hospitalised. Stool diagnostics were performed for 13% of patients and were more frequent in patients with recent travel history. Campylobacter spp. was the most frequently identified pathogen.

CONCLUSIONS AG leads to a considerable burden of disease and socio-economic burden due to absence from work. Data from national mandatory infectious disease surveillance underestimates the burden of AG considering that the majority of patients does not undergo stool testing. The significant socio-economic impact and health system burden due to AG in Switzerland needs to be urgently addressed by public health authorities.

ACKNOWLEDGMENTS We thank all Sentinella physicians for their contribution.

DISCLOSURE The complete study was funded by the Swiss Federal Office of Public Health, Bern, Switzerland.

3.6.2. Nutrition

INV.3.6.2.002

Vitamin D and tuberculosis

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Vitamin D was used to treat active tuberculosis (TB) in the pre-antibiotic era, and its active metabolite, 1,25-dihydoxyvitamin D, has long been known to enhance the immune response to mycobacteria *in vitro*. Vitamin D deficiency is common in patients with active TB in diverse settings, and several clinical trials have evaluated the role of adjunctive vitamin D supplementation in its treatment. Vitamin D deficiency is also recognised to be highly prevalent among people with latent *M. tuberculosis* infection (LTBI) in both high- and low-burden settings, and there is a wealth of observational epidemiological evidence linking vitamin D deficiency with increased risk of both acquisition and reactivation of LTBI. In this talk, I will discuss the potential for vitamin D supplementation to be used in the prevention of LTBI and active TB, and in the treatment of active TB.

DISCLOSURE Nothing to disclose.

INV.3.6.2.004

New insights into the role of iron in the etiology and pathogenesis of malaria, severe anaemia and invasive bacteraemia

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Both iron deficiency and inflammation-induced hypoferraemia are believed to protect the human host against invading pathogens. Iron supplementation can thwart this protection and increase rates of febrile malaria episodes in young children, perhaps by transiently enhancing the production of young erythrocytes that are more susceptible to invasion and propagation by *P. falciparum* merozoites than mature erythrocytes. In children with deficiency, however, iron supplementation also results in increased haemoglobin concentrations, which may act as a reservoir and prevent the development of severe anaemia during subsequent febrile malaria attacks. Thus, paradoxically, iron supplementation can increase or decrease malaria rates, depending on case definitions and the method of case detection.

The hypoferraemic effect of inflammation is mediated by upregulation of hepcidin, a hormone produced by hepatocytes that integrates multiple and often conflicting signals reflecting iron stores, erythropoietic activity and host defence, and thus acts as the master regulator of the body's iron metabolism.

Limited evidence suggests, however, that children with severe anaemia have reduced circulating hepcidin concentrations compared to non-severely anaemic controls. Thus in the course of developing severe anaemia, these children seem to be able to pass a tipping point whereby the hypoxic drive to down-regulate hepcidin and increase iron availability for erythropoiesis overrides the inflammation-mediated effect that upregulates hepcidin and withholds iron. The resultant increase in circulating iron may enhance susceptibility to infections, which may be exacerbated by iron supplementation. The role of the erythroferrone in these processes remains to be elucidated, because this recently discovered hormone is produced by erythroblasts in response to erythropoietin, and mediates hepcidin suppression following blood loss.

The implications of this model would be that iron deficiency can predispose to severe anaemia and death in malaria-endemic areas. It is presumably safe to prevent or correct iron deficiency by iron supplementation under cover of antimalarial drugs. On the other hand, therapeutic supplementation of iron during severe anaemia may inadvertently result in enhanced susceptibility to malaria, invasive bacteraemia and death.

DISCLOSURE Nothing to disclose.

3.6.3. Nutrition and immunology

O.3.6.3.001

Malaria chemoprevention, undernutrition and anaemia in children: findings from three randomized intervention trials in Southern Mali

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Children born in sub-Saharan Africa face increased risks of undernutrition and infectious disease, increasing stunting and potential to impact ultimately on educational achievement. Iron is important in brain function, and interventions that reduce iron-deficiency and anemia may improve cognitive function and learning. Mali experiences some of the highest rates of malaria and anaemia in the world. Sikasso in the south, is one of the regions with the highest level of malnutrition: 45% of children under five are stunted, 16% wasted and 88% are anaemic. It is also the region where the prevalence of malaria is highest. A series of trials undertaken by Save the Children in collaboration

with national partners, aimed to identify intervention approaches to effectively address malaria and undernutrition to support child development.

This research culminated in a trial to examine the combined impact of two newly-recommended interventions in early childhood: seasonal malaria chemoprevention and home fortification with micronutrient powders. A cluster-randomized controlled trial was conducted in 60 rural communities with community-based pre-schools in Sikasso region. Children aged <5 years living in 30 intervention communities received two rounds of seasonal malaria chemoprevention in Oct and Nov 2013, followed by daily supplementation of micronutrients for 4 months from January–April 2014. Delivery of the two interventions at community-level was organized by pre-school management committees. The combined impact of the interventions was evaluated in May 2014 through cross-sectional surveys to compare study trial outcomes in children aged 3 and 5 years living in intervention and control communities. A significant reduction in malaria infection was observed in May, 6 months after the last anti-malarial treatment, in intervention compared to control communities (3y olds: 21% vs. 45%, $P < 0.001$; 5y olds: 32% vs. 55%, $P < 0.001$). However, no differences were observed in prevalence of anaemia, mean hemoglobin concentration or nutritional indices. These findings were in marked contrast to the results from trials of iron supplementation and malaria chemoprevention in schoolchildren, previously conducted in the same area.

In this presentation, we shall contrast findings from the three trials to highlight differences in epidemiology of malaria and anaemia in southern Mali according to age; design of each intervention used; and implications for future work.

DISCLOSURE Nothing to disclose.

O.3.6.3.002

Social costs of iron deficiency anemia in 6-59 month-old children in India

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Inadequate nutrition has a severe impact on health in India. According to the WHO Global Burden of Disease project iron deficiency is the single most important nutritional risk factor in India, accounting for more than 3% of all disability adjusted life years (DALYs) lost.

METHODS AND MATERIALS We estimated the social costs of iron deficiency anemia (IDA) in 6- to 59-month-old children in India in terms of intangible costs (DALYs) and production losses (income lost). The life-time costs of a birth cohort suffering from IDA between the age of 6 and 59 months are calculated with a health economic model. The model is stratified by two age groups (6–23 and 24- to 59-months), two geographical areas (urban/rural), 10 socio-economic strata (SES) and three degrees of severity of IDA (mild, moderate, severe). Prevalence of anemia is calculated with the last available National Family Health Survey. We verify the robustness of the results with a multivariate sensitivity analysis and evaluate the effect of recent changes in the DALY methodology.

RESULTS IDA prevalence among 6- to 23-month-old children is 50.4% in rural and 46.6% in urban areas. 24- to 59-month-old children are slightly less affected with a prevalence of 41.1% in rural and 36.7% in urban areas. Children living in poor households are particularly affected and the differences between poor and wealthy are especially pronounced among older children. We find that the yearly burden of IDA in India amounts to production losses of 24 001 m USD and 8.3 m DALYs lost. These DALYs correspond to 125 699 potential lives lost every year due to IDA. Poor households incur considerably higher costs, with the poorest 20% experiencing 2.4 times higher intangible costs and 2.1 times higher production losses than the wealthiest 20%. The rural population suffers disproportionately high losses. Changes in the DALY methodology have led to a threefold increase in the estimated number of DALYs. As the new disability weights are based on a more sound methodology, we find that previous calculations considerably underestimated the social costs of IDA.

CONCLUSIONS Despite years of iron supplementation programs and substantial economic growth IDA remains a crucial public health issue in India and an obstacle to the economic advancement of the poor. Young children are especially vulnerable due to irreversible effects of IDA on cognitive development. Our research may contribute to the design of new effective interventions aiming to reduce IDA in early childhood.

DISCLOSURE The study was supported by the Nestlé Nutrition Institute and Nestec S.A. The supporting sources had no influence on study design; in the collection, analysis, and interpretation of the data; in the writing of the manuscript; and in the decision to submit the results for publication

O.3.6.3.003

When malnutrition meets TB and HIV: prevalence of microcytic hypochromic anaemia and associated risk factors among adult TB cases and household contacts in urban Dar es Salaam, Tanzania

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BACKGROUND Tuberculosis (TB) is known to induce a systemic inflammatory state which can change iron metabolism. Together with existing nutritional deficiencies this can cause a transient iron deficiency that has been associated with worse clinical outcomes. We describe the burden of microcytic hypochromic anaemia (MHA) in a large cohort of TB patients and controls from the urban region of Dar es Salaam, Tanzania.

METHODS As part of an ongoing TB Cohort Study (TB-DAR), we included smear-positive adult TB patients (>18 years, cases), and controls without TB from the household contacts. Clinical and laboratory data were collected during recruitment. Anaemia was defined as hemoglobin (hb) concentration <11 g/dL, low mean corpuscular volume (MCV) as <80 fL, and low mean corpuscular hb (MCH) as <27.5 pg/cell. Logistic regression models were adjusted for age, sex, active TB, white blood cell count, red blood cell distribution width (RDW-CV), HIV and helminth infection, presented as adjusted Odds Ratios (aORs).

RESULTS Data was available from 344 cases and 296 controls. The median age was 33.6 years (interquartile range [IQR] 26.4–42.3); 384 (60%) were male and 97 (15.2%) HIV-infected (18.3% among cases vs. 11.5% among controls). The proportion of underweight (body mass index < 18.5) was more frequent among cases compared to controls (24.7% vs. 5.4%). Prevalence of helminth infection was similar in both groups (11.6% vs. 11.5%).

The median hb concentration was 12 g/dL (IQR 10.3–13.3), and lower among cases than controls (11.2 g/dL vs. 12.4 g/dL).

The median MCV and MCH were lower among cases compared to controls: 76.7 (IQR 70.5–83) vs. 81.3 (IQR 75.9–86.5) for MCV, 24.9 (IQR 22–27) vs. 26.4 (IQR 23.6–29) for MCH. MHA was more common among cases than controls (23.1% vs. 14.2%, $P < 0.0001$).

In multivariate analyses, the risk for MHA was higher in cases compared to controls (aOR 2.2, 95% confidence interval [95% CI] 1.25–3.8, $P = 0.006$), and MHA was associated with HIV infection (aOR 2.4, 95%CI 1.3–4.4, $P = 0.007$). Among TB patients, MHA was associated with male sex (aOR 0.4, 95%CI 0.2–0.7), and unit increase in RDW-CV (aOR 1.2, 95%CI 1.07–1.4).

CONCLUSION Prevalence of MHA was high contributing to the morbidity among TB cases in urban Dar es Salaam, and associated with HIV. Clinical management of anaemia and nutritional interventions need to be considered to improve clinical outcomes and reduce the burden of anaemia and TB/HIV.

DISCLOSURE I have no any conflict of interest.

O.3.6.3.004

Predictive score of severe acute malnutrition in children under 5 years in developing countries: development and validation

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INTRODUCTION The nutritional status is the best indicator of the well-being of the child. Inadequate feeding practices are the main factors that affect physical growth and mental development. Poor growth in infancy has a significant impact in adult life. The aim of this study was to develop a prediction score of severe acute malnutrition (SAM) in children 6–59 months.

METHODS Case-control study. Cases were children 6–59 months admitted to hospital for SAM which was defined by a z-score weight / height <−3 SD or <−2 SD with presence of edema; the control were children of the same age admitted to the same hospital for another condition other than the SAM. They were included consecutively and prospectively and matching was 1 by 1 on the date of consultation. Those with HIV infection, heart disease, birth defects or other disease that produces malnutrition were excluded. The number of subjects included in the study was 263 cases and 263 controls. We performed a univariate and multivariate analysis. The inclusion of variables was made by the stepwise method in the multivariate model. Discrimination score was assessed using the ROC curve and the calibration of the score by Hosmer-Lemeshow test. STATA software 12 was used for various statistical analyses.

RESULTS After logistic modeling, new criteria emerge as predictive factors of SAM; to each of these criteria we assigned a coefficient. Thus a score is calculated as follows: low birth weight X(1.0) + repeated or chronic diarrhea X(2.3) + daily meals's number less than 4 X(1.3) + age of breastfeeding cessation <6 months X(2.2) + age of dietary diversification <6 months X(1.16) + age of mother less than 29 years X (2.8) + parity below 5 X(1.8) + family history of malnutrition X (3.2) + number of children aged less than 5 years in siblings X (1.7). The area under the ROC curve was 0.9685, the sensitivity of 93.5%, specificity 93.2%, positive predictive value of 93.2% and positive likelihood ratio of 6.8%.

CONCLUSION No score published is adapted to predict the risk of occurrence of SAM in a population of <5 years in developing countries. We propose a simple and efficient score predictive of the risk of SAM which will require external validation study. This predictive score of SAM would be a useful and simple clinical tool to identify people at risk, limit high rates of malnutrition and reduce disease and child mortality in developing countries.

DISCLOSURE Nothing to disclose.

O.3.6.3.005

High intestinal parasitic infections and malnutrition in school-aged children in Burkina Faso

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BACKGROUND The present study undertaken in the framework of the 'Vegetable Go to School' (VGtS) project aimed to assess the baseline prevalence of parasitic infections and nutritional status among school-aged children in two regions of Burkina Faso at the onset of the project's complementary nutrition- and health-sensitive interventions.

METHODS The study was carried out in February 2015. Children aged 9–14 years were randomly selected in four intervention and four control schools in the Plateau Central and Centre-Ouest regions of Burkina Faso. Standardized, quality-controlled anthropometric and haemoglobin measurements were performed. Additionally, children were subjected to parasitological examinations using stool and urine samples collected on two consecutive days. Stool samples were examined by the Kato-Katz and formalin ether-concentration method. 10% of the samples were re-examined for quality control.

RESULTS A total of 445 school-aged children (231 boys and 214 girls) had complete data records. Intestinal parasitic infections were highly prevalent; 360 children (81.2%) were infected with at least one species of intestinal parasites. Intestinal protozoa infections showed particularly high prevalence rates (83.4%), while helminth infections were found in 7.5% of the children. The most frequent intestinal protozoa species encountered were: *Entamoeba histolytica/E. dispar* (67.4%), *Entamoeba coli* (35.2%) and *Giardia intestinalis* (25.7%). *Hymenolepis nana* (6.8%) was the predominant helminth species. Co-infections were common, affecting more than half of the children, whilst 14.7% of the study subjects suffered from triple species infections. With regards to children's nutritional status, the prevalence of stunting was 42.1% and that of thinness 15.3%. The prevalence of anaemia was 21.2%. Overweight/obesity rate was low (2%) and restricted to one school.

CONCLUSION This study shows that malnutrition and parasitic infections are important and concerning public health issues in school-aged children in the Plateau Central and Centre-Ouest regions of Burkina Faso. Our findings and further analyses of underlying risk factors determined by an accompanying questionnaire survey will be utilised for the design and implementation of complementary school garden, nutrition and health intervention strategies to jointly tackle ill-health and malnutrition, particularly for children in this age group.

DISCLOSURE Nothing to disclose.

O.3.6.3.006

Prevalence and associated factors of fruit and vegetable consumption among university students in 26 low, middle and high income countries

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OBJECTIVES The aim of this study was to assess the prevalence of fruits and vegetable consumption and associated factors among university students from 26 low, middle and high income countries.
METHODS Using anonymous questionnaires, data were collected in a cross-sectional survey from 17 789 undergraduate university students (mean age 20.8, SD = 2. 8) from 27 universities in 26 countries across Asia, Africa and the Americas.
RESULTS Overall, 82.8% of the university students consumed less than the recommended 5 servings of fruits and/or vegetables. The mean fruit and vegetable consumption varied by country, ranging from ≤2.5 mean daily servings in Jamaica, Philippines and Barbados to ≥3.9 mean daily servings in Mauritius, Tunisia and Ivory Coast. In multivariate logistic regression analysis, sociodemographic factors, psychosocial factors, and behavioural factors (inadequate dietary behaviours, binge drinking and physical inactivity) were associated with low prevalence of fruit and vegetable intake.
CONCLUSION Findings stress the need for intervention programmes aiming at increased consumption of fruit and vegetables considering the identified sociodemographic, psychosocial and behavioural risk factors.
DISCLOSURE Nothing to disclose.

TRACK 4: Health and Social Systems and Their Determinants

4.1.1. When people have a say. Participatory health governance, social accountability and access to local resources

INV.4.1.1.003

Public accountability practices of district health management teams: a realist inquiry in two local health systems in Ghana

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In today's local health systems in low- and middle-income countries, district health management teams, together with local authorities, bear the responsibility for health sector performance. This infers not only a responsibility for coordination of the multiple actors in pluralistic health systems and the organisation of services and programmes, but also for ensuring accountability towards the population. This explorative study appraised actual public accountability practices of district health management teams in two local health systems in Ghana and explored how these could be improved.

We used a comparative case study design based on realist inquiry principles. An initial middle range theory was developed on the basis of a literature review of governance and accountability spanning different social science research traditions. It was tested in one urban and one rural health system. Data collection included in-depth interviews, informal discussions, and review of documents, reports and routine data.

In both districts, the health management teams had strong upward accountability systems through which they accounted to the regional and central level authorities of the Ghana Health Service. This accountability was enforced by command-and-control mechanisms such as centrally set priorities and planning directives, audits and performance reviews. In the rural local health system, the district health management team had strong horizontal accountability practices towards the District Assembly and INGOs with whom they collaborate in health service delivery programmes. These relations were based on shared interests and reciprocity. However, in both sites, public accountability strategies were found to be virtually absent. Apart from complaint boxes, there were no formal channels of communication nor for participation of the public in local priority-setting and performance assessment. As a result, none of the district health management teams achieved full public accountability.

The study identified ways to improve public accountability. First, there is a critical need for more transparency and information sharing with the public. Existing performance appraisals, for instance, should be open to public representatives. Public accountability practices should be enforced by a 'meta-governor' (Bell and Hindmoor, 2009), recognised in this role by all other actors, capable of overseeing local health system governance.
DISCLOSURE Nothing to disclose.

4.1.2. From global health diplomacy to global health actions: the northen and southern perspectives

O.4.1.2.002

The Global Fund's new funding model in the context of international funding shortfalls: does it foster ambition in scale-up and quality of HIV programs?

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INTRODUCTION In 2014 the Global Fund to fight Aids, TB and Malaria (GFATM) launched its new funding model (NFM) replacing annual 'rounds' of country funding requests. For the first time since the cancellation of round 11 (2011), countries submit new proposals for urgently needed scale-up, including new tools and approaches to improve program quality. The NFM provides allocations based mainly on country income level and disease burden, with additional funds potentially available through competition from a restricted pool of 'incentive funds'. A first group of countries applied through the NFM process and analysis of the effects can guide necessary adaptations.
METHODS AND MATERIALS We studied how NFM criteria and pre-defined allocations affected programmatic ambition in proposals, reflected 'full expression of program demand' and current country program needs. Qualitative methods were used to analyse processes and proposals in selected countries where MSF teams contributed. Key informants involved in the processes in DRC, Guinea, Mozambique and Malawi from MSF and partners (incl. Country Coordinating Mechanisms, UNAIDS, WHO, Pepfar) were selected and interviewed over a 6–12 months period. Data collection included application documents, national strategic plans, GFATM and technical partners' guidelines, epidemiological statistical data etc.
RESULTS While in theory ambitious requests were possible, countries encountered confusing and conflicting guidance on acceptable funding levels and application modalities.

Indicative funding allocations and preliminary or final grant results corresponded poorly to country plans and current funding needs, including a shortfall for even critical continuity of services in some

CONCLUSIONS

1 While the NFM should encourage rather than hamper country ambition, there was limited and conflicting guidance regarding capped allocations.
2 The NFM appears to have fostered country ambition to some extent despite countries' awareness of limited funding prospects.
3 The methodology to determine initial allocations should be reviewed to better correspond to the present funding needs in countries.
4 Findings should feed into review of NFM methodology and process.
5 The ability to reward country ambition is undermined by scarce GFATM funding and needs urgent political attention. The core GFATM principle of country driven ambition and demand is at risk, with major implications for scale up and quality in programs.

DISCLOSURE Nothing to disclose.

O.4.1.2.003

Spectrum of diseases occurring in refugees and asylum seekers treated in three clinical settings in Munich, Germany

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INTRODUCTION In 2014 the number of refugees and asylum seekers (R/AS) in Germany rose steeply. Overcrowded initial reception facilities (IRF) posed logistic and medical problems to public health offices and services. In Munich the registered society REFUDOCS (RD) was founded to provide basic medical care for R/AS. Those with suspected infectious or tropical diseases were further treated at the department of infectious diseases and tropical medicine (DITM) of Munich University or at the infectious disease ward of the Munich municipal hospital Schwabing (MHS). As data on the spectrum of illnesses in this group in Germany are lacking, we provide the first exemplary data on this topic.

MATERIAL AND METHODS Anonymized data were retrospectively collected from two outpatient (RD, DITM) and one inpatient (MHS) setting by checking medical records and patient databases for treated R/AS.

RESULTS Records of 548 R/AS patients could be evaluated. Common countries of origin were Eritrea, Somalia, Syria, Senegal, Kosovo, and Albania. At the general medical office of RD in the Munich IRF, 329 patients with 522 visits were seen in 2 1/2 months starting from January 2015. Leading causes of visits were acute respiratory, neuropsychiatric, and gastrointestinal/hepatological illnesses (152, 67, 56 visits, respectively). At DITM 44 R/AS patients were treated in 2014. Most common diagnoses were tropical diseases (17 patients, e.g. vivax/falciparum malaria, schistosomiasis) followed by dermatologic conditions (11 patients, e.g. bacterial skin infection, scabies). Leading diagnoses in the inpatient setting of MHS were tuberculosis (53 cases), vivax/falciparum malaria (39 cases), and bronchopneumonia (19 cases). In seven months starting from July 2014 175 refugees were treated.

CONCLUSION The growing number of R/AS arriving in Germany poses special challenges. Lack of knowledge concerning diseases in R/AS can lead to missed or delayed diagnosis and treatment. The exemplary data from this study mostly show occurrence of illnesses well known to German general practitioners. However, depending on the country of origin, infectious/tropical diseases uncommon in Germany have to be considered. In the setting of IRFs infectious diseases such as tuberculosis or scabies, and – currently of major concern - measles can spread easily and prevention and case-finding are important. Larger and prospective studies are needed to gain knowledge about the medical problems of this group of patients.

DISCLOSURE Nothing to disclose.

O.4.1.2.004

The challenges for global governance for health and universal health coverage under sustainable development goals

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INTRODUCTION From 2001, the Millennium Development Goals (MDGs) have been associated with new structures in governance for health at global and country level. The World Bank adopted MDG reporting as the metric for Poverty Reduction Strategy Papers and grants; multilateral and bilateral donors shaped their development programs to support MDG health priorities. The GAVI Alliance and the Global Fund to Fight AIDS, Tuberculosis and Malaria emerged to respond to these same priorities. Annual MDG reporting now benchmarks development progress at national, regional and global levels, but global governance for health remains fragmented.

METHODS The results are based on interviews with key multilateral stakeholders, and a discourse analysis of the literature around emergent global governance structures for health, analysing their implications for health systems and Universal Health Coverage (UHC).

RESULTS The Sustainable Development Goals (SDGs) health goal has expanded to include non-communicable diseases and mental health, neglected tropical diseases and additional communicable diseases, diseases associated with environmental pollution and road traffic injury. While the progress against the MDGs resulted in increased and focused commitment, the expanded scope of the 17 SDGs is unwieldy, and may distort development assistance priorities, with selected programs privileged in terms of financial and technical support, and resultant mal-distribution of financial and human resources. UHC continues to be advocated as a framework for addressing these new priorities, with additional mechanisms to address tobacco, alcohol and substance abuse. SDG indicators for the 169 targets are being negotiated. The World Bank and World Health Organization are mapping indicators for UHC, including those for chronic conditions and injury. New global governance models have been mooted: Global Funds for Health; Framework Conventions for Global Health; similar mechanisms for global governance of alcohol or food. The Chinese have launched an alternative Asia Infrastructure Investment Bank, and the Third International Conference on Financing for Development in Addis Ababa will explore financing options for the SDGs, with clear implications for governance.

CONCLUSIONS Analyses of global governance for health under the MDGs pointed to multiple players, networked fora and no

singe locus of governance for health; under the SDGs, governance may prove more fragmented, to health's disadvantage.
DISCLOSURE Nothing to disclose.

O.4.1.2.005
Is UHC's position within the emerging post-2015 health and sustainable development goals consistent with its prioritisation by the UN General Assembly in December 2012?

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INTRODUCTION In December 2012 the UN General Assembly unanimously adopted a Global Health and Foreign Policy Resolution. UHC was central: The resolution emphasized the fundamental role universal coverage plays in achieving the Sustainable Development Goals (SDGs), and links to states' foreign policy agenda. Despite this, UHC's status in subsequent post-2015 health and SDG negotiations became murky; contra to the UN resolution of late 2012.
METHODS UHC's trajectory in the post-2015 health and SDG debate's three phases will be investigated. Following a review of UHC's framing within the key post-2015 reports from 2013–2015, findings will be contrasted with responses on UHC's prioritisation in the emergent post-2015 landscape offered by key informants recruited from multilateral and associated agencies responsible for health and the post-2015 development agenda; informants who frequently sat at the cross-road of UN and Member State post-2015 dialogue.
RESULTS Our findings will focus on UHC's integration in the competing configurations of the proposed post-2015 health goals and targets as they temporally emerged in 2013–2015. UHC's main proponents and detractors within the dynamic post-2015 landscape will also be identified.
CONCLUSIONS This study's findings point to an erosion of UHC's primacy; arguably undermining the content of the UN General Assembly's resolution of December 2012. Unless UHC is expressly incorporated in the post-2015 health goal 'title' or target/indicator 'content', it will likely lose conceptual significance and prioritisation in future health and development activities. Alternatively, if UHC becomes one of many health and development goal targets, then its import will also likely be diluted on the world stage.
DISCLOSURE Nothing to disclose.

4.1.3. Health insurance for rural population – innovations and challenges

O.4.1.3.002
Financing healthcare through micro health insurance in Bangladesh

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BACKGROUND Healthcare financing in Bangladesh suffers from insufficient spending ($27 per-capita), inefficient resource use and high out-of-pocket (OOPs) expenses (64%) impeding universal health coverage (UHC). The country's current national health-financing strategy highlights the need for an insurance mechanism to raise more funds, ensure efficiency and reduce OOPs. Micro health insurance (MHI) has been identified as a transitional mechanism towards achieving this goal. ICDDR,B, a research organization in Bangladesh, initiated an MHI scheme in a rural area in 2012 with an aim to reduce reliance on OOP, ensure equity and efficiency in healthcare delivery and financing.
METHOD The study was carried out among the clients of the MHI scheme in Chakaria, under Cox's Bazar District of Bangladesh. Real time program data spanning February'12–January'15 was used for analysis.
FINDINGS AND INTERPRETATION Initially the scheme launched a general package including certain out-patient and in-patient services for a premium of Tk.1200/household/year ($15). After 8 months of operation the scheme was struggling on two grounds: ensuring equity and financial sustainability. A revised scheme was thus introduced with two packages of varying benefits [in-patient at Tk.1200/household/year and out-patient at Tk.500/household/year ($6.5)]. A safety net was built with an out-patient package where the poor have similar entitlements at a discounted premium [Tk.200/household/ year ($2.5)]. After the revision, enrolment increased rapidly and currently stands at around 5,500. Equity in access has been achieved with similar representation of 5 wealth quintiles in client-pool. To date the scheme could collect a total revenue of Tk.12 33 200 ($15 730) for the in-patient package and Tk.15 56 250 ($19 860) for the out-patient and poor packages. Benefit disbursed to date on average stands at Tk.3870/Household/year ($50) for the in-patient and Tk.1320/household/year ($17) for the out-patient and Tk.510/household/year ($7) for the poor package. Full cost recovery has been established for out-patient package while in-patient component is yet to reach break-even due to inadequate pool size.
CONCLUSION This experience indicates that an MHI scheme with a strong value proposition can potentially attract clients in low resource settings and generate adequate revenue to ensure effective risk pooling. Constant monitoring and modification is essential for any such scheme to be financially sustainable.
DISCLOSURE Nothing to disclose.

O.4.1.3.003
Applying technology in informal sector health insurance schemes – the example of the Insurance Management Information System in Tanzania, Nepal and Cameroon

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An estimated 100 million individuals are impoverished in any given year because of direct health expenditure incurred. This raises serious questions on the performance of health systems of low income countries which are grappling with limited resources, the inability to ensure equity and the desire to increase quality of providers. Increasing number of developing countries are now looking at health insurance schemes to address such challenges and move towards their national aspirations of Universal Health Coverage. Reaching out to the informal sector, which constitutes the largest part of the population in low and middle income countries, however, is difficult due to a multitude of challenges ranging from poor understanding of the concept of insurance to

finding financially viable outreach models. Lack of professionalized insurance systems makes informal sector schemes inefficient, in some cases unsustainable and in a lot of cases non scalable. Technology can play a significant role in success of insurance schemes but associated cost in most cases remains a deterrent for schemes targeting the informal sector. The Insurance Management Information System (IMIS) developed under a Swiss – Tanzanian cooperation project in Tanzania is an example of a technology which provides cost-effective operability in a rural and informal sector context. Experience of implementing this Insurance Management Information System gained in three countries (Tanzania, Nepal and Cameroon) shows how outreach to informal sector can be increased at low cost, and common problems (towards professionalizing schemes) like identification mechanisms, accountability towards clients, reaching out to remote areas, accessibility to all network facilities, flexibility of insurance model regarding benefit packages and pooling of funds, and operational monitoring can be better dealt with such a technology. The technological innovation has been able to support three different insurance models with district level (Tanzania), national level (Nepal) and community level (Cameroon) fund pooling. The system now covers close to 200 000 individuals across its implementation sites, having achieved a household coverage rate of 19% at the implementation sites in Tanzania. Projections in a rural district of Tanzanian show that administrative cost ratio (from total revenue) can be brought to below 40% with a population coverage rate of only 35%, which is a positive achievement for an informal sector scheme.
DISCLOSURE The IMIS development and implementation in Tanzania was done in the framework of the Health Promotion and System Strengthening Project, funded by the Swiss Agency for Development and Cooperation. The implementation in Cameroon was done in the framework of a Swiss Tropical and Public Health project with its partner Bamenda Ecclesiastical Provincial Health Assistance (BEPHA) funded by MISEREOR. The implementation in Nepal was done in the framework of a Swiss Tropical and Public Health Institute project with the Ministry of Health and Population in Nepal, funded by Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), Nepal.

O.4.1.3.004

Healthcare financing and outcomes in low and middle income countries: a model-based approach

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Despite the vast research done on health financing, little research has been conducted to determine the effects not only of public health expenditures but also of private health expenditures on health outcomes, particularly in low and middle income countries. Past studies have instead concentrated on public health financing and outcomes. This paper provides empirical evidence on the relationship between key health financing indicators, which include both public and private health expenditures, and different measures of health outcomes, including infant mortality rates, child mortality rates, life expectancy rates and a combined index, using cross-country data from 137 low and middle income countries. Findings discuss existing health financing and outcome indicators and highlight current gaps in its use. Descriptive statistics were then calculated to estimate health financing and outcomes in low and middle income countries. Bivariate analyses were conducted to examine the relationships between the variables of interest. Statistically significant associations between independent and dependent variables were identified and the results of the estimation procedure are presented. Our estimation shows statistically significant relationships for external resources for health and health outcomes, particularly mortality rates, in low and middle income countries. Out-of-pocket expenditures also showed statistically significant associations across any health outcome variable of interest, including mortality rates and life expectancy. Geographic information systems were also used to visualize current status of health financing in LMICs. Discussions focus on how these findings can be used in priority setting and in enhancing health financing arrangements or reforms, particularly in low and middle income countries.
DISCLOSURE Nothing to disclose.

O.4.1.3.005

Health care utilization among users of community-based health insurance after the implementation of subsidies to poorest households in Nouna, Burkina Faso

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BACKGROUND Access to health care is low in developing countries. Poor people are less likely to seek care than those who are better off. Community-based health insurance has been less effective in securing equity than expected. Poor people, who probably require greater protection from catastrophic health expenses, are less likely to enrol in such schemes. Even once enrolled, they use health care less frequently. This study investigated the utilization behaviour of health care among different CBHI members after the implementation of a subsidy program for the poorest households in Nouna area.
METHODOLOGY Using descriptive statistics and a zero-inflated binomial model, we analysed the utilization behaviour among CBHI members for a period of 18 months after the implementation of the subsidy program. We used the data from the Nouna Health and Demographic Surveillance System (HDSS) and the CBHI enrolment and utilization of health services register.
RESULTS During the evaluated 18 months of possible insurance coverage, 4572 people enrolled into the CBHI in Nouna. 2818 (62%) had at least one health care contact. 1189 (26%) CBHI members benefitted from the subsidy program and 616 (52%) of them used health care at least once. Our model showed there is a significant interaction between being a member in the subsidy program and the length of enrolment of 18 months (RR = 2.88) for more frequent health care utilization.
CONCLUSION The differences in the health care utilization among those CBHI members, with and without subsidy, disappeared after being enrolled for 18 months in the scheme. CBHI needs further improvement to increase the enrolment behaviour and retention in the scheme, especially among the poorest, to achieve equity in health care utilization.
DISCLOSURE Nothing to disclose.

4.2.1. Improving access to essential quality health services

INV.4.2.1.001

Improving access to healthcare – a critical element for advancing universal health coverage in Sub-Saharan Africa

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Access to health care has become a major political and economic concern in the pursuit of advancing Universal Health Coverage (UHC). Ensuring that all people obtain the health services they need, of good quality, without suffering from financial hardship when paying for them is a huge challenge for any country. Evidently, big disparities exist between the poor and the betteroff with respect to access to health care services. Even public subsidies for facilitating access to healthcare frequently benefit rich people more than poor people. To ensure more equitable access, innovative and community-based approaches are needed to better align health care services with poor people's needs, expectations, and resources.

Based on a comprehensive access framework that moves beyond conventional biomedical and public health approaches by placing access to health care in a wider context of people's livelihoods and poverty, this key note will present evidence on how selected Sub-Saharan African countries have addressed access issues in order to advance UHC. The framework is based on the assumption that once a person recognizes symptoms of an illness and decides to initiate treatment, five access dimensions (availability, accessibility, affordability, adequacy and acceptability) affect the health seeking behavior. What degree of access is reached along the five dimensions depends essentially on the interplay between: (i) the health care services and the broader policies, institutions, and processes that govern the services; and (ii) the households' and communities' socio-cultural and economic context that influence norms and livelihood patterns in a particular society.

The key note will provide evidence on three major areas relevant to improving the five access dimensions: First, reforms on health financing which result in an increase in the level and progressivity of funding for the health sector and in elimination of out of pocket expenditures at least for vulnerable populations. Second: Improvement in quality of care at the level of service delivery. In various countries there is a move to link quality with financing i.e. results based financing and to generate reliable disaggregated data that is critical to inform the planning process, ensure proper monitoring and evaluation as well as to provide the basis for accountability.Third: coordinated reforms across the health system, and even beyond the health sector, are neededto address barriers to demand side of health care.

DISCLOSURE Nothing to disclose.

O.4.2.1.002

Identifying and addressing structural quality gaps in primary health care in Tanzania

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INTRODUCTION Regular supportive supervision is a crucial element in improving the performance and quality of health facilities. To make supportive supervision more effective, a situation analysis needs to be conducted on a regular basis in all health facilities and identified problems discussed and addressed with all involved. An electronic *Tool to Improve Quality of Health Care* (*e-TIQH*) was introduced in seven districts in southern Tanzania with the objective of making supportive supervision of primary health care services more manageable, efficient and sustainable through reducing time and costs and by removing technical challenges in entering, cleaning and analyzing the collected data.

METHODOLOGY A comprehensive assessment of the quality of health care provision in all health facilities in the project districts is done annually. The tool assesses performance in six areas:

1 physical environment, tools and equipment,
2 job expectations,
3 professional knowledge skills and attitude
4 management and administration of the facility,
5 staff motivation and
6 clients' satisfaction.

With help of electronic tablets, the results are immediately made available to allow for timely feedback to providers and health system managers.

RESULTS At baseline, weak performance prevailed with regard to staff motivation, job expectations, and professional knowledge, skills and attitudes of health care personnel. Shortage of trained staff, lack of essential equipment and non-adherence to basic principles of infection prevention and control measures were important issues across all districts. A comparison of the baseline and follow-up assessments in project districts showed quick improvements in job expectations and professional knowledge skills and attitudes as a result of targeted on-the-job training and supply of treatment guidelines to health facilities. However, staff motivation remains a major structural issue that requires a multidisciplinary approach to address it.

CONCLUSION AND POLICY IMPLICATIONS e-TIQH helps to identify the major quality gaps across districts, regions and the country. By providing immediate results and feedback to providers and health managers, the e-TIQH approach facilitates immediate, mid- and long term planning to address the identified gaps. Thus, it has a potential for informing the planning process and making resource allocation more efficient in view of achieving the envisaged Sustainable Development Goals.

DISCLOSURE Nothing to disclose.

O.4.2.1.003

Heterogeneity of fever case management and provider performance at private clinics and pharmacies on the Kenyan coast: results from client exit and mystery client studies and competency assessments

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The private health sector is increasingly recognised for its potential as a key player in malaria case management. However, the 'private health sector' covers a variety of providers with varying competencies and behaviours, and differences are often poorly understood. Population Services International is implementing a three-year project to introduce malaria rapid diagnostic tests (RDTs) in private clinics and pharmacies in Kwale and Mom-

basa counties in Kenya. To better understand provider performance, client exit and mystery client surveys were conducted at a random sample of project facilities in Q4 2014. 526 client exit interviews were conducted at 86 clinics and 44 pharmacies with adult clients seeking treatment for fever for themselves or on behalf of someone else. 260 mystery client visits were conducted by known test-negative volunteers at 97 clinics and 58 pharmacies. Point estimates from studies were weighted, and standard errors calculated taking account of the clustered design. Concurrent routine competency assessments were done with 75 private physicians and 52 pharmacists. Exit interview clients were more likely to be tested for malaria at clinics than at pharmacies (84.1% vs. 39.7%, $P < 0.0001$). Overall 84.9% of 216 malaria test-positive clients received an antimalarial, with no difference between facility types ($P = 0.9$). However, clients at clinics were twice as likely to receive an antibiotic independent of test outcomes ($P < 0.001$). When mystery clients actively requested a test, there was no difference in testing levels by facility type (clinic: 95.0%, pharmacy: 93.8%). However, mystery clients at clinics reported being told they'd tested positive more often than at pharmacies (40.3% vs. 22.6%, $P = 0.02$). Almost all tests conducted at pharmacies were RDTs (92.6%) compared with 43.2% at clinics ($P < 0.001$). Overall, 9.3% of test-negative clients received an antimalarial, with no difference between facilities. Provider routine assessment scores were comparable: 54.4% of pharmacists and 57.7% of physicians scored over 80% when assessed on RDT procedure, though differences were observed in some key areas. Provider heterogeneity should be considered when conceiving projects within the broad private health sector in order to better define provider profiles and design tailored interventions that improve cost-effectiveness. Results from these studies are being used to tailor future training and supervision sessions with participating providers.

DISCLOSURE Nothing to disclose.

O.4.2.1.004

Official invitation letters are highly effective to increase male partner participation in antenatal care services in Mbeya Region, Tanzania

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BACKGROUND The benefits of male partner involvement in antenatal care (ANC) services for maternal and infant health outcomes and for HIV testing uptake among couples have been widely recognised. Despite this fact, male involvement in ANC remains disappointingly low in most sub-Saharan African settings. Invitation letters for partners could be an effective strategy to increase attendance rates. Hence, our study aimed at assessing acceptability and effectiveness of official invitation letters for male partner participation in ANC services in Tanzania.

METHODS We conducted implementation research at three health centres in Mbeya Region, including both urban and rural sites. Pregnant women approaching ANC without their partner were given an official letter from the health facility, inviting the partner to attend the next ANC session. If the partner attended, couple voluntary counselling and testing for HIV (CVCT) was offered. Questionnaires were administered to the women after the sessions. We analysed partner return rates at two subsequent visits, as well as social consequences of the letters and joint sessions for couples.

RESULTS Of 318 recruited women who received an invitation letter for their partner, 170 (53.5%) returned with their partners for a joint ANC session, 81.3% of whom proceeded to CVCT. Relatively higher age of women ($P = 0.042$) and self-reported HIV-positive status at baseline ($P = 0.046$) were negatively associated with partner return. Male attendance varied significantly between the rural and urban study sites ($P < 0.001$) with rates as high as 76% at the rural site, compared to 31% at the urban health centre. Most women assessed the joint ANC session as a favourable experience, however, 80% of women in HIV-positive discordant or concordant relationships reported problems during disclosure. Social outcomes reported one month after the session included improved client- provider relationship, improved intra-couple communication and enhanced sexual and reproductive health decision-making.

CONCLUSION Official invitation letters are a feasible intervention in a resource limited sub-Saharan African context, they are highly accepted by couple members, and are an effective way to encourage men to attend ANC and CVCT. Pre-intervention CVCT rates of 2–19% were clearly improved in all sites. However, more anonymous urban settings might require extra emphasis to reach high rates of partner attendance compared to smaller rural health centres.

DISCLOSURE Nothing to disclose.

O.4.2.1.005

The One-Stop Clinic of Ifakara: a model for integration of prevention of mother-to-child transmission and pediatric HIV services

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INTRODUCTION Family-centered approaches may facilitate access to HIV and primary health services. We describe the procedures and preliminary outcomes of the One-Stop Clinic of Ifakara (OSC), an integrated model of mother and child HIV care in rural Tanzania.

METHODS The OSC is a facility that integrates HIV and reproductive and child health care (RCH) under one roof. It was launched in 1/2013 aiming to facilitate linkage into care, reduce vertical transmission, and improve clinical outcomes and retention in care. A bundle of strategies was implemented: (i) Provider Initiated Testing and Counselling (PITC) in the pediatric and maternal wards; (ii) integration of HIV services for families within the RCH clinic; (iii) structured follow-up for HIV-exposed infants (HEI) and implementation of HIV PCR for Early Infant Diagnosis (EID); (iv) electronic medical records; and (v) development of a network with the peripheral health centres to foster the decentralisation of HIV care. We compared clinical outcomes between the first two years of the OSC (2013–14) and the previous five (2008–12).

RESULTS The mean number of pregnant women enrolled/year increased from 22 (SD 7.2) to 45 (SD 4.9), while the mean number of children enrolled/year was 91 (SD 44.4) and 80 (SD

23) respectively. Yet, it varied largely during 2008–12: 138 (SD 6.3) in 2008–09, and 58 (SD 10) in 2010–12. Median age at enrolment was 3.8 years (IQR 1.2, 7.9) vs. 2.6 (IQR 1.2, 8.1), *P* 0.67. Median CD4% at diagnosis was 19 (IQR 10, 34) vs. 17 (IQR 9, 26), *P* 0.007. The number of children with WHO stage 3/4 increased from 32% to 71%, $P < 0.001$. Among eligible children, antiretroviral treatment (ART) coverage rose from 80% (261/325) to 97% (116/119), $P < 0.001$. Retention in care 6 months after enrolment increased from 85% to 92%, $P = 0.09$. In 2013–14, 261 HEI were enrolled. By the time of analysis, 24 were HIV-infected, 76 uninfected,13 (5%) transferred, 31 (12%) lost to follow-up, and 117 had not yet reached a final HIV status. After EID was implemented, the median turnaround time of results was reduced from 7 months to 13 and 35 days for positive and negative results respectively. CONCLUSION The integration of services combined with PITC and EID resulted in an increased number of mothers and children diagnosed and linked into care, an increased detection of children with AIDS, and a greater ART coverage and retention in care. The OSC may provide a feasible and scalable model for maternal and pediatric HIV care in Tanzania. DISCLOSURE The One-Stop Clinic receives funding from Merck for Mothers Global Giving Program. The Chronic Diseases Clinic of Ifakara receives funds from the Government of the Canton of Basel-Stadt, the Government of Tanzania, and from USAID through the local implementer, TUNAJALI-Deloitte

4.2.2. Determinants of health and help seeking behavior

INV.4.2.2.001

Towards a comprehensive framework for community study of vaccine acceptance

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Explaining determinants of health- and help-seeking behaviour are challenges for disease control and long-standing interests of health social sciences. Help seeking for treatment and health seeking for prevention are sensitive to the influence of both health system and community determinants. Questions about vaccine effectiveness in the real world illustrate the point, but attention to community awareness and willingness to use available vaccines has been a neglected aspect of vaccine studies. The concept of hesitancy has recently become an important framework for explaining delayed acceptance or refusal of vaccination despite availability. A working group report of the WHO Strategic Advisory Group of Experts (SAGE) on immunization has elaborated this concept and approaches to assessing vaccine hesitancy. Matters of confidence, complacency and convenience all play a role, and the issues vary for different vaccines and across regions.

Cultural epidemiological studies have addressed a salient example of underutilization of vaccines, by examining community determinants of actual and anticipated acceptance of influenza vaccination in Pune, India, during the pandemic of 2009. Findings showed that hesitancy is a relevant consideration for both at-risk populations and health professionals. Furthermore, research is needed that not only assesses hesitancy, but also channels findings into programme strategies that measurably improve uptake and coverage.

Based on experience in the pandemic influenza vaccination study in Pune, we present a research design that applies findings to a designated public health priority, namely, improving seasonal influenza vaccination coverage in low- and middle-income countries for pregnant women. This group has been identified by the SAGE as most important among high-risk groups for influenza. The strategy involves focussed dissemination of at-risk community study findings to a group of antenatal care providers and comparing vaccination rates for patients of these providers with patients receiving standard antenatal care. The approach examines the value and indicates the need for a comprehensive framework for research on community issues to facilitate development of vaccine-specific research designs and implementation strategies.

DISCLOSURE Nothing to disclose.

O.4.2.2.002

Cultural beliefs are not the key determinants of treatment-seeking behaviour: lessons from ethnographic fieldwork in regions of Benin's Ouémé River valley endemic for Buruli ulcer

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Global health campaigns often consider sociocultural beliefs and local illness conceptions to have an almost determinist influence on health-seeking behaviours, particularly in the developing world. This is particularly true for a disease like Buruli ulcer, whose unknown route of transmission and unusual presentation foster interpretations of mystical etiology in many places where it is found. Ethnographic fieldwork in Buruli-endemic regions of Benin, where the physical attributes of the disease intersect with local epistemologies to suggest 'sent' rather than biomedical cause, therefore provides an excellent opportunity to closely investigate the logic of treatment-seeking behaviour and the actual relationship between illness perceptions and household practices.

This paper draws upon anthropological fieldwork conducted from 2009 to 2011 in communities endemic to Buruli ulcer near Dasso, Benin. Formal and informal interviews were conducted with former and current patients, community members, and health workers in villages and clinics. Participant-observation of everyday community life and health-seeking behaviour, and particularly of the actions and rationales of households in moments of health crisis, contributed strongly to the arguments here presented.

Fieldwork strongly suggests that the reasons for delaying or abandoning treatment are much more closely tied to economic, structural, and pragmatic considerations than to cultural beliefs. The links between belief and treatment-seeking behavior are often ambiguous or non-causal. While direct education campaigns have limited efficacy in reforming local beliefs, the impact of belief on health-seeking behaviour is strongly affected by the kind of demonstrable biomedical efficacy that current antibiotic protocols for Buruli ulcer provide. Furthermore, although justifications for biomedical delay or non-compliance are often grounded in explanations of cultural belief, these justifications generally appear as *post hoc* rationalisations rather than as determinants of health-seeking actions.

While it is necessary to attend to local beliefs in the design and execution of health campaigns, it is equally necessary to examine the underlying factors that distort the perceived significance of their impact on health-seeking behaviour. Resources

devoted to reform local beliefs might be better expended in addressing the structural factors that serve as the primary constraints for the poor to access appropriate care.
DISCLOSURE Nothing to disclose.

O.4.2.2.003

Healthcare-seeking behaviour and experiences of rehabilitation among disabled youth in Ghana

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INTRODUCTION Disabled youth in low and middle-income countries often face barriers to accessing healthcare and are confronted with limited and inadequate rehabilitation services. For instance, more than 90% of the disabled population in Ghana have no access to rehabilitation services. However, little is known about healthcare-seeking behaviour and experiences of rehabilitation among disabled youth in low- and middle-income countries. This presentation explores the healthcare-seeking behaviour of youth with different sensory and physical impairments in the particular case of Ghana. It also presents their experiences of different forms of rehabilitation, including conventional and traditional medicine.
METHODS This study used a combination of different qualitative research techniques, including life-story interviews, focus group discussions, participant observation, solicited diaries, self-directed photography and videography to shed light on the everyday realities of 50 youth with different impairment types (physical, visual, and hearing impairments) in Ghana. This approach offered disabled youth the opportunity to participate in methods that suited their abilities and preferences.
RESULTS The healthcare-seeking behaviour of disabled youth is influenced by a combination of different factors, including conceptualisations of disability, location (rural or urban area), type of impairment, knowledge of health-care and rehabilitation facilities and socio-economic and socio-cultural determinants. Due to inadequate rehabilitation services, limited knowledge about options for treatment and socio-economic constraints, traditional medicine and spiritual and faith healing play a significant part in the healthcare-seeking behaviour and experiences of rehabilitation in the lives of disabled youth. The impact of these alternative methods on the health status of disabled youth varied.
CONCLUSION This research offers valuable insights regarding the availability, benefits and challenges of different rehabilitation services for disabled youth in Ghana and can be used for further studies aiming to meet the rehabilitation needs of disabled people in low- and middle-income countries more generally.
DISCLOSURE Nothing to disclose.

O.4.2.2.004

Predicting non-communicable disease in Canada based on behavioral risk factors and social determinants of health

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In Canada, the concern over non-communicable diseases (NCDs), also known as chronic diseases, has become a major issue. With the significant increase of chronic disease risk factors, Canadians are facing chronic disease challenges. Two of five Canadians above the age of 12 years have at least one chronic disease and 80% are at risk of developing a chronic disease. Chronic disease rates are affected by a complex interaction of factors including the underlying socioeconomic, cultural, political and environmental conditions. This study assessed the impact of social determinants of health (SDOH) and behavioral risk factors (BRFs) on individuals' probability of getting a NCD in Canada. Both the independent effect of each risk factor and their multi-function effects were assessed. BRFs include fruit and vegetable consumption, physical activity, tobacco use and alcohol consumption. The SDOH considered in this study include income, education level, marital status, age and work stress. The Canadian Community Health Survey (2010) data set was used in the analysis of this study. A sample of 62 909 individuals were investigated in the CCHS 2010 survey. Univariable and multivariable logistic regression models were used in the analysis. These results indicate that the socio-economic status is related to an individual's probability of getting a NCD. Individuals with higher socio-economic status are more likely to have fewer NCDs. Respondents who reported higher levels of education and income experienced fewer NCDs than respondents with lower education and income levels. Respondents with the highest work stress levels were more likely to have chronic diseases than those not so stressed. A healthy lifestyle, i.e. more fruit and vegetable consumption, being physically active, less smoking, is important to maintain better physical health in order to reduce the risk of having a NCD. Respondents who were obese and overweight were more likely to have NCD than those of normal weight. Recommendations from both institutional level and community involvement policies were made in the conclusion.
DISCLOSURE Nothing to disclose.

O.4.2.2.005

Measuring the status of household water, sanitation and hygiene behaviours in rural Bangladesh: an application of qualitative information system

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INTRODUCTION Ensuring the condition of safe water, sanitation and hygiene facilities is the early step to behaviour change. However, mere provision of facilities does not ensure the desired health benefits. To improve health of the rural poor, the water, sanitation and hygiene (WASH) program of Bangladesh Rural Advancement Committee (BRAC) has been working in 250 rural sub-districts since 2006. Some of the major interventions are hygiene education, loan for installing deep tubewell, construction of tubewell platform and hygienic latrine. The quality of practice measured through an information system has gained recent attention by the program to monitor WASH services and improve quality of practices.
METHODS AND MATERIALS This was a cross-sectional comparative study between intervention and comparison areas. A multi-stage random sampling technique was used to select study samples, where each sub-district was considered as a cluster. Assuming 80% power, 5% significance level and 1.5 times design effect, the total sample size was estimated at 960 households. Thirty-six interviewers grouped into twelve were trained intensively on data collection tools and techniques. Both observed (spot check) and self-reported data were collected using structured questionnaire to assess the quality of WASH practices. The scaling principles of qualitative information

system (QIS) were applied to analyze data on WASH behaviours. The uniqueness of QIS method is that WASH practices are monitored and measured by collecting quantitative information on qualitative aspects.
RESULTS More households in intervention areas than comparison areas (65.5%. vs. 53%) scored above benchmark in using arsenic free and protected drinking water source. Hygienic latrine use (ring-slab with water seal) was found significantly higher in intervention areas over comparison areas (75% vs. 44%, *P*-value = 0.000). However, 0.3% of households in intervention areas defecated in the open indicating that the majority of them used a fixed place for defecation. More households in intervention than the comparison areas (58.3% vs. 52.6%) covered the pit with soil after disposing of the sludge to make the latrine reusable when pit was full.
CONCLUSIONS In sludge management, we found environmental consciousness about the pollution among the households in intervention areas, but they were unaware about the potential benefit of compost making out of the sludge and using it eventually for productive purposes.
DISCLOSURE Nothing to disclose.

4.2.3. Health workers patients interactions – key to compliance and adherence

O.4.2.3.001
Poor retention in care of HIV-infected pregnant and lactating women starting Option B+ ART in rural Mozambique

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INTRODUCTION In 2013, Mozambique adopted WHO-option B+ as the national strategy for PMTCT of HIV. We aimed to analyze retention in care of pregnant and lactating women (PLW) starting antiretroviral treatment (ART) under option B+ in Ancuabe, a rural district in Northern Mozambique with a decentralized ART provision system.
METHODS We compared outcomes of PLW starting ART under option B+ with those of non-pregnant non-lactating childbearing age women starting ART following clinical and/or immunological criteria between July 2013 and June 2014. Patients were followed until database closure on December 2014. LTFU was defined as not coming back to the clinic for >180 days after last visit; no-follow-up (NFU) was defined as not coming back for >180 days after first visit. Competitive risk regression was used to analyze factors associated to LTFU and logistic regression to factors associated with NFU. Models were adjusted for type of facility, age, baseline CD4, WHO stage and time from HIV diagnosis to ART.
RESULTS Six hundred and twenty-five women started ART between July 2013 and June 2014; 308 under option B+ (243 pregnant, 65 breastfeeding) and 317 following clinical and/or immunological criteria. They were followed up for 305.21 person-years. B+ pregnant and lactating women were more likely to be LTFU (67.5% vs. 55.4% vs. 32.5%; $P < 0.001$) and NFU (42.4% vs. 29.2% vs. 16.4%; $P < 0.001$) than women starting ART for their own health. In an adjusted multivariate analysis, B+ pregnant women (SH: 2.22; CI 95%:1.60–3.09; $P < 0.001$), B+ lactating women (SH: 2.02; CI95%:1.31–3.12; $P = 0.001$) and women that started ART at a peripheral type 2 health centre (SH: 1.66; CI95%: 1.20–2.29; $P = 0.002$) had a higher risk of LTFU. The risk of NFU was significantly higher in B+ pregnant women (HR: 2.75; CI95% 1.61–4.72; $P < 0.001$).
CONCLUSIONS Retention among PLW starting ART under option B+ in rural Mozambique was poor. A significant part of these losses to follow-up were early losses, therefore compromising PMTCT effectiveness. Women started on ART in peripheral health centres were more likely to be LTFU.
DISCLOSURE Nothing to disclose.

O.4.2.3.001a
Prevention of mother-to-child-transmission of HIV in the Option B+ era: uptake and adherence during pregnancy in Fort Portal, Uganda

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BACKGROUND Many sub-Saharan African countries have adopted the WHO guidelines of Option B+ as recommended regimen for prevention of mother-to-child transmission of HIV (PMTCT). Option B+ implies initiation of lifelong antiretroviral treatment for all pregnant HIV-positive women, regardless of clinical condition and gestational week. Uganda has introduced this regimen for PMTCT in 2012, but longer-term outcomes have not yet been evaluated.
METHODS We conducted an observational study to describe acceptability of the new regimen for women during pregnancy. HIV-positive women approaching antenatal care (ANC) services in two hospitals in Fort Portal, Western Uganda were enrolled in PMTCT- Option B+ and followed-up at every monthly ANC visit until delivery. We collected socio-demographic and clinical data and assessed drug adherence through pill counts at each subsequent ANC visit.
RESULTS In total, 124 HIV-positive pregnant women were initiated on Option B+ between January and December 2013 in our study sites. From these, 80.8% had not been aware of their positive HIV status before their first ANC visit. Lack of prior status knowledge and status disclosure were significantly associated with immediate loss to follow-up after the first visit ($P = 0.049$ and 0.019), which occurred in 45 clients (36.3%). Among those continuing Option B+ after the first visit, the median pill count adherence until delivery was 91.03%. The overall adherence level remained stable in the cohort throughout the course of pregnancy. Rather low adherence below 80% pill intake was observed in 21 clients (26.9%), while moderate adherence of 80–95% was achieved by 28 clients (35.9%), and high adherence >95% was achieved by 29 clients (37.2%). From these, 17 clients (21.8%) achieved full adherence of 100%. Higher adherence was significantly linked to higher gestational age at first ANC visit. Full adherence was also significantly linked to HIV status disclosure.
CONCLUSION HIV status awareness seems to be a large unresolved problem in our study setting. Also, one out of three PMTCT clients was lost to care already after the first visit. Program implementers should place special emphasis on comprehensive counselling for new PMTCT clients at their first visit, to prepare them adequately for Option B+ uptake.

However, those clients who remained in the program showed encouragingly high adherence levels throughout pregnancy, possibly demonstrating a consequence of the simplified Option B+ regimen.
DISCLOSURE Nothing to disclose.

O.4.2.3.002

The human factor in the clinical management of infectious diseases of poverty in remote, low-resource settings – a discussion of four qualitative studies on healthcare provider attitudes and practices

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The control and clinical management of infectious diseases of poverty is challenging in the best of circumstances, but becomes even more arduous in remote, low-resource settings where healthcare providers are faced with a range of additional factors that impact on their capacity to provide an optimal quality of care. This presentation will summarise findings from a series of qualitative studies on healthcare provider attitudes and practices regarding the management of a range of clinical syndromes and associated infectious diseases.

The studies were performed in remote areas in four different countries: the Democratic Republic of Congo, Indonesia, Nepal and Australia using various qualitative research techniques (non-participatory observation, in-depth interviews and focus group discussions). A different clinical syndrome was considered for each of the countries. These were respectively the neurological syndrome, the digestive syndrome, the persistent fever syndrome and skin infections. From these case studies we will distill and discuss the determinants that affect quality of care in such settings.

The following three main issues were identified from this body of work:
1 technical limitations (such as a lack of practical point-of-care diagnostic tests),
2 health system challenges (such as issues arising from a breakdown in communication between health facilities and health policy institutions) and
3 socio-cultural factors (such as patient expectations regarding the role of healthcare providers and their capacity to diagnose and treat).

We will argue that although the first two are important barriers, they are relatively well established in the literature, and more or less easy to overcome by technical and system innovation. The latter group of issues however, more akin to the human factor that is inherent to any intervention, is under-acknowledged and requires more consideration when developing strategies for the improvement of health service delivery.

While behavioural studies often tend to focus on 'the community' in itself, it is precisely the interaction of these socio-cultural determinants with the role model and role expectations of health professionals working in those socio-cultural contexts that can have a major influence on health outcomes.
DISCLOSURE Nothing to disclose.

O.4.2.3.003

Quality improvement of antenatal and intrapartum care services in Southern Tanzania: the health care workers' perspective

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INTRODUCTION Despite of the high use of antenatal care (ANC) in Tanzania, the quality of services provided in these clinics is still poor including the counselling sessions. Furthermore, the proportion of health facility deliveries is very low comparing to high ANC visits. A problem solving quality improvement (QI) approach was used to improve antenatal and intrapartum care in rural health facilities in Ruangwa district, Southern Tanzania. In order to learn about the impact of the intervention health workers' perspectives were explored.
METHODS AND MATERIALS The QI intervention was implemented in 21 dispensaries and two health centres from January 2010 to June 2011. The key areas targeted were ANC counselling and partograph use during labour. Qualitative in-depth interviews were conducted with 13 randomly selected healthcare workers from different health facilities and two district officials.
RESULTS The healthcare workers highlighted that the regular and targeted on-site follow up visits offered by the QI intervention assisted them to improve their services. The training content and close supervision increased the use of the partograph. Furthermore, the QI intervention contributed to the improvement of counselling during ANC, which allowed pregnant women to prepare themselves for delivery and to get timely help from their partners.
CONCLUSIONS Health care workers highlighted the potential of problem solving quality improvement interventions. However, the cost effectiveness of the problem solving QI intervention approach should be evaluated to prove its feasibility in developing countries. In addition, sustainability and harmonization of different maternal and newborn interventions need to be addressed.
DISCLOSURE Nothing to disclose.

O.4.2.3.004

Knowledge about Chagas disease of patients and health professionals in a non-endemic areas: are there differences?

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INTRODUCTION WHO is promoting the detection and management of neglected tropical diseases at Primary Health Care level as the best control strategy for them. Chagas disease (CD) is a challenge issue in most of the European countries, and its knowledge and management protocols are essential to ensure accessibility to the diagnosis and comprehensive treatment.
OBJECTIVES The aims were: to determine the knowledge level about CD of health professionals and patients and to evaluate the efficiency of a formative session about CD given by a training physician fellow (trained at the Unit of International Health of Drassanes-Vall Hebron) to the health professionals of their Primary Health Care (PHC) centres.

METHODS Descriptive study with two phases: firstly comparing knowledge about CD between health professionals and patients, and secondly comparing knowledge of health professionals before and after formative session. Knowledge was measured using a standardized questionnaire. Fellows answered before and after their stay at Unit of International Health of Drassanes-Vall Hebron, and a formative session was given by them at the PHC centres.

All data were collected after informed consent was signed, and were processed confidentially.

RESULTS A total of 111 health professionals from 6 PHC centres of Barcelona were included: 71.2% family doctors, 23.4% nurses, and 5.4% paediatricians; 94.6% attending Latin American population and 21.6% of them had previously diagnosed CD.

A total of 103 CD patients were interviewed: 98.1% Bolivian, 69.9% women with mean age of 37.5 years, and 47.6% reporting any relative affected by CD.

Health professionals knew less about CD than patients with $P < 0.05$. Answers regarding congenital transmission were right in 82.5% of the patients vs. 64% of the health professionals; heart involvement in 93.2% patients vs. 87.4% professionals; importance of CD screening of relatives in 99% of the patients vs. 85.6% professionals; treatment in children in 78% patients vs. 57.7% professionals.

Regarding the health professionals knowledge about CD before and after the formative session, a mean increase of 25.5 points was achieved (CI95% 16.8–34.1) with $P < 0.001$ value.

CONCLUSIONS Lack of knowledge becomes a barrier to guaranteeing access to comprehensive care to people affected by CD, it also generates mistrust. We need strategies to improve the general knowledge about CD, involving an educational intervention from Primary Care level.

DISCLOSURE Nothing to disclose.

O.4.2.3.005

An operational comparative study of quinine and artesunate for the treatment of severe malaria in hospitals and health centres in The Democratic Republic of Congo: the MATIAS study

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BACKGROUND The Democratic Republic of the Congo (DRC) has the highest number of severe malaria cases in the world. In 2012, the National Malaria Control Programme (NMCP) changed the policy for treating severe malaria in children and adults from injectable quinine to injectable artesunate. To scale up injectable artesunate nationwide, operational research is needed to identify constraints and challenges in the DRC's specific setting.

METHODS We compared the implementation of injectable quinine treatment in 350 patients aged two months or older with severe malaria in eight health facilities from October 2012 to January 2013, and in the same facilities injectable artesunate in 399 patients from April to June 2013. Since this was an implementation study, concurrent randomised controls were not possible. Four components were evaluated in each phase: (i) clinical assessment, (ii) time and motion, (iii) feasibility and acceptability, and (iv) financial cost.

RESULTS The time to discharge was lower in the artesunate (median = 2, 90% central range 1–9) compared to the quinine group (3 (1–9) days; $P < 0.001$). The interval between admission and the start of intravenous (IV) treatment (2 (0–15) compared to 3 (0–20) hours; $P < 0.001$) and parasite clearance time (23 (11–49) compared to 24 (10–82) hours; $P < 0.001$) were lower in the artesunate group. The overall staff pre-administration time (13 (6–38) compared to 20 (7–50) minutes; $P < 0.001$) and the personnel time spent on patient management (9 (1–24) compared to 12 (3–52) minutes; $P < 0.001$) were lower in the artesunate group. In hospitals and health centres, the mean (standard deviation, SD) total cost per patient treated for severe malaria with injectable artesunate was USD 51.94 (16.20) and 19.51 (9.58); and USD 60.35 (17.73) and 20.36 (6.80) with injectable quinine. Among 201 patients treated with injectable artesunate and with complete follow-up 23 (11.4%) had a delayed Hb decrease between 2 and 5 g/dl 7–21 days after treatment. Five patients (2.5%) had a decrease in Hb below 5 g/dl during at least one follow-up visit. In all patients Hb recovered by day 28.

CONCLUSIONS This study demonstrates that injectable artesunate in the DRC is easier to use and that it costs less than injectable quinine. Delayed anaemia was clinically manageable with appropriate and prompt care in all patients. These findings provide the basis for practical recommendations for rapid national deployment of injectable artesunate in the DRC.

DISCLOSURE SD, and PH are employees of MMV.

4.2.4. Promoting multi-sectorial approaches in health: what kind of science do we need?

O.4.2.4.002

Cross-sectoral partnerships for health in real-life: a case study of the Global Fund's country coordinating mechanism (CCM) in Ethiopia

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Over the last two decades, there has been a high proliferation of cross-sectoral partnerships in the field of global health governance. Partnerships are widely celebrated for advancing egalitarian objectives as they involve state and non-state actors in governance processes. However, their conduct in *real-life* is less understood. Especially, their 'embeddedness' in national contexts in developing countries remains unexplored.

This study set out to explore real-life interactions between multi-sectoral actors in developing countries in and around globally initiated partnership mechanisms. To this end, the study undertook a case study of the Global Fund's Country Coordinating Mechanism (CCM) in Ethiopia. Drawing on the critical realist research paradigm, the study first describes the defining features of interactions between actors, followed by an analysis of explanatory factors that underlie observed trends. It is a qualitative study employing in-depth interviews with 43 policy makers, non-participant observation of CCM meetings, and document review. The data was analysed through the thematic analysis method.

Actors' interactions in the CCM were mainly characterised by: dominance by the public sector, prioritisation of clinical care over population based health promotion interventions, a consensus based decision-making approach that actually favours powerful actors, and predominance of discourses that bolster the positions of dominant actors. The explanatory factors underlying these trends include: the ideology of the government (Developmental State), the historical relationship between actors, the broad set of geopolitical issues that define the relationship between donors and the Ethiopian State, the legal frameworks for regulation of non-State actors and the inherent organisational challenges that afflict non-state actors. Furthermore, the findings expose the ways in which partnership requirements emanating from the Global Fund interact with these contextual factors to reproduce the relative ordering of actors that exists in the setting.

Rather than an uncritical acceptance of partnerships as egalitarian governance solutions, there needs to be a careful scrutiny of the ways in which they facilitate interactions between actors in real-life. Specifically, the influence of broader contextual factors need to be taken into account, along with how these factors interact with the design of partnerships to influence interactions between actors.

DISCLOSURE Nothing to disclose.

O.4.2.4.003

A qualitative evaluation of stakeholder perspectives on the Millennium Village Project successes and challenges in Sauri, Kenya

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The Millennium Villages Project (MVP) is a 10-year, multi-sectorial, rural development program that strives to achieve the Millennium Development Goals at an annual cost of US$110 per capita through implementation of evidence-based interventions across sectors, including agriculture, health, and education. Focusing on early implementation of the first MVP site in Sauri, Kenya, perspectives held by major stakeholders ($N = 27$) in the planning and implementation of project activities were examined using semi-structured interviews. Key stakeholders represented implementing agency and partners from village sector committees (VSCs), local and regional government agencies, international health agencies, non-governmental organizations, and academic and policy institutions. Interviews were recorded, transcribed, and analyzed using NVivo10, a qualitative software. Interviews were coded inductively and independently by three researchers to ensure high inter-rater reliability. Data suggest differing views among stakeholders around program successes. Additionally, although MVP sought to impact changes in three areas -namely, agriculture, health, and education- during its early phase, most emphasized positive effects in health and agriculture, with fewer mentioning achievements on education. Distinctions in expressed challenges were found with most indicating planning difficulties regarding development and mobilization of VSCs and others identifying implementation barriers associated with program adoption and adaption. Conflict was apparent in stakeholder comments around resolving village-level power struggles and reconciling conflicts between MVP activities and government policies.

Findings also suggest enhancement in community cohesion and capacity. This qualitative evaluation of stakeholder perspectives on MVP successes and challenges contributes to the current debate at national and international levels in setting and implementing rural development policies.

DISCLOSURE Nothing to disclose.

O.4.2.4.004

The living and working conditions including accessibility to healthcare of migrants working in rubber plantations in eastern Thailand

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INTRODUCTION New land use patterns and replacement of forested area with mono-agricultural land resulted in high demand for labour workers and influx of human migration across the Thai borders. This situation coincided with the disease outbreak and transmission of epidemic infections. Working in rubber plantations had the reputation for being a better occupation when compared to construction and fishery, since the ratio of profit divided between owners and labour workers was typically 60:40. Intensive hours of working conditions from midnight to midday of migrant workers could make them more vulnerable to vector-borne diseases and other health problems.

MATERIALS AND METHODS This study gathered information on health risk factors related to the living and working conditions including accessibility to social welfare and health services of 84 migrants from Myanmar, Cambodia, and Lao PDR. Systematic interviewed questionnaires with migrants, semi-structured interviews with 6 local authority public health and hospital officers; group discussions with 30 owners of rubber plantations; and informal home visits with 6 selective migrant families were methods used in this study.

RESULTS AND CONCLUSION It was found that 19% of migrants accessed social welfare and health services and 64% paid their own health service. About 50% of the study population reported to seek healthcare from pharmacy shops, and 14% went to private clinics for quick examination. The owners of rubber plantations paid for annual health examination and government health insurance for their registered migrants, but an ineffectiveness of health insurance implementation discouraged the use of health insurance. We concluded that improved accessibility to social welfare and health services, along with effective health policy implementation, could help in solving economic issues of migrants and reducing vector-borne diseases and other health risk due to their occupational habits.

DISCLOSURE Nothing to disclose.

O.4.2.4.005

Using regional socio-ecologic models to identify system barriers and enablers for the adoption of Improved Cook Stoves in rural Peru

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INTRODUCTION Adoption, continued uptake and use of Improved Cook Stoves (ICS) are influenced by determinants at personal, household, community, institutional and policy levels. Thus, the dynamics and prominence of levels within a local socio-ecological framework are key for sustainability of ICS programmes. We describe the local socio-ecological frameworks of three Peruvian ICS programmes in Cajamarca, La Libertad and Cusco areas and determine system level enabling and hindering factors for ICS adoption.
METHODS We used a mixed methods approach to explore the barriers and enablers for adoption; we compared programme characteristics, key actors and stakeholders in the three environments using questionnaire-, focus groups- and key informant data. Data analysis was structured around the newly proposed descriptive model of large scale uptake of ICS (Rehfuess et al, 2014).
RESULTS Considering individual and interpersonal levels of the socio-ecological models of stove programmes main enabler and barriers for household ICS-uptake were linked to fuel and technology characteristics, mainly time saving, durability and stove design. For householders pre-existing and provided knowledge and perception of health issues and air pollution-related respiratory health, safety of the stove, cleanliness, homes improvements and total perceived benefits were decisive factors for adoption. At community level programmatic factors and policy mechanisms were more essential e.g. creation of competition, training and operational issues linked to stove maintenances. At institutional level, main barriers appear founded in authoritative action plans; community voices demanding a functioning ICS supply chain were disregarded as were requests of communities for 'service agreement' for an ICS technical and maintenance follow-up. Institutions unknowingly create dependency with beneficiaries potentially reducing longterm programme effectiveness. At policy level main enablers are coherent clean energy policies. However barriers are linked to the high-level monitoring and quality control of the various governmental and non-governmental ICS programme deliveries.
CONCLUSION Sustained adoption and equity in ICS adoption can be enhanced. The different levels of the local socio-ecological framework from policy to beneficiary need to be understood and key enablers and barriers at each level of the framework considered for ICS programme implementation.
DISCLOSURE Nothing to disclose.

4.2.5. Determinants of health, knowledge attitude and practice

O.4.2.5.001

Community awareness, experience and preference for use of pandemic influenza vaccines in Pune, India

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INTRODUCTION Vaccination is a cornerstone of influenza prevention, but experience during the 2009–2010 influenza pandemic suggested problems in vaccine uptake worldwide. Community acceptance of a vaccine is a critical determinant of vaccine effectiveness. Despite acknowledged cross-cultural differences in public responses to pandemic influenza and need for country-specific studies, few have been conducted in lower income settings.
METHODS We conducted a cross-sectional, mixed-methods study in urban and rural Pune, India, in 2012–2013. Semistructured explanatory model interviews were administered to 436 community residents to study awareness, preferences and experience with pandemic influenza vaccination. Five focus group discussions and 12 in-depth interviews complemented the survey.
RESULTS Findings suggest trust in vaccines for pandemic influenza, but awareness of these vaccines was low (26.6% for nasal and 23.4% for injectable vaccines). Reported vaccine uptake was 8.3%. Some respondents did not consider vaccines as relevant for adults, but almost all (94.7%) believed that a vaccine would prevent swine flu. Main themes identified as reasons for vaccine uptake were having heard of a death from swine flu, health care provider recommendation or association with the health system, influence of peers and information from media. Reasons for non-use of influenza vaccines were low selfperceived risk, problems with access and cost, insufficient information and lack of a perceived government mandate endorsing influenza vaccines. A majority indicated a preference for injectable compared to nasal vaccines, especially in remote rural areas.
CONCLUSIONS Low community awareness of pandemic influenza vaccines limited coverage. A clear message from the government endorsing pandemic influenza vaccines, which the community indicated was missing in the 2009 influenza pandemic, would likely have improved coverage. Training for health care providers would also have helped. Hesitancy from a lack of confidence in pandemic influenza vaccines appears to have been less of an issue than access, complacency and other sociocultural considerations. Recent influenza outbreaks in 2015 in India highlight a need for government policy to reconsider the priority for influenza vaccination beyond use in pandemics alone.
DISCLOSURE Nothing to disclose.

O.4.2.5.002

Household and community level factors associated with use of mosquito nets for under-five children in Nigeria: a multilevel analysis

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BACKGROUND Malaria remains a public health concern in Nigeria despite enormous global investments in the distribution of mosquito nets to protect individuals from *Plasmodium* parasites. Children under 5 years of age are most susceptible to severe malaria and should be given preference for sleeping under a mosquito net. It is important to understand the household and community-level factors associated with use of mosquito net for under-five (U-5) children.
METHODOLOGY The study was a secondary analysis of data obtained in the 2010 Nigeria Malaria Indicator Survey (MIS). The survey encompasses all the 36 states of Nigeria. The 2010 NMIS sample was selected using a stratified, two-stage cluster design consisting of 240 clusters. SPSS version 20 and STATA version 12 were used for the analysis.
RESULTS Overall, 28.2% of the households had mosquito nets out of the total household population. Two-thirds (67.6%) of households reported using mosquito nets for U-5 children out of all households with U-5 children. There was an association between living in areas covered by mosquito net scale-up programs and U-5 use of mosquito nets ($P < 0.05$). U-5 households living in areas covered by World Bank project areas and other project bodies were 1.5 times (OR = 1.5. 95% C.I = 1.07–2.22) and about 2 times (OR = 1.80. 95% C.I = 1.19–2.73) respectively more likely to use mosquito nets than households without mosquito net scale-up programmes. There is a significant association between sex of head of households and U-5 use of net. U-5 households headed by females were about 2 times (OR = 1.94. 95% C.I = 1.14–3.23) more likely to use mosquito nets than U-5 households headed by males. Furthermore, U-5 household heads above 50 years were about 2 times (OR = 0.59. 95% C.I = 0.44–0.79) less likely to use mosquito nets than households whose head is below 51 years.

Finally, the community level random effect was statistically significant ($P < 0.01$); the residual intra-class correlation for the community was significantly large (9.7%), suggesting that even after controlling for household level and community level factors there were still substantial clustering of net use at the community level.
CONCLUSION This study has shown that living in areas covered by mosquito net scale-up programmes, gender and age of household head were significant factors associated with use of mosquito nets for U-5 children in Nigeria.
DISCLOSURE Nothing to disclose.

O.4.2.5.003

Mixed-methods design to promote deeper understanding of how socioeconomic change influences health: the experience of a middle-age population in Poland

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INTRODUCTION Relatively few studies have examined the effect of a current and past socioeconomic position on health, but those who did found that the class of origin has a long-lasting effect on health, regardless of current social position. There was however no such research in Eastern Europe so far, which is surprising given how deep social and economic change this region has been.
MATERIAL AND METHODS This study applied a sequential-mixed methods approach by integrating a cross-sectional representative data with an ethnographic study. We looked at 7500 individuals aged 45–59 residing in Poland, and a qualitative set of 18 in-depth interviews in an attempt to describe and understand the health differences of people with very different socioeconomic trajectories.
RESULTS Approx. 60% of the sample changed their social class between childhood and adulthood, which is a very high rate of vertical social mobility. In addition to that, we observed a deviation in health pattern of mobile groups compared to the evidence from the UK or Scandinavia. Namely, the protective effect of belonging to a higher socioeconomic class in childhood was low and sometimes even non-existent. Qualitative, ethnographic follow-up provided some possible explanations for this pattern. We postulate that during the communist times social classes in Poland were poorly isolated, and the state promoted uniformisation of lifestyles. Thus the impact on socioeconomic class in childhood on health may be lower than could be expected, based on evidence form well established democratic societies.
CONCLUSIONS Supplementing an otherwise quantitative study with a qualitative component provided a better insight into the nature of factors shaping health status of a post-transformational society. Ethnographic investigation created also an opportunity for people from very different socioeconomic backgrounds to communicate their views on the factors that influence their health and their rationale for health choices. Such participation is too rarely possible in classic epidemiological studies, even those within the domain of social determinants of health.
DISCLOSURE Nothing to disclose.

O.4.2.5.004

Risk perception for HIV infection by multi-stage stratified random cross-sectional survey, South Africa 2012

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BACKGROUND South Africa (SA) has a high HIV prevalence (12.2% in 2012). Incidence of HIV among male and females aged 15–49 years has been decreasing: from 1.9% during 2005–2008 to 1.7% during 2008–2012. However, prevention efforts must focus on high risk groups and assess their risk perception. We describe identified factors associated with perceived risk of HIV infection in an SA population using a national representative survey.
METHODS To assess factors associated with perceived risk of HIV infection we used data from a multi-stage stratified random cross-sectional survey conducted in 2012 with South Africans aged 16–55 years. Multivariable logistic regression was used to determine factors associated with perceived risk of HIV infection. Forward selection, variables with P-value <0.05 and improved fit model were retained in the final model. Analyses were adjusted for clustering and done using STATA. Results

were summarized using Adjusted Odds Ratios (AOR) with their corresponding 95% confidence intervals.
RESULTS Of 8756 respondents 19.9% (1743) perceived themselves to be at high risk of HIV infection. Female gender (AOR 1.76, 95% CI: 1.53–2.04), living in Mpumalanga compared to Western Cape Province (AOR 3.53, 95% CI: 2.33–5.36), low socio-economic status (SES) (AOR 1.28, 95%CI: 1.05–1.57), having multiple sexual partners (AOR 2.58, 95%CI: 2.11–3.13), and low self-esteem (AOR 1.67, 95% CI: 1.23–2.27) were significant predictors of high risk of HIV perception.
CONCLUSION Heightened risk perception of HIV infection in SA is associated with specific gender, geographic, economic, behavioral and self-esteem factors. To expand on HIV prevention efforts, initiatives targeted at groups linked to these identified risk factor should be developed.
DISCLOSURE Nothing to disclose.

O.4.2.5.005
The effect of two different intervention approaches on a Nipah virus prevention intervention in Bangladesh

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INTRODUCTION Nipah virus infection (NiV) is a bat-borne zoonosis transmitted to humans through consumption of contaminated raw date palm sap. In Bangladesh, raw sap is a traditional delicacy. The objective of this study was to measure the association between exposure to two different intervention approaches and changes in date palm sap consumption to prevent NiV transmission.
METHODS We developed and implemented a behavior change communication intervention to reduce the risk of NiV transmission using community mobilization, interpersonal communication, posters and television. In one district, we recommended stopping drinking raw date palm sap ('no raw sap'). In a different district, we promoted the use of a skirt-like barrier, a traditional method used by local sap harvesters that interrupts bats' access to sap, recommending drinking only skirt-protected sap ('only safe sap'). We conducted surveys with randomly selected respondents, in April 2014, 2 months after the intervention, to measure the proportion of people reached and their change of behavior.
RESULTS We interviewed 1776 respondents equality distributed in the 'no raw sap' and 'only safe sap' districts. Respondents from the 'no raw sap' district reported 30% direct exposure to the intervention and 28% indirect exposure by learning from others. In the 'only safe sap' district direct and indirect exposure to the intervention were 41% and 38%. In the 'no raw sap' area, neither direct exposure (18% vs. 18%, OR 1.0, CI 0.7–1.5, $P = 0.95$) nor indirect exposure (22% vs. 16%, OR 1.4, 95% CI 0.9–2.3, $P = 0.09$) were associated with stopping raw sap consumption. In the 'only safe sap' area, respondents who mentioned direct exposure were less likely to consume raw sap from an unprotected source than those who were not exposed to the intervention (22% vs. 29%, OR 0.68, 95% CI 0.5–0.9, $P = 0.01$). Indirect exposure was not associated with reduction of raw sap consumption from an unprotected source (27% vs. 33%, OR 0.7, 95% CI 0.4–1.1, $P = 0.18$).
CONCLUSION The results from the 'no raw sap' district suggest that convincing people to abstain from drinking a traditional delicacy are difficult to achieve. Promoting the use of skirts, an existing preventive method, in the 'only safe sap' area seems like an effective approach to modify raw sap drinking behavior. To reduce the risk of NiV transmission, a future 'only safe sap' intervention should focus on increasing direct exposure to help prevent NiV infection.
DISCLOSURE Nothing to disclose.

4.3.1. Effective development cooperation in a complex environment

O.4.3.1.003
Are Global Health Initiatives contributing to health system strengthening in Zanzibar?

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INTRODUCTION It is widely agreed that Global Health Initiatives (GHIs) should contribute to Health Systems Strengthening (HSS) in the countries in which they operate. However, examples of this being achieved are few. The objective of this study was to examine GHI contributions to the health system beyond its own vertical objectives in Zanzibar, where substantial progress has been made in controlling malaria through a GHI program.
METHODS A range of health indicators recommended by the World Health Organisation (WHO) for the overall assessment of health systems was examined for the period 2000–2010 to identify trends indicating changes in the status of the health system. Interviews were conducted with representatives of the government, primary health care (PHC) and organisations involved in malaria control to evaluate GHI interaction with health services not directly involved in malaria control.
RESULTS Analysis of health indicators confirmed improvement in all malaria indicators but did not show improvements in other areas. Analysis of interview data showed agreement on the need for GHI's to contribute to HSS but with little consensus on how this should be accomplished. Further, while there was an extensive interaction between the GHIs and health services involved in malaria control, there was little interaction with other stakeholders. The development community has recognised that GHI interaction with a wide range of stakeholders is essential for HSS. This policy was pursued in Zanzibar but was limited to stakeholders directly involved in malaria control. Further, while mechanisms existed to promote interaction between stakeholders, sustained underfunding prevented its effective operation so opportunities to extend the benefits of the malaria control program to other health services were not identified or pursued.
CONCLUSIONS To enhance GHI contributions to HSS, governments must facilitate communications between all stakeholders and ensure this process is coordinated by people with a broad understanding of the health system who can identify opportunities for inter-service collaborations. Further, GHIs must include support for these mechanisms within their budgets.
DISCLOSURE Nothing to disclose.

O.4.3.1.004

Political pressure from donors to reduce or end health aid on basis of country income classification risks damage to people's health in middle income countries and undermining effectiveness of global health initiatives

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INTRODUCTION Increasingly, donors shift development aid away from countries classified as middle income countries (MIC). This trend affects development health aid (DHA), both bilaterally and through global health initiatives (GHI), as reflected in GAVI's graduation policy and increased pressure on the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) to exclude countries from grants based on income. In addition, there are indicators that MIC-classification will negatively influence access and pricing of medical commodities for these countries.
METHODS AND MATERIALS Interviews with key actors included governmental donors, international agencies, GHI, international and national NGOs. Analytic mapping of bilateral donors' policies and aid instruments towards health aid allocation based on country income classification was compared to actual and projected level, type and modalities of health aid in selected countries (Lesotho, South Africa, Myanmar, Kenya, South Sudan, Kyrgyzstan). Analysis of donors' positions influencing restrictions applied to GHI. Country case studies to explore consequences for health due to DHA reduction in MIC.
RESULTS Evidence linking country income classification and health aid needs or poverty is weak and inconclusive. Factors such as fiscal space, limited tax base, restricted political influence of the health sector, governance and disbursement problems delay and hamper domestic allocations to health. Implications of MIC status include: increased international prices of drugs, vaccines and diagnostics; increased patient fees plans and end of waivers for vulnerable patients. GHIs adapting to income-classification based policies, risk undermining countries' ambitions and hinder GHI's own strategic objectives. Shortfall of international funding has repetitively been invoked as argument for restrictive measures.
CONCLUSION The present donor tendency to exclude MICs from development health aid through bilateral and GHI channels is based on insufficient evidence; reveals weak links between country health needs and financing gaps; exposes inability and/or unwillingness of states to allocate sufficient domestic funding for necessary health results. Vulnerable groups in particular suffer risk of increased exclusion from essential health services. GHIs cannot mitigate increased commodity prices, nor other negative consequences of shifting burden of health financing to unavailable or insufficient domestic funding.
DISCLOSURE Nothing to disclose.

4.3.2. Maternal and infant health

O.4.3.2.002

Decline in infant mortality in Guinea-Bissau – trends and risk factors

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INTRODUCTION Although the infant mortality rate in Guinea-Bissau has declined over the past two decades, it remains high. We aimed to identify risk factors for infant mortality in the rural population of Guinea-Bissau and assess whether these risk factors changed from 1992–3 to 2002–3.
METHODS AND MATERIALS The Bandim Health Project (BHP) continuously surveys children in randomly selected clusters of villages in rural Guinea-Bissau. We investigated whether several maternal and infant factors were associated with infant mortality and assessed whether the risk factors changed from children born in 1992–3 to children born in 2002–3. Mortality rate ratios (MRR) for risk factors were assessed in multivariate cox regression, stratified by cohort and age group (0–45 days, 45 days–5 months, 6–8 months and 9–12 months). We tested for interactions with sex and cohort to assess whether the risk factors were the same for boys and girls and in 1992–3 and 2002–3.
RESULTS A total of 3706 live born children were followed in 1992–3 and 4526 in 2002–3. In spite of a civil war disrupting health services in 1998–2000, the infant mortality rate declined from 1992–3 to 2002–3 (MRR = 0.88; 95%CI: 0.77–0.99), and more so among girls [MRR = 0.77 (0.64–0.94)] than among boys [MRR = 0.97 (0.82–1.15)] ($P = 0.10$). The decline was especially evident among girls aged 9–12 months [MRR = 0.55 (0.37–0.83)]. Median age at vaccination, as a measure of vaccination coverage, declined from 1992–3 to 2002–3 – thus coverage increased. Previous loss of child, being twin and being the oldest sibling were the main risk factors for infant mortality in the multivariate analyses and were especially profound among 0–45 day old children. No health facility within the village was a risk factor in 1992–3 but not in 2002–3, whereas long distance to hospital was a risk factor in 2002–3 but not in 1992–3. We saw no effects of maternal schooling, delivery at health facility or season of birth. The risk factors varied by age group. There were no formal interactions with cohort and sex.
CONCLUSIONS Infant mortality declined significantly from 1992–3 to 2002–3 especially among 9–12 month old girls. Factors associated with being twin, firstborn and previous death of child are still important contributors to infant mortality and have not changed particularly over time. However, the large decline seen among 9–12 month old girls may be due to increased measles vaccination coverage.
DISCLOSURE Nothing to disclose.

O.4.3.2.003

Mortality, morbidity and developmental outcomes in children born to women receiving either mefloquine or sulphadoxine-pyrimethamine as intermittent preventive treatment of malaria in pregnancy: a randomized controlled trial

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INTRODUCTION Malaria infection during pregnancy confers substantial risks for the woman, her fetus and the newborn child. Mefloquine (MQ) has showed to be an effective antimalarial in sub-Saharan Africa, though controversy about its safety in pregnancy has been subject of debate. A recent trial showed that African pregnant women receiving MQ for intermittent preventive treatment of malaria in pregnancy (IPTp) had less clinical malaria than those receiving sulphadoxine-pyrimethamine (SP) while the safety profile was similar. Furthermore, MQ is recommended for prophylaxis in non-immune pregnant women travelling to endemic areas and is a potential partner drug in artemisinin-based combination treatment (ACT) recommended in pregnancy or for women of childbearing age. However, safety of MQ in pregnancy has been poorly assessed in children over the first month of life and little is known about its long-term impact on infant's morbidity, mortality and development.

METHODS AND MATERIALS In the context of a multicenter randomized controlled trial to evaluate the safety and efficacy of IPTp with MQ compared to SP in pregnant women from Mozambique, Benin, Gabon and Tanzania, 4247 newborns were followed up until 12 months of age. Nutritional status and psychomotor development were assessed at months 1, 9 and 12 and incidence of malaria, anemia, hospital admissions, outpatient visits and mortality calculated for their first year of life.

RESULTS No differences in the proportion of stunting, underweight, wasting and severe acute malnutrition at month 1, 9 and 12 of age between infants born to women who had IPTp with MQ or SP were found. Higher risk of being unable to stand without help, walk without support and bring solid food to the mouth were observed in the MQ group at month 9 [RR 1.07 (95%CI 1.00–1.14) $P = 0.040$, RR 1.10 (95%CI 1.01–1.21) $P = 0.039$ and RR 1.32 (95%CI 1.03–1.70) $P = 0.031$] though no significant differences were found in the other psychomotor development milestones assessed. Incidence of malaria, anemia, hospital admissions, outpatient visits and mortality were similar in both groups.

CONCLUSIONS We did not find any associations between MQ administered in pregnancy and infant's mortality, morbidity, and nutritional status. Our findings from the psychomotor development assessment show significant differences in the achievement of 3, out of 20, items assessed. Impact of MQ in pregnancy on infant's psychomotor development should be further investigated.

DISCLOSURE Nothing to disclose.

O.4.3.2.004

Epidemiology of malaria in pregnancy in Central East India

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BACKGROUND Data on epidemiology of malaria in pregnancy in India are limited. This study describes the burden of malaria in a cohort of pregnant women that was enrolled in different ecological zones in Jharkhand and Odisha State, India for a clinical trial of two different artemisinin-based combination therapies (ACTs) for the treatment of malaria in pregnancy.

METHODS Women attending routine antenatal care clinics with a gestational age between 12 and 36 weeks were enrolled into the cohort from October 2010 till January 2014. At each monthly visit blood slides and filter paper samples were collected from all women. Women having fever or history of fever were screened with a rapid diagnostic test (RDT) for malaria and if positive, blood slides were examined prior to starting treatment. Women who had malaria parasitaemia were treated either with artesunate+sulphadoxine-pyremithamine or artesuante+mefloquine. Microscopy was done on all blood slides from all visits collected throughout the study period. Diagnostic PCR was done on samples collected at the first and last visit of each woman enrolled in one full calendar year (August 2011 to July 2012).

RESULTS A total of 7139 women were enrolled into the cohort; 3506 were enrolled in the ISPAT General Hospital in Rourkela, 1853 in the Mahadevi Birla Hospital in Ranchi and 1780 in the TATA Main Hospital in Jamshedpur. The mean prevalence of fever was 2.27% (0.85% in Rourkela, 4.95% in Ranchi and 2.34% in Jamshedpur). The mean prevalence of microscopic infection was 2.93% (2.15% in Rourkela, 3.51% in Ranchi, 3.59% in Jamshedpur). The incidence of sub microscopic infections in a subset of 2494 pregnant women and the incidence of asymptomatic malaria in pregnancy will also be presented.

CONCLUSIONS The incidence of malaria in pregnancy is low but not negligible and suggests the need for active case detection and targeted interventions. The current policy of passive case detection of malaria during pregnancy in Jharkhand and Odisha States needs to be reviewed.

DISCLOSURE Nothing to disclose.

O.4.3.2.005

Relation of haemoglobin measured at different times in pregnancy with newborn's anaemia and low birthweight in the district of Allada, Benin

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BACKGROUND Because of the high prevalence of gestational anaemia (GA) in sub-Saharan Africa, anaemia-related adverse effects on birth outcomes are expected to have an important public health impact.
METHODS Between January 2010 and May 2012, a prospective cohort of 1005 Beninese HIV-negative women was followed from early pregnancy until delivery to investigate the relationship between maternal and newborn's haemoglobin (Hb) and birthweight. Linear regressions were performed to evaluate the relation between maternal Hb at each antenatal clinic (ANC) visit and newborns' Hb. Afterwards, total, direct and indirect associations between maternal and newborn's Hb were tested using a Path analysis.
RESULTS GA was common in the study population and anaemia affected 63.5% of newborns. GA at the 1st ANC visit and at delivery were associated with a decrease of 4.3 g/L ($P = 0.02$) and 3.5 g/l ($P = 0.05$) respectively in newborn's Hb concentrations. The Path analysis confirmed a strong direct association between maternal and newborn's Hb at delivery (Standardised beta (SB) = 0.12, $P = 0.003$), and also showed an indirect association of maternal Hb at 1st ANC and newborn's Hb (SB = 0.07, $P = 0.006$). No association was found between GA and birthweight.
CONCLUSIONS Our findings show that late GA has an important effect on newborns' health and suggest that current anaemia preventive measures play an important role to lower the consequences of anaemia during pregnancy on newborns'. Current preventive measures should then be reinforced by new strategies such as pre-gestational iron and folic supplementations.
ACKNOWLEDGMENTS We thank the study staff, the authorities of the health district of Allada, the European and Developing Countries Clinical trial Partnership, the Malaria in Pregnancy consortium and the MiPPAD Executive Committee.
DISCLOSURE Nothing to disclose.

4.3.3. Health systems and social exclusion

O.4.3.3.002

Integrating medical and social care for the elderly: effectiveness of different types of home care services in Belarus

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INTRODUCTION Belarus is increasingly confronted with an ageing society with almost 20% of inhabitants being 60 years and older. Care for the elderly is provided through the medical and social structures of the Belarus Government system either in institutions or at home. The Belarus Red Cross Society (BRC) is the only organization in Belarus which provides integrated care which means medical, social, individual and household care through their Visiting Nurses Service. Since the government is interested in increasing service quality and quantity of care for the elderly, the operational effectiveness and cost-effectiveness of the Visiting Nurses Service was studied in order to make informed decisions on future investment.
METHODS The study was carried out in two districts of the Grodno region (Lida and Oshmyany) and two districts of the Vitebsk region (Lepel and Polotsk). The medical and financial performance reports from 30 different governmental health providers, social care providers and the integrated care provider BRC over a span of 8 years were analysed. Health-related quality of life (HRQoL) of 780 elderly patients from the different service providers was assessed using SF 36© (Russian version). Additionally, all patients filled in a questionnaire survey related to their health-seeking behaviour. Data were entered and analyzed in STATISTICA 6.
RESULTS In terms of medical effectiveness, 45% of integrated care clients ($\chi^2 = 7.7$. $P < 0.01$) did not call an ambulance in the last year and 21% of clients ($\chi^2 = 12$; $P < 0.001$) preferred to be cared for at home rather than in hospital. General home care clients were 10 times more frequently hospitalized than integrated care clients. Integrated care receivers required longer stays at hospital, but were 50% less often hospitalized than general home care clients. A total 65% of integrated care receivers perceived an improvement of self-care and mobility.

Costs of integrated home care proved between 1.5 and 6.2 times lower than hospitalization. Integrated care services prove more cost effective for mental factors and physical factors remain constant over the different age and disability groups. Integrated care is most cost effective for the clients with highest disability grade.
CONCLUSION Merging health and social care services in home care prove to be an efficient service model at low costs and with high beneficiary satisfaction, which frees resources and eases the workload of government medical and social providers.
DISCLOSURE Nothing to disclose.

O.4.3.3.003

Assessment of work-time allocation of health workers at family medicine level in rural Tajikistan through direct observation

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INTRODUCTION Tajikistan is a low-income country transitioning from a specialized health care system toward a system based around family medicine. Information about time spent by family doctors (FD) and nurses (FN) on tasks such as administration, outreach activities, and direct patient care is essential for work force planning and health service delivery. As there is hardly any data available on rural health workers' use of time, we assessed time-allocation of FDs and FNs in central district and village clinics.
METHODS AND MATERIALS We developed a data collection instrument to record activities and time-allocation using predefined categories as well as a questionnaire about health centres and professional backgrounds of health workers observed. In July-August 2014, 52 randomly selected health workers (24 FDs, 24 FNs and 4 narrow specialists) from rural health centres in

4 districts were observed over 5 consecutive full working days. In order to diminish the Hawthorne effect, observers kept a distance and limited interaction with health workers. Data was recorded using CSPro and analysed using R software.
RESULTS Total observation time was 1483 hours. On average, health workers worked 5.7 hours per day and saw 17.5 patients. FDs spent on average 43% of their working time on administrative tasks, 25.7% on patient care, 15.7% on outreach activities, and 14.2% unproductive. FNs spent on average 40.9% of their working time on administrative tasks, 21% unproductive, 20.3% on patient care, and 16.8% on outreach activities. More than half of time allocated to administrative tasks was used for collecting data for the health information system. FNs in central district clinics spent significantly more time unproductive than FNs in village clinics (24.4 vs. 17.3%).
CONCLUSIONS Direct observation of government health workers at family medicine level in Tajikistan showed them devoting a substantial amount of their working time to administrative tasks to the detriment of patient care and resulting in inefficient use of resources. As for many other operational problems, there is no blueprint or general receipt on how to increase productivity, and little is known about how best to address the performance of the health care workforce as an essential element of health service delivery in low-income countries. There is a need for an increased focus on reasons why health workers perform suboptimally, and feasible approaches to improve their productivity need to be developed.
DISCLOSURE This study was conducted in the frame of the Medical Education Project supported by the Swiss Agency for Development and Cooperation.

O.4.3.3.004

Management strengthening using health workforce performance problems in decentralised contexts: lessons from Ghana, Tanzania and Uganda

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INTRODUCTION Improving the performance of the existing health workforce is one way to reduce the impact of staff shortages. However, general prescriptions for improving workforce performance may not be useful, because problems and contexts differ. Our research question was how to strengthen district management to improve health workforce performance.
METHODS We used an action research (AR) approach with district health management teams (DHMT) in Ghana, Tanzania and Uganda to steer health workforce performance improvement. The events to facilitate the AR approach were fitted around the busy schedules of three DHMTs in each country. After a situation analysis, two participatory inter-district workshops were conducted in 2013/14 to refine the problem solving and integrated strategy development outputs. Follow-up support and inter-district meetings were facilitated over an 18-month implementation phase.

AR or similar approaches are commonly used for implementation projects, but the process is rarely documented to derive lessons on management strengthening. Process monitoring was carried out throughout the project and an in-depth evaluation was conducted at the end of the project – both using mainly qualitative methods.
RESULTS The two most common strategies selected for improving workforce performance were strengthening supervision and controlling staff absence. Other strategies included improving competencies, use of incentives, better appraisal systems, and increased use of volunteers. Modest improvements in workforce performance were reported. Wider health systems strategies were also included, such as setting performance indicators for immunisation logistics, to address service delivery problems.

Reports of management strengthening included the greater use of teamwork and more participatory decision-making processes and the application of the problem analysis process to other areas of management. Some managers found the lack of additional funding a major barrier to implementing the strategies they developed, while others found the sole reliance on existing resources challenging and educational. The AR approach was popular, especially ownership of the process, and most teams wanted to continue using it.
CONCLUSIONS Whilst the improvements to workforce performance may be modest after the short implementation period, the management strengthening was welcomed by DHMTs and resulted in improved teamwork and human resource management practices.
DISCLOSURE Nothing to disclose.

O.4.3.3.005

Towards a programme theory in the application of systems thinking to complex public health issues

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INTRODUCTION Increasingly, disease is seen as a result of an interaction of many diverse, socio-environmental, economic and other interacting variables. Addressing public health issues from this perspective requires a shift from a reductionist focus on pathogens, vectors and behavioural change to a multi-sectorial, systems approach. This paper draws on an evaluation of state-wide Otitis Media management and prevention framework in Aboriginal and Torres Strait Islander children in Queensland, Australia. Based on an examination of the evaluation findings and the literature, we reflect on the challenges in applying a systems thinking approach.
METHODS AND MATERIALS A qualitatively-led evaluation was undertaken using in-depth stakeholder interviews (n = 32) and complemented by a review of the programme documentation, available quantitative data and the broader literature. Data was analysed using a mix of deductive and inductive analysis and guided by the programme framework and using a systems thinking lens.
RESULTS The findings show that despite stated commitments to a systems approach, moving away from a health sector and primarily medical model of disease is not easy. In this evaluation stakeholders grappled with the challenges posed by the paradigm shift to a systems approach, including conceptualising the changes required. These challenges were often compounded by the prevailing political context.
CONCLUSIONS Reflecting on this experience, we offer a programme theory and 'simple rules' or principles that can help promote systems thinking. It includes research and on-going

feedback loops, political commitment, leadership at all levels and community participation. The programme theory can be used to help policy-makers, programme managers and evaluators gain a better understanding of how these simple rules work and how context influences the way in which programmes unfold. Such an understanding, we argue, is critical if programmes are going to shift from a narrow, disease-focussed approach to one that also tackles the determinants of health, understands how they interact and their interdependencies, and promotes sustainability.

ACKNOWLEDGEMENTS The evaluation was undertaken with support from Queensland Health.

DISCLOSURE Nothing to disclose.

4.3.4. The good, the bad and the ugly of global targets: Will the SDGs be different?

INV.4.3.4.001
From Alma Ata to sustainable development goals

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International and global health have been shaped by a series of historical hallmarks: from the Alma Ata declaration defining Primary Health Care up to the most recent Sustainable Development Goals, and going through Health For All by year 2000, the World Bank report Investing in Health and the Millennium Development Goals.

In most of these documents, common issues, such as the right to health care or equity, are approached in slightly different ways.

We will briefly review and compare those issues along the historical hallmarks to inspire the debate around what have we done right and wrong when setting international health care targets and approaches to achieve them.

DISCLOSURE Nothing to disclose.

INV.4.3.4.003
Unmet Agenda in post-MDG era and role of the Global Fund for SDGs

O. Kunii

The Global Fund to fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland

Since its creation in 2002, The Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund) has mobilized resources, fostered partnerships, and promoted catalytic innovation to combat the three diseases.

Globally, great progress has been made in reducing morbidity and mortality amongst the three epidemics over the past decade, and many low and middle income countries have achieved or are expected to achieve MDG 6.

However, the Ebola outbreak in 2014 and the fact that its 1-year death toll was equal to 2-day average deaths of the three diseases underscored that the fight against infectious diseases is still an unmet agenda in the post-Millennium Development Goals (MDG) era and the Sustainable Development Goals (SDGs) are critical for ending epidemics as global public health threats.

To end the three epidemics and fight public health emergencies such as Ebola it is also crucial to strengthen health and community systems and develop synergy with various programs such as reproductive, maternal, newborn, child and adolescent health.

In this session, I will discuss the Global Fund's contributions and current effort towards health and community system strengthening, and a potential component of the new strategy in building resilient and sustainable systems for health towards achieving the SDGs and Universal Health Coverage.

DISCLOSURE Nothing to disclose.

INV.4.3.4.004
GAVI contribution to the MDGs and plans for the SDGs

A. Bchir

GAVI, Geneva, Switzerland

GAVI was created to enable developing countries introducing new vaccines they cannot afford to pay for (Pentavalent, Rota, Pneumo, HPV…), strengthening their health systems and using safety injection devices (Safety boxes and AD syringes. The main objectives were to reduce the incidence and the mortality of vaccines preventable diseases contributing therefore to achieve the MDG 4 and 5 targets. In addition GAVI was instrumental supporting the measles elimination and polio eradication initiatives.

I will present GAVI's achievements and discuss the difficulties faced and the plans to address them to better contribute to the SDGs.

DISCLOSURE Nothing to disclose.

4.3.5. Innovative community-based Buruli ulcer management programs: outcomes, impact, and lessons for other disease programs

INV.4.3.5.001
Buruli ulcer outreach education: an exemplar for community based tropical disease interventions

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BACKGROUND In this presentation, we describe an innovative approach to Buruli ulcer (BU) outreach education as a means of increasing community awareness about the disease, early identification, decreased treatment delay, enhanced treatment adherence, and decreased treatment drop-out. The shortcomings of top-down education approaches are well documented. Education is never introduced into a vacuum and needs to address existing cultural perceptions and concerns. We describe the development and piloting of a BU education program based on 3 years of research carried out in three West African countries.

METHODS Six months of formative research was conducted on local understandings and responses to BU in Benin, Cameroon and Ghana. An interactive education program was then developed and pretested utilizing a question: answer format addressing issues of concern to both health staff and local populations. The program encompassed BU signs/symptoms and ways of distinguishing BU from other common diseases, BU progression, perceptions of possible causes of BU, and treatment. The program was driven by a power point presentation that can easily be updated when new questions arise and translated into local languages. Presentations incorporated images explaining actions taken by clinic staff in identifying and managing BU, and time series images of stages of the BU healing process. Education

programs also included the testimonials of former patients conveying a message of hope instead of fear.
RESULTS The results of a three country evaluation were very promising. Over 200 education programs were held in the three countries attended by over 75 000 community members. Knowledge of BU increased as did trust in local clinics offering BU care. BU identification in the community increased substantially, most notably category one cases. The education program had a positive impact on community volunteers empowered to organize outreach programs and clinic staff reported the reputation of their clinics increased, as did working relations with volunteers.
CONCLUSION This innovative BU education program facilitated the formation of BU Communities of Practice in each of the three countries. It established common ground for collaboration between clinic staff, community volunteers, former patients, and traditional healers. The program is offered as an exemplar for other neglected tropical disease education programs.
DISCLOSURE Nothing to disclose.

INV.4.3.5.002

Developing a Buruli ulcer community of practice in Bankim Cameroon as a model for BU outreach in Africa

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BACKGROUND Buruli Ulcer (BU) is a neglected tropical disease primarily found in West Africa with a known cause and cure, but an unknown route of transmission and incubation period. If not treated early and in a timely manner by a 56-day course of antibiotics, BU often progresses to an advance state requiring prolonged wound care and skin grafting. BU does not kill, but may render the afflicted permanently disabled. In the Cameroon, previous efforts to identify BU early in the community by community health workers (CHW) yielded poor results. In this paper, we describe the successful creation of a BU community of practice (BUCOP) composed of clinic staff, former patients, community health workers and traditional healers. A COP is based on all stakeholders sharing a common objective, basic understanding of a focal problem, and mutual respect for what each stakeholder contributes to a process of problem solving.
MATERIAL AND METHODS A BUCOP including CHW, former patients and traditional healers was set up to improve the care for BU from 2013–2014 following formative research. Patient support in the form of transport and lodging was also provided when needed. Cumulative data was collected on member collaboration, the identification and confirmation of patients, and treatment outcomes.
RESULTS A successful BUCOP was established. This resulted in a notable improvement in staff: community relations, BU identification, reduction in health care seeking delay, and a decline in treatment drop out leading to better treatment outcomes. In the 3 years prior to the intervention 224 cases of BU had been identified through a household survey of which only 20 (8.9%) cases was category one. During the 2 year intervention 91 cases were identified through community education outreach of which 35 (38.4%) were category one. Prior to the intervention there was a 52% treatment adherence rate and 93% occurred during the intervention. Material and psychosocial support improved quality of care and patient satisfaction.
CONCLUSION The successful creation of a BUCOP in a remote part of Cameroon demonstrates the vitality of the COP model which may prove useful in the control of other neglected tropical diseases.
DISCLOSURE Nothing to disclose.

INV.4.3.5.003

Role of traditional healers in a community of practice (COP) for Buruli ulcer (BU) care in Cameroon, Africa

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BACKGROUND The role of traditional healers (TH) in outreach health programs has been a matter of considerable debate. Supporters of TH involvement uphold that healer have contributed to health interventions. Opponents hold that TH have undermined programs using them as a means to promote their BU healing capacity. For BU, it is recognized that TH are often the first practitioner consulted by the afflicted. To date, no well executed TH program has tested their contribution to community based BU control. This study addresses this lacuna.
MATERIAL AND METHODS A pilot project was conducted from 2013–2014 in Bankim Cameroon. TH here are active, BU is prevalent and referral to clinics by TH uncommon. Members of a TH group were invited to join a BU Community of Practice (COP). Interested healers received education and agreed to abide by a contract that: (i) they would refer patients with BU like symptoms after treating mystical aspects within 10 days; (ii) treatment would not involve treating the skin of the patient. TH received a small honorarium for referring patients/accompanying them to clinic. They were asked to continue providing psychosocial support and spiritual protection on demand. TH were also invited to participate in outreach programs (OP). Data was collected on patients referred by healers, their adherence to BU treatment, healer adherence to quick referral/not treat the skin contract and healer participation in OP.
RESULTS Prior to the pilot project TH had referred no BU cases to Bankim clinic. During pilot project they were responsible for 1/3 of all referrals of suspected BU cases. Half of all cases referred in year one were confirmed to be BU. By year two it rose to 80%. Notably, 50% of cases referred were category one. No patient referred by TH abandoned treatment. TH participation was found to be more motivated by social status gained from community recognition and a good working relationship with clinic staff, than financial gain. A majority of TH continued to operate as role models by adhering to contract. A small minority of TH was non-adherent with the contract.
CONCLUSION TH collaboration is possible under certain cultural conditions: careful selection of TH, healer groups support, establishing respectful relations with health staff, recognition of the role of TH in providing psychosocial and spiritual support, training in BU that addresses cultural issues and resources to organize ongoing meetings and dialogue about BU.
DISCLOSURE Nothing to disclose.

INV.4.3.5.004

Steps toward creating a BU therapeutic community: lessons from Allada Hospital Benin

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BACKGROUND Providing in-patient care for people afflicted with diseases requiring long term hospitalization is a major challenge in low income countries where patients struggle to maintain a positive attitude while far from their families. Patients and hospital staff live and work in close quarters, yet are often socially distant. Research on hospitals as therapeutic communities is virtually non-existent in Africa. This paper describes a pioneering attempt to establish a therapeutic community for Buruli ulcer patients requiring long term care in Benin.
METHODS A 6 month pilot project was undertaken at Allada Hospital in Benin with the objectives of establishing a BU therapeutic community, and evaluating its impact on practitioner: patient relations. The project was designed and implemented by a team of social scientists working closely with the director of the hospital which serves as a centre for BU treatment. Patients histories were taken, psychosocial status monitored, and concerns about treatment identified. Weekly meetings were held during which time health education was provided followed by an opportunity for patients to express concerns and discuss problems. Patient groups then met with staff to problem solve in a non confrontational manner.
RESULTS Formative research revealed that most patients had very little information about their illness, and the duration of their treatment. This knowledge gap surprised clinic staff members, who assumed someone had provided this information. Weekly meetings corrected this knowledge gap, and offered patients the chance to express their concerns. This led to changes in staff: patient interaction. There was widespread consensus among both patients and staff that the quality of communication and increased. Patients reported they felt better care for. However, patients with ulcers unrelated to BU questioned why BU patients were receiving preferential treatment, given special medicines, and charged less for their care. The idea of subsidized treatment for one disease and not another was hard to convey, especially as BU is not contagious.
CONCLUSION This pilot project is a pioneering effort to introduce some of the basic principles of therapeutic communities into hospitals in Africa treating long term residential patients. Although the focus of this case study is BU patients, the model presented is relevant for other types of patients with cultural adaptation.
DISCLOSURE Nothing to disclose.

4.3.6. Health economics

O.4.3.6.001

Acute gastroenteritis and campylobacteriosis in Switzerland: how expensive are our patients?

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INTRODUCTION More than 7000 campylobacteriosis cases annually of which about 1000 or 15% are hospitalised are likely to cause considerable health care costs within the Swiss health care system. Laboratory-confirmed campylobacteriosis cases are only a fraction of all patients consulting a physician due to acute gastroenteritis. This study aimed at estimating health care costs due to acute gastroenteritis and campylobacteriosis in Switzerland.
METHODS We combined expert opinions, official health statistics and data from published and unpublished literature to define four different patient models (A-D) and estimated their individual treatment costs for two case management scenarios. By estimating the frequency of the patient models we extrapolated individual costs to overall health care costs for Switzerland due to acute gastroenteritis and campylobacteriosis.
RESULTS Total national health care costs due to acute gastroenteritis and campylobacteriosis are estimated at €42–78 million annually. Patients consulting a physician due to acute gastroenteritis who are not being tested (model A, estimated frequency: N = 251 970–679 555) are assumed to generate costs of €12.4–48.1 million annually. Patients with a negative stool test for *Campylobacter* (model B, N = 75 423) are estimated to account for €12.7 million and patients tested positive for *Campylobacter* (model C, N = 7325) generate costs of €1.9 million. Data suggest that hospitalised patients with laboratory-confirmed campylobacteriosis (model D, N = 1242) cost €15.0 million per year.
CONCLUSION Acute gastroenteritis and campylobacteriosis are not only a public health problem in Switzerland but also cause considerable costs for the health care system, health insurance companies and patients. The observable increase in campylobacteriosis case numbers in the National Notification System for Infectious Diseases suggests that costs are rising. Potential cost savings in the health care sector must be considered when planning and evaluating interventions targeted to reduce campylobacteriosis in Switzerland.
DISCLOSURE Nothing to disclose.

O.4.3.6.002

The public health impact and cost-effectiveness of the RTS, S malaria vaccine candidate in malaria endemic Africa: estimates based on phase III clinical trial results

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The potential role of the RTS,S/AS01 malaria vaccine candidate is currently being evaluated on the basis of Phase III trials results in 11 African sites. A WHO recommendation on its use in endemic African countries is expected in late 2015 or early 2016 and will depend on clinical trial results and potentially projections of

expected public health impact and cost-effectiveness in endemic sub-Saharan African countries. Whilst the data from the trial provides estimates of cases averted in the 11 sites, models are required to extend these estimates across the full range of *Plasmodium falciparum* malaria parasite prevalence settings currently observed in Africa and to make country-specific predictions taking into account local context.

Bayesian analysis and the Phase III site-specific clinical trial data were used to estimate vaccine efficacy against infection and duration of protection. Using an existing simulation model of malaria epidemiology and control, the public health impact and cost effectiveness of the vaccine if implemented in countries across Africa was determined. Our analysis indicates that the initial efficacy against infection of RTS,S/AS01 is likely to be high, but the effect decays relatively rapidly. Even with quick decay, however, the vaccine is predicted to have substantial public health impact and likely to be cost-effective.

Based on our analysis, adding RTS,S to existing interventions has the potential to avert 100–600 malaria deaths and 45 000–80 000 clinical cases for every 100 000 fully vaccinated children in endemic Africa for the first 10 years of the program, depending on age of immunization and vaccination schedule. Estimates will be updated as new data/information become available. The predictions take into account country-specific contexts of health systems, immunization coverage, country costs and malaria exposure. Further analysis across a range of parasite prevalence settings indicates the vaccine is potentially cost-effective compared to current malaria interventions and childhood vaccines.

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DISCLOSURE Nothing to disclose.

O.4.3.6.003

Modelling the cost-effectiveness of diagnosis of *Schistosoma mansoni* infection: a comparison of Kato-Katz and urine-circulating cathodic antigen cassette test

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Accurate diagnosis of schistosomiasis is important to monitor the progress of ongoing control efforts, assess drug efficacy and improve patient management. The most widely used method for the diagnosis of intestinal schistosomiasis due to *Schistosoma mansoni* is the Kato-Katz technique performed on fresh stool specimens. Despite its relative ease of use, the technique requires standard laboratory equipment and well-trained laboratory staff to perform the test. Although a point-of-care (POC) assay to detect circulating cathodic antigen (CCA) in urine as a rapid diagnostic test for *S. mansoni* has been commercially available for a number of years, its use in epidemiological survey and clinical settings is still limited. Findings from a cross-sectional survey in three settings in Côte d'Ivoire have shown that the POC-CCA has a similar sensitivity to triplicate Kato-Katz thick smears, but neither its cost nor cost-effectiveness relative to the Kato-Katz technique has been assessed.

Using a decision tree and sensitivity analysis, we evaluate the average and incremental cost-effectiveness of the Kato-Katz and POC-CCA techniques for the diagnosis of *S. mansoni* among patients presenting with persistent diarrhoea and/or persistent abdominal pain (≥2 weeks) at rural health facilities in Côte d'Ivoire and Mali. The analysis is conducted from the perspective of the public health care services. Primary data is collected as part of the NIDIAG project (www.nidiag.org) and combined with data from the literature and expert opinion. Outcome measures include cost per diagnostic strategy and the cost per disability-adjusted life year (DALY) averted. Sensitivity analysis is conducted on variables with considerable uncertainty to assess the robustness of the results.

DISCLOSURE Nothing to disclose.

O.4.3.6.004

Seeing beyond 2020: cost-effectiveness analysis of contemporary and emerging strategies for human African trypanosomiasis (HAT) *Trypanosoma brucei* (*T.b.*) *gambiense* for elimination

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Human African trypanosomiasis (HAT) *Trypanosoma brucei gambiense* has been selected as a neglected tropical disease (NTD) to reach elimination as a public health problem by 2020, and full elimination by 2030. Economic evaluations of older interventions have been done, however, further evidence of how new interventions may contribute to elimination is needed. The following analysis was undertaken to evaluate strategies based on current and emerging technologies that could lead to elimination and be cost-effective (CE).

A total of 12 strategies were simulated over 30 years using a dynamical transmission model for low, moderate and high risk transmission areas. The analysis took on a National Health Service perspective, discounting for both costs and DALYs was 3%, and input parameters regarding costs, transmission rates, treatment event rates and surveillance coverage estimates were taken from the literature, national reports or experts. All prices were converted to USD and inflated to 2013. The outcomes included prevalence, total costs and total DALYs making predictions for elimination and cost-effectiveness feasible. A probabilistic sensitivity analysis (PSA) was conducted to determine the uncertainty of the model results.

Elimination in high and moderate areas was most probable and most CE when vector control (VC) was implemented in addition to new tools for diagnosis and treatment. In the low transmission areas, strategies that included emerging technologies were key in reaching elimination, however only the strategy with newest treatments and diagnostics (no VC) was considered to be CE.

New and emerging technologies play a large role in reducing HAT disease transmission towards elimination. In high and moderate areas, implementing all new technologies as they come to the market is CE. In low transmission areas, new diagnostics

and treatments alone are CE, but to accelerate elimination, vector control would be required.
DISCLOSURE This project was funded by Grant #: OPP1037660 from the Bill and Melinda Gates Foundation

O.4.3.6.005

Budget impact analysis of using dihydroartemisinin-piperaquine to treat uncomplicated malaria in children in Tanzania

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BACKGROUND Dihydroartemisinin-piperaquine (DhP) is a very cost-effective anti-malarial drug. This study aims to predict the budget impact of using DhP as a first- or second-line drug to treat uncomplicated malaria in children in Tanzania.
METHODS A dynamic Markov decision model based on clinical and epidemiological data was developed to estimate annual cases of malaria in under-five children. The model was then used to predict the budget impact, from the providers' perspective, of adopting two different treatment policy options containing DhP as a first- or second-line drug. A probabilistic sensitivity analysis was performed for a period of 1 year.
RESULTS The model predicts that the recently adopted treatment policy for malaria, in which DhP is used as a second-line drug (AL + DhP), will save about 66 800 US$ per year, while achieving a 3% reduction in the number of malaria cases, compared to the previous policy of AL + quinine. However, a treatment policy in which DhP is used as a first-line drug (DhP + AL), will consume an additional 671 000 US$ per year, while achieving an 8% reduction in the number of malaria cases, compared to AL + quinine. Therefore, if AL + DhP is replaced by DhP + AL, it will consume an additional 737 800 US$ per year, while achieving a 5% reduction in the number of malaria cases in children.
CONCLUSION The use of DhP as a second-line drug (AL + DhP) to treat uncomplicated malaria in children is slightly cost-saving. However, a policy in which DhP is used as a first-line drug (DhP + AL) is somewhat more expensive but with more health benefits.
DISCLOSURE Nothing to disclose.

O.4.3.6.006

Feasibility, costs and benefits of the Global Technical Strategy 2016–2030 for accelerating global progress towards malaria elimination

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Rapid declines in malaria transmission and burden have been achieved globally due to increased coverage of malaria control interventions. Yet the burden remains unacceptably high. The Global Technical Strategy (GTS) provides a vision for malaria reduction and elimination for 2016–2030. We assessed the feasibility, costs and benefits of reaching the GTS goals.

Using a published malaria transmission model, the impact of different coverage scenarios on reducing malaria cases and deaths and on the number of countries expected to eliminate was estimated. The costs of implementing the GTS were estimated from a public provider perspective using modelled coverage data combined with unit delivery cost estimates sourced from procurement databases and peer-reviewed and grey literatures. The potential value of reaching the GTS goals was estimated in term of direct savings to households (reduced out of pocket payments) and health systems due to the reduction in malaria incidence; and to societies due to increased longevity with an application of the full income approach.

Findings demonstrate that substantial additional gains can be made over the next 15 years with local elimination a feasible prospect in approximately 30 countries. Reducing malaria cases and deaths by close to 90% and elimination in at least 35 countries by 2030 are estimated to cost US$102.3 billion (95% CI : US$73.6–141.9 billion) compared to US$62.9 billion (US$50.4–78.4 billion) to retain current coverage levels. Costs are concentrated in high burden countries, with 21 accounting for 80% of the global financial need. The estimated global economic benefits are high and increase with greater intervention coverage, giving a more than 60-fold return on investment by the time the 2030 goals are realized.

Achieving elimination and preventing resurgence will deliver significant returns and pave the way for sustainable investments for a malaria-free world.
DISCLOSURE Nothing to disclose.

4.4.1. Emergent diseases: immigrants and potential diseases with impact in and for Europe

O.4.4.1.002

Dengue serotypes and genotypes circulating in recent years in the Caribbean and imported to Europe

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INTRODUCTION Dengue viruses (DENV) are the most widespread arthropod-borne viruses endemic in the tropics and transmitted to humans through the bites of Aedes mosquitoes. Travelers can act as vectors to introduce DENV to uninfected areas or regions. Travelers can also serve as sentinels for ongoing outbreaks and dominating serotypes and genotypes in the source countries. We set out to describe the importation of dengue virus from the Caribbean via travelers to Europe.
METHODS From 2011 to 2014, we collected samples from viraemic travelers returning from the Caribbean with confirmed dengue to 11 TropNet clinics in Europe that are participating in the DengueTools project. Sequences of the Envelope gene were used to identify serotype and genotype.
RESULTS The main countries of importation were Barbados, Cuba, Dominican Republic, Guadeloupe, Haiti, Martinique, Netherlands Antilles and Puerto Rico. All 4 DENV serotypes

were identified. DENV 1 strains were grouped within genotype V creating a new clade. All DENV 2 sequences clustered within a clade in the American/Asian genotype which was recently also identified in other Caribbean and Brazilian strains. DENV 3 strains were grouped within genotype III. All DENV 4 strains were phylogenetically grouped within a modern Caribbean basin clade in genotype II.

CONCLUSIONS Travelers provides unique insights into the global picture of circulating DENV strains. This study from the Caribbean region led to the identification of novel clades. Moreover, we were be able to detect dengue strains circulating in Cuba from 2011 to 2013, although officially no dengue was reported during that time period. Travelers serve as sentinels to provide timely information about current distribution of dengue serotypes and genotypes associated or not with outbreaks and track the spread of DENV strains in areas with scarce epidemiological information.

DISCLOSURE Nothing to disclose.

O.4.4.1.003

Identification of potential novel *P. vivax* vaccine candidates: naturally-acquired immune responses to a panel of *P. vivax* blood-stage antigens are associated with reduced risk of clinical malaria episodes in Papua New Guinean children

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Dramatic reductions in the burden of malaria have occurred in the last few decades, with several countries now attempting to permanently eliminate this disease. Eliminating *Plasmodium vivax*, now the most prevalent species in almost all endemic sites outside Africa, is particularly challenging, but would be greatly facilitated by an effective *P. vivax* vaccine. While individuals living in endemic areas rapidly acquire protective immunity to *P. vivax* malaria, the targets and mechanisms underlying this process are complex and poorly understood. We therefore assessed antibody responses to an extended panel of *P. vivax* blood-stage protein antigens, investigating their relationship with prospective risk of malaria in a cohort of 264 children aged 1–3 years in a region of very high malaria endemicity in Papua New Guinea. The levels of total IgG specific for each protein were measured using a Luminex bead array. Our results show that antibody levels tended to be higher in children with concurrent infections and in those with a higher overall exposure to *P. vivax* blood-stage infections (as measured by molecular force of infection). For multiple antigens tested (e.g., GAMA, P41, P12, AMA1, MSP3a, MSP9, RBP, DBP and hypothetical proteins), high levels of antibodies were associated with protection against clinical malaria, independently of exposure, age, and transmission season. These data identify antigens that appear to be key targets of naturally-acquired immunity and thus promising *P. vivax* vaccine candidates.

DISCLOSURE Nothing to disclose.

O.4.4.1.004

Mathematical models for *P. vivax* elimination

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The importance of spatial transmission heterogeneity and human movement is often entirely neglected in vector borne transmission models, including those for malaria. Most models assume homogenous transmission (i.e., spatial features such as human households and mosquito habitats are not considered).

It is now widely acknowledged that malaria transmission is maintained in *hotspots* i.e., very focal areas with high transmission. *Plasmodium vivax* hypnozoites pose an additional challenge for the elimination of hotspots, as they facilitate persistence of transmission.

Methods to attack residual transmission hotspots are being tested, including focalized drug administration e.g., after reactive case detection. It is not possible to use conventional models to forecast the impact these control strategies as their impact is directly linked to local, micro-scale (few metres) variation in transmission. The only class of mathematical models that can be used to simulate such heterogeneous transmission environments are spatially explicit, individual based simulation models.

Here, we built such a spatial mathematical transmission model for *Plasmodium vivax*. The model allows for the transmission of multiple parasite clones as well as heterogeneous human and mosquito populations embedded in a realistic village structure based on that on the North Coast of Papua New Guinea.

Using the model we simulate mass drug administration, mass screening and treatment, as well as focal screening and treatment interventions and compare the results with predictions from a standard transmission model.

DISCLOSURE Nothing to disclose.

O.4.4.1.005

Prevalence of strongyloidiasis in immigrants and in the autochthonous, elderly population in a formerly endemic area of Northern Italy

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INTRODUCTION Strongyloides stercoralis (Ss) causes a neglected parasitic infection that may affect more than 300 million people. This soil transmitted helminth (STH) infection is underestimated, primarily because most cases, including severe

and often fatal ones in immunosuppressed subjects, remain undiagnosed, due to lack of suspicion and to low sensitivity of conventional diagnostic methods in stool. Ss is highly prevalent in many areas of the tropical continents, but is/was also still endemic in Europe. The peculiar, self-maintaining life cycle causes Ss to persist indefinitely in the host if not properly treated. Cases are regularly observed in Italian elderly subjects that were exposed at young age when hygiene and sanitation were more precarious.

METHODS Prospective study carried out from February 2013 to July 2014 in 7 medical centres of three regions of Northern Italy, recruiting Italian patients born before 1952 and immigrants aged ≥ 18. During twenty, randomly selected weeks, every centre had to recruit 10 "cases", defined as patients with a eosinophil count ≥500/µl, consecutively enrolled among those presenting for any reason to the local laboratory as outpatients, and 10 "controls", belonging to the same age groups, consecutively enrolled in a random day of the same week among those who had a normal eosinophil count. The planned sample was 1400 cases plus 1400 controls. The diagnosis relied on stool culture and on serology (2 concordant positive samples in IFAT and ELISA required if negative stool).

RESULTS In autochthonous subjects, prevalence was 97/1137 (8.5%) for cases (with a clear rising trend with age) and 13/1178 (1.1%) for controls (p=0.000). Peak prevalence of 13% was found in cases from an agricultural area of Veneto region. In immigrants, prevalence was 36/214 (16.8%) vs. 3/172 (1.7%) (p=0.000). Peak prevalence of 29% was found in cases from sub-saharan Africa. In both main groups, prevalence showed a clear, rising trend with eosinophilia.

CONCLUSIONS In the three regions we can estimate a prevalence of several thousand subjects with Ss infection. Practically all, as well as their doctors, are unaware of the infection and related risks. Systematic screening of subjects with eosinophilia is recommended.

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DISCLOSURE Nothing to disclose.

4.4.2. Travel medicine

O.4.4.2.002

Diagnostic guidance for patients presenting with persistent fever in neglected tropical disease endemic areas of Cambodia, the Democratic Republic of Congo, Nepal and Sudan

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INTRODUCTION Patients with neglected tropical diseases (NTD) such as visceral leishmaniasis (VL), human African trypanosomiasis (HAT) and enteric fever occasionally or nearly always present with persistent (≥1 week) fever. Existing diagnostic algorithms usually focus on a single disease (e.g. VL, HAT). We established the differential diagnosis in patients with persistent fever in several NTD endemic countries, with a focus on potentially severe and treatable diseases. We then developed guidance for diagnostic management by integrating specific clinical features with the results of rapid diagnostic tests. This study (acronym: NIDIAG) is funded by the EU (FP7).

METHODS AND MATERIALS Patients ≥5 years (18 years in Cambodia) presenting with ≥1 week fever were recruited after informed consent at five hospitals in Cambodia (Phnom Penh), the Democratic Republic of Congo (Mosango, Bandundu Province), Nepal (Dharan & Dhankuta, Eastern Region) and Sudan (Tabarakallah, Gedaref Province). Data from in depth history taking and physical examination were reported on a case-report form. Blood and urine reference diagnostic tests were performed on site and in referral laboratories for malaria, HIV, brucellosis, leptospirosis, relapsing and enteric fevers, VL (Nepal and Sudan) and HAT (DRC). Other investigations (e.g. chest X-ray, abdominal ultrasound, sputum or CSF examination) were done if requested by the physician. All patients were followed-up at 1 month post hospital discharge to assess clinical outcome. Final case-ascertainment was done by an experienced physician based on pre-specified definitions.

RESULTS A total of 1927 patients (Sudan: n = 670; Nepal: n = 578; Cambodia: n = 378; DRC: n = 301) were included in the study between January 2013 and October 2014. At the time of initial abstract writing, database cleaning and laboratory tests at the international referral laboratory are ongoing, and final case-ascertainment and workshops on development of diagnostic guidance are planned. All study results will be available at the time of the congress.

CONCLUSIONS Persistent (≥1 week) fever is a frequent reason for seeking health care in the tropics, with a broad differential diagnosis. There is an urgent need to support frontline clinicians with appropriate diagnostic guidance that goes beyond single disease algorithms and includes accessible diagnostic tools. More specific conclusions will be presented at the ECTMIH congress.

DISCLOSURE Nothing to disclose.

O.4.4.2.003

Clinical spectrum, main etiologies and outcome of neurological disorders in the rural Hospital of Mosango, Province of Bandundu, Democratic Republic of the Congo

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INTRODUCTION Neurological disorders account for an important proportion of hospital admission in sub-Saharan Africa, but have been poorly investigated so far in rural settings due to evident resource constraints. A hospital-based clinical and diagnostic study has recently been completed by the consortium for Neglected Infectious Diseases Diagnosis (NIDIAG) in the

rural Province of Bandundu, Democratic Republic of the Congo (DRC).
METHODS All patients >5 years admitted with ongoing (non-traumatic) neurological disorders were prospectively evaluated at the 'Hôpital Général de Référence' of Mosango, a 400-bed district hospital located in Bandundu, DRC. All consenting patients were examined by a neurologist investigator, submitted to a systematic laboratory workup on blood and cerebrospinal fluid (CSF) and clinically followed-up until 6 months after discharge. Blood and CSF samples were sent to reference laboratories in Kinshasa, DRC and in Antwerp, Belgium for further testing.
RESULTS From September 2012 to June 2014, 351 patients were enrolled [male: 46%; mean age: 39 years (range: 6–76)], with follow-up until January 2015. Main presenting symptoms/syndromes were (often present in combination): severe daily headache, with or without meningismus (n = 160; 46%), walking disturbance (n = 97; 28%), convulsion (n = 87; 25%), focal sensory-motor deficit (n = 77; 22%); behaviour disturbance (n = 66; 19%) and altered consciousness (n = 54; 15%). Pending the results of ongoing analyses, severe and treatable infections were strongly suspected or confirmed in at least 95 patients (27%), including mainly unspecified meningo-encephalitis (n = 18; 5.1%), bacterial meningitis (n = 15; 4.3%), HIV-related neurological disorders (n = 12; 3.4%), second stage human African trypanosomiasis and malaria (n = 10; 2.8% for each). Other main clinical diagnoses were epilepsy (n = 58; 16.5%), neuropsychiatric condition (n = 54; 15.4%) and cerebrovascular accident (n = 22; 6.3%). Twenty-eight (8%) patients died and another 73 (21%) had still neurological sequels 6 months after discharge.
CONCLUSIONS The pattern of neurological disorders in district hospitals of rural DRC is extremely varied. Preliminary data show that treatable infections are strongly suspected or confirmed in about 30% of the admissions (more accurate diagnostic data will be available at the time of presentation). Mortality and long-term morbidity were very important in this remote setting.
DISCLOSURE Nothing to disclose.

O.4.4.2.004
Diagnostic accuracy of a LAMP kit for diagnosis of imported malaria in Switzerland

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BACKGROUND The diagnosis of acute malaria in non-endemic countries is still carried out largely by microscopic examination of thick and thin smears or rapid diagnostic tests. Low-density infections might be missed, however, but the more sensitive PCR is more expensive, complex and requires considerable more time.
METHOD We examined the suitability of a new loop-mediated isothermal DNA-amplification kit (LAMP) for malaria diagnosis in febrile returning travelers in comparison to qPCR and microscopic examination in a prospective study in a non-endemic setting at the Swiss TPH.
RESULTS Among 205 complete datasets, 43 samples were positive for malaria by microscopy, with *P. falciparum* (35 cases) being the most frequent species. All these samples were positive by both LAMP and qPCR, too. An additional 4 samples negative by microscopy were positive by both LAMP and qPCR. Three of these samples were follow-up samples taken after start of treatment in patients originally identified as positive by microscopy.
CONCLUSIONS The LAMP performed exactly as did the qPCR and is a very valuable diagnostic alternative with a potential of being used also in endemic settings.
DISCLOSURE H. Marti and Ch. Stalder have no conflict of interest to declare. I. Gonzalez is an employee of FIND, a co-developer of the malaria LAMP kit.

O.4.4.2.005
Dengue in Africa: sustained and silent circulation of multiple serotypes and genotypes, detected in travelers from 2010 to 2014

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INTRODUCTION Dengue is caused by 4 different related viruses, DENV 1 to 4, transmitted to humans via Aedes mosquitoes. The disease is endemic in more than 100 countries. In Africa, the estimated dengue burden is 15 million of clinical cases and about 48 millions of inapparent infections. However, dengue remains largely unrecognized in Africa. Due to the lack of laboratory confirmation, a febrile syndrome is frequently misdiagnosed as malarial infection. The circulation of different dengue serotypes is also poorly documented. However, some information is provided by reports of dengue infections in travellers returning from Africa. In the present study we attempt the identification of dengue serotypes and genotypes circulating in Africa from 2010 to 2014 detected in travellers returning to Europe.
METHODS We collected samples from viraemic travellers returning from Africa who attended TropNet clinics in Europe from 2010 to 2014. Sequences of the Envelope gene were used to identify the serotype and genotype.
RESULTS During the study period we identified 3 DENV serotypes circulating in Africa. DENV 1 strains were detected in East Africa in 2010 (Eritrea) and in 2012 (Kenia), whereas in Central Africa in 2013(Angola and DRC). Strains from East Africa were grouped within Asian genotype, close to virus isolated in previous years in Djibouti and Kenia; we found American /African genotype in Central Africa. Both genotypes have circulated in West Africa for many years. DENV 2 strains were detected in West Africa (Senegal) and in East Africa (Tanzania) in 2014. Dengue 2 from Tanzania belongs to cosmopolitan genotype, but form a distinct clade different from the old African group. However, DENV 2 from Senegal surprisingly fell into genotype America /Asia. To our knowledge this is the first time identified in Africa. Finally, DENV 3 was detected in 2010 in Mali and Burkina Faso and again in Burkina Faso in 2013. All DENV 3 belong to genotype III and form a cluster with the African strains identified since 2008.
CONCLUSION DENV 1 of both genotypes was identified previously in Africa indicating endemic transmission as well as with DENV 3. Meanwhile, a new DENV 2 appeared in

Tanzania, introduced from South East Asia, and in Senegal from the Americas. These results confirm silent and sustained circulation of dengue in Africa and show the usefulness of travelers for sentinel surveillance to unmask the dengue problem in Africa.
DISCLOSURE Nothing to disclose.

4.5.1. Health of pastoralists and the science of zoonoses elimination

O.4.5.1.002

Neglected zoonoses at the human and livestock interface in Northern Côte d'Ivoire

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INTRODUCTION Neglected zoonotic diseases are less prioritized in West Africa. However they likely contribute greatly to morbidity in humans and livestock. Brucellosis, Q fever and Rift Valley Fever (RVF) are important zoonoses already eliminated in high-income countries, but persist in the developing world. Northern Côte d'Ivoire is the main livestock-raising zone in the country and most mobile pastoralism and livestock cross-border movements occur in this area. No animal disease control program has been in place for 20 years and veterinary services are not operational since the armed conflict in 2002.
METHODS We conducted a cross-sectional study in livestock and humans from 2012 to 2014 using a random selection of 63 villages in Korhogo and Niakaramandougou. We randomly selected a cluster sample of 633 cattle, 622 small ruminants and 88 people. We performed serological tests including the Rose Bengal Plate Test (RBPT); indirect ELISAs for *Brucella abortus*, *Brucella ovis* and *C. burnetii*; and competitive ELISA for *Brucella melitensis* and RVF. We also administered epidemiological questionnaires on relevant risk factors for zoonoses.
RESULTS Human seroprevalence for *Brucella* spp. was 5.3%. RBPT-positive small ruminants were negative by indirect and competitive ELISAs. Two RBPT-positive sheep reacted to *B. ovis* indirect ELISA. Seroprevalence of *Brucella* spp. in cattle adjusted for clustering was 4.6%. Cattle aged 5–8 years had higher odds of seropositivity than those aged <4 years (OR = 3.5; 1.5–8.2). Seropositivity to brucellosis in cattle was significantly associated with having joint hygromas (OR = 9; 1.3–59), grazing with small ruminants (OR = 5.8; 2.2–15.4) and transhumant herds (OR = 11.3; 3.3–38.1). Seroprevalences of Q fever were 13.9%, 9.4% and 12.4% in cattle, sheep and goats, respectively. Sheep from Niakaramandougou had greater odds of seropositivity (OR = 4.2; 2–8.4) compared to Korhogo. Seroprevalence of RVF was 3.9% in cattle, 2.4% in sheep and 0% in goats. Seropositive ewes had greater odds (OR: 4.7; 1.02–21.3) of abortion than seronegative ones. In cattle, short distance from the night pen to the closest permanent water bodies was a significant protective factor (OR = 0.13; 0.02–0.72).
CONCLUSION Our results provide recent epidemiological evidence on zoonoses, to understand their occurrence and transmission at the human and livestock interface in West Africa and eventually on possible control options.
DISCLOSURE Nothing to disclose.

O.4.5.1.003

A retrospective study on 182 cases human hydatidosis based on hospital records, from 2006 to 2013 in Hamadan, West of Iran

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INTRODUCTION AND OBJECTIVES Hydatidosis is a zoonotic disease common in the Middle East countries and Eastern Mediterranean region. Iran, classified as an endemic area for hydatid disease according to WHO classification. In humans, hydatidosis lead to economic losses from treatment costs and lost wages and even death from surgery side effects in some cases. The reservoir and intermediate hosts of *Echinococcus granulosus* and human hydatidosis are more prevalent in the Alborz and Zagros Mountains slop as two rich and good pastures for livestock. Many cases of hydatid cysts were operating annually in Iranian hospitals and some of them die from surgery complications. A 7-year (2006–2013) retrospective study was carried out to investigate the occurrence of hydatidosis in patients at main hospitals in Hamadan Province, Iran.
MATERIALS AND METHODS This study reviewed the files of patients with hydatid cysts treated surgically in the main public and private hospitals in Hamadan province between 2006 through 2013. The data extracted from 8 hospitals in the public and private sectors. Demographic data, diagnostic measures including laboratory and radiological findings, clinical manifestations, site of the cyst, surgical approaches, and final outcome were noted in the prepared check list and analyzed.
RESULTS A total of 182 hydatidosis patients were diagnosed and operated giving an average of 26 cases per year, equivalent to approximately 15 cases per 1 000 000 people per year. High proportion of cysts (70.9%) occurred in the liver, 24.7% in the lung and 2.2% in both organs; and more females had higher cysts (52%) than males (48%). Mean age of patients were 44.5 years at range of 3–91 years. The most cysts were at the 5th decade of the life. The majority the patients were illiterate (32.2%) and residence in the rural areas (61.7%) and their occupations were house wife (36.8%). The most of patients were from Hamadan, and then from Malayer city. Finally, almost 90% of patients diagnosed by CT and 8% had history of surgery for hydatid cyst.
CONCLUSION These findings indicate, hydatidosis is a major health problem in this area and more extensive epidemiological investigations of CE is necessary to better determine the prevalence, economic impact and risk factors for the disease in this province and other provinces of Iran as well.
KEYWORDS Hydatidosis, surgery, hospital, Iran
DISCLOSURE Nothing to disclose.

O.4.5.1.004

Molecular detection of *Echinococcus granulosus* and *Taenia* spp. infections in dogs in rural areas of southwest Iran

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INTRODUCTION *Echinococcus granulosus* is the causative agent of cystic echinococcosis (CE), a global zoonotic disease in humans and animals. The parasite life cycle is perpetuated in the domestic life cycle, which domestic dogs are typical definitive hosts and humans or ungulates are intermediate hosts. In some endemic regions, wild carnivores such as wolves play a role as definitive hosts. Geographically, *E. granulosus* has a worldwide distribution, and is found in all continents. Iran is an endemic area for *E. granulosus*, and dogs act as definitive hosts.
MATERIALS AND METHODS From April 2013 to June 2014, faecal samples of 167 household dogs from rural areas in southwest Iran were collected, and processed using the flotation/sieving technique. For isolating taeniids eggs, zinc chloride solution with specific gravity 1.45 g/ml was used. All samples were analyzed by multiplex PCR of mitochondrial genes for identification of *E. granulosus, Echinococcus multilocularis,* and *Taenia* spp.
RESULTS Multiplex PCR revealed mono infections for *E. granulosus* in 7 (4.2%) and *Taenia* spp. in 29 (17.4%), but co-infections were detected with *E. granulosus* and *Taenia* spp. in 11 (6.6%). A total 120 samples (71.9%) were negative for both *E. granulosus* and *Taenia* spp. infections. *Echinococcus multilocularis* infection was not found in any faecal samples.
CONCLUSIONS Based on obtained results, infection of owned dogs from rural areas of southwest Iran with *E. granulosus*, may be a potential source of human cystic echinococcosis in the studied regions. Therefore, implementation of control and prevention programs by local health centers and comprehensive educational programs to increase public awareness, particularly for dog owners, should be established in the area.
DISCLOSURE Nothing to disclose.

O.4.5.1.005

A dog rabies elimination campaign in N'Djamena, Chad

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The risk of transmission from rabies reservoir animals to people prevails until to date despite the availability of potent vaccines both for human and animal use. The most effective strategy to control and eliminate dog related rabies in humans is to immunize dog populations at high coverage. The dynamic and semi feral nature of dog populations in most rabies endemic areas is one of the obstacles to achieve sufficient coverage levels. Other major challenges are commitment of policy makers, allocation of resources and awareness of the public.

We conducted two consecutive parenteral dog mass vaccination campaigns in Ndjamena, Chad. From October to December 2012 and during the same period in 2013 10 vaccination teams progressed from district to district vaccinating dogs from Fridays to Sundays each week at central locations previously identified together with district and quarter chiefs. A poster and radio campaign together with loudspeaker announcements in the respective district preceded the vaccination. A Bayesian statistical analysis was done on capture-mark-recapture data to estimate vaccination coverage and the proportion of ownerless dogs. Dog rabies incidence data are routinely collected at the rabies laboratory of the Institut de Recherche en Elevage pour le Développement (IRED).

In 2012 over 18 000 dogs were vaccinated and this number was outperformed in 2013 by vaccination of 22 300 dogs. The overall coverage reached by the intervention was >70% in both years. Yet, coverage percentages vary greatly from district to district reflecting the various cultural and socio-economic backgrounds of the city. Rabies incidence in dogs dropped from 0.5/1000 June to October 2012 to 0.03/1000 for the same period in 2014.

Key to success was cooperative collaboration between the three implicated partner institutions, a sufficient information and communication strategy to access local leaders, careful operational planning and the motivation of staff. Future challenges for the control program remains the lack of long term funding, the high dog population turnover and the lack of any legislation on dog registration and movement restriction.
ACKNOWLEDGMENTS We are grateful to all vaccinators and supervisors for their huge effort. We also thank all authorities for their support and the dog owners for their participation.
DISCLOSURE Nothing to disclose.

4.5.2. Innovations in public health entomology

INV.4.5.2.001

Innovative vector control tools to address residual malaria transmission, dengue fever and other vector borne diseases

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Mosquito borne diseases such as dengue and malaria are causing an intolerable burden on human health and economy. On one hand studies estimate that 3.9 billion people in 128 countries are at risk of dengue fever infection. There is no specific treatment for dengue and its prevention relies solely on effective vector control. Dengue vectors are active indoor and outdoor and transmission of dengue fever is often increased outdoors where mosquitoes and humans spend most of their time.

On the other hand, it is estimated that 3.3 billion people are at risk of malaria worldwide. Indoor residual spraying (IRS) of chemical insecticides, and long-lasting insecticide treated nets (LLINs) have greatly contributed to the decline in malaria particularly in sub-Saharan Africa where mortality rates have declined by 54% in the last decade. However, these gains are threatened by the now widespread development of resistance in mosquitoes against all classes of insecticides currently used on nets and most of those used in IRS. Another alarming challenge in malaria vector control is the increasing proportion of vectors biting outdoors. Without addressing the challenge of outdoor transmission of malaria, it will not be possible to eliminate the disease.

Developing innovative ways of controlling mosquitoes outdoors before they enter human dwellings or bite humans outdoors will help control residual malaria transmission but also

dengue and other vector borne diseases such as lymphatic filariasis in an integrated vector management fashion.

Potential interventions that have been proposed include larval source management; adult mosquito contamination with biological or chemical agents which can be autodisseminated into mosquito habitats; oviposition traps for mass mosquito removal; mosquito repellents (topical, spatial or clothing); paratransgenic bacteria or toxic sugar baits; pheromone trapping and space spraying to control mosquito swarms; zooprophylaxis; endectocides (Ivermectin); release of competitive sterile males or other genetically modified mosquitoes; physical barriers and house modification or improvement, etc.

Here we discuss potential innovative vector control strategies that are being tested for the control of malaria, dengue and other vector borne diseases. For these innovative tools to be implemented effectively there is a need to increase local human capacity in disease endemic countries to plan, implement and monitor new vector control interventions.

DISCLOSURE Nothing to disclose.

O.4.5.2.002

Efficacy of permethrin-impregnated clothing on knock-down and mortality of dengue mosquito vectors

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INTRODUCTION As vector control for dengue has proven to be elusive, additional methods to protect against dengue are urgently needed. We have previously shown that pre-fabricated clothing impregnated with permethrin in a proprietary manner had a close to 100% 1 h knock-down and 24 h-mortality effect on *Aedes* mosquito vectors. However, this effect rapidly declined with repeated washing. Here we investigated different impregnation techniques to assess the best method with the lowest waning efficacy after washing.

MATERIALS AND METHODS School clothes were impregnated with permethrin by two different technologies: pad-dry-cure versus exhaustion. Impregnated products were tested for their efficacy using laboratory-reared *Aedes* mosquito vectors using WHOPES cone test, before and after 10 washes.

RESULTS The 1 h knock down effect and 24 h mortality rate of school clothes treated by both technologies were both found to be 100%. However, the clothes treated by pad-dry-cure technology could stand frequent washing better than those treated by exhaustion technology. The decrease in efficacy of up to about 60% of the clothes treated by pad-dry-cure technology was observed after washing 8 times while those treated by exhaustion technology showed decrease in knock-down effect (67.27%) and mortality rate (74.29%) after washing only 4 times.

CONCLUSION The knock-down and 24 h mortality results look very promising to support impregnated clothing as a potential strategy to protect against day-biting *Aedes* mosquito vectors to prevent dengue infections. However, rapid waning efficacy of impregnated clothing after <10 washes suggests that impregnation techniques for sustainable effect are sub-optimal and hence such an approach is not recommended at this point in time. Either new impregnation technologies will need to be developed to overcome the waning efficacy after washing, or clothing such as aprons or vests will need to be employed. Since school aprons are hanged in classrooms after daily use without washing through out the school term, they could potentially have a prolonged impact of permethrin on mosquito vectors (in terms of knock-down and mortality) and eventually dengue transmission in school.

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DISCLOSURE Nothing to disclose.

O.4.5.2.003

The complementary advantage of combining spatial repellent treated sisal decorative baskets with long lasting insecticide treated nets

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BACKGROUND Spatial repellents (SRs) interfere with host attractiveness of mosquitoes, consequently preventing bites and may substantially reduce malaria transmission. The goal of this study was to determine the advantage of combining Transfluthrin treated sisal fiber decorations with long lasting treated nets (LLINs).

METHODS Efficacy of Transfluthrin treated sisal baskets against malaria vectors that bite in the early evening before humans are protected by LLINs was investigated in experimental huts. The proportion of mosquitoes in experimental huts with Transfluthrin treated sisal baskets and LLINs was compared to huts that had LLINs only using a 3 × 3 Latin square design. Treatments included: (i) untreated sisal baskets and LLINs, (ii) 2.5 ml Transfluthrin treated sisal baskets and LLINs and (iii) 5.0 ml Transfluthrin treated sisal baskets and LLINs. One male volunteer was allocated to each hut to conduct human landing catches at 1900 hours–2300 hours and retired to bed until 0600 hours. Mosquitoes were collected from exit traps, the floor and resting surfaces inside huts.

RESULTS Results indicate that 2.5 and 5.0 ml Transfluthrin sisal baskets reduced the proportion of *Anopheles arabiensis* mosquitoes inside huts by almost three quarters [Relative Rate (RR): 0.26 (0.22, 0.29); $z = -19.00$, $P < 0.000$ and RR: −0.31 (0.27, 0.36); $z = -16.97$, $P < 0.000$] respectively. Both 2.5 and 5.0 ml Transfluthrin baskets treatments prevented more than three quarters of *An. arabiensis* mosquitoes from biting humans [RR: −0.17 (0.11, 0.24); $z = -9.78$, $P < 0.000$].

CONCLUSION This study shows that combining spatial repellents with LLINs inside huts significantly reduces house entry as well as biting rate of *An. arabiensis*. This is especially useful where residual malaria transmission occurs in the early evening before people go to bed and are under the protection of LLINs. Nevertheless, there is need to conduct further studies that determine the epidemiological impact of combining spatial repellents with LLINs.

DISCLOSURE There is no conflict of interest.

O.4.5.2.004
Interactions between endosymbiotic *Spiroplasma* and anopheline mosquitos

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Endosymbiont-based strategies to block disease transmission by vector insects have shown promise for the control of arboviral diseases (e.g. Dengue). There is great interest in using endosymbionts to control vector borne parasites (e.g. *Plasmodium*), however, more research is needed to identify and study endosymbionts that confer hosts with parasite-specific protection. One widespread endosymbiotic bacterium, *Spiroplasma*, confers fly and aphid hosts with protection against a variety of parasitic and fungal infections. *Spiroplasma* has previously been identified in a number of mosquitos, including members of the genus *Anopheles,* but the effects of this endosymbiont on vector biology have not previously been investigated in detail. We report the discovery of *Spiroplasma poulsonii* in a population of *Anopheles arabiensis* from Kirinyaga district, Kenya. We use confocal microscopy to demonstrate the tissue tropism of this endosymbiotic bacterium and further investigate the implications harboring *Spiroplasma* on the longevity, fecundity and other aspects of mosquito host biology. In addition, we examine the potential utility of this strain of *Spiroplasma* for *Plasmodium* transmission blocking.
DISCLOSURE Nothing to disclose.

O.4.5.2.005
Breeding conditions influence susceptibility to insecticides in mosquitoes

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BACKGROUND As insecticide resistance increasingly threatens malaria control programmes, it is very important to understand the processes and factors that interact to produce observed insecticide resistance phenotypes. The contribution of the environmental and breeding conditions to the susceptibility of the mosquito has been largely ignored. In this study, we evaluate how temperature, population density (crowding) and nutrition during the larval stage interact to influence the susceptibility of the adult mosquito to public health insecticides.
METHODS Using a factorial experimental design, we bred *Anopheles gambiae* and *A. stephensi* larvae under different combinations of temperature, population density and nutrition. Emerging adults were tested in the World Health Organization insecticide susceptibility test against a concentration of permethrin that would kill 50% of the mosquito population under standard rearing conditions. Dry weights of both dead and alive mosquitoes were measured to test the association of mosquito body weight in susceptibility to insecticides in terms of immediate knockdown and 24 h mortality. A dose-response assay of mosquitoes of extreme sizes was done to evaluate the practical implications of breeding conditions on mortality
RESULTS Mosquitoes bred under different conditions showed significant differences in body sizes and mortality. Dry weight was strongly related to mortality (OR = 0.0000992, $P < 0.001$) in both experiments but was not significantly associated with time-to-knockdown. The results for the dose-response would be ready by the time of the conference.
CONCLUSION The breeding conditions of mosquito larvae have a significant impact on the dry weight as well as susceptibility status of the adult mosquito. It is therefore important to incorporate the size of the mosquito when studying insecticide susceptibility in mosquitoes.
DISCLOSURE Nothing to disclose.

4.5.3. Dengue and Chikungunya viral infections: a box of surprises

INV.4.5.3.001
Chikungunya in the Americas, emergence and dissemination

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Chikungunya virus is a mosquito borne alphavirus, transmitted by *Aedes* mosquitoes, first identified in 1952 in Tanzania. It caused sporadic outbreaks in Africa and Asia until it re-emerged in 2005 and caused a major epidemic in the Indian Ocean. There are 3 genotypes – African, East Central South African (ECSA) and Asian. The Americas had been spared by the 2005–09 chikungunya epidemics despite several imported cases. However, due to the abundance of vectors and travel exchanges, the risk of local transmission was considered high.

In early December 2013, evidence of local transmission came from St Martin Island in the Caribbean, during a dengue epidemic. The virus was of the Asian genotype, related to strains recently identified in Asia. Within 6 months it had disseminated throughout the Caribbean. It reached the South American in February 2014. In July 2014, 11 locally acquired cases were confirmed in Florida. In September 2014, 2 different introductions were reported in Brazil. The Asian strain circulating in French Guiana was identified in North Brazil and an ECSA strain was identified in Northeast Brazil, presumably imported from Angola. On June 2015, 18 months after the St Martin cases, over 1 and a half million cases were identified in the Americas.

Outside the Americas, an epidemic occurred in French Polynesia in September 2014 with a strain related to the Caribbean isolate. In Europe, no local transmission originating from the Americas occurred despite a high number of imported cases. The only episode of local transmission, in France, was from an imported case from Cameroon (ECSA lineage).

The emergence and dissemination of chikungunya in the Americas was not unexpected, however several questions remain about the factors driving them. Its rapid spread in the Americas, the introduction of an ECSA strain in Brazil and the evidence of a high number of imported cases world-wide, are evidence that vector borne diseases and globalization remain high on the agenda of public health and prevention.
DISCLOSURE Nothing to disclose.

O.4.5.3.002
Distinct cytokine and chemokine patterns are generated among patients with Chikungunya infection

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INTRODUCTION Chikungunya reemerged in 2005–2006 in several parts of India and later reaching West Bengal. We

investigated the serum levels of 7 cytokines/chemokines, circulating immune complexes (CIC) and complement consumption (C3) during the acute phase of Chikungunya disease and 6 month post-infection.
MATERIALS AND METHOD A longitudinal study was performed at Calcutta School of Tropical Medicine, West Bengal, India during 2013–2015. Confirmed chikungunya patients along with patients with rheumatoid arthritis, dengue and healthy donors were enrolled. Their profiles of clinical disease and immune mediators were investigated.
RESULT In acute stage of Chikungunya the patients had significantly higher levels of Interferon (IFN) gamma, Interleukin-6(IL-6), IL-12, Chemokine (C-X-C motif) ligand 9 (CXCL9) than the control population ($P = 0.01$, $P = 0.0003$, $P = 0.039$, $P < 0.0001$) and decreased levels of Regulated on Activation, Normal T Expressed and Secreted (RANTES) ($P < 0.0001$). Very high titres of C3 and CIC were also obtained ($P < 0.0001$, $P < 0.0001$). A novel arthralgia severity marker in serum CIC of patients with Chikungunya infection was also identified. The 39 kDa protein also had good clinical correlation and was completely absent in healthy persons as well Dengue and Rheumatoid arthritis patients. In contrast, acute dengue patients had higher levels of RANTES and CXCL10 ($P < 0.0001$, $P < 0.0001$). With disease resolution in Chikungunya patients increased levels of RANTES along with decreased levels of IL6, IL7, IL12, CXCL10 were obtained. The titres of CXCL9 decreased markedly ($P = 0.04$) in chikungunya follow-up patients.
CONCLUSION Distinct cytokine patterns in acute chikungunya and post infection were obtained. CXCL9 could serve as signature molecule for acute chikungunya infection whereas 39 kDa CIC protein could serve as novel arthralgia marker. Additionally, contrasting cytokine and chemokine patterns were obtained in chikungunya and dengue suggesting differential disease manifestation in the two viral infections.
ACKNOWLEDGEMENT The study was funded by National Rural Health Mission, Government of West Bengal.
DISCLOSURE Nothing to disclose.

O.4.5.3.003

Urbanisation in Côte d'Ivoire increases *Aedes* mosquito hatching rate and contributes to dengue and yellow fever outbreaks by selecting *Aedes aegypti*

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BACKGROUND Single and combined *Aedes* mosquito-transmitted outbreaks of dengue and yellow fever are repeatedly reported in rural and urban areas of Côte d'Ivoire. The present study aimed at assessing the effects of urbanisation on *Aedes* mosquito egg eclosion rate and its dynamics in rural, suburban and urban settings of Côte d'Ivoire.
METHODS The study was conducted from January 2013 to April 2014. *Aedes* spp. eggs were sampled using a standardised World Health Organization (WHO) ovitrap method. Emerged larvae were reared until adult stage. Eggs, larvae and adult of *Aedes* spp. were identified and recorded.
RESULTS A total of 5146, 3796 and 3854 eggs of *Aedes* spp. were collected in rural, suburban and urban areas, respectively, providing overall respective densities of 5.72, 6.33 and 6.42 eggs/ovitrap/week. Egg eclosion rate progressively increased from rural (52.3%) to suburban (74.6%) and urban (89.9%) areas with significant difference between rural and urban areas ($F = 5.45$; $P < 0.05$). The adult species density also rose from rural (2.69 *Aedes*/ovitrap/week) to suburban (4.07 *Aedes*/ovitrap/week) and urban (5.16 *Aedes*/ovitrap/week) areas with significant differences between rural and suburban areas ($\chi^2 = 11.23$; $P < 0.001$), and between rural and urban areas ($\chi^2 = 36.97$; $P < 0.001$). Inversely, species diversity gradually decreased from rural (8 species) to suburban (3 species) and urban (1 species) areas. *Ae. aegypti*, the main vector of dengue and yellow fever, was the predominant species in the urban setting (100%; $n = 3098$), while its prevalence increased from rural (72.5%; $n = 2421$) to suburban (88.5%; $n = 2440$) settings. Effectiveness of the WHO ovitrap method for *Ae. aegypti* collection was three times higher in urban compared to rural area.
CONCLUSIONS Our study reports a significant increase in *Aedes* egg eclosion rate in correlation with urbanisation. Furthermore, urbanisation also correlates with an exclusion of the *Aedes* wild species to the benefice of *Ae. aegypti* that adapt well its oviposition to artificial receptacles. These results open new perspectives in dengue and yellow fever vector control and surveillance strategies.
DISCLOSURE Nothing to disclose.

O.4.5.3.004

Dengue fever outbreak in the native and expatriate communities of Dar es Salaam, Tanzania

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INTRODUCTION Uncontrolled urbanization and human mobility has led to a rapid increase of dengue over the last decade and its geographic distribution is now expanding to Africa. We describe the epidemiology of a dengue outbreak in Dar es Salaam, Tanzania, that occurred in both native and expatriate populations, which gives a unique opportunity to study differences in clinical presentation.
METHODS Consecutive adult patients with temperature ≥38°C were recruited prospectively between July 2013 and 2014 in public clinics. Several rapid and conventional diagnostic tests for causes of fever, including dengue, were performed. Patients with confirmed dengue (NS1 and/or IgM and/or PCR positive) were also recruited in a private clinic. The clinical outcome of patients was assessed by a visit/call at day 7.
RESULTS Between July–December 2013, none of 187 Tanzanian patients had dengue, while 5% had malaria. Between January–July 2014, 185/517 (36%) Tanzanian patients had dengue (serotype 2 virus, genotype Cosmopolitan) and 15%

malaria; 225 additional dengue patients were detected in a private clinic (178 expatriates and 55 Tanzanians).

Tanzanians dengue patients ($N = 232$) were younger than expatriates ($N = 178$; mean 33 vs. 42 years, $P < 0.001$), had more often headache (93% vs. 81%, $P = 0.001$), rarely presented with a rash (4% vs. 48%, $P < 0.001$) and were more often co-infected with malaria (5% vs. 1%, $P = 0.03$). Tanzanians tended to present with less warning signs (24% vs. 31%, $P = 0.08$), but the same rate of severe dengue (1%). Mucosal bleeding (5% vs. 13%, $P = 0.005$) was more frequent among expatriates, while severe thrombopenia was more common among Tanzanians (7% vs. 1%, $P = 0.005$). Two (1%) Tanzanians died. GPS localisation showed a concentration of Tanzanian dengue cases in a poor and overcrowded neighbourhood while expatriate cases came from a privileged area of the city.

CONCLUSIONS In this dengue outbreak, clinical presentation differed between native and expatriate populations but severity was overall similar. Although Tanzanians and expatriates acquired dengue in different areas, they were all infected with the same genotype that has been described in Indian Ocean islands and Asia. This outbreak, which completely disturbed the febrile diseases distribution, highlights the necessity of introducing point-of-care tests other than malaria and to have sentinel clinics with enhanced diagnostic capacities to rapidly document the pathogen.

DISCLOSURE Nothing to disclose.

O.4.5.3.005

Serotype influences on dengue severity

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INTRODUCTION Dengue is a mosquito-borne disease caused by a RNA virus of the Flaviviridae family, a complex with four distinct serotypes (DENV-1 to DENV-4), capable to induce hemorrhage and associated with epidemics of different levels of severity. The present study evaluates the serotype influence on dengue outcome.

METHODS AND MATERIAL The study presents a cross-sectional design, including dengue cases occurred between 2007 and 2013 in Vitória, Espírito Santo, Brazil, accessed through the Information System for Notifiable Diseases.

RESULTS The sample analyzed was 496 dengue cases, mainly males (53.2%) witha median age of 26.3. Severe dengue affected 6.7% ($n = 33$) of the cases. DENV-1 was the serotype dominant ($n = 385$, 77.6%), followed by DENV-4 ($n = 79$, 15.9%) and DENV-2 ($n = 31$, 6.3%). One non-severe case caused by DENV-3 (0.2%) occurred in a male. Severe dengue was more frequent in DENV-2 cases, affecting 32.3% of them ($n = 10$, $P < 0.01$), being rarer in DENV-1 cases, affecting only 4.7% of these cases ($n = 18$, $P < 0.01$). Severe clinical form affected 6.3% of DENV-4 cases ($n = 5$, $P = 0.9$).

CONCLUSION The results demonstrate a higher risk to severe dengue in DENV-2 infection, indicating that when this serotype is identified by surveillance, an increased number of severe outcomes has to be expected, necessitating preparation of the health system to allow for early diagnosis, patient follow up and allocation of treatment resources.

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DISCLOSURE Nothing to disclose.

4.5.4. Arthropode-borne diseases

O.4.5.4.001

Seasonality of dengue epidemic potential in Europe – based on vectorial capacity for *Aedes* mosquitoes

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INTRODUCTION Dengue is a mosquito-borne viral infection that has become a major public health concern. About 390 million people are infected yearly. Increased global connectivity and population movement as well as climate change affect the global distribution of both dengue vectors and the virus, facilitating the spread of dengue to new geographic areas. Weather is an important factor determining mosquito behaviour and effectiveness of dengue virus transmission. Dengue epidemic potential depends on vectorial capacity of *Aedes* mosquitoes, which depend on climate, such as, temperature and diurnal temperature range. This study aims at identifying high-risk areas and high-risk time windows in Europe based on temperature, in order for timely vector surveillance and control.

METHODS Relative vectorial capacity (*rVc*) was used to estimate dengue epidemic potential. Using historical and projected temperature data over two centuries (1901–2099) and temperature dependent vector parameters for *Aedes* vectors, *rVc* was calculated for 10 selected European cities from Stockholm in the North to Malága in the South.

RESULTS Compared to dengue endemic areas, *rVc* in Europe was lower and showed more prominent seasonality. The peak and width of the seasonal windows in *rVc* were generally higher in the South than the North. Currently, only South and Central-East Europe and the summer season corresponds to *rVc* that is over the threshold for possible dengue transmission. By the end of this century, in the best case scenario, all the Central and Southern European cities would be at risk for dengue transmission during the warmer months; in the worst case scenario, this risk would extend to Northern European to include Stockholm if dengue vectors were established and virus introduced.

CONCLUSION As travel and globalization become more frequent channels for dengue vector and virus introduction, Europe may face the reality of more frequent dengue outbreaks in their warmer months. Madeira's outbreak in 2012 underlines this concern. The future's high risk area and time window depend sensitively on climate scenarios. Therefore, it is important to emphasize climate change mitigation and enhance vector surveillance and control in Europe.

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DISCLOSURE Nothing to disclose.

O.4.5.4.002

NS1 rapid test for detection of dengue virus infection

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INTRODUCTION Rapid diagnosis during the early phase of dengue is crucial for prompt public health measures and proper patient management. Dengue diagnosis as early as on day 1 of fever is now possible with the use of the DENV non-structural protein 1 (NS1) antigen detection. Here, we report the performance of the dengue NS1 Ag STRIP test (Bio-Rad, France) using actual suspected dengue patients' samples.
MATERIAL AND METHODS DENV NS1 antigen test was performed using the Dengue NS1 Ag Strip following the manufacturer's protocol. The performance of the NS1 Ag Strip for detection of DENV infection was evaluated and compared to that of the quantitative reverse transcription-polymerase chain reaction (qRT-PCR).
RESULTS Among the primary infection samples ~95% were positive with the NS1 Ag Strip assays and ~75% with qRT-PCR. Whereas, among the secondary dengue samples, ~40% and 50% of the samples tested positive by the NS1 Ag Strip and qRT - PCR, respectively. Almost 80% of the samples tested negative by qRT-PCR but positive with NS1 Ag Strip were samples obtained after day 5 of illness onset. On the other hand, over 95.0% of the samples tested positive by qRT-PCR but negative by NS1 Ag Strip were from secondary dengue samples.
CONCLUSION The NS1 Ag STRIP test is sensitive to detect acute DENV infection. NS1 negative results, however, should be cautiously interpreted especially in dengue hyperendemic regions where the prevalence of secondary DENV infection is high. Molecular test is needed to complement the NS1 test for more conclusive dengue diagnosis.
DISCLOSURE This research was funded by the European Union 7th Framework Programme through 'DengueTools' (www.denguetools.net).

O.4.5.4.003

A school-based intervention trial using insecticide-treated school uniforms to reduce dengue infections in school-aged children

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BACKGROUND There is an urgent need to enhance our armamentarium to prevent dengue infections in children. Since dengue vectors (*Aedes* mosquitoes) are active mainly during the day, a potential target for control should be schools where children spend a considerable amount of their day. School uniforms are the cultural norm in most developing countries, worn throughout the day. We hypothesized that insecticide-treated school uniforms will reduce the incidence of dengue infection in school-aged children. Our objective was to determine the impact of impregnated school uniforms on dengue incidence.
METHODS A randomised controlled trial was conducted in 10 schools in eastern Thailand in 2012. Pre-fabricated school uniforms were commercially treated to ensure consistent high quality of insecticide impregnation with permethrin. The 1-h-knock-down effect and 24 h mortality of *Aedes* mosquitoes by the impregnated cloth was tested at baseline and then once per month using WHOPES cone test. Blood samples were taken at baseline and at the end of the school-term for the hemagglutination-inhibition assay to identify serologically confirmed dengue infections during the study period. Students were randomized into intervention schools (all students wearing impregnated uniforms) versus control schools (uniforms had the same appearance and odor, but were not impregnated).
RESULTS A total of 1808 students in 10 schools were enrolled, mean age 10.07 years. Of these, 1651 had paired blood samples taken, which showed an incidence of new dengue infection of 3.3 % over the school term (5 months). There was no difference in the incidence of dengue infections in intervention versus control schools. Both the knock-down and mortality at baseline were close to 100%, but rapidly waned after only 8 washes to 20% e.g. after only 1 month of wearing the uniform.
CONCLUSION Although the results of mosquitoes' knock-down and mortality of impregnated schools looked very promising, we did not see a protective effect of impregnated uniforms on reducing dengue infections in this school-based trial. The most likely reason for the apparent failure was the rapid waning efficacy of impregnation after washing. New technologies need to be developed to overcome rapid waning efficacy of impregnated clothing.
DISCLOSURE This research was funded by the European Commission 7th Framework and was conducted by 'DengueTools' partners.

O.4.5.4.004

Household-related risk factors of tungiasis and severe disease in Kilifi County, Kenya

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Tungiasis is a neglected tropical skin disease caused by female sand fleas (*Tunga penetrans*). The disease is common among impoverished communities in South America, the Caribbean and sub-Saharan Africa and is associated with important morbidity. Tungiasis is endemic along the Coast of Kenya with a prevalence ranging from 11% to 50% in nursery and lower primary school. This research intends to reveal behavioral and environmental risk factors of tungiasis in rural Kenya.

In a cross-sectional study we investigated 1086 individuals from 233 households in 8 villages located in Kakuyuni and Malanga Sub-locations, Kilifi County, on the Kenyan Coast. Study participants were examined clinically and established severity scores for acute and chronic tungiasis were calculated. Risk factors were assessed using a structured questionnaire and household GPS locations were recorded. Data were analyzed using regression analysis and spatial methods.

The overall prevalence of tungiasis was 25.0%. In 42.5 % of the households at least one individual had tungiasis. Bivariate analysis showed that the occurrence of tungiasis was significantly related to the number of people per sleeping room (OR = 4.17; 95 % CI 1.56–11.14), presence of sandy/dusty floors

(OR = 1.81; 95 % CI 1.01–3.24), low level of school education (OR = 3.40; 95 % CI 1.51–7.65) and a low frequency of washing (OR = 3.00; 95 % CI 1.41–6.39). The odds of having tungiasis was inversely associated with socio-economic status. Using a selection procedure, a multivariate model included only sandy floors (OR = 10.43; 95 % CI 1.54–70.43) and male sex (OR = 2.48; 95 % CI 1.59–72.33).

The results show that in rural Kenya tungiasis is associated with important morbidity and is poverty-related. Future domiciliary transmission is very likely.

DISCLOSURE Nothing to disclose.

O.4.5.4.005

Topically applied dimeticones are highly effective against embedded sand fleas (*T. penetrans*)

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Tungiasis (sand flea disease) is a neglected tropical disease associated with debilitating acute and mutilating chronic morbidity. Since there is no effective treatment at hand, patients in the endemic areas attempt to remove embedded sand fleas with non-sterile sharp instruments, such as safety pins, needles or thorns – a hazardous procedure in itself.

In a randomized-controlled trial in rural Kenya, the efficacy of the topical application of a mixture of two dimeticones of low viscosity on embedded sand fleas was compared to bathing the feet in 0.05% $KMnO_4$ (the government-approved treatment in Kenya). The viability of the embedded parasites was assessed by a handheld digital video microscope and the degree of inflammation was determined by means of an inflammation score. In a second clinical trial, a targeted application of the dimeticone (i.e. placing a few drops onto the rear cone of the parasite) was compared to wetting the whole foot.

In the first study, in the dimeticone group, 78% (95% CI 67–86%) of the embedded sand fleas lost all viability signs within seven days. In the $KMnO_4$ group viability signs disappeared in 39% (95% CI 28–52%; $P = <0.001$). The inflammation score decreased from 6 to 4.7 points in the dimeticone group ($P < 0.001$), but remained unchanged in the KMnO4 group (4.5 vs. 5 points). The targeted treatment increased the efficacy of the dimeticone treatment by 10.2% (95% CI 7–14%) and simultaneously minimized the necessary volume of the dimeticone to a few drops.

It is concluded that the topical application of appropriate dimeticones effectively kills embedded sand fleas. As soon as the parasites are dead, tungiasis-associated inflammation regresses and the healing process begins. In view of the high efficacy and safety of dimeticone, the hazardous extraction of embedded sand fleas with sharp instruments is no longer warranted.

DISCLOSURE Nothing to disclose.

O.4.5.4.006

Efficacy of deltamethrin applied as ULV- and thermal aerosols for control of *Aedes albopictus* in Nice, France

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INTRODUCTION Insecticidal aerosols dispensed from vehicle-mounted cold-foggers (ULV) or hand-held thermal-foggers are considered the methods of choice for control of *Aedes aegypti* and *Ae. albopictus* during outbreaks of dengue and chikungunya. Nevertheless, their effectiveness has been poorly studied, particularly in Europe.

METHODS We used two techniques – ovitraps baited with hay infusion and 'B-G Sentinel' adult traps – to monitor *Ae. albopictus* populations on a 24-h cycle in three residential areas in Nice, France. The impact of deltamethrin applied from vehicle-mounted ULV fogging-machines was assessed by comparing trap results in treated versus untreated areas for 5 days before and 5 days after treatment. Four trials were conducted at the maximum permitted application rate (1gm/ha) and two (on a much smaller scale) with hand-held thermal foggers.

RESULTS Susceptibility to the insecticide was high: LD50 and LD95 for females were 0.0131 ng/mg and 0.0469 ng/mg – yet there was no discernable change in oviposition rate or in catch of adult female mosquitoes, nor was there any change in their physiological stage (parous versus nulliparous). Curiously, however, there was a marked reduction in adult males. Hand-held thermal foggers were much more effective, with more than 90% reduction of both males and females.

CONCLUSIONS We believe that direct monitoring of the wild population gives a more realistic assessment of treatment impact than the widely used approach with caged mosquitoes. By these measures, thermal fogging is clearly more effective than ULV treatments although much more labor-intensive.

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DISCLOSURE Nothing to disclose.

4.6.1. Clinical challenges in global health and patient management in health facilities with limited resources

O.4.6.1.002

Development of guidance for the diagnostic management of patients with neurological disorders in hospitals in Bandundu, Democratic Republic of the Congo, with a focus on not-to-miss infections of the central nervous system

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INTRODUCTION In Bandundu province in the Democratic Republic of the Congo (DRC), infections of the central nervous system (CNS) still cause considerable morbidity and mortality. NIDIAG is a European Union-funded research project that aims at improving diagnostic approaches in settings where neglected infectious diseases are frequent. We report on the development of diagnostic guidelines for neurological disorders.
METHODS AND MATERIALS The diagnostic guidelines are based on evidence from two previous NIDIAG studies conducted in Bandundu: a diagnostic study of 352 patients with neurological disorders and a qualitative study on knowledge, attitudes and practices of local clinicians. The guidelines were developed during a 3-day workshop in which Congolese and foreign experts in clinical tropical medicine and diagnostic research participated.
RESULTS Acknowledging gaps in knowledge and aiming for ease of use by a broad range of health workers, the workshop participants decided to make flexible guidelines rather than rigid dichotomous algorithms. They chose to represent likelihood ratios (LR) qualitatively without asking guideline users to calculate odds. It was considered important to include all not-to-miss CNS infections in one tool. The tool targets adults and children >5 years with a broad set of symptoms and signs, i.e. altered consciousness, severe increasing headache, sleeping abnormalities, new onset convulsions or focal neurological deficit. The guidance consists of two parts: initial diagnostic workup and diagnostic panorama. Each part can be printed as a poster or on A4 format so that it fits in patient files.

1 The recommended workup consists of three rapid diagnostic tests (RDT for HIV, malaria, sleeping sickness) and a general clinical and neurological exam. This should be done systematically and immediately. In some cases, based on clinical/RDT criteria, lumbar puncture is recommended.
2 The diagnostic panorama lists 8 severe and treatable infectious diseases that cause neurological problems in Bandundu. The most important (LR ≥ 5) clinical and lab arguments in favour and against each diagnosis are given. Rather than specifying a discrete final diagnosis, this format provides a visual representation of how likely or unlikely alternatives are.

CONCLUSIONS Evidence-based guidance is now available for the diagnosis of not-to-miss infections of the CNS in hospitals in Bandundu. The operational effectiveness is currently under evaluation.
DISCLOSURE Nothing to disclose.

O.4.6.1.003

Bloodstream bacterial infection among outpatient children with acute febrile illness in North-Eastern Tanzania

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INTRODUCTION Fever is a common clinical symptom in children attending hospital outpatient clinics in rural Tanzania, yet there is still a paucity of data on the burden of bloodstream bacterial infection among these patients.
METHODS The present study was conducted at Korogwe District Hospital in north-eastern Tanzania. Patients aged between 2 and 59 months with a history of fever or measured axillary temperature ≥37.5°C attending the outpatient clinic were screened for enrollment into the study. Blood culturing was performed using the BACTEC 9050® system. A biochemical analytical profile index and serological tests were used for identification and confirmation of bacterial isolates. *In vitro* antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion method. The identification of *Plasmodium falciparum* malaria was performed by microscopy with Giemsa-stained blood films.
RESULTS A total of 808 blood cultures were collected between January and October 2013. Bacterial growth was observed in 62/808 (7.7%) of the cultured samples. Pathogenic bacteria were identified in 26/808 (3.2%) cultures and the remaining 36/62 (58.1%) were classified as contaminants. *Salmonella typhi* was the predominant bacterial isolate detected in 17/26 (65.4%) patients of which 16/17 (94.1%) were from patients above 12 months of age. *Streptococcus pneumoniae* was the second leading bacterial isolate detected in 4/26 (15.4%) patients. A high proportion of *Salmonella typhi* 11/17 (64.7%) was isolated during the rainy season. *Salmonella typhi* isolates were susceptible to ciprofloxacin (n = 17/17, 100%) and ceftriaxone (n = 13/17, 76.5%) but resistant to chloramphenicol (n = 15/17, 88.2%). *Plasmodium falciparum* malaria was identified in 69/808 (8.5%) patients, none of whom had bacterial infection.
CONCLUSION Bloodstream bacterial infection was not found to be a common cause of fever in outpatient children; and *Salmonella typhi* was the predominant isolate. This study highlights the need for rational use of antimicrobial prescription in febrile paediatric outpatients presenting at healthcare facilities in rural Tanzania.
DISCLOSURE Nothing to disclose.

O.4.6.1.004

Application of the Luminex xTAG gastrointestinal pathogen panel for the detection of gastrointestinal pathogens in a rural African setting

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BACKGROUND Despite high morbidity and mortality, the laboratory diagnosis of gastrointestinal infections is largely neglected in tropical African settings. While multiplex PCR assays are increasingly used in industrialized countries, their rational use for patients with high numbers of different co-circulating pathogens has not yet been evaluated. This study aims to apply the Luminex multiplex PCR assay for the diagnosis of gastrointestinal pathogens in rural Ghana to evaluate its usefulness as a routine method.
METHODS A case-control study was conducted at the Outpatients Department of the Agogo Presbyterian Hospital in Ghana. Stool samples were collected from children below 6 years of age with (cases) and without (controls) diarrhoea. Samples were screened for 15 different diarrhoeal pathogens by the Luminex xTAG GPP assay. Associations between diarrhoea and gastrointestinal infections and fractions attributable to diarrhoea (AF) were determined by performing age adjusted logistic regressions.
RESULTS The Luminex PCR assay identified organisms in 96.6% (n = 428) of 443 cases and in 92.5% (n = 221) of 239 selected controls. A mean of 2.5 (SD: ±1.3) and 2.3 (SD: ±1.3) organisms were detected in cases and controls respectively. An association with diarrhoea was found for rotavirus [adjusted odds ratio (aOR) 7.2; 95% CI 2.9–18.1], norovirus (aOR 2.7; 95% CI 1.4–5.3) and *Shigella* spp. (aOR 1.7; 95% CI 1.2–2.4) with respective AFs of 12.5% (95% CI: 9.6–15.3), 7.9% (95% CI: 3.8–11.7) and 16.9% (95% CI: 6.9–25.9).
CONCLUSION The high proportion of positive stool samples with a high number of co-infections in cases and controls suggests a substantial amount of transient or colonizing microorganisms in the study population. Therefore, the application of a multiplex PCR assays might reveal frequently positive results, which do not necessarily implicate treatment. The use of sequential diagnostic algorithms with pathogen specific or quantitative PCRs might be more appropriate for diagnosing gastrointestinal infections in tropical settings.
DISCLOSURE Nothing to disclose.

O.4.6.1.005

Characterising the health facility infrastructure in countries with endemic sleeping sickness for effective targeting of diagnostic resources

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Human African Trypanosomiasis (HAT) is a highly debilitating vector born disease that is endemic in a number of sub-Saharan African countries. It is important to identify cases early in infection when clinical signs can be mild but the highly toxic and onerous treatment makes it vital to obtain the correct diagnosis. Being forced to travel long distances can form a barrier to reporting and diagnosis, whilst poorly targeted resources can result in an infrastructure that is difficult to maintain and support. Therefore, in order to correctly target HAT diagnostics, it is necessary to have up to date information on the location and capacity of diagnostic facilities.

To collect these data, we worked with HAT control programmes in 8 African nations to compile databases of health infrastructure in their HAT foci. Data collected include the location, equipment and staffing resources and history of diagnosing HAT cases. In most countries these data were collected by ground surveys.

All facilities in foci in Uganda, Tanzania, Nigeria and Guinea have been characterised, whilst in South Sudan, Chad and the DRC, the foci with the greatest prevalence have been characterised. These countries account for 93% of gambiense sleeping sickness cases and 91% of rhodesiense sleeping sickness cases. In these countries, detailed data have been collected on 4803 facilities. The data have been used to inform HAT elimination programs in all countries except Tanzania. These programs have involved the delivery of enhanced diagnostics in an integrated hierarchical structure in the passive surveillance systems. As part of these programs, 1310 facilities have been equipped with new rapid diagnostic tests, 53 with new fluorescence microscopes and 13 large facilities with loop mediated isothermal amplification of DNA (LAMP) incubators. This required the selection of appropriate facilities for improvement of diagnostics to ensure full coverage of the population at risk and on-going monitoring of diagnostic activities at the facilities. The data have also being analysed to identify gaps in the surveillance infrastructure.

By improving HAT screening infrastructure in all levels of health systems, new cases have been identified through enhanced passive surveillance in participating countries. Crucial to this surveillance model is the detailed characterisation of health facilities. These data are owned by the countries and so can be used for many other aspects of healthcare provision.
DISCLOSURE Nothing to disclose.

4.6.2. Medical and public health education in Africa

O.4.6.2.003

What are the mutual benefits for universities participating in teaching networks?

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BRIEF INTRODUCTION tropEd is a worldwide network for education in global and international public health, especially at Master's level training: Since its inception in 1995 it has grown to an association of more than 30 universities and research institutions in Africa, Asia, Australia, Europe and South America. Whereas its impact on the quality assurance of teaching at European universities and on career development of fellows could be shown in several studies, the outcomes in terms of quality enhancement at African universities is at least not evident. At the same time not much is known about mutual benefits for partners from North and South as a result of real partnership in teaching and learning approaches.

METHODS AND MATERIALS Interviews with representatives of two African partner universities, having been member of the network, but dropped out for several reasons, will be held. In addition, representatives of African universities which are not member but expressed their interest in joining will be interviewed to get more insight into the opinions of African universities in the field of quality assurance in teaching. Regional networks like ASPHA (Association of Schools of Public Health in Africa) will be approached for interviews.
RESULTS This study is still ongoing. One of the expected results is to define strategies, how a longtime existing teaching network can effectively support public health studies at Northern and Southern universities in building up capacities for high quality teaching at Master's level.
CONCLUSIONS Following a partnership approach it is expected that partners can learn from each other, no matter on which continent they are located. A better knowledge about the demands of possible African partners and the opinions of Northern partners is expected, which would have also an impact on the design and content of programmes of network partners and the future strategies to support both sides in teaching of public health programmes.
DISCLOSURE Nothing to disclose.

O.4.6.2.004
APARET (African Programme for Advanced Research Epidemiology Training)

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AIM APARET supported African researchers to initiate and implement their own research initiatives with own funding.
TARGET GROUP Graduates of Field Epidemiology (and Laboratory) Training Programmes – FE(L)TP- in Africa.
TRAINING STRUCTURE APARET workshops were a two-week initiation workshop on research funding, proposal writing, ethical issues; a one-week project management workshop and a final seminar, attached to an international conference. Mentors from European African and American institutions supported the APARET fellows.
CORE OBJECTIVES FOR THE FELLOW A core part of the fellowship was the development of an epidemiological research project assessed and funded by APARET (with around 5000 USD) and the application for a major research grant.
OUTCOME EU-funding covered 3 successive cohorts of 8 fellows. Of 24 fellows, 23 successfully completed APARET and were awarded a certificate. While APARET funded projects were all implemented, most major grant applications were rejected. Smaller external funding was e.g. acquired for research on bovine tuberculosis or cervix cancer. One fellow acquired a grant of >70.000 € for a project on rotavirus vaccination and was later appointed principal investigator for a National rotavirus vaccination assessment project. Other fellows became FETP programme leader or epidemic preparedness trainers.
CONCLUSIONS FROM OUR EXPERIENCE APARET fellows work on their own projects and thus identify with activities of the learning process, more than in an artificial exercise. As an individualised postgraduate-level training programme APARET needs high resources. For a successful fellowship the selection of good fellows, strong mentorship and strong support of the host institute are crucial.
DISCLOSURE Nothing to disclose.

O.4.6.2.005
A public health laboratory for global capacity building in sub-Saharan Africa

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INTRODUCTION The Public Health Laboratory Ivo de Carneri (PHL-IdC) located in Pemba Island, Zanzibar, is a partnership between the Ministry of Health Zanzibar and the Ivo de Carneri Foundation. The PHL-IdC is WHO Collaborating Centre for Neglected Tropical Diseases and collaborates with national and international institutions to implement public health interventions, educational programmes and research projects to assess, monitor and evaluate national and global strategies for disease surveillance and control.
METHODS AND RESULTS Since 2005 the PHL-IdC is implementing capacity building of local and international health staff. 50 PHL-IdC employees receive on-the-job training by senior staff and international experts. Students from the College of Health Science, Zanzibar, and PhD and MSc students from other Universities are hosted every year for internship. Through PHL-IdC, local staff has been sent to East African Universities for further training on: PhD (1), MSc (4), BSc (1), MD (1), Diploma (2), Certificate (1). About 400 peripheral health staff were trained on data management, computer science and basic epidemiology through the Health Management Information System. Selected staff received yearly residential training for ultrasound and are referral personnel for this diagnosis in Zanzibar. 30 Programme managers from sub-Saharan African (SSA) countries benefited from NTD training under the leadership of WHO. The 7 editions of the training on Global Health Priorities in SSA, now part of the Italian Master in Tropical Medicine and Global Health, and the 2 editions of the 'East Africa DTM&H' in collaboration with the London School of Hygiene and Tropical Medicine, were attended by 120 and 40 health operators, respectively, from SSA and European countries.
CONCLUSIONS A training centre of international standard in SSA is an asset for sharing knowledge between experts from SSA and developed countries. The benefits of the capacity building in this setting are threefold:
1 allow on the job training of local staff who continues to work in an efficient infrastructure for the health of the Zanzibar community;
2 serve as a SSA centre in which international training courses are carried out at affordable cost and permits African researchers to meet their training needs without seeking alternatives overseas;
3 offer the opportunity to expatriates health providers to be trained in an tropical disease endemic setting facing unique public health challenges.

DISCLOSURE Nothing to disclose.

TRACK 5: Methodology/Approaches: Innovation – Validation – Application
5.1.1. Molecular approaches for health

O.5.1.1.002
A multi-protein complex between the GPI-anchored CyRPA with PfRH5 and PfRipr is crucial for *Plasmodium falciparum* erythrocyte invasion

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Erythrocyte invasion by *Plasmodium falciparum* merozoites is a highly intricate process in which PfRH5 is an indispensable parasite ligand that binds with its erythrocyte receptor, Basigin. PfRH5 is a leading blood-stage vaccine candidate as it exhibits limited polymorphisms and elicits potent strain-transcending parasite neutralising antibodies. However, the mechanism by which it is anchored to the merozoite surface remains unknown as both PfRH5 and its interacting partner (PfRipr) lack transmembrane domains and GPI-anchors. Here, we have identified a novel conserved GPI-linked parasite protein, Cysteine-rich protective antigen (CyRPA) as an interacting partner of PfRH5-PfRipr that tethers the PfRH5-PfRipr-CyRPA multi-protein complex on the merozoite surface. CyRPA was demonstrated to be GPI-linked, localized in the micronemes and essential for erythrocyte invasion. Specific antibodies against the three proteins successfully detected the intact complex in the parasite and co-immunoprecipitated the three interacting partners. Importantly, full-length CyRPA antibodies displayed potent strain-transcending invasion inhibition as observed for PfRH5. CyRPA does not bind with erythrocytes suggesting that its parasite neutralising antibodies likely block its critical interaction with PfRH5-PfRipr leading to a blockade of erythrocyte invasion. Further, CyRPA and PfRH5 antibody combinations produced synergistic invasion inhibition suggesting that simultaneous blockade of the PfRH5-Basigin and PfRH5-PfRipr-CyRPA interactions produced an enhanced inhibitory effect. Our discovery of the critical interactions between PfRH5, PfRipr with the GPI-anchored CyRPA clearly defines the components of the essential PfRH5 adhesion complex for *P. falciparum* erythrocyte invasion and offers it as a novel potent target for anti-malarial strategies that could abrogate formation of the crucial multi-protein complex.

KEYWORDS Malaria, Erythrocyte Invasion, Protein-Protein interactions, Blood-stage vaccines, PfRH5

DISCLOSURE Nothing to disclose.

O.5.1.1.003
Assessing the *var* gene expression of CIDRα1-subtypes associated with EPCR-binding in *Plasmodium falciparum* parasites isolated from hospitalized Tanzanian children with severe malaria

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INTRODUCTION Severe malaria syndromes are precipitated by *Plasmodium falciparum* parasites binding to endothelial receptors on the vascular lining. This binding is mediated by the highly variant *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) family. We have previously identified a subset of PfEMP1 associated with severe malaria1 and found that the receptor for these PfEMP1 variants is Endothelial Protein C Receptor (EPCR). The binding is mediated through the amino-terminal cysteine-rich interdomain region (CIDRα1) of Domain Cassette 8 (DC8) and group A PfEMP1 subfamilies. However, it is still unresolved if particular variants confer particular/expressed during severe malaria.

METHOD In this study parasitized blood samples were collected from hospitalized Tanzanian children presented with severe malaria syndromes. The isolated parasites were cultured, purified and tested for their ability to bind EPCR on petri dishes. PfEMP1 var genes expression was tested by quantitative PCR using specific primers targeting CIDRa1 subtypes and assessed for interplay between CIDRa1 variants expression and parasites binding phenotypes.

RESULTS Of 248 isolated parasites, only 122 parasites were able to be cultured and 50 parasites grew sufficiently for binding assay, and only about 30% bound rEPCR. From designed primers to amplify all known CIDRα1-subtypes associated with EPCR binding: CIDRα1 subtypes of group A (DC13) and subtypes of group B/A (DC8) show high transcript levels among children with severe anemia, hyperlactate, prostration and cerebral malaria: Though there were very high *CIDRα1* transcript levels in some isolated parasites that did not bind EPCR.

CONCLUSION 30% of isolated and cultured parasites from hospitalized children bound to rEPCR in our assay and showed very high transcript levels of *CIDRα1*, both of DC8 and group A *var* genes. However, the *CIDRα1* transcript levels were also very high in some parasite isolates that did not bind EPCR but with manifestations of severe malaria syndromes. Hence, it seems that the static petri dish assay used is not optimized to define the EPCR phenotype of patient isolates, though, transcript levels were measured at diagnosis and parasites were cultured for up to three cycles before assay; maybe petri dish binding assay alter the parasites binding phenotypes. Thus antibodies obtained to future CIDRα1 vaccine candidates may be tested in this assay, bearing in mind the limitations of the number of working assays.

DISCLOSURE Nothing to disclose.

O.5.1.1.004

A hybridization-based enrichment strategy to increase the accuracy of next generation sequencing in phylogenetic analysis of dengue viruses in Sri Lanka

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INTRODUCTION Sri Lanka has experienced confirmed dengue outbreaks since the 1960s although severe dengue disease (DHF/DSS) didn't appear until 1989. Since then, cyclical outbreaks associated with severe disease have occurred throughout the island. The most recent epidemic began in 2009 with the apparent introduction of a new genotype of DENV-1. To better understand the mechanisms underlying the persistence of this ongoing epidemic, a longitudinal study was conducted in hospitals in the Colombo district from April 2012 to March 2014. In order to glean as much information as possible about the viral genetics from this large cohort, we developed a novel Next Generation Sequencing (NGS) platform that can function without any *a priori* knowledge of the target dengue genome.
METHODS The principle problem encountered when employing NGS directly on patient samples is the high ratio of host to viral RNA. To compensate for this, we developed a hybridization-based enrichment strategy consisting of DENV-specific 120nt, biotinylated oligodeoxynucleotides to capture DENV genomic material from an NGS library prepared directly from patient sera.
RESULTS The strategy developed here allowed us to enrich DENV genomic material over 5000 fold relative to unenriched material. Full genome data and phylogenetic analysis indicate that the DENV-1 are predominantly genotype 1 although a smaller number of genotype 5 isolates was also identified.
CONCLUSION The platform developed for this study has the inherent ability to capture all four serotypes of DENV and can significantly increase the virus to host RNA ratio. The principle driver of the current dengue epidemic in Sri Lanka is the same DENV-1 genotype that has been in circulation since 2009.

This research was funded by the Singapore Infectious Disease Initiative (SIDI/2013/012) and the European Union 7th Framework Programme through 'DengueTools'. (www.denguetools.net).

DISCLOSURE Nothing to disclose.

O.5.1.1.005

Protein transport mechanisms in *Plasmodium falciparum* as novel anti-malarial drug targets

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BRIEF INTRODUCTION *Plasmodium falciparum*, a human malaria parasite, displays sophisticated protein secretion mechanisms modulating host cell invasion and remodelling. Central to these complex pathways are signal recognition particle (SRP), a chaperone involved in translocation of secretory proteins to the endoplasmic reticulum and adaptor protein complex-1 (AP-1) which targets proteins beyond the ER. Using transgenic approaches we characterized components of SRP and adaptor protein mu-1 (Pf-μ1) and studied their localisation, protein interactions and inhibitors based studies in *in-vitro* cultured parasite.
METHODS AND MATERIALS We employed molecular biology tools for cloning these genes into expression vectors, generating GFP expressing lines along with cell culture techniques and super-resolution microscopy. We generated anti-sera against these proteins in rabbit, mice and rat and carried out ELISA based interaction studies and confirmed these results using bacterial two hybrid system and co-immunoprecipitation techniques.
RESULTS The study revealed nucleo-cytoplasmic shuttling for SRP polypeptides followed by their transport to ER membrane, establishing them as the key targeting chaperone for introducing proteins into early secretory pathway, whereas, adaptor protein (Pf-μ1) showed Golgi/ER localization. Co-localization studies showed considerable overlap of Pf-μ1 with rhoptry proteins RAP1 and Clag3.1 suggesting involvement of Pf-μ1 in rhoptry targeting of proteins. Treatment of Pf-u1 transgenic parasites with Brefeldin-A and AlF4 altered the localization of Golgi-associated Pf-μ1 indicating its role in post-ER targeting. However hand, treatment of PfSRP transgenic parasites with ivermectin, an inhibitor of nucleo-cytosolic import/export confined its localisation to cytosol resulting in death of parasites.
CONCLUSIONS These findings provide significant insights into dynamic structure of *P. falciparum* SRP and AP-complex and use of these protein transport mechanisms as future anti-malarial drug targets. Together, these results help us to fill the loopholes in building up the roadmap of protein transport in *P. falciparum*.
DISCLOSURE Nothing to disclose.

5.2.1. How to bridge between health systems researchers and practitioners in the field of international health cooperation

O.5.2.1.001

Challenges and solutions in collaboration between non-governmental implementing organizations and local research institutions in developing countries

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Enfants du Monde, Geneva, Switzerland

INTRODUCTION The non-governmental organization (NGO) Enfants du Monde (EdM) supports Ministries of Health (MoH) and NGOs to operationalize the World Health Organization's (WHO) framework for Working with Individuals, Families and Communities (IFC) to improve maternal and newborn health in several countries. Conducting research is a priority in order to generate evidence for advocacy and programme fine-tuning. In 2014, EdM and its partners collaborated with local research organizations (ROs)/researchers in Bangladesh, Burkina Faso and Haiti to conduct baseline studies within this context.
METHODS Studies employed a rigorous mixed-methods approach. With technical support from WHO and the University of Geneva (UNIGE), EdM drafted terms of reference (ToR), following which ROs submitted research protocols. Protocols, including methodology, were finalized jointly with EdM and MoH. Researchers collected and analysed data and the report was finalized jointly.

RESULTS Common challenges emerged in the processes throughout all studies, including:

1 Expectations of NGOs and ROs regarding research: ToR proved insufficient for communicating completely the programme contexts and theories of change. A solution to this was investing in capacity building of ROs through exchanges and workshops;
2 Budget challenges: The costs of carrying out research are high, and NGOs are limited in their ability to justify research in their budgets. Agreeing required give and take on both sides. This included an understanding of ROs that mid-sized NGOs have limited resources for research and a willingness of NGOs to increase investment in research;
3 Involvement of MoH and other partners: While necessary for a high degree of engagement by all partners, it proved time consuming;
4 Different expectations and requirements in ethical considerations: Our solution was to insist on holding to the highest standards and submit the protocol to MoH for ethical approval. In every case research skills within the NGO, support of WHO and UNIGE, and input from other ROs were critical to success. This facilitated supporting local researchers, ensuring quality and accountability. The final result was three high-quality baseline reports.

CONCLUSION Effective collaboration between implementers and ROs requires give and take and a high degree of investment on both sides. In our case, the ultimate result was a synergistic relationship which met the needs of all organisations.
DISCLOSURE Nothing to disclose.

O.5.2.1.002

Key determinants for a successful collaboration between NGOs and universities in health research

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INTRODUCTION Non-governmental Organisations (NGO) are often close to the action, know the reality and needs of their partners and beneficiaries, and are best situated to investigate their surroundings. However, they often lack resources (time, human and financial) to perform sound research. This abstract explores the potential to define key determinants of success for collaborations between NGOs and universities in health and development based on 6 years of experience validated through a case example.
METHODS SolidarMed (SM) is a Swiss NGO implementing evidence-based health system strengthening projects in 5 southern-eastern African countries. The University of Sheffield, UK, offers a Masters programme in Public Health & International Development (MPHID), which includes a thesis based on original research. The University looks actively for placement opportunities where students can carry out this research in collaboration with a host NGO. A Placement Agreement between the NGO, the University, and the student enshrines the common understanding, roles and responsibilities behind the collaboration. Financial responsibility for most of the placement lies with the student. Hosts and students separately evaluate the placement experience at the end of the programme to address any shortfalls in the future.
RESULTS From 17 students on the MPHID programme in 2014/15, 2 (12%) selected 2 projects, respectively, from a list of 21 research topics in four countries (9.5%) offered by SM. Nine additional international organisations offered placements specifically related to public health, which were selected by another 13 students, whilst the remaining students chose non-health related placements. Based on previous experience, some of the key determinants of success for such collaboration include a clear structured frame within which the collaboration takes place; focussed, realistic research topics meeting all expectations; the student's maturity to manage the project; as well as the host organisation's motivation and support at the placement site and during preparation.
CONCLUSIONS The experience shows that key determinants for successful collaborations between NGOs and Universities can be defined and may be beneficial to students, universities and host organisations worldwide. SM and University of Sheffield will be able to validate the above findings with its ongoing case example and share these late breaker findings during the ECTMIH conference.
DISCLOSURE Nothing to disclose.

O.5.2.1.003

From well-researched, tested and documented pilot interventions to health impact for all; from laboratory systems research to changing lives: in search of the holy grail of scalability

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INTRODUCTION For many years the Novartis Foundation has been piloting a number of projects focusing on enabling better health outcomes for more people in LMIC. Most of these have been well documented, and as pilots, are deemed to have successfully demonstrated proof of concept. The huge challenge however is to ensure that these examples of innovation transit through to having lasting impact at scale. Sustainability and scalability are important characteristics of innovations that determine the true long term impact they will eventually have. The Foundation is on a journey to ensure that creating solutions goes beyond short-lived pilot successes, by instilling from the start preconditions to scale and sustainability. We present a framework we use in our due diligence to select, implement and monitor our projects.
METHODS AND MATERIALS We reviewed our existing project portfolio and those in our shortlist pipeline against a combined set of scalability factors. Based on existing literature that combines lessons learned from success and failure in scale-up of innovations in health service delivery and structured interviews with key opinion leaders, we distinguish 34 factors in 2 broad categories: Differentiators/catalysts, and contributors/promotors; across 5 domains: communities and patients, providers, strategic approach, financing and leadership and governance.
RESULTS The structured and outcome-at-scale focused review enabled us to better understand limitations encountered, strategically re-orient current initiatives and engage more forward looking with new opportunities. Our projects of generation 2.0 have different characteristics as those from the generation 1.0; and continued evaluation and fine-tuning using the scale framework will ensure that this transformation allows us to go beyond the pilot-phase.
CONCLUSIONS A cemetery filled with successful and well documented pilots has failed billions of poor people in their aspiration to good health. By going beyond a proof of concept towards a proof of concept+scalability framework, and discussing sustainability and scale at the start of the project, we

believe we do not only deliver innovation, but innovate delivery towards having lasting impact at scale. Embracing concept+scalability thinking allows systems research to align more strategically with realities in practice, and ensure bolder steps towards universal health coverage.
DISCLOSURE The described approach was developed and implemented during the authors employment at the Novartis Foundation.

O.5.2.1.004

Improving programme implementation through embedded implementation research (iPIER)

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BRIEF INTRODUCTION Implementation research is most likely to be useful where implementers such as programme managers have played a part in the identification, design and conduct of the research undertaken, and are not just a passive recipients of results. In order to effectively integrate implementation research into the decision-making processes it is not enough to simply open lines of communication with implementation researchers at an early stage; implementation research needs to be embedded in the overall design, planning and decision-making endeavour.
METHODS AND MATERIALS The Alliance for Health Policy & Systems Research, in collaboration with 3 WHO Regional Offices, is implementing a program of implementation research to support the implementation of current programmes in these regions with the objective of facilitating improvements in programme implementation through research that is embedded within existing implementation processes. This programme comprised two components:

1 capacity development for implementers such as programme managers and district health officers in identifying implementation barriers and on the application of basic research approaches to understand and solve these barriers;
2 small grants (USD 15-20K) to support the conduct of implementation research activities by programme managers and district officers to resolve implementation barriers.

RESULTS Initial calls for expressions of interest (EOI) yielded an overwhelming response from implementers demonstrating the relevance of this type of research to the work of implementers as well as their interest in engaging in research. To-date, 8 projects are being supported in the Americas, 13 in the Eastern Mediterranean region, and 6 in the South and Eastern Asia region. Projects range from issues relating to non-compliance of guidelines to the expansion of e-health platforms.
CONCLUSIONS Embedding research within programme processes can facilitate the use of evidence by decision-makers. Implementation research is critical to the successful implementation of proven effective interventions and should be embedded as a core function of the system in which these programmes are being implemented. Programme managers and other implementers have an important role in this effort and rather than be viewed as potential recipients of research results, should lead it.
DISCLOSURE Nothing to disclose.

O.5.2.1.005

Fairness in international collaborative research partnerships for health, time for a certification process: COHRED Fairness Index

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INTRODUCTION Global support for health in low middle-income countries has resulted in many improved products and services, but has not consistently improved the systems that countries need to conduct or partner research and to translate results into effective policy and practice. The Council on Health Research for Development (COHRED) is developing the COHRED Fairness Index™ (CFI) that will provide a recognized global benchmark of 'good practices' in health research collaborations taking place in low and middle income countries.
METHODS The development of CFIs the result of a multi-sector consultation approach involving a Technical Working Group comprised of key stakeholders from NGOs, International organizations, philanthropies, donors, the public and private sector as well as academia.
RESULTS Based on a series of precisely developed indicators, the CFI is designed to provide an assessment tool to stakeholders to measure and report vital information that reflects their performance with respect to transparency, level of engagement, accountability and equity in their collaborations. Governments, institutions or researchers can use the CFI to examine and evaluate their respective research collaboration standards in order to get the confidence of where they stand in the 'fair standards' arena or how they can bring productive changes for improvement in their practices.
CONCLUSIONS The CFI through a verification and certification procedure that includes reporting and auditing processes shall strengthen contracting competences, articulate the needs and expectations of the different actors involved and increase trust. It can minimize reputational risk and posterior resource consuming litigation. The added values of its implementation will be to improve the alignment of interests of all partners in global health research and to reduce inequity in health research.
DISCLOSURE Support for COHRED CFI Colloquium 4, 16–17 April 2015 from Sanofi - Aventis Group, Pfizer and Celgene

O.5.2.1.006

Successfully connecting NGO practice and health systems research – getting evidence into NGO practice and NGO practice into research

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INTRODUCTION For driving the best science to meet global health challenges, the system has to build on researchers, policy-makers and practitioners creating, sharing and applying knowledge. NGOs translate needs into action. Researchers generate systematic knowledge for evidence-based decisions and actions.
METHODS AND MATERIALS The aim of the study was to develop a framework on how to get evidence into NGO practice and for supporting researchers to get NGO practice into their research. Enablers, barriers, and supportive tools are identified for NGOs to integrate more evidence into their work; and for NGO-research Collaborations. A literature review, an online questionnaire collected information from 30 NGOs, face to face

interviews and two workshops involving 18 NGOs and 8 researchers were conducted. Case studies showing good practices of NGOs integrating evidence into their work and of NGO-research collaborations were identified.
RESULTS The findings highlight challenges for NGOs to integrate health systems research in their work, and difficulties with the uptake of research findings into practical NGO work. Larger NGOs especially have increased investments in research and show institutional buy-in. NGOs and researchers alike see collaborations as beneficial for both (e.g. NGOs benefit from technical expertise on research methodology; researchers from access to the field). However, they are challenged by different time lines, incentive structures, and working cultures.
CONCLUSION For successful collaborations between practitioners and researchers, sufficient time has to be invested to build a relationship that is based on trust, respect, transparency and equity. Available tools and resources have been compiled in a web-based 'toolbox' (www.ngo-research-toolbox.org) for NGOs and researchers to facilitate collaboration, as well as for NGOs to integrate evidence into practice. Tools alone will however not be sufficient to support the process – an enabling environment is required within NGOs ('doers' becoming 'doer-thinkers'), research communities ('thinkers' becoming 'thinker-doers') as well as funding agencies ('funders of results' becoming 'funders of processes, results and research uptake'). Only the collective capacity of all stakeholders will enable creating, sharing and applying knowledge to meet global health challenges.
DISCLOSURE This study was conducted as part of a Master Thesis in International Health at the Swiss Tropical and Public Health Institute and in coordination with Medicus Mundi International. The research questions and objectives of the study have been developed based on the Medicus Mundi International Research Policy. Supervisor of the thesis: Nicolaus Lorenz, Deputy Director, SwissTPH

5.3.2. The reality of open source drug discovery: a move towards multilateral collaborations

INV.5.3.2.001

Re-engineering how we innovate for public health

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We need to design an alternative system to prioritise, conduct, and finance biomedical development that responds to public health priority needs, and where the primary payback is improved global health, not shareholder profits. This can only be achieved if we have strong public health leadership that views medicines as public goods, not commodities to generate profit.

Despite the dominant narrative that biomedical innovation has led to unprecedented medical progress, there is increasing recognition that the current model for medical innovation is deficient. Even with significant public and private investments into pharmaceutical R&D, critical medical needs remain unmet, while a significant number of new medicines developed have little added therapeutic value to what already exists. The few new drugs that do represent true therapeutic advances are priced out of reach for most.

Correcting these deficiencies will require targeting and prioritizing unaddressed health needs and designing medicines with the appropriate product profile; improving the efficiency of R&D (decreasing costs and time, and avoiding redundancy and duplications); and making use of unexploited opportunities (promising leads which would address public health priorities and are not being pursued).

This means pursuing alternative models to the current closed system (prevailing in academia and pharma industry alike) that builds upon exclusive ownership of knowledge that can be monetized. Sharing of information and open-source R&D is a possible means to render R&D more efficient and equitable, coupled with a range of incentives including adequate financing.

The demonstrable inadequacy of today's biomedical R&D system has inspired various conceptual models and mechanisms aiming to promote medical innovation as a public good. We will present the results of a comprehensive overview of the R&D landscape focusing on a typology of models and mechanisms that address the systemic problems and gaps that exist in the current system, highlighting models that are being actively developed and are genuinely innovative and different.
DISCLOSURE Nothing to disclose.

INV.5.3.2.002

The NTD Drug Discovery Booster: an innovative multiparty collaboration on early drug discovery

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Screening for new leads against kinetoplastid parasites is evolving with increased throughput and as a result some new hits have been identified, but there are still insufficient number and variety of starting points to give high confidence of delivering new clinical candidates. The NTD Drug Discovery Booster will rapidly expand these few, precious hits from screening through cross-collaboration with several Pharma companies and also enable scaffold-hopping to identify related series. DNDi will be able to generate additional structure activity relationships (SAR) before commencing time consuming and expensive chemistry to make new analogues. The Booster project will also benefit from the pooling of structures and information from the consortium members to inform decision-making and further development of the series. Overall this approach will accelerate drug discovery and reduce costs.

A big experiment in drug discovery and a leap towards open research for NTDs.

The Booster will uniquely take advantage of simultaneously exploring high quality libraries to rapidly and cost effectively develop hit series for optimization with the goal of generating a clinical candidate. As compared to existing 'pre-competitive' models of R&D, the innovation of the NTD Booster lies in companies simultaneously accepting to share with DNDi upfront structural and biological information about a promising chemical series that is essential for its rapid development. Thus, by exploring the combined libraries containing several million compounds, the chances of pulling out the best possible hit series with a pooled collection of valuable information are dramatically increased. All members of the Consortium will be acknowledged for any results coming out of the NTD Booster, and thus con-

tribute to a potential successful new treatment for leishmaniasis or Chagas disease.

During the first 2 years the Booster project will rapidly expand at least 4 promising hits each against *Leishmania* and *T. cruzi*, the causative agents of leishmaniasis and Chagas disease, respectively. As products of the Booster project we aim that at least one novel chemical series will provide promising *in vivo* activity for each parasite, providing solid foundations for further optimization towards clinical candidates.

DISCLOSURE Nothing to disclose.

O.5.3.2.003
MMV malaria box and pathogen box projects: the application of open science

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Medicines for Malaria Venture, Geneva, Switzerland

To further stimulate open science, MMV launched the MMV Malaria Box[1], a collection of 400 anti-malarial compounds, distributed for free, with the sole condition that researchers agree to place the results in the public domain. To date over 200 copies of the Malaria Box have been distributed, with 500 distinct assays having been run, generating more than 200 000 data points and 20 scientific publications. The presentation will highlight results from the Malaria Box project in the fields of malaria and other neglected diseases. In malaria, groups have screened for liver and sexual stage activity and against specific biological targets. Malaria Box screening has also identified compounds with activity against many other neglected diseases, including cryptosporidium[2], toxoplasmosis[3], and kinetoplast diseases[4].

As a follow-on project MMV is now assembling the Pathogen Box[5], a set of ~400 diverse, drug-like molecules active against various neglected diseases, which will be available free of charge at the end of 2015. Upon request, researchers around the world will receive a Pathogen Box of molecules to help catalyze neglected disease drug discovery. In return, researchers are asked to share any data generated in the public domain. The presentation will detail the strategy adopted to select compounds for inclusion in the Pathogen Box, alongside recent results.

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DISCLOSURE Nothing to disclose.

INV.5.3.2.005
Creating a global community for clinical drug repurposing and development

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Drug development for many tropical and parasitic infections has little commercial appeal, often leaving us with situations where treatment is unavailable or inadequate. Under these circumstances, caregivers are forced to borrow drugs used for other diseases to treat their patients. This 'clinical repurposing' of drugs has been a useful source of treatment options. Unfortunately, clinical experience using old drugs in new ways is not systematically captured, and potentially helpful or harmful treatments may not be recognized.

An internet base program is under development to capture the global experience using drugs in new ways for infections that are difficult to treat. Caregivers around the world will be able to share their experiences and concerns in these situations. These data may serve as a valuable resource to inform formal drug development.

DISCLOSURE Nothing to disclose.

5.3.3. Where there is no market – exploring novel approaches to R&D for diseases of the poor

O.5.3.3.003
The challenge of product R&D initiatives for neglected tropical diseases that currently rely on product donation programs

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The access strategies for medicinal products for diseases disproportionally affecting populations in developing countries, particularly the so called poverty related diseases, can be broadly divided on strategies that are based on product purchase programs and donation programs. In the first category we have products for diseases such as malaria, tuberculosis, HIV, Chagas, leishmaniasis. In the second category we have for example onchocerciasis, lymphatic filariasis (LF), schistosomiasis, soil transmitted helminthiasis and others. This division may have created the expectation that innovative products resulting from R&D activities will follow automatically this access pattern that has been established for a given disease, which means access to products from category 1 will be provided through existing reimbursement mechanisms (e.g. Global Fund, GAVI, UNITAID) while new products from category 2 do not have any alternatives today other than donation programs. This expectation creates a challenge for those engaged in product R&D for diseases in category 2, not only because of the uncertainty associated with a potential replacement of the products in use, but also because of the high expectation on effectiveness above the standard products. As a result, R&D efforts for products in category 2 that could have a significant incremental public health value (new formulations, enhanced potency or new treatment paradigms) are very limited and the number of products in the R&D pipeline is considerably low for helminthic diseases, onchocerciasis and LF compared to the 'Big Three' diseases.

As a case study, the 'Pediatric Praziquantel Consortium' which includes public and private partners from developed and developing countries, will be presented. The Consortium was created in 2012 to address an unmet medical need to develop and register a new pediatric formulation of praziquantel to treat younger children (<6 year) suffering from schistosomiasis. The R&D costs are covered by innovative approaches of resource and risk sharing between public, private and philanthropic sectors. The product is currently completing phase 1 clinical development and a clear development strategy until registration is in place. How to place and incentivise this product in order to keep engagement of R&D and manufacturing partners, especially from developing countries needs to be discussed in order to ensure access to treatment for young children that are left untreated today.
DISCLOSURE Nothing to disclose.

O.5.3.3.004

Looking at alternative models for innovation and access for neglected infectious diseases

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BACKGROUND Neglected Infectious Diseases suffer from not presenting sufficiently attractive markets to the private sector. Innovations for and access to products in this field often rely on public grants, philanthropic foundations and donation programmes. R&D for new tools, in spite of initiatives of the last decade, remains insufficient and relies heavily on conventional push funding, often not supported by solid access provisions or plans.
PRESENTING ALTERNATIVE MODELS The lack of appropriate tools to address the recent Ebola crisis has emphasized urgent need to assess alternative models for Innovation and Access (I + A). Current mechanisms and architecture (e.g. Global Fund, UNITAID) that promote market shaping and access provide a good starting point but are unlikely to work considering institutional and donor reluctance to expand mandates. Additionally an urgent funding and innovation gap remains for diseases such as TB.

Alternative models should look at three key aspects. First, recognizing and pulling together key priorities for funding and support. For instance, antibiotic resistance, emerging infectious diseases and Neglected Tropical diseases could be grouped for a global R&D fund based on long term, sustainable and innovative funding mechanisms. Second, implement alternative ways of promoting innovation such as twinning conventional push and using alternative pull incentives (e.g. prizes). This should be done in parallel with pooling of knowledge, data and intellectual property. Third, a facility to promote rational introduction of drugs and diagnostics and pooling of procurement could be useful. Implementation of these may be achieved in tandem with existing WHO mechanisms such as the Essential Medicines List and Pre-qualification Programme, ensuring quality-assured production and conservation of drugs.
CONCLUSIONS While significant public action, ownership and funding is required, it may allow increased involvement of the private sector in the long term. Furthermore, previous policy analysis conducted at WHO to support such concepts and has been published as the report of the Consultative Expert Working Group on R&D: financing and coordination (CEWG report). In 2016, WHO will discuss with member states further action in process initiated by CEWG report. It is imperative the scientists, public health officials and relevant public and private sector actors work together to ensure comprehensive solutions are supported and implemented.
DISCLOSURE Nothing to disclose.

O.5.3.3.005

Cell-based drug discovery model at the Novartis Institute for Tropical Diseases using Human African Trypanosomiasis as an example

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The Novartis Institute for Tropical Diseases (NITD) is dedicated to finding new medicines to treat neglected, infectious diseases including Dengue fever, Human African Trypanosomiasis (HAT) and Malaria. NITD was set up as a public-private partnership between Novartis and the Singapore Economic Development Board in 2002. NITD drug discovery model involves close collaboration with both internal and external partners to leverage drug discovery and disease area expertise.

A high-throughput screen of the entire Novartis compound deck was performed and triaged using in silico physiochemical parameters, potency and cytotoxicity to identify the most promising chemical series. For each chemical series, structure activity relationship (SAR) was established. Front-runner compounds were also tested for kill kinetics. The most advanced compounds from each chemical series were tested in a stage 1 animal efficacy model, which includes investigation of *in vivo* pharmacology. Chemical series with good pharmacokinetics, *in vivo* efficacy in stage 1 animal efficacy model and some brain penetration were tested in a stage II animal efficacy model. In parallel to the above work each chemical series were tested *in vitro* combination studies. Chemical series not showing antagonistic activity in combination studies will be prioritised for *in vivo* combination studies providing they show some degree of brain penetration. For each chemical series a variety of techniques are being used to elucidate the mechanism of action.

Following hit triaging 36 chemical series were identified, the number of series was further reduced to 7 on the basis of either lack of cidality, lack of SAR, poor metabolic stability and lack of efficacy against clinical strains. These series showed significant reduction in parasitemia and delay in relapse in the stage 1 animal efficacy model. One of the chemical series showed complete clearance of brain parasite in half of the animals in the treatment group in the stage II animal efficacy model. To date no *in vitro* combination studies have revealed antagonistic activity. Mechanisms of action studies have identified the possible targets of two chemical series.

NITD has quickly and efficiently initiated drug discovery against HAT resulting in the identification of 7 chemical series. A key role in this was the optimal use of internal and external collaborators expertise in either drug discovery and/or the disease.
DISCLOSURE Nothing to disclose.

5.4.1. Threats to health systems – emergency situations

INV.5.4.1.001

Evidence Aid: a resource for those preparing for and responding to disasters, humanitarian crises and major healthcare emergencies

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BACKGROUND Evidence Aid (www.evidenceaid.org) was established following the Indian Ocean tsunami in 2004, to improve access to systematic reviews of the effects of healthcare interventions of particular relevance in the aftermath of disasters and both short onset and protracted humanitarian crises which often affect fragile states.
METHODS In recent years, Evidence Aid has developed from being an opportunistic and reactive initiative to being one which is moving towards strategic development and advocating for evidence in policy. The 1st Evidence Aid Conference was held in 2011 in Oxford; the 2nd conference was hosted by the Belgian Red Cross in 2012. In June 2013, a 2-day priority setting exercise was undertaken to identify 30 priority questions for the humanitarian community. In September 2014, a symposium was held in Hyderabad, India, a fitting end to the first 10 year period of Evidence Aid, and 2015 will culminate with a policy delphi study and meeting in Washington, USA, related to the use of evidence by policymakers.
RESULTS A needs assessment survey showed that 82% of respondents thought that systematic reviews are useful; 51% had used them as a basis for decision-making; 81% thought that improved access to systematic reviews could play a role in improving the response to natural disasters and other humanitarian emergencies and the majority said that they would use online systematic review training if it were available. These results indicate that there is a lack of accessibility to relevant systematic reviews in the field of disaster and humanitarian emergency management. Evidence Aid addresses this imbalance by providing a free at the point of use database of relevant tagged information.

In August 2013, Evidence Aid launched its new website which now has more than 200 systematic review resources relevant to the disaster and humanitarian emergency setting plus bundles relating to specific emergencies such as Ebola, windstorms and earthquakes. It is searchable and free at the point of use. Evidence Aid continues to search for relevant information to add to the resource.
CONCLUSIONS Evidence Aid has outlined short, medium and long-term goals, including a mission statement, identification of potential partnerships and target audience, content (with an initial focus on interventions or actions with health-related outcomes), governance, communication, funding and training.
DISCLOSURE Claire Allen is an employee of Evidence Aid.

O.5.4.1.002

Pandemic preparedness, disease surveillance and health systems in West Africa: the case of The Gambia

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INTRODUCTION The rapid spread of SARS in 2003, the 2009 H1N1 influenza pandemic and the ongoing multi-country Ebola outbreak demonstrate the urgent need for a long-term global perspective on pandemic/epidemic preparedness and response. Effective preparedness and response requires a multi-scalar and multi-pronged approach of risk reduction, early detection and prompt reporting, rapid response and surge capacity, as well as operational collaboration in medical and non-medical measures.
METHODS AND MATERIALS Here, we present an in-depth case study of pandemic preparedness in The Gambia, a small country in West Africa that remained on high alert throughout most of 2014, based on its recent experience and its geographic proximity and socio-cultural closeness to the epicenter of the Ebola epidemic. Results are based on qualitative analysis of key informant interviews with health leaders at multiple levels of the health system across the entire country.
RESULTS AND CONCLUSIONS Whilst many countries have pandemic preparedness 'plans' in place, operationalizing them remains a challenge – particularly in settings where health systems are fragile and vastly under-resourced. National strategic goals remain unclear and under-developed and the improved health system capacities called for in the modified International Health Regulations (IHR) have not been met in a majority of IHR signatory countries. Moreover, concepts, methods and indicators of 'preparedness' remain crucial issues to consider, in relation to complex political factors traditionally seen as domestic. The Gambia escaped narrowly and numerous lessons have been learnt for effective preparedness and response in the country and region.
DISCLOSURE Nothing to disclose.

O.5.4.1.003

Environmental factors and fatal injuries during Typhoon Haiyan: a framework for assessing impact, mitigating risk, and promoting resilience during natural disasters

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INTRODUCTION Typhoon Haiyan (locally known as 'Yolanda') made landfall in central Philippines on 8 November 2013 and caused an estimated 6300 deaths. Many deaths were due to injuries but it is unclear what role the environment played on mortality. The purposes of this study are: to assess the impact of environmental factors on fatal injuries, and to use findings to develop a framework for the mitigation of risk and promotion of resilience during natural disasters.
METHODS The study has two phases. First an epidemiological study will assess the relationship between exposure to environmental factors and mortality (i.e. fatal injury rate) in the population ($N = 6300$). Environmental factors are categorized as: water-related (i.e. drowning), vegetation-related (i.e. being hit by an uprooted tree), and built environment-related (e.g. electrocution, roof collapse). Existing data from the Philippines' National Disaster Risk Reduction and Management Council (NDRRMC) will be used. Second a literature review will identify and characterize impact assessment methods related to environment and health. Search terms/descriptors, such as Medical Subject Headings (MeSH), will be used in the MEDLINE database according to a predefined search strategy. An integrative Natural Disaster Impact Assessment (NDIA) framework will be developed based on the findings.
EXPECTED RESULTS Mortality rates will be calculated as: overall, fatal injury only, and fatal injury by mechanism (e.g. asphyxiation, hypothermia). Uni-variable analysis, with

frequencies and counts, as well as bi-variable analysis, with measures of associations and trends, will be performed in SPSS. The level of significance (*P*) will be explicitly stated prior to data analysis. Measurements of effect size (correlation, odds ratios, and relative risk) will be reported and confidence intervals (CI) will be estimated at a level of 95%. Stratification will be used to adjust findings for the effects of confounding variables. Sensitivity analysis will assess the quality/strength of the measurements and statistical models used. The study's proposed contributions will be: quantifiable health impacts of Typhoon Haiyan; assessment of the relationship between environmental factors and fatal injuries; development of an integrated NDIA framework; and set of evidence based recommendations for mitigating risk and promoting resilience during natural disasters.
DISCLOSURE Nothing to disclose.

O.5.4.1.004
Trends and factors associated with dengue mortality and fatality in Brazil

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BACKGROUND The increase in the incidence of dengue and the potential to progress to lethal forms made this disease the most important arbovirus in the world. Studies that generate information that may help to reduce the risk of death are essential. The aim of this study was to analyze time trends and risk factors for dengue mortality and fatality in Brazil, for the period 2001–2011.
METHODS Time trends of dengue mortality and fatality rates were analyzed using simple linear regression. The association between dengue mortality rate, case fatality rate and socioeconomic, demographic and health care indicators at the municipality level was analyzed using negative binomial regression.
RESULTS Dengue Hemorrhagic Fever case fatality rate increased in Brazil over the study period ($\beta = 0.67$, $P = 0.036$) both in cases aged 0–14 ($\beta = 0.48$, $P = 0.030$) and 15 years and older ($\beta = 1.1$, $P < 0.001$). Factors associated with dengue fever case fatality rate were average income per capita (RR = 0.99, $P = 0.038$), and number of basic health units per population (RR = 0.89, $P = 0.000$). Mortality rate also increased over the period ($\beta = 0.350$, $P = 0.002$). Factors associated with mortality rate were low inequality (RR = 1.02, $P = 0.001$), high income per capita (RR = 0.99, $P = 0.005$) and high proportion of the population living in a urban area (RR = 1.01, $P < 0.001$).
CONCLUSION The increase in dengue mortality and case fatality and the associated socioeconomic and health care factors, at the municipality level, suggest that structural and intersectoral investments to improve living conditions are needed for a sustained reduction in those outcomes.
DISCLOSURE Nothing to disclose.

O.5.4.1.005
Maintaining low mortality rates in displaced populations: MSF experience in Minkaman

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INTRODUCTION Population displacement in camp settings can lead to high mortality, especially early following displacement. Addressing the main needs of the population ('10 priorities') can prevent this. Since December 2013, armed conflict led to a massive displacement of the population in South Sudan. As of April 2014, approximately 80 000 internally displaced persons were living around Minkaman in Awarial County of Lakes State, where MSF was one of the main humanitarian actors.
METHODS Provision of safe drinking water was assured immediately by a water treatment station with water trucking distribution system and bucket chlorination. By January 2014, 4 primary health care clinics, a hospital, nutritional program and a network of oral rehydration points to address the high number of diarrheal cases in the camp were functional. In addition, mass vaccination campaigns were organized to prevent outbreaks of main epidemic prone diseases: measles, cholera and meningitis. A network of community health workers was ensuring community surveillance and spread of health promotion messages. Food and non-food items were provided by other actors. A cross-sectional mortality survey was carried in May 2014, using two-stage cluster design.
RESULTS From January 1st to October 15th 2014, 52 047 people attended the outpatient department and 2032 patients were admitted in the hospital. 731 children were admitted in the nutritional programs (161 of them requiring admission in intensive care) and 2778 women received antenatal care. In addition 480 m^3 of treated water were delivered daily ensuring the minimum of 5 l of drinking water/person/day. The crude mortality rate (CMR) between end of December 2013 and May 2014 was estimated at 0.59/10 000/ day [95%CI: 0.43–0.82], and the under-5 mortality rate (U5MR) at 0.50 deaths/10 000/ day [95%CI: 0.43–0.82]; 45% of those deaths were due to trauma and occurred before arrival to the camp. No outbreak of vaccine preventable disease occurred in Minkamman, although there was widespread measles outbreak ongoing in the region, and sporadic cases were reported in the camp. Cholera outbreaks were reported throughout South Sudan from May on, with no cases in Minkamman.
CONCLUSION CMR remained below national average at all times. While several outbreaks of vaccine preventable diseases ravaged across South Sudan, Minkaman was spared. We believe the population well-being was assured by rapidly addressing most important needs.
DISCLOSURE Nothing to disclose.

5.4.2. Large cohorts and big data and disease/risk mapping-predicting

O.5.4.2.002
Modification of ambient air pollution and diabetes association by type 2 diabetes genetic risk score of 48 variants

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INTRODUCTION Exposure to ambient air pollution (AP) has been associated with risk of type 2 diabetes (T2D). Genetic

factors may influence susceptibility to environmental stressors in the aetiology of T2D. The effect of T2D genetic variants on susceptibility to air pollution has not been studied. Compared to single variants, joint genetic variants contribute substantially to disease risk.
METHODS We studied the modifying effect of genetic risk score (GRS) of 48 European T2D risk variants on the association between AP and diabetes in 2825 follow-up participants of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults aged 29–73 years, with complete genotype and covariates data. AP exposure was estimated by the 10-year residential mean of particulate matter <10 μm in diameter (PM_{10}). Genotyping of 48 European T2D risk variants was done using the Illumina HumanOmniExpressExome chip. We computed two risk scores, count-GRS and weighted-GRS, and applied PM_{10}-specific interaction term with each risk score in a mixed logistic regression model.
RESULTS Diabetes prevalence was 5.9%. Mean PM_{10} exposure was 22 $\mu g/m^3$. Odds of diabetes increased by 10% ($P < 0.0001$) per T2D risk allele and by 55% ($P < 0.0001$) per 10 $\mu g/m^3$ exposure to PM_{10}. There was a positive gradient in the association between PM_{10} and diabetes across quartiles of count-GRS [OR_{Q1}:1.26 (0.67, 2.38); OR_{Q4}: 1.72 (1.00, 2.97); $P_{interaction} = 0.38$). We observed a positive interaction between PM_{10} and count-GRS ($OR_{int} = 1.83$; $P = 0.05$) among participants with low education. Two risk variants (rs1531343 near *HMG2A* and rs8042680 near *PRC1*) showed interactions with PM_{10}. Evidence from pathway analyses indicated interactions with risk variants associated with insulin sensitivity (IS) ($OR_{int} = 1.17$; $P = 0.08$), which became stronger when limited to participants with normal respiratory function ($OR_{int} = 1.22$; $P = 0.03$). Participants at the highest IS risk quartile had twice the odds of diabetes compared with those at the lowest quartile ($P = 0.07$). We did not observe any positive interactions with risk variants associated with beta-cell function or fat cell metabolism ($0.9 < OR_{int} \leq 0.99$, $P > 0.5$). We observed similar patterns with weighted-GRS and results were robust across sensitivity analyses.
CONCLUSIONS Our results suggest that genetic risk factors for diabetes may modify susceptibility to air pollution through altered insulin sensitivity. These results need to be confirmed in diabetes cohort consortia.
DISCLOSURE Nothing to disclose.

O.5.4.2.003

Malaria mortality in a hypoendemic area of North-Eastern South Africa: population-based surveillance from 1992 to 2013 reveals an increasing malaria burden

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INTRODUCTION Most of South Africa is malaria-free, but hypoendemic levels of transmission persist in lowveld areas in the north-east of the country, adjacent to Mozambique. Many families have links to relatives in Mozambique, where malaria transmission remains much higher, and cross-border travel is commonplace, although the Kruger National Park provides something of a depopulated buffer zone along the border. Malaria diagnosis and treatment is relatively easily available at public and private facilities in the endemic area.
METHODS The Agincourt Health and Socio-Demographic Surveillance Site has monitored population health in a defined area within Mpumulanga Province, around 24.7°S, 31.2°E, since 1992.

A circumscribed semi-rural area with a population ranging from approximately 60 000 in 1992 to 90 000 in 2013 was covered. All households were visited regularly to consistently record demographic and health data, including the documentation of deaths and their causes using verbal autopsy.
RESULTS From 1992 to 2013 a total of 13 251 deaths were documented over 1.58 million person-years observed. Of that total mortality burden, 1.2% of deaths were ascribed to malaria. Half of the malaria deaths were among children aged under 15 years, with most of the remainder among working-age adults. Malaria deaths were strongly correlated with temperature and rainfall. The malaria mortality rate was over 50% higher during the last 5 years of the surveillance period, compared with earlier years. A huge HIV/AIDS epidemic that developed and receded in this population during the period of observation had no apparent effect on malaria mortality.
CONCLUSIONS This detailed longitudinal examination of malaria mortality showed that although malaria is a relatively minor cause of death in this population, it has become more common in recent years, and shows no sign of retreating despite rapid socioeconomic development. In addition to local relevance, these findings are important for understanding potential population burdens of hypoendemic malaria in other areas of sub-Saharan Africa as progress towards malaria control and elimination targets is realised.
ACKNOWLEDGEMENTS Support for the Agincourt site comes from the School of Public Health and Faculty of Health Sciences, University of the Witwatersrand, and the Medical Research Council, South Africa, with core funding from the Wellcome Trust, UK (Grants 058893/Z/99/A; 069683/Z/02/Z; 085477/Z/08/Z; 085477/B/08/Z).
DISCLOSURE Nothing to disclose.

O.5.4.2.004

High participation and engagement rate in a systematic hospital-based genomic medicine research project with broad consent

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INTRODUCTION Hospitals represent a unique opportunity to recruit patients into genomic research projects. Little is known about hospital patient's willingness to engage in such projects.
METHODS AND MATERIALS Within the framework of the Lausanne, Switzerland, University Hospital Institutional Biobank (BIL), inpatients and selected outpatients are systematically invited to grant researchers access to their biomedical data and to donate blood for future whole genome sequencing. Additionally, participants are offered the options to be re-contacted in case of incidental findings and to receive an electronic newsletter. Multivariable logistic regression analysis was used to identify personal factors associated with willingness to participate in BIL and with interest in these options. Analyses were restricted to the initial 11 099 invited patients for whom full dataset was available, and were stratified by age groups.
RESULTS Overall participation rate was 82.4% (9141/11 099) and was higher in the <64-year old group [odds ratio (OR) 1.70;

95% confidence interval (CI) 1.53 to 1.90]. In the ≥64-year old group, participation was lower among women (OR 0.77; 95% CI 0.68 to 0.89), among non-Swiss citizens (OR 0.66; 95% CI 0.55 to 0.79) and those with emergency admissions (OR 0.59; 95% CI 0.51 to 0.69). A total of 8576 (93.8%) and 3020 (33.0%) participants were willing to be re-contacted for incidental findings and to receive the newsletter, respectively.
CONCLUSIONS A large proportion of patients are willing to actively participate in this particular systematic hospital-based genomic research program. Hospitals adopting broad consent represent an efficient setting to recruit participants into 'precision medicine' initiatives.
DISCLOSURE Nothing to disclose.

O.5.4.2.005

MIDATA cooperatives – citizen-controlled use of health data is a pre-requiste for big data analysis, economic success and a democratization of the personal data economy

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Technological advances in genome sequencing and the automatic recording of health data via sensors and smartphones generate new, large data sets. These data in combination with other medical, personal and publically available data (open data) are extremely valuable for personalized medicine and disease prevention. Already today, lives could be saved, treatments made more effective and drug side effects detected earlier through the more efficient secondary use of personal health data. In principle, individual persons are the only stakeholders possessing the right to aggregate all their personal data and to decide on any secondary use of that data. Thus, in theory only the individual is capable of unleashing the huge economic and societal value of aggregated personal data. In praxis, however, citizens often neither have access to their data nor do they possess a personal data account in which to store, manage and decide on the secondary use of their data.

Personal data are amongst the few assets of which all humans possess similar amounts. For example, all people are billionaires in genome data since the human genome consists of 6 billion base pairs. Because of this, the 'One-Member-One-Vote' governing principle of cooperatives is ideally suited for banks that manage one's personal data. Members of MIDATA cooperatives possess an account in which they can safely store, manage and share all or subsets of their personal data from different sources. At their request, data are automatically deposited in their account (e.g. via Apple Healthkit). The different national or regional MIDATA cooperatives are linked by a common platform (analogous to the financial transaction platform SWIFT) such that data can be shared for secondary use whenever cooperative members request it. In this way, patients with rare diseases, for instance, can find similar patients and make their data available to the global research community for finding better treatment. Acting as the democratic representatives of its members, MIDATA cooperatives generate financial revenues through the secondary use of the data members have assigned for this purpose. Members decide how financial revenues will be invested. In this way, MIDATA cooperatives enable their members to regain their digital self determination. At the same time they enable the democratization and maximal value creation in the personal data economy.
DISCLOSURE Nothing to disclose.

5.4.3. Population health – the use of health and demographic surveillance systems

O.5.4.3.002

Measuring population health: costs of alternative survey approaches in the Nouna Health and demographic surveillance system in rural Burkina Faso

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BACKGROUND To improve data quality and collection efficiency in the Nouna Health and Demographic Surveillance System (HDSS) in Burkina Faso, stand-alone data collection activities of the HDSS and the Household Morbidity Survey (HMS) were integrated, and the paper-based questionnaires were consolidated into a single tablet-based questionnaire, namely the Comprehensive Disease Assessment (CDA). This study aims to assess the comparative implementation costs of the two different survey approaches to measure health at the population level.
METHODOLOGY Financial costs of stand-alone (HDSS and HMS) and integrated (CDA) surveys were estimated from the perspective of the implementing agency. Fixed and variable costs of survey implementation and key drivers of costs were identified, and costs per household visit were calculated for both survey approaches.
RESULTS While fixed costs of survey implementation remained similar across the two survey approaches, there were significant variations in variable costs, resulting in an estimated annual cost-saving of about US$45 000 with the integrated survey approach. This was primarily because costs of data management for the tablet-based CDA survey were significantly lower than the paper-based stand-alone surveys. The integrated survey approach was estimated to reduce the cost per household visit from US$25 to US$21 to collect the same amount of information from 10 000 HDSS households.
CONCLUSION The CDA survey appears to be a feasible and efficient method of data collection in the Nouna HDSS in rural Burkina Faso. The tablet-based data collection platform is likely to increase the quality of population and health data collected and this should be further explored.
DISCLOSURE Nothing to disclose.

O.5.4.3.003

Adult mortality in sub-Saharan Africa: evidence from INDEPTH member health and demographic surveillance systems

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There is still a considerable dearth of knowledge regarding adult mortality and premature deaths in low-and middle-income countries (LMICs) in sub Saharan Africa (SSA). With very few countries able to maintain a reasonably functional vital registration system, our knowledge of the adult premature mortality remains somewhat scanty. The data collection constraint is further compounded by a methodological challenge since there is yet no adult mortality measurement approach as robust as the birth histories approach widely used for childhood mortality analysis (Hill et al. 2005; Hill and Pebley 1989; Preston et al. 2001).

Moreover, adult mortality is a rather infrequent event even in high mortality populations (Preston et al. 2001). Attempts to measure adult mortality using censuses and cross-sectional surveys rely mainly on indirect techniques that are affected common biases or by the likelihood that assumptions underlying the development of these techniques no longer hold in contemporary LMICs.

The growing number of Health and Demographic Surveillance Systems (HDSSs) grouped under the INDEPTH Network offer a medium term solution to the dearth of knowledge regarding adult mortality and premature deaths in low-and middle-income countries (LMICs) of Africa. With a current membership of 52 HDSSs located mainly in the remote parts of 20 LMICs in Africa, Asia and Oceania (majority of whom are in Sub Saharan Africa), the INDEPTH members collectively monitors a population of over 3.0 million people annually and generate on continuous basis vital information on population and health dynamics of small well-defined areas. This paper compares adult mortality estimates from 20 HDSSs in 11 countries in sub Saharan Africa. Life table techniques are use to generate the adult mortality estimates, specifically the probability of a 15-year old dying before the 60th birthday (45q15). We examine differences in adult mortality and their patterns in geographic regions of sub Saharan Africa and identify mortality clusters and sex differential patterns.

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Disclosure

Nothing to disclose.

O.5.4.3.004

Health and demographic surveillance system profile: the Muzaffarpur-TMRC Health and Demographic Surveillance System

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Introduction The Muzaffarpur-TMRC Health and Demographic Surveillance System (HDSS), established in 2007, was developed as an enlargement of the scope of research collaboration on the project Visceral Leishmaniasis in Bihar, which had been ongoing since 2005. The HDSS is located in a visceral leishmaniasis (VL)-endemic area in the Muzaffarpur district of Bihar state in India. It is the only HDSS conducting research on VL, which is a vector borne infectious disease transmitted by female phlebotomine sand flies and is fatal if left untreated.

Method Currently the HDSS serves a population of over 105 000 in 66 villages. The HDSS collects data on vital events including pregnancies, births, deaths, migration and marriages, as well as other socio-economic indicators, at regular intervals. Incident VL cases are identified.

Results We have a comprehensive dataset of over 6000 patients of visceral leishmaniasis and their clinical characteristics (including laboratory data) since 2002. Our demographic database contains data of 16 283 households and their members' information since 2007. The household level database contains information on household structure, family size, type of houses and housing conditions, and socio-economic data including household assets, animal ownership and other peri-domiciliary data. The individual database contains information of each family member including name, age, sex, education, marital status, migration etc. The HDSS team is experienced in conducting both qualitative and quantitative studies, sample collection and rapid diagnostic tests in the field. In each village, volunteers connect the HDSS team with the community members and have encouraged greater participation of the community in the HDSS.

Conclusion The Muzaffarpur-TMRC HDSS provides opportunities for studies on VL and other neglected tropical diseases (NTDs) and their interaction with demographic events such as migration.

Disclosure Nothing to disclose.

O.5.4.3.005

Mortality and cause of death in children aged below 5 years: the utility of Health and Demographic Surveillance Sites in monitoring key health indicators in rural Uganda

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Introduction Under five mortality is still a global public health problem with about 9–10 million children dying every year, the majority from developing countries where many deaths still go unrecorded since substantial deaths occur outside formal health facilities. Health and demographic surveillance sites (HDSS) provide mortality estimates in a fairly large and well defined populations including causes of deaths using the International Classification of Diseases version 10 (ICD 10). This paper examines trend in under-five mortality, causes of death and associated individual and contextual factors to inform health planning.

Methods and materials Data on deaths of children collected between January 1, 2008 and 31st December 2012 in Iganga-Mayuge HDSS was analysed. 783 deaths were registered and 491(62.7%) with cause of death information is analysed using Stata version 10.

Results The average under-five and infant mortality rate was 81 and 42 deaths per 1000 live birth respectively. A mortality decline (17.2%) was observed between 2009 (93/1000 live births) and 2011 (77/1000 live births). Majority of deaths (43%) occurred in rural poor households and mothers with primary or less education were 23% more likely to experience death than those in peri-urban and rich households. Neonatal pneumonia (29%), sepsis (15%) and birth asphyxia (12%) were major causes of neonatal deaths, while malaria (27.7%), pneumonia (18%), HIV related diseases including diarrhea (15%) were cause of infant deaths. Case fatality rate for malaria, pneumonia

and HIV related diseases including diarrhea was 24.5%, 20.5% and 23.5% respectively among 1–4 years.
CONCLUSION Preventable causes of deaths are still major killers of children. More examination of community and household health practices and promotion of community led preventive programs is recommended.
DISCLOSURE Nothing to disclose.

5.5.1. Innovative technologies and approaches to strengthen health

O.5.5.1.002

Managing research and surveillance projects in real-time using a novel open-source eManagement tool designed for low-resourced countries

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BACKGROUND Paper forms are still commonly used to collect data.This often leads to time-consuming data management and data errors.The introduction of tablet computers and smartphones offer new opportunities for software applications.We aimed to develop a software tool to facilitate data entry and real-time monitoring of research projects in low-resourced countries.
METHODS The *e*Management tool 'odk_planner'was written in the scripting languages PHP and Python,designed to be lightweight and for use with minimal internet resources. It was developed to be used with the open-source software Open Datakit (ODK) and uses the same database as ODK Aggregate. 'odk_planner' can be easily configured according to the needs of the user and the online interface will display the collected data from ODK forms in a graphically informative way. 'odk_planner' contains additional utilities including uploading of pictures (such as X-rays) and laboratory results,Xray reader, 2D barcodes and automated sending of text messages.Data protection and privacy is controlled by user-defined access rights. The source code and a detailed documentation are hosted on GitHub.
RESULTS We successfully used the *e*Management tool for three field applications in Tanzania:
1 A longitudinal Tuberculosis (TB) Cohort Study with a complex visit schedule: graphical display of missing case report forms on tablets, upload and reading of digitalized chest X-rays, GPS recording of residents' homes, lab reports, and text message reminders sent to the patients to reduce drop outs.
2 Intervention study at pharmacies to improve TB case detection: tablet-based electronic referral system involving different levels (pharmacies, clinics), monitoring of referred patients, automated messages to remind pharmacy customers to visit a TB Clinic.
3 Monitoring of TB retreatment cases in Tanzania to improve drug resistance surveillance in Tanzania: smartphone-based application used by clinicians at four public TB Clinics and lab technicians at the TB Reference Laboratory, combining tracking of sputum samples, collection of clinical and lab data.

CONCLUSION The user-friendly open-source 'odk_planner' is a simple but multi-functional *e*Management tool with a set of add-ons to support the conduct of studies in low-resourced countries. It can be used on any mobile device and proved to be well-suited for longitudinal and intervention studies but also for surveillance purposes at governmental clinics and laboratories.
DISCLOSURE Nothing to disclose.

O.5.5.1.003

An exploratory study using mHealth technology to describe health risks to travelers

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INTRODUCTION Emerging mHealth technology shows great potential in more accurately and completely documenting travel itineraries and mapping health and disease risk patterns of travelers, in particular the growing numbers of vulnerable travelers such as pregnant women, the elderly, and those with underlying conditions.
METHODS AND MATERIALS In partnership with the ETH Wearable Computing Lab, the Epidemiology, Biostatistics, and Prevention Institute at the University of Zürich have developed a novel data collection instrument: a smartphone application that collects data on travelers' exact itinerary using passive GPS localization, and daily information via a daily smartphone-administered questionnaire on health risk behavior, accidents, and symptoms while traveling. This ongoing study consists of 100 adult travelers to Thailand recruited from the Travel Clinic network of Zürich and Basel between January and July 2015.
RESULTS More than half ($n = 61$) of the planned study participants were enrolled by March 31, 2015. The incidence of identified health risk behaviors, symptoms, and accidents will be described and mapped by region and destination type (e.g. city, beach resort, national park). The itinerary and traveler demographic characteristics will be analyzed as predictors for health risk behavior and the development of symptoms. In addition, questionnaire completion rates will be compared to traditional travel questionnaire methodology to determine the feasibility of the app as a data collection tool in travel medicine. During an interim analysis, completion rates of the study were high (83.8%, 31/37).
CONCLUSIONS Use of a smartphone app to collect health information is technically feasible and acceptable among the traveler population, minimizes recall bias, and greatly increases the quality and quantity of data collected during travel. MHealth technology shows great potential for innovation in the field of travel medicine.
DISCLOSURE Nothing to disclose.

O.5.5.1.004

Ghana telemedicine – using mHealth to bridge the gaps in health service availability and accessibility

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The Ghana telemedicine project uses information and communications technology (ICTs) in the Bonsaso Cluster to connect rural CHWs to medical specialists at the district referral hospital to manage complicated emergency cases, and to reduce unnecessary referrals and improve health services. The purpose of the

project is to improve the access to and availability of healthcare services at the point-of-care by enhancing the referral system in rural areas, reducing unnecessary transportation resources and cost through a teleconsultation center (TCC), and expanding the reach of physicians to rural facilities. The project also aims to strengthen the triage process. Healthcare personnel are trained in the use of mobile technologies to perform 24-h health consultations from a distance, while CHWs conduct home visits and follow-up appointments.

Research was conducted to determine the impact of the project while services are scaled-up to the entire district. Included in the evaluation was a pre- and post-study with two evaluations, cross sectional in nature, one conducted before (baseline) and another conducted 12 months after the full introduction of the intervention into the scale-up communities (end line). A mixed methods approach, qualitative and quantitative data collection, was used.

Preliminary analysis shows an average of 46 calls per month mostly made from midwives, community health extension workers, and CHWs. 58% of cases were female. Calls made to the TCC were mainly related to patients between the ages of 15–35 (60%), and the main conditions were obstetrics and gynaecology (30%). Fever was the second main condition reported at 17%. In terms of referrals, preliminary results indicate 37% of referrals were avoided once the TCC was established, saving an average of 110 Ghana cedis (31 USD) per avoided referral. Among the referred cases reported, 50% were designated as emergency referrals, requiring ambulatory services. Additionally, for the calls that were referred to the district hospital, the TCC offered support in stabilizing emergency and delivery related cases.

Informal interviews have also shown that participants and users of the TCC – nurses, midwives, CHWs, and patients – reported positive impacts and improved primary health services from the pilot project.

DISCLOSURE Nothing to disclose.

O.5.5.1.005

The influence of mobile health on patient adherence in the case of effective management of type 2 diabetes in Bangladesh

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BACKGROUND Lack of awareness about type 2 diabetes and adherence to treatment, together with accessibility, availability and affordability of services are the main barriers to ensure quality management of disease in resource-poor settings such as Bangladesh. Therefore, mobile health (mHealth), due to its rapid growth and wide range of coverage, was discussed as an option to help overcome these challenges.

METHOD The study was a randomized controlled trial with a sample size of 160 patients per group. It was conducted during the period of January–December 2014 with the study population receiving treatment from the Bangladesh Institute of Health Sciences and Hospital, Dhaka. The intervention group received mobile health services (patients were reminded to follow physicians' advice regarding drug, diet, other life style activities), whereas the non-intervention group did not. Simple random sampling was followed and every 5th patient was taken as sample coming to the out-patient department. Data were collected through questionnaire survey.

RESULTS According to baseline data, the mean ages of the patients were 52 ± 10.5 years and 49 ± 10 years in the intervention and non-intervention group, respectively. The majority of the respondents were female (76% – intervention and 85% – non-intervention). Adherence to drug intake was 97% in the intervention group and 92% in non-intervention group. In the intervention group 59% patients showed adherence to physical exercise – walking for at least 30 min per day as advised, whereas 54% were adherent in non-intervention group.

INTERPRETATION The end-line data collection ended in April 2015. The end-line data will be compared with baseline data to measure the adherence to drug, diet, exercise and other lifestyle improvement advice.

CONCLUSION The comparison of the different indicators between end-line and baseline will allow us to draw conclusions about the impact of mHealth interventions on diabetic patients in urban Bangladesh.

DISCLOSURE Nothing to disclose.

5.6.1. Challenges of surveillance-response in the disease elimination phase

INV.5.6.1.001

Feasibility and roadmap analysis on malaria elimination in China

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To understand the current status of malaria control programme at the county level in accordance with the criteria of World Health Organization, the gaps and feasibility of malaria elimination either at county and national levels were analyzed based on three kinds of indicators, such as transmission capacity, capacity of profession team, and intensity of intervention. Finally, the roadmap of the national malaria elimination in P.R. China was proposed based on the results of feasibility assessment at national level.

The national malaria control programme in P.R. China could be classified into 2 stages in the history. The formulation of the national disease surveillance and reporting system since 2004 allowed for individual case to be reported nationwide. Population distribution of malaria cases nationwide from 2004–2011 showed an increasing proportion in the 20–45 age group which might be attributed to the occupations in this population including farming, business, production and others, who are more susceptible to be infected. For occupational distribution, the proportion of farmers is still in the first place, but with a declining trend, while the proportions of mobile workers, businessmen, and government staff rise significantly. Particularly in the mobile workers who migrated back from the African countries after working in Africa for years.

The classification approach used in 'China's Action Plan for Malaria Elimination (2010–2020)' relies on the incidence at county level during the period of 2006–2008, without considering the capacity of local institutions as well as vector capacities. This approach has provided useful information to design the strategy in the initiation of the National Malaria Elimination Programme but it could not fully reflect malaria transmission risks in a whole picture. To overcome this gap, our research takes comprehensive considerations of transmission risks and control capability into one picture. The results of classification is helpful to assess risks annually for the decision makers, and to find out the key factors that may reduce or increase the malaria transmission for the professionals who involve in the National

Malaria Elimination Programme, so that appropriate response easily tailor into local setting and may take place in a shorter time.
DISCLOSURE Nothing to disclose.

O.5.6.1.002
Enhanced dengue sentinel surveillance in Sri Lanka

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INTRODUCTION Dengue poses a significant socioeconomic and disease burden in Sri Lanka, where the geographic spread, incidence and severity of disease has been increasing since the first dengue hemorrhagic fever (DHF) epidemic occurred in 1989. Periodic epidemics have become progressively larger, peaking in 2012 with 44 456 cases. Passive surveillance was established nationwide more than a decade ago but dengue notifications have been based on clinical diagnosis, with infrequent laboratory confirmation. To obtain more accurate data on the disease burden, a laboratory-based enhanced sentinel surveillance system was established in Colombo Municipality, the area with the highest dengue incidence. Here we describe the study design and the results of the first 2 years (2012–2014).
METHODS Three government hospitals and two outpatient clinics in Colombo District were selected for the sentinel surveillance. All patients presenting with undifferentiated fever were enrolled, if consent given, capped at a maximum of 60 patients per week. Acute blood samples were taken from all enrolled subjects and tested by dengue-specific PCR, and NS1, and IgM – ELISA at the time of first presentation. A sub-set of 536 samples was sent to Duke-NUS Singapore for quality assurance, virus isolation and serotyping.
RESULTS Between 1 April, 2012 and 31 March, 2014, 3127 patients were enrolled, 964 (30.9%) as outpatients and 2160 (69.1%) as inpatients. The mean age was 22.3 years (SD = 17.5) and the time of first presentation was at day 4 of illness. For inpatients, 1687 (78.1%) of all febrile cases had laboratory-confirmed dengue. For outpatients, the proportion of confirmed dengue was 237 (24.6%). The mean duration of hospitalization was 4.1 days (SD = 1.85). The proportion of DHF in lab-confirmed hospitalized dengue cases was 22.1% and 4 patients (0.21%) died. Serotypes 1 and 4 were the only viruses detected in this sample (serotype 1: 85%; serotype 4: 15%). The clinicians' diagnosis for dengue at time of first presentation had a sensitivity of 92% and specificity of 23%.
CONCLUSIONS Dengue infection was responsible for a high proportion of febrile illnesses during 2012–2014, with serotypes 1 and 4 circulating. A significant proportion (22%) of hospitalized dengue cases developed DHF, but the case fatality rate was low. Clinicians' judgment was associated with good sensitivity, but to enhance specificity it is important to add laboratory confirmation of dengue.
DISCLOSURE This research was funded by the European Commission under the 7th Framework and conducted by DengueTools partners (www.denguetools.net).

O.5.6.1.003
Fine scale participatory mapping of malaria infection clusters by using routinely collected health facility data in urban Dar es Salaam, Tanzania

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BACKGROUND Standard methods for assessing malaria infection burden have limitations regarding the spatial resolution they can achieve. This study investigated whether routine data collected at health facilities can provide an affordable alternative for accurately identifying malaria transmission hot spots.
METHODS The study was performed in two adjacent wards of urban Dar es Salaam, Tanzania, with a total population of 178 000. Anonymised patient data comprising malaria rapid diagnostic test results were collected from June 2012 to January 2013 from the laboratory registry book of the area's main health facility. In the absence of a residential address system, patients' residential locations were traced by asking them to provide the name of the elected local leader of their residential housing cluster, and geo-referencing these leaders' houses. Geographic information systems and spatial scan statistics were deployed to detect clustering of malaria cases.
RESULTS Among 2407 patients tested for malaria, 46.6% (1121) could successfully be traced to their residential location. Of the traced patients, 21.4% (240) tested positive for malaria. Six spatial clusters ($P < 0.05$) of high infection risk (*hot spots*) and four of low risk (*cold spots*) were identified, with radii not exceeding 500 m. Once identified, all could be rationalised on the basis of local topography and hydrology.
CONCLUSION Participatory mapping by recording simple points of reference that community members can readily relate to during routine health facility visits can be used to map hot and cold spots of malaria infection on fine geographic scales, offering an affordable approach to targeting malaria control interventions under programmatic conditions.
KEYWORDS Malaria, clustering, hot spots, mapping, participatory, GIS, targeting
DISCLOSURE Nothing to disclose.

O.5.6.1.004
Evaluation of the national case-based measles surveillance system in South Africa: January 2009 to December 2013

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INTRODUCTION Measles is a vaccine-preventable disease but remains the leading cause of death among children under 5 years. In South Africa the case-based measles surveillance was initiated in 1998 in line with the recommendation from the World Health Organization (WHO) to monitor progress towards measles elimination. Blood specimens are collected from

suspected measles cases at all health facilities at district and provincial level. This study described the epidemiology of measles in South Africa from 2009–2013 and evaluated seven specific performance indicators for measles surveillance recommended by the WHO.
METHODS A retrospective descriptive analysis was conducted on secondary measles surveillance data routinely collected from measles suspected cases in all age groups from 2009–2013.The blood samples were tested at the measles serology laboratory at the National Institute for Communicable Diseases (NICD). The percentage for each of the indicators was calculated and compared with the WHO minimum standard values for measles surveillance.
RESULTS In 2009–2011, there were 18 000 confirmed measles cases reported, which included cases identified during the measles outbreak from June 2009 to July 2010 in all nine provinces. The number of cases decreased to 335 between 2011–2013. From 2009–2013 the age group most affected were those >14 years, while the least affected were those between the ages of 2–4 years. Out of the seven performance indicators evaluated, five met WHO specified targets, including all districts reporting at least one measles case per year (WHO target ≥80% of the districts) and blood specimens collected in more than 80%of the suspected measles cases (WHO target of ≥ 80%).Two laboratory indicators did not meet the WHO targets; between 2009 and 2013, 32%, 28%, 46%, 49% and 52% of blood specimens respectively reached the laboratory within 3 days of being sent (WHO target ≥ 80%) and between 2009 to 2013,14%,15%,65%, 68% and 66% of blood samples respectively were tested within seven days (WHO target ≥ 80%).
CONCLUSION The case-based measles surveillance met most of the WHO-specified performance indicators. Addressing timeliness of specimen delivery to the laboratory, timeliness of laboratory testing and subsequent feedback of the results to the health facility will ensure proper management of cases and rapid response to outbreaks.
DISCLOSURE Nothing to disclose.

O.5.6.1.005

Operational challenges during implementation of the 1, 3, 7 malaria surveillance strategy in China: a qualitative study

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BRIEF INTRODUCTION China has achieved great progress in malaria control over the last century and now aims at malaria elimination by 2020. In 2012 China launched its 1, 3, 7 malaria surveillance strategy. The strategy refers to case reporting within one day, case investigation within three days, and focus investigation and control action within seven days. Since being rolled out nationally, the strategy has accumulated a lot of experiences and confronted also operational difficulties. As this strategy could also become a model for other countries on the road to elimination, more information is needed on how to best deal with challenges.
METHODS This qualitative study was conducted in two provinces of China, Gansu Province in the northwestern China and Jiangsu Province in southeastern China. Key informant interviews (n = 6) and in-depth interviews (n = 36) were conducted with malaria experts, health staffs, laboratory practitioners and villager doctors at provincial Disease Control Centers (CDCs)/Parasitological Institutes, city CDCs, county CDCs, township health centers and village health stations. The participants were recruited through stratified purposeful sampling, intensity sampling and snowball sampling. A thematic analysis was conducted by identifying themes related to enablers and difficulties when implementing the 1, 3, 7 surveillance system. Ethics approval was obtained from responsible ethics committee and individual written informed consent was obtained from participants. Resulted will be presented.
RESULTS Broad themes related to barriers to the implementation of malaria 1, 3, 7 surveillance system were identified according to the case reporting, case investigation and focus investigation procedures. They included, for example, logistic aspects, population movement, imported malaria, working motivation of health workers, financial support, technical support, knowledge of health works, coordination between different sectors, lack of standard operating procedure (SOP) and quality control. We also identified themes relevant for opportunities to improve surveillance according to different administrative levels (province/city/county/township/village).
CONCLUSION Well functioning malaria surveillance and response systems are of major importance for malaria elimination programmes. China has accumulated great experience with malaria surveillance, which could be helpful for modifying other national malaria eliminating programmes.
DISCLOSURE Nothing to disclose.

5.6.2. Novel approaches for clinical trial design for poverty-related diseases

O.5.6.2.002

Randomized controlled trials using human challenge studies for influenza: a systematic review

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BACKGROUND Controlled human infections, the intentional infection of healthy volunteers, allows diseases to be studied and vaccines and therapeutic interventions to be evaluated. Seasonal and pandemic influenza contribute to major social and economic burden. Controlled human infections are integral in developing influenza vaccines and antivirals. We performed a systematic review of randomized controlled trials for influenza, using the controlled human infection platform. Our primary objective was to document trials to-date and their main findings. Our secondary objectives was to review the challenge virus, dose, attack rate and identify serious adverse events.
RESULTS Between 1947 and 2014, 21 randomized controlled trials fit our inclusion criteria. Two thirds of these trials investigated antivirals and one third influenza vaccines. 1878 subjects underwent challenge with influenza virus, and the incidence of serious adverse events was only 0.05%. These challenge studies down-selected at least three antivirals that were subsequently FDA approved. We will present the attack rates, inoculation dose and the most frequently used challenge virus.
CONCLUSIONS Controlled human infection studies are an important research design in selecting promising influenza vaccines and antivirals. These studies are performed quickly, are cost effective and safe with low serious adverse events incidence.
DISCLOSURE Nothing to disclose.

O.5.6.2.003

Data collection in a high-risk infectious zone: challenges and lessons learned in an Ebola clinical trial in Conakry, Guinea

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BACKGROUND Clinical trials require implementation of sophisticated data collection systems, i.e. in terms of traceability and validity. Data originally collected in medical files (source data) are subsequently entered into validated databases, that fulfill the stringent requirements. In Ebola treatment centers, clinical source data originate from high-risk infectious zones, thus the original medical files cannot simply be moved to the low-risk zone where data entry will take place. Various solutions are possible to overcome these challenges.
METHODS The Ebola_tx trial (ClinTrials.gov NCT02342171), sponsored by the Institute of Tropical Medicine and carried out at the Ebola Treatment Center of Médecins Sans Frontières (MSF) in Donka, Guinea, evaluates convalescent plasma added to standardized supportive care in Ebola Virus Disease. We listed and analysed the methods of data transfer used at this site in 'routine' from the start of the outbreak, and compared them with the scanning method adopted for the trial.
FINDINGS The approaches for the transfer of source data from the high-risk to the low-risk zone used in routine setting include 'shouting over the fence', the use of walky-talkies and the use of wired scanners. Conversely, in the trial we used a scanning system based on mobile phones, mounted in custom made stands and positioned in strategic places (study room, decontamination area and medical office) in the staff circuit. Documents scanned in the high-risk zone were transmitted over a secured local wireless network to a central server and automated printer.

The synoptic comparison of advantages and disadvantages of each system shows that the new system allows more control on source data and improves both quantity and quality of trials data, while minimizing infection-related risks and limiting required time of transmitting information. However, avoiding missing data during initial data collection remains a challenge.
CONCLUSIONS Digitizing paper copies in high-risk zone can provide more security and control over source data used in Ebola clinical research, while minimizing the safety risks for the staff. For future outbreaks, the development of tools for electronic data capture inside the high-risk zone could represent a further improvement for reliable and more complete datasets, by using intelligent skip patterns and mandatory data fields. But flexibility will still be needed to choose the system on a case-by-case basis, based on local constraints.
DISCLOSURE Nothing to disclose.

O.5.6.2.004

Improving efficiency and quality in clinical trials in sub-Saharan Africa

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Clinical research is indispensable for efficient health systems. Research centers in sub-Saharan Africa face particular constraints through increasing trial related workload and administration paired with capacity limitations. We therefore investigated the main challenges in the conduct of clinical trials to optimize processes for resource-effective and high quality trials in low-resource settings. The working hypothesis was that the main difficulty was that existing regulations are not adapted to these particular situations and that the possible leeway for interpretation was not sufficiently exploited.

Key informant in-depth interviews with 69 clinical trial staff were performed in 2014 and 2015 in three English- and two French-speaking African countries (Kenya, Tanzania, Ghana, Burkina Faso and Senegal). In each country clinical trial staff representing different levels in two clinical research centers was interviewed. The interview guide consisted of general questions about quality, guidelines, challenges, and perceived inefficiencies in clinical trials. The interviews were transcribed verbatim. Content analysis was performed to identify themes relevant both across settings and positions.

Poorly developed protocols, patient management and ineffective trial management were the main emerging themes. Protocols were often poorly adapted to the respective research settings ignoring capacity limitations and local culture and values. This contributed to difficulties with patients: Lack of sufficient and appropriate community and patient information and identification of balanced incentives led to fears, rumors and consequently inadequate recruitment or losses to follow-up. This together with unrealistic deadlines contributed to time loss in trials. Unclear delegation of tasks was another frequently described challenge. In turn, unexpectedly, the administrative burden resulting from the guidelines was not mentioned as a difficulty; rather, researchers were grateful for having guidance in their daily work.

Protocols need to be adapted to local contexts by early involvement of local staff and careful consideration of local capacity, systems and conditions. In addition, careful and realistic planning with regular exchange between sponsors, sites and authorities and a test run before the enrolment of the first patient are recommended to guarantee efficient and high quality trials.
DISCLOSURE Nothing to disclose.

O.5.6.2.005

Data Management Protocol: blueprint to stamp good data management procedures – experience from a multicountry study in East and South Africa

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INTRODUCTION A Clinical Data Management Protocol (DMP) describes the data management (DM) processes, systems and responsibilities in a clinical study. We will describe how its implementation in the study 'Characterization of Novel Microbicide Safety Biomarkers in East and South Africa' was coordinated with a capacity building initiative.
METHODOLOGY This multicountry study, funded by the European & Developing Countries Clinical Trials Partnership (EDCTP) and sponsored by the International Centre for Reproductive Health (ICRH), was carried out at the WITS Reproductive Health and HIV Institute in South Africa (WRHI), Rinda Ubuzima (RU) in Rwanda and at the ICRH in Kenya.

The Institute of Tropical Medicine (ITM) in Belgium was a collaborating partner. Partner data managers met with an objective of sharing best practices, to build and strengthen the implementation: the WRHI data manager wrote the DMP, ICRHK designed the database and trained data-entry staff, RU designed the DM study documentation, while ITM provided coordination, training and ongoing remote support.
RESULTS The DMP guided the study on the following: design of the case report form, database development, procedures/timelines, data quality control, training, roles and responsibilities and communication flow. Adherence to the DMP ensured standardizing and harmonizing and it promoted timely communication across the research teams, resulting in coordination of key-activities such as data review/cleaning. The DMP became a useful reference for monitors during their monitoring visits to the sites. Concomitantly, the capacity building plan contributed to innovation of local capacity by enhancing skills in database design,validation and documentation.
CONCLUSION A DMP is an essential document that guides the DM process likewise a study protocol guides the study procedures. When working in low-income settings and/or in new research sites, the DMP should envisage a capacity building component, to strengthen local capacity.
DISCLOSURE Nothing to disclose.

5.6.3. Surveillance of substandard and falsified medicines

O.5.6.3.002
The quality of paediatric medicines supplied by private wholesalers in Kinshasa, DRC

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The global pharmaceutical market is characterised by multiple qualitative standards. Low and middle-income countries are particularly permeable to poor quality medicines: in sub-Saharan Africa their proportion ranges from 12% to 48%, though accurate estimates are not available. In the Democratic Republic of Congo, the reduction of infant mortality and the availability of good quality medicines are objectives of the national Health Development Plan 2011–2015. In the context of a North-South bilateral cooperation program, a cross-sectional survey of the quality of paediatric medicines available in the private market in Kinshasa was carried out with the national medicine regulatory authority and the results were reported following the Medicine Quality Assessment Reporting Guideline. Amoxicillin (AX) and artemether/lumefantrine (AL) powder for suspension in paediatric dosage and paracetamol tablets 500 mg (PCT) were selected as tracers of medicine quality, based on 8 public health criteria. To obtain a representative sample of the most marketed products, samples were weighted on the distribution figures provided by the wholesalers and a subset of 80 samples per molecule was randomly extracted. Analyses were performed following the US-Pharmacopoeia (USP) and results were compared to the specifications of the International Pharmacopoeia for AL, and of the USP for AX and PCT. An in-depth visual inspection of the packaging and labelling was performed based on a structured checklist. In April 2014, 417 products were purchased covertly from 61 of the 80 licensed wholesalers of Kinshasa and 238 of 239 samples have been tested so far. Overall, 27% were found non-conform for the content in active ingredient (API): 21% containing AL, 3% AX and 3% PCT. Notably, 48% of all the antimalarials were underdosed in artemether. Analyses of visual inspection and correlation with risks factors are ongoing and will be presented. The overall proportion of substandard products is similar to that reported in the literature. The failure rate of AL-containing products due to artemether underdosing has not been described so far, and might be explained by artemether's higher risk of degradation under improper storage or packaging conditions, as well as by the higher cost of artemether that, coupled with the analytical difficulty of testing its content, might incentivize voluntary mismanagement during manufacturing.

The overall results are expected by June 2015 and will be presented.
DISCLOSURE Nothing to disclose.

O.5.6.3.003
DIFAEM-EPN Minilab-network

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In 2010 DIFAEM, a Christian NGO in Germany and member of EPN (Ecumenical Pharmaceutical Network), started to assist Drug Supply Organizations (DSOs) in African countries and India in implementing a system to control the quality of medicine used in central pharmacies and hospitals of Christian churches.

So far 14 partners in 11 countries have been equipped and trained to run the 'Minilab', a scientific thin layer method to test medicine samples on identity, assay (semi quantitative) and dissolution. One focus is the visual inspection, for example checking the information on the label and blisters. All samples not passing these tests are sent for confirmation to qualified laboratories, such as the WHO prequalified laboratory of MEDS in Kenya. These results are anonymously shared (to protect the partner in the field from harassment of wholesalers or manufactures) with WHO in Geneva (SSFFC Surveillance and Monitoring Department) for further action. Some of the previous WHO alerts (http://www.who.int/medicines/publications/drugalerts/en/) are based on these findings.

More than 1200 different samples have been tested so far, including substandard medicines and 14 falsified medicine. The most recent cases:

Coartem found with prolonged falsified expiry date (batch F 2951) from 2 to 4 years. Falsified Lumartem without active ingredients and error in writing Cipla (CLIPA) (batch FD3016 on pack, blister different). Cloxzem (Cloxacillin) badly substandard. Company name and address on pack does not exist in Germany. Duo Cotexcin: one batch contained Aspirin and one Acetaminophen instead of Antimalarial APIs. Recently DIFAEM started to support its partners enabling them to buy samples from uncontrolled markets e.g bus stations and street markets. More than 1000 products will be tested and most certainly some of these samples will be of low quality or even fake medicine.

A training module and flyer to raise awareness on quality of medicines in health facilities will be launched on this occasion.

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DISCLOSURE Nothing to disclose.

O.5.6.3.004

Quality assessment of the pharmaceutical products management system in Chad

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The access to essential drugs remains an issue in several low-income countries. In Chad, studies carried out in 2004 showed that median availability of generic drugs in public health care establishments was 31.3 % and that their price was not in accordance with international norms.
OBJECTIVE To assess the quality of the pharmaceutical products management system in Chad.
METHODS We conducted across-sectional study from May 30 to July 29, 2014 in a sanitary district of Middle Chari (one provision center, four hospitals and six health care centers). Availability, stock management, conservation and prices of the main essential medications were assessed using a WHO standardized questionnaire.
RESULTS Regarding national programs, drug availability was 100% for antimalarials, 46.67% for antiretroviral drugs and 50% for tuberculosis medications. Median availability of the studied drugs was 46.33% in health care centers, 75.5% in hospitals and 88% in the provision center respectively. Conservation conditions were appropriate in 60 % of cases. Stock management and monitoring tools were suitable in 41.7% of cases. The price of medicines in the sanitary district was higher than international standards.
CONCLUSION Quality of the drugs management system remains low. Despite advances regarding availability, the storage, conservation and accessibility to essential medicines should be improved.
DISCLOSURE Nothing to disclose.

O.5.6.3.005

Systematic sampling approach reveals fewer falsified first line antimalarials than previously reported

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Malaria is a curable disease provided patients have timely access to efficacious drugs, namely artemisinin based-combination therapies (ACTs), recommended as first line treatment by the World Health Organisation (WHO). The threat posed by falsified and substandard drugs is drawing increasing international attention, heightened by reports indicating that up to 35% (796 of 2296) of antimalarial drugs purchased following the convenience approach from 21 Sub-Saharan African countries failed content analysis.

To investigate the threat we purchased over 10 000 ACTs using three sampling approaches (convenience, mystery client and overt) and updated sampling frames, to provide comprehensive surveillance of ACTs available in a given geographical region. The ACTs were collected in 6 countries – Cambodia, Ghana (Kintampo), Equatorial Guinea (Bioko Island), Nigeria (Enugu metropolis and Ilorin city), Rwanda and Tanzania (nationwide). Content analyses using mass spectrometry (qualitative) and high performance liquid chromatography with photodiode array detection (quantitative) were used to measure the amount of active pharmaceutical ingredients (APIs) in 3 independent laboratories. Results were expressed as percentage of APIs stated on the packaging and used to categorise each sample as quality assured, substandard, degraded, or falsified.

Our findings were reassuring in that out of the 10 092 samples (142 brands) we only found falsified formulations that did not contain the stated APIs in 2 countries: Nigeria [both Enugu state (1%) and Ilorin city (0.8%)] and Equatorial Guinea [Bioko Island (7.3%)]. In contrast, although substandard drugs were found in all 6 countries, this did not exceed 7% of the samples analysed from Africa. The results were disseminated to the country-specific Ministry of Health, as well as the stated manufacturers and WHO.

Data will be presented to illustrate that a representative sampling approach is essential, and that both mystery client and overt sampling approaches can be used, to accurately quantify and track the scale of ineffective drugs which jeopardise treatment of a life threatening disease.
DISCLOSURE Nothing to disclose.

5.6.4. Measuring effectiveness: approaches to evaluate large-scale programs

O.5.6.4.002

Effective coverage and systems effectiveness for malaria case management in sub-Saharan African countries

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INTRODUCTION Scale-up of malaria preventive and control interventions over the last decade resulted in substantial declines in mortality and morbidity from the disease in sub-Saharan Africa and many other parts of the world. Sustaining these gains will depend on the health system performance. Treatment provides individual benefits by curing infection and preventing progression to severe disease as well as community-level benefits by reducing the infectious reservoir and averting emergence and spread of drug resistance. However many patients with malaria do not access care, providers do not comply with treatment guidelines, and hence, patients do not necessarily receive the correct regimen. Even when the correct regimen is administered some patients will not adhere and others will be treated with counterfeit or substandard medication leading to treatment failures and spread of drug resistance.
METHODS We apply systems effectiveness concepts that explicitly consider implications of health system factors such as treatment seeking, provider compliance, adherence, and quality of medication to estimate treatment outcomes for malaria case management. We compile data for these indicators to derive estimates of effective coverage for 43 high-burden sub-Saharan African countries. Parameters are populated from the Demographic and Health Surveys and other published sources. We assess the relative importance of these factors on the level of effective coverage and consider variation in these health systems indicators across countries.
RESULTS Our findings suggest that effective coverage for malaria case management ranges from 8% to 72% in the region. Different factors account for health system inefficiencies in different countries. Significant losses in effectiveness of treatment are estimated in all countries.

CONCLUSION The patterns of inter-country variation suggest that these are system failures that are amenable to change. Identifying the reasons for the poor health system performance and intervening to tackle them become key priority areas for malaria control and elimination policies in the region.
DISCLOSURE Nothing to disclose.

O.5.6.4.003

How effective are demand-side incentives in improving utilisation of delivery services in the Oyam district of northern Uganda? A quasi-experimental study

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BRIEF INTRODUCTION Lack of skilled attendance at birth remains a major contributor to the persistently high maternal mortality in Uganda. We aimed to evaluate the effects of transport vouchers and baby kits on institutional delivery and other maternal health services in Oyam district, Uganda.
METHODS AND MATERIALS We conducted a quasi-experimental study involving purposively selected intervention and comparable control sub-counties in the Oyam District, for 12 months (2013–2014). Study participants were women attending antenatal (ANC), delivery and postnatal care (PNC) services at facilities in the intervention and control sub-counties. Two interventions were evaluated: transport vouchers and baby kits. Transport vouchers were given to pregnant women attending ANC and or delivering in Acaba sub-county, which has two health centre (HC) IIs, whilst baby kits were given to pregnant women who delivered at Ngai HC III, the only HC in Ngai sub-county. Baseline and end line data were collected in 2013 and 2014 respectively. Study outcomes included coverages of institutional delivery, ANC visit 4, PNC and percentage 'by-passing' (proportion of women accessing services outside their resident sub-counties). The effect of each intervention on study outcomes was calculated using difference in differences (DID) analysis. A falsification exercise was performed based on outpatients' attendance.
RESULTS Overall, transport vouchers had a greater impact on ANC 4 and PNC, whilst baby kits had a greater influence on institutional delivery. The absolute increase in institutional delivery coverage attributable to baby kits was 22.1%. Similarly, transport vouchers increased ANC 4 and PNC coverages by 24.2% and 28.6% respectively. 'By-passing' was mainly transport voucher-related and ranged from 7.2% (PNC) to 11.9% (delivery). None of the interventions affected outpatients' attendance.
CONCLUSIONS Overall, the demand side incentives effectively increased utilisation of ANC, delivery and PNC services and could potentially improve maternal and newborn health in our setting.
DISCLOSURE Nothing to disclose.

O.5.6.4.004

Health monitoring in a changing social-ecological context of a biofuel project in Sierra Leone

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INTRODUCTION A large-scale biofuel project facilitated by sugarcane plantations in Sierra Leone impacts on the local environment, existing ecosystems, social structures and health of affected communities. The acquisition of 14 300 ha arable land, a subsequent change in vegetation and the usage of large water quantities for irrigation purposes are examples of impacts, which link environments and ecosystems to health issues, such as food security, access to water and altered breeding habitats for disease vectors (e.g. *Anopheles* mosquitoes) and intermediate host snails. In order to monitor project-related impacts, the Addax Bioenergy Sierra Leone project conducted a health impact assessment (HIA) that included primary data collection of health and health-related environmental and social indicators.
METHODS Two cross-sectional health surveys were conducted; a baseline in December 2010 prior to major project developments and a 3-year follow-up in December 2013. Data collection included
1 biomedical indicators;
2 knowledge, attitudes and practices indicators; and
3 environmental indicators, in both, project-impacted and non-impacted control communities.

RESULTS The prevalences of stunting, wasting, and *Plasmodium falciparum* in children under 5 years of age decreased significantly in impacted (all $P < 0.05$) and non-significantly in control sites. Anaemia in children and in women of childbearing age decreased significantly in impacted and control sites ($P < 0.05$ and $P < 0.001$, respectively). Health facility-based deliveries increased significantly in the impacted sites ($P < 0.05$). The prevalence of helminth infections in children aged 10–15 years remained approximately at the same level with focal increases in impacted sites. Access to improved sanitation decreased significantly ($P < 0.05$) in control and non-significantly in impacted sites. Water quality remained poor without notable changes.
CONCLUSION The comparison of health and related indices from two cross-sectional surveys as part of the initial HIA and long-term monitoring provides an interesting case study to quantify burden of disease, study the underlying causes of changing health patterns and guide mitigation measures in the context of a highly dynamic social-ecological system due to a large-scale infrastructure project in sub-Saharan Africa.
DISCLOSURE Nothing to disclose.

O.5.6.4.005

Using social network analysis to assess communication between programme and district managers on HIV programme monitoring and evaluation in South Africa

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INTRODUCTION Internationally there is a push to maximise synergies between disease control programmes (DCPs) and health systems. Methods are needed that can measure the extent of collaborative interactions (communication and joint working) between DCP and health system actors. Social network analysis (SNA) is a useful actor analysis method that has not previously been applied to these interactions in health systems research. In South Africa programme and district managers are supposed to collaborate in the monitoring and evaluation (M&E) of programme interventions within a policy context that makes district managers the lead actors in programme implementation with programme actors as specialist advisors. This research innovates by applying SNA to measure communication amongst these actors on HIV M&E.

MATERIALS AND METHODS Data were collected from 51 managers using a structured SNA survey during 2010 to 2011. We measured:

1 one-on-one task-related communication – talking about collation (verification, reporting) and use of HIV data; and
2 group communication through co-participating in management committees where HIV data were used for monitoring HIV interventions.

UCINET software was used to compute SNA measures of: centrality (to identify the most prominent actors), whole network density (cohesiveness of networks), and homophily (extent of communication within and between programme and district manager sub-groups). Block modelling identified committees that linked managers.

RESULTS Data collation networks were more cohesive than those for data use. Programme managers were the most prominent network actors. As a group, programme managers located at higher levels tended towards homophily (talking mostly amongst themselves) and shared weakly cohesive networks with district managers and seldom participated with them in management committees.

CONCLUSION This SNA study illustrates the relationship between programme and district managers, so identifies bottlenecks and synergies, and suggests potential areas of intervention. Bridging communication gaps would promote synergies in the monitoring of HIV interventions, as envisioned in policy.

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DISCLOSURE Nothing to disclose.

5.6.6. Implementation research – key to effectiveness

INV.5.6.6.002

Research capacity strengthening and knowledge management for health teams towards improvement in disease control in Ghana (Ghana RCS4FIVE)

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BACKGROUND Infectious diseases form a substantial proportion of the disease burden in Ghana, like most sub Saharan African countries. With increasingly limited resources, solutions to operational bottlenecks to disease control efforts need to be evidence-based. Health Management Teams are limited in basic skills to systematically process, analyze and interpret relevant data including routine to answer their questions or solve operational challenges to disease control.

OBJECTIVES We proposed to carry out capacity development for operational research among five 4-member regional teams over the course of 1 year. The overall aim was to equip the five health teams with relevant knowledge and skills to address specific health problems through operational research. Teams processed, analyzed and interpreted relevant routine data. They disseminated the findings locally and widely and applied them in their disease control efforts.

METHODS A total of 5 health teams were selected from 4 regions of Ghana for capacity development. Included in the 6-member multidisciplinary team were one scientist from a research Institution and an expert in the Routine Health Management Information Data System (DHIMS2). The teams participated in 3 capacity building workshops over the period of 1 year. This included a 5-day proposal development workshop during which they developed their selected research topics into full proposals and subsequently applied for ethical approval with support from the study Investigators. The second workshop was for data extraction and analysis in the team's home region. During the third and final workshop, 6 months after the first, teams finalized their draft papers for publication and slides for presentation at their next regional Annual Review Conference.

RESULTS Reviewing of data facilitated dialogue among the research team members as well as between them and the heads of the departments where the data was primarily generated. Teams carried out studies on a wide range of disease areas such as HIV, TB cases, Malaria and cholera. The study results served to initiate follow-up actions for improvement of disease control following dissemination in the areas where data were collected and to leverage additional funds for training other such teams in Ghana.

CONCLUSIONS Equipping heath teams with skills to systematically process, analyze and interpret relevant data including routine data leads to evidence based actions for improved disease control.

DISCLOSURE Nothing to disclose.

INV.5.6.6.003

Effectiveness of short term training on health economics in improving knowledge and economic way of thinking to help break vicious cycle of infectious disease and poverty: an evidencefrom Nepal

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Knowledge of health economics and its commensurate way of thinking enhances the allocative and technical efficiency for contributing to the elimination of infectious diseases. As poverty is a root cause of infectious diseases as well as an important consequence of these diseases endogenizing economic way of thinking has an important implication for having a holistic understanding of solution. This broad, holistic, perspective uses many facets of economic analysis and its tools can identify areas of waste and inefficiencies to map out options and facilitate better use of scarce resources. Thus short term training on health economics was conducted funded by WHO/TDR.

As evidences are rarely found in low income countries whether the short term trainings are effective in improving the knowledge and economic way of thinking in health service and policy research, the objective of this paper is to assess the effectiveness of the training in the above regard using pre- and post- questionnaires and the innovative approach. A quasi experimental design was adopted with the use of a pre-test intervention and post-test design. The training package included various tools and techniques of economic analysis and appraisal, demand and supply analysis, production economics, health care financing and catastrophic payments with practical hand-on experience with tools and techniques. The approach taken to evaluate the training was by measuring its reflection rather than the just the technical content of training is innovative. The effectiveness of the training was measured in three dimensions – (i) general understanding of economics from health policy perspective; (ii) application of economic analysis and appraisal tools and techniques; and (iii) economic way of thinking for issues related to disease control and poverty. The results show that there is a significant improvement in these three dimensions after the training intervention. The paper concludes that indigenizing knowledge of economics and way of thinking has important implications for designing alternative policy and resource utilization.

DISCLOSURE Nothing to disclose.

INV.5.6.6.004

Estimating of the level of insecticide availability in some samples of sprayed surfaces (IRS) using insecticide quantification kits (IQK) in Benin

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Indoor Residual Spraying (IRS) are key weapons in the fight against malaria in Benin. This programme is rarely assessed because of the limited choice of methods available for quantifying insecticide content in the field. The available methods are too expensive and technically demanding for field operations. This study, evaluated a user-friendly tool to identify potential improvements for detecting insecticide content after routine IRS operations were conducted.

This study was conducted in Toucountouna municipality at Natitingou (north Benin). IRS was conducted with pyrimiphos methyl (PM). Two types of samples were collected: (i) pre-spraying filter papers were placed in the selected households to determine what the real deposit of insecticide was during spraying, (ii) post-spray removal of insecticide with adhesive to assess the extraction efficiency of the Bostik dots as a post extraction sampling method. The insecticide content on the pre-spray filters was quantified using both colorimetric assay (IQK) and High-performance liquid chromatography (HPLC), while post-IRS samples (Bostik dots) were analysed using HPLC.

One hundred and twenty three households in 20 villages were sample using both pre-spray filter papers and post spray Bostik dots sampling methods. Overall, the pre-spray data indicates an average spray rate of ~3 g/m^2, ranging from 1.3–4.5 g/m^2. Although the range is large, reflecting numerous variables such as individual/team spray performance, most of the variation lies with one SD, indicating reasonably consistent spray performance across the board. When comparing data generate with IQK versus HPLC results using only pre-spray filter papers, we observed excellent correlation ($r^2 > 0.9$). We also evaluated the use of Bostik dots for post spray monitoring. Results of the average recovered PM from Bostik dots post-spray averaged ~6% compared with pre-spray filters. This was much lower than expected from laboratory tests (25%–30%), and too low to provide meaningful interpretation of spray values. Although disappointing, this is a valuable result since it establishes the suitability of post-spray sampling methods.

Our data suggests that the new organophosphate IQK assay can be used instead of HPLC for the analysis of IRS samples facilitating timely decision making and reporting for program managers. Furthermore, data indicates that Bostik doesn't work well with mud walls. However, an alternative methods need to be explore for post spray.

DISCLOSURE Nothing to disclose.

INV.5.6.6.005

The new 1,3,7 strategy and implementation for malaria elimination in China

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Jiangsu Institute of Parasitic Diseases (JIPD) was founded in 1950. JIPD received the institution-building grants from WHO/TDR in 1989 and 1991 and has now become one of best professional insitutions for research, technical training and diseases control on malaria and other parasitic diseases in China. Housing the National Key Laboratory for Parasitic Disease and Provincial Key Laboratory for Molecular Biology of Parasitic Diseases in JIPD as well as Master and PhD- degree programs and Post doctor training, JIPD has become an international malaria training centers in China. The international malaria training courses and workshops hold in JIPD every year have attracted more than 700 participates from 52 countries, most of them from Africa since 2002.

Jiangsu province used to be highly endemic for malaria. There were two large outbreaks with over 10 million annual malaria cases in 1970's. After successful malaria control activity, falciparum malaria was eliminated in Jiangsu since 1990. The National Malaria elimination program began in 2010 and there has been no local infected malaria cases in Jiangsu province since 2013. The '1,3,7' new malaria elimination strategy established in Jiangsu has become the national malaria elimination strategy.

DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

INV.5.6.6.006

Implementation of a mentorship programme on knowledge translation/management to improve policymakers' capacity for evidence-informed policymaking for the control of infectious diseases of poverty in Nigeria

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BRIEF INTRODUCTION Mentorship can be used to enhance capacity for effective job performance. In this study, we implemented a mentorship programme to enhance the capacity of policymakers for evidence-informed policymaking in the control of infectious diseases of poverty (IDP) in Ebonyi State Nigeria.
METHODS AND MATERIALS A 'before and after' intervention design was used in which outcomes were measured on target participants both before intervention is implemented and after. Strategies used included a training workshop on information/communication technology (ICT); a training workshop on health-policy information literacy; an evidence-to-policy meeting; and a policy dialogue. Pre/post-workshop questionnaires developed in a 4 point likert scale were used to assess the outcome of each meeting. The 52 participants enrolled were divided into three IDP groups (malaria, schistosomiasis, lymphatic filariasis) and were mentored by four senior researchers and a senior policymaker for 2 months. The mentorship meetings were held by each group to identify potential policy options for the policy brief. The policy options were subjected to research evidence synthesis by each group to identify options supported by research evidence (mostly systematic reviews) from PUBMED, COCHRANE DATABASE and GOOGLE SCHOLAR. The policy brief was subjected to a multi-stakeholder policy dialogue.
RESULTS Percentage increase in mean of knowledge and capacity from the ICT workshop ranged from 8.3%–39.1%. Outcome of the information literacy workshop indicated a percentage increase in mean of knowledge of participants ranging from 22.6%–55.3%. Outcome of the group mentorship/evidence-to-policy meetings indicated percentage increase in mean of knowledge and capacity for preparation/use of policy briefs ranging from 20.1%–45%. Participants rated the policy brief and policy dialogue very high and noted that both achieved their purpose. A Director from health ministry noted thus: 'We used the knowledge from the trainings to influence the final policy documents on free maternal health services.' A consultant family physician, said 'the programme opened my eyes on how research should not end in published papers only, but on how to translate research into policy'.
CONCLUSIONS The outcome suggests that this type of mentorship can improve policymakers' capacity for evidence-informed policymaking in low income setting.
ACKNOWLEDGEMENT Authors are grateful to TDR for funding support.
DISCLOSURE Nothing to disclose.

INV.5.6.6.007

Implementation research dashboard tool for district health management

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BACKGROUND In Tanzania, the districts serve as hubs for implementation of national health policy and thus they host large number of implementation research efforts. However the products of information from such efforts are rarely available to the host districts. Due to resource limitation effective utilization of available evidence would improve planning capacity of the districts. We designed a dashboard tool to support streamlining of procedures related implementation research projects at the districts.
RATIONALE There is big volume of research efforts that use district health system as their platform. They create an additional workload but also have potential input into planning and reposting processes. So far members of the district health management teams do serve as logistic serving as agents but the resulting information products are not utilized by the district health system.
MAIN OBJECTIVE To assemble value of research initiatives to enhance planning and reporting capacity of the host districts specific objectives (i) to assemble and analyze existing metadata of implementation research projects and generate baseline profile (ii) to establish mechanism for systematic registration of research initiatives and alignment of research results with planning indicators; (iii) to design, implement and evaluate an information system to facilitate documentation and alignment of research results with CCHP environment and (iv) to *Package* any successful and challenging experience with a view to further testing to additional districts to facilitate in-depth understanding of possible operational gaps and fine-tuning of proposed solutions
RESULTS Majority (89%) of researchers came from universities and most of them (92%) were students of higher learning institutions. Majority (81%) of the research students was undergoing their academic studies at undergraduate and masters and most of them (78%) were dealing with public owned health facilities than otherwise. As far as the distribution of implementation research efforts priority areas of the Comprehensive Council Health Plan (CCHP), maternal, newborn and child health was the most researched area (38%) followed by communicable diseases control (20%), treatment and care of other common diseases (9%) and non-communicable diseases (8%), out of 13 priority areas of the CCHP. Software tool is in place to facilitate all the procedures
DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

Late Breaker Oral Abstract Sessions

LB1 Late Breaker Abstract Session 1

O.LB1.001

Pyrethroid and DDT resistance in Anopheles gambiae from Taabo, south-central Cote d'Ivoire

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Malaria prevention can be done by the use of insecticides as Indoor Residual Spraying (IRS) or by the use of Insecticide Treated Nets (ITNs). The development of resistance to insecticides in malaria vectors constitutes a real threat given the emphasis on the use of IRS and ITNs for malaria control. This highlights the importance of assessing the level of resistance to insecticides in vectors before any vector control action. In this context, the resistance level of the major malaria vector, Anopheles.gambiae s.l, was evaluated for the four main families of insecticides used in public health and agriculture (pyrethroids (Deltamethrin 0.05%, permethrin 0.75%), organochlorine (DDT 4%), organophosphate (malathion 5%), carbamate (propoxur 0.1%) in three locations (Taabo-Cité, N'denou, Tokohiri) in the subprefecture of Taabo, Côte d'Ivoire. Susceptibility test were performed according to WHO test cylinders with adult females of An. gambiae aged 2–5 days. The results showed that the three mosquito populations were resistant to DDT (Taabo-Cité: mortality = 17.1%, N'denou: mortality = 5.6%, Tokohiri: mortality = 0%). Mosquitoes from Taabo-Cité and N'denou were resistant to deltamethrin respectively with 89.7% and 85% mortality rates. A probable resistance was suspected with permethrin in these two populations with 97% and 93% of mortality respectively. Contrarily, at Tokohiri, mosquitoes were resistant to permethrin (mortality = 54.4%) and had a decreased sensitivity to deltamethrin (mortality = 91.6%). The molecular forms M and S were identified in overall with the predominance of S form (80.4%). The resistance mechanism involved was the kdr mutation with a frequency of 56.3%. A widespread resistance of wild populations of An.gambiae s.l to DDT and pyrethroids was observed in the three communities, contrarily to the other family of insecticides where the levels of resistance observed varied. Any vector control program in these areas should take into account these observations.

DISCLOSURE There is no conflict of interest.

O.LB1.002

Stool-based polymerase chain reaction for the diagnosis of multiple pathogens in Mali: a case-control study

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BACKGROUND The diagnosis of infectious gastrointestinal diseases in resource-constrained settings is hampered by the low sensitivity of conventional stool culture and the need for multiple tests to cover all target pathogens. Multiplex polymerase chain reaction (PCR) assays have been proposed as a sensitive alternative, but data from highly endemic tropical settings are scarce and most previous studies did not include asymptomatic controls.

METHODS Between August 2014 and May 2015, the European research consortium NIDIAG conducted a prospective, non-interventional case-control study in Niono, central Mali. Ethanol-fixed stool samples stemming from patients with persistent diarrhoea (≥2 weeks) and/or persistent abdominal pain (≥2 weeks) and from matched asymptomatic controls were transferred to Germany and subjected to real-time multiplex PCR (R-Biopharm; Darmstadt, Germany) for detection of diarrhoeagenic bacteria (*Campylobacter* spp., diarrhoeagenic *Escherichia coli* pathotypes, *Salmonella* spp. and *Yersinia enterocolitica*), intestinal protozoa (*Cryptosporidium* spp., *Dientamoeba fragilis*, *Entamoeba histolytica* and *Giardia intestinalis*) and viruses (adenovirus, astrovirus, norovirus and rotavirus).

RESULTS Preliminary analysis of 345 patients and 177 matched controls revealed that enteroaggregative *E. coli* (EAEC) and *Campylobacter* spp. were the most frequent pathogens, with an overall prevalence of 44% and 36%, respectively. The protozoon *G. intestinalis* was found in 25% and adenovirus in 22% of all samples. In contrast, *Cryptosporidium* spp., *E. histolytica*, *Salmonella* spp., *Yersinia enterocolitica* and most viruses were detected in <5% of all samples. Strikingly, *Campylobacter* spp., *G. intestinalis* and rotavirus were significantly more common in symptomatic patients than healthy controls.

CONCLUSION The application of highly sensitive real-time PCR on stool samples from endemic settings detects surprisingly high infection rates with multiple enteric pathogens. The inclusion of asymptomatic controls in epidemiological studies is recommended to enhance the clinical relevance of such findings.

DISCLOSURE Nothing to disclose.

Abstracts of the 9th European Congress on Tropical Medicine and International Health

O.LB1.003

Why such a high prevalence of epilepsy in the Orientale Province in the Democratic Republic of the Congo (DRC)?

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OBJECTIVE To determine the prevalence, distribution, and risk factors of epilepsy in villages in an onchocerciasis endemic region of the DRC.
METHODS In July 2014, an epilepsy prevalence study was carried out in Dingila and Titule in the Bas-Uélé district, Orientale Province. The distribution of epilepsy cases was investigated using the Moran's I statistic of spatial auto-correlation. In a case control study, 59 individuals with epilepsy were compared with 61 healthy controls from the same village.
RESULTS Among the 12776 individuals of Dingila, 373 (2.9%) individuals with epilepsy were identified. In a house-to-house survey in Titule, 68 [23.4 ‰ (IC 95%: 16.7–27.3)] of 2908 people were found to present episodes of epilepsy. Epilepsy showed a marked spatial pattern with clustering of cases occurring within and between adjacent households. Individual risk for epilepsy was found to be associated with living close to Simulidae infested fast flowing rivers. Peak onset of epilepsy was around the age of 14–15; neuro-psychiatric abnormalities were present in 31%, important growth retardation in 17% and delayed sexual development in 3%. *Onchocerca volvulus* (OV) DNA was detected in the skin of 26/34 cases (76%) and 10/14 controls (71%) ($P = 0.7$) but was not detected in the cerebrospinal fluid of cases. However, 49% cases and 48% controls had taken ivermectin 7 months earlier. Cases reported a greater frequency of daily bathing in the river compared to controls, respectively 24/57 (42%) vs. 12/60 (20%) OR 3.07 (95% CI 1.19–7.93) ($P = 0.02$). Blood PCR tests for*Toxoplasmosis* and *Wuchereria bancrofti* were negative in all cases and controls. A *Loa loa* infection was found in only one case and one control. In none of the participants were antibodies to *Taenia solium*, *Toxocara* and*Trypanosoma sp*. detected. In an age matched nested case control study 16/18 (98%) cases did not take ivermectin the year before they developed epilepsy compared to 7/18 (39%) controls that same year ($P = 0.002$).
CONCLUSION The epilepsy prevalence in the Bas-Uélé district was higher than in non-onchocerciasis endemic regions in Africa. The nodding syndrome like appearance of some epilepsy cases requires more in depth neurological investigations. Frequent contact with Simulidae infested rivers, and a historical lack of ivermectin treatment were associated with the presence of epilepsy suggesting that OV infestation is the main cause of epilepsy in onchocerciasis endemic regions.
DISCLOSURE Nothing to disclose.

O.LB1.004

Evaluation of sulphadoxine-pyrimethamine for intermittent preventive treatment of malaria in pregnancy: a retrospective birth outcomes study in Mansa, Zambia

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BACKGROUND Intermittent preventive treatment of malaria in pregnancy (IPTp) with sulphadoxine-pyrimethamine (SP) decreases placental parasitaemia, thus improving birth outcomes. Zambian policy recommends monthly SP-IPTp doses given presumptively during pregnancy at each antenatal examination, spaced 1 month apart after 16 weeks of gestation. The effectiveness of SP-IPTp was evaluated in Zambia where a recent study showed moderate prevalence of Plasmodium falciparum parasites with genetic mutations that confer SP resistance.
METHODS HIV-negative women were enrolled at the time of delivery at two facilities in Mansa, Zambia, an area of high malaria transmission. Women were interviewed and SP exposure was determined by antenatal card documentation or self-reports. Using Poisson regression modelling, the effectiveness of SP-IPTp was evaluated for outcomes of parasitaemia (microscopic examination of maternal peripheral, cord, and placental blood films), maternal anaemia (Hb < 11 g/dl), placental infection (histopathology), and infant outcomes (low birth weight (LBW), preterm delivery, and small for gestational age) in women who took 0–4 doses of SP-IPTp.
RESULTS Participants included 435 women, with a median age of 23 years (range 16–44). Thirty-four women took zero doses of SP-IPTp, while 115, 142 and 144 women took one, two, or ≥three doses, respectively. Multivariate Poisson regression models considering age, mosquito net usage, indoor residual spraying, urban home, gravidity, facility, wet season delivery, and marital status showed that among paucigravid women ≥two doses of SP-ITPp compared to one or less doses was associated with a protective effect on LBW (prevalence ratio (PR) 0.33, 95% confidence interval (CI) 0.12–0.91) and any infection (PR 0.76, CI 0.58–0.99). Multivariate models considering SP-IPTp as a continuous variable showed a protective dose-response association with LBW (paucigravid women: PR 0.54, CI 0.33–0.90, multigravid women: PR 0.63, CI 0.41–0.97).
CONCLUSIONS In Mansa, Zambia, an area of moderate SP resistance, ≥ two doses of SP-IPTp were associated with a protective effect from malaria in pregnancy, especially among paucigravid women. Each dose of SP-IPTp contributed to a 46% and 37% decrease in the frequency of LBW among paucigravid and multigravid women, respectively. SP-IPTp remains a viable strategy in this context.
DISCLOSURE Nothing to disclose.

O.LB1.005

Strengthening Publications Reporting Infections in Newborns Globally (SPRING) international survey on the criteria for reporting neonatal infections

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BACKGROUND Globally about 630 000 neonates die each year from severe bacterial infections: this is a higher death toll than

both malaria and HIV together in children under five. In South Asia, Sub Saharan Africa and Latin America alone an estimated 7 million neonates are affected by severe bacterial infections every year. However the literature on the subject is limited, of variable quality, and reporting criteria have never been harmonised, making it difficult to appreciate the extent of the problem. As a step to agree standards of reporting, we set up a survey to establish what clinicians and researchers across the world consider essential criteria for reporting neonatal infection.
METHODS Following the extraction of criteria from published studies through an extensive literature review, an online survey consisting of 12 sections and 109 questions was drafted. The criteria were refined through a discussion amongst a group of clinicians and researchers from different institutions and piloted amongst the group.

The refined online survey was sent to 32 international experts who distributed it to their peers through neonatal and infectious diseases networks and personal contacts in the 5 continents.
RESULTS 145 respondents from 35 countries and 97 institutions from all continents participated. Essential criteria according to over 70% of participants were for the method: clear definitions, study context (health facility or community), timing of infection (including proportion of cases captured on the first day), postnatal age, birth weight and gestational age ranges; for the results: the proportion of babies meeting the case definition, proportion of culture-proven infections, positive cultures and their classification as pathogens or contaminants, incidence of infection and mortality.
CONCLUSIONS There was good agreement in choosing core criteria for reporting neonatal infections globally, indicating that selecting appropriate criteria for this condition is feasible. We believe that the dissemination and implementation of essential criteria for reporting neonatal infections will greatly improve the quality of the studies and publications leading to raising the profile and visibility of this global problem. The results from this survey informed a process including a consensus meeting to define guidelines for Strengthening Publications and Reporting Infections in Newborns Globally (SPRING).
DISCLOSURE Nothing to disclose.

O.LB1.006

Effectiveness and sustainability of a 6 month peer support based physical activity intervention trial among sedentary women in Thiruvananthapuram City, India

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BRIEF INTRODUCTION Evidence on physical activity (PA) interventions targeting women in India is limited. The objective of the study was to assess the effectiveness and sustainability of a peer supported PA intervention targeting sedentary women in Thiruvananthapuram City, India.
METHODS AND MATERIALS A non – randomized quasi-experimental design was used. Intervention was developed using intervention mapping approach. Intervention components were developed based on the findings from formative research: focus group discussions; and cross sectional survey, and behavioral theories. Sedentary women (n = 401) aged 18–64 years identified through a cross sectional survey, based on the Modified Global Physical Activity Questionnaire were enrolled into the trial. Culturally relevant intervention components: educational workshop; individual counselling and goal setting; health information booklets; peer leader training and subsequent peer leader led sessions; with group specific activities were delivered at three intensities: intense, less intense and no intervention. Assessments were made at the baseline, 4th, 7th and 13th month of intervention and mixed model analysis was employed.
RESULTS The proportion of women who became active was significantly higher in the intervention arm compared to the control arm at fourth (58.5% vs. 10%, P value < 0.001), seventh (48.5% vs. 6%, P value < 0.001)) and thirteenth month (29.6% vs. 0.6%, P value < 0.001) respectively. The improvements from the baseline in amount of PA expended by the intervention arm when compared to the control arm were 990.02 MET-min/week, 575.2 MET-min/week and 466.3 MET-min/week at the fourth, seventh and thirteenth months respectively.
CONCLUSION More attention has to be given to the environmental and policy determinants of PA apart from the behavioural and social approaches for sustainability. Simultaneous use of multiple strategies required to promote PA.
DISCLOSURE Elezebeth is supported by the Fogarty International Centre, National Institutes of Health, Award Number: D43TW008332 (ASCEND Research Network).

LB 2 Late Breaker Abstract Session 2

O.LB2.001

Acceptability of plasma donation for clinical trial on Ebola virus disease in Conakry, Guinea

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INTRODUCTION Since July 2014, the World Health Organization has been leading discussions on emergency evaluation of experimental therapies targeting Ebola Virus Disease (EVD), such as transfusion of Ebola convalescent plasma. In February 2015, the trial '*Emergency evaluation of convalescent plasma for Ebola Virus Disease in Guinea*' started in Donka Hospital, Conakry, Guinea (NCT02342171). To implement plasma donation, a mobile plasmapheresis was installed at the National Blood Transfusion Centre (NBTC) possessing the latest technology to produce pathogen-reduced plasma. Recruitment of survivors as plasma donors was facilitated by collaborating with Ebola survivors acting as mediators. Challenges were anticipated because of evidence that social meanings of blood and rumours surrounding blood sampling have previously hampered medical research in this region. There were concerns about the acceptability of plasma donation for highly stigmatised Ebola survivors in a setting where collection of blood in healthy volunteers is already challenging.
METHODS Qualitative formative research was carried out to support the trial. It included informal conversations and semi-structured interviews with various types of actors, as well as observations during different trial stages and at different places linked to its implementation (i.e. NBTC, Plasma Mobile, Ebola Treatment Unit).
RESULTS Preliminary data show that two main factors increased the acceptability of plasma donation at NBTC: firstly, the confidence of survivors in other survivors introducing them to the plasma donation process, based on their common identity

of having suffered from and survived Ebola; secondly, the sophisticated technology and highly professionally environment of plasma donation. Main reasons explaining the more positive perception of plasma versus WB donation were the sensitization and welcoming process; the return of red blood cells; the faster recovery of plasma donors compared to WB donors; the impressive plasmapheresis technology and the devoted health staff.
CONCLUSIONS Despite being an innovative intervention in Guinea, plasma donation was found acceptable if presented under favourable conditions. This experience can contribute to our understanding of how the acceptability of voluntary and non-remunerated donation of blood products can be enhanced, and this, specifically in a West-African context.
DISCLOSURE Nothing to disclose.

O.LB2.002

Comparison of the molecular staphylococcal epidemiology in sub-Saharan Africa versus Germany: a prospective, multicenter cohort study on community associated *Staphylococcus aureus*

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OBJECTIVES African-German-multicenter cohort study comparing genotypic and phenotypic signatures of *Staphylococcus aureus* associated with geographic mapping and virulence of colonizing and infection strains between Africa and Germany (www.African-German-Staph.net).
METHODS Prospective collection of 1200 community associated *S. aureus* isolates from 600 patients (wound infections, blood cultures) and 600 healthy volunteers (nasal swabs). Identification was performed by MALDI-TOF and genotyping by *spa*-analysis. Clonal complex (CC) assignment, and regulatory, virulence, metabolic and antimicrobial resistance gene profile analysis by 174 gene-locus DNA microarray (MA) (Identibac®), followed by advanced bioinformatics (affinity propagation, principal component analysis, Kolmogorov–Smirnoff-test).
RESULTS In this community associated study cohort, the overall rates of MRSA rates was low (<3%). CC5, CC8, CC9, CC25 and CC707 were highly abundant in African and German cohorts. Other CCs were clearly predominant either in Africa (CC121, CC152) or Germany (CC45, CC398), associated with disease (CC45, CC121, CC152) or carriership (CC101, CC707). Recent PCA and affinity propagation analysis of abundant clonal complexes allowed identification of nine clonal subgroups with specific geographical and clinical characteristics. Eight clusters could be characterized by significant associated genes such as PVL found in the isolate clusters of CC8 and CC45 isolates. Moreover, two CC45 subclusters could be discriminated with respect to clinical versus nasal significance. More detailed PCA analysis of only CC45 or CC121 isolates showed that the nasal CC45 isolates could be characterized by specific genes such as *vwb* (gene encoding for von Willebrandt factor binding protein), *sec, sel* (staphylococcal enterotoxin genes) and that a clinical CC121 isolate subcluster could be characterized by *luks/F-PV* (PVL encoding genes) and *etA* (exfoliative toxin gene).
CONCLUSION These results from a large, prospective, microarray-based study comparing exclusively community African and German *S. aureus* isolates indicate genetic profile association with disease and/or geographical origin. Such knowledge will be valuable to ascertain the relevance of selected genes and/or genetic profiles throughout developed and developing global regions.
DISCLOSURE The DFG as sponsor of this study had no part in study design, experiments, data collection, data analysis, data interpretation or writing of the report.

O.LB2.003

Rapid point-of-need diagnostics for Chikungunya virus using recombinase polymerase amplification assay

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INTRODUCTION Chikungunya virus (CHIKV) is a mosquito-borne virus identified in 60 countries. CHIKV causes acute flu-like symptoms and in many cases prolonged musculoskeletal and joint pain. Detection of the infection is mostly done using RT-RCR or ELISA, which are not suitable for point-of-care diagnosis.
METHODS In this study, a reverse transcription recombinase polymerase amplification (RT-RPA) assay for the detection of the CHIKV was developed. The assay sensitivity, specificity and cross-reactivity were tested. A field trial was conducted in Thailand to assess the possibility of using the CHIKV RT-RPA assay at point-of-need.
RESULTS CHIKV RT-RPA assay detected down to 80 genome copies/reaction in a maximum of 6 min. It successfully identified 18 isolates representing the three CHIKV genotypes. No cross-reactivity was detected to other alphaviruses and arboviruses except O′nyong′nyong virus, which could be differentiated by a modified RPA primer pair. In Thailand, fifty-eight samples were screened by RT-RPA. The result was compared with real-time RT-PCR and viral culture. The clinical sensitivity and specificity of the CHIKV RT-RPA was 100%. Moreover, the RT-RPA reagent was stable at ambient temperature during transportation and handling. The total weight of the RPA mobile laboratory including reagent for 500 samples was 23 kg and was 158 cm in size (length + width + hight), which was easy to carry and transport.
CONCLUSION The developed RT-RPA assay represents a rapid and sensitive method for the molecular detection of CHIKV. In addition, the mobile laboratory can be implemented easy at site of outbreak or for epidemiological studies in low resource settings.
DISCLOSURE Nothing to disclose.

O.LB2.004

Quality of medicines in resource-limited settings: an analysis of the compliance of pharmaceutical distributors with the WHO Quality Assurance standards

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The globalization of pharmaceutical production has not been paralleled by globalization of regulation, and the international market is characterised by multiple qualitative standards. Poor-quality medicines are especially prevalent in low and middle-income countries (LMICs). When regulatory supervision is weak, pharmaceutical distributors play a key-role in ensuring medicine quality within their country.

QUAMED, a network hosted by the Institute of Tropical Medicine (Belgium), promotes appropriate quality standards for medicines in LMICs. We analysed retrospectively the results of audits conducted by QUAMED at 10 African and 8 European wholesalers working with LMICs. Audits were conducted according to the criteria of WHO Model Quality Assurance System (MQAS, 2007). The analysis was supplemented by qualitative data from interviews with relevant stakeholders.

Compliance with MQAS was on average better in European than in African distributors. However, the most critical parameters, i.e. the capacity to select suppliers and products based on stringent quality criteria, and to re-evaluate them regularly, tend to be limited in both groups. Qualitative data indicate that political commitment is needed to invest on quality, i.e. on training/retention of qualified staff, and on measures to enhance the capacity of products selection. The regulatory environment and the market competition may negatively influence the choices of distributors.

The traditional focus on good storage/distribution practices is insufficient to ensure the quality of medicines supplied by distributors in LMICs. Financial investments and operational enhancements are needed by distributors and donors to ensure that products are selected (and not only stored) according to stringent quality standards.

DISCLOSURE Nothing to disclose.

O.LB2.005

Impact of patient education and frequent contacts on various factors responsible for poor glycemic control in Type 2 diabetes mellitus patients on high dose Insulin therapy

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METHODS AND MATERIALS The study was a prospective, interventional study. We enrolled 30 patients who required insulin >1 U/kg body weight along with metformin and/or sulfonylurea and having HbA1c >7.5. There were 3 patient visits (Week 0, 6 and 12) and 2 telephonic contacts (Week 3 and 9) over 12 weeks. A structured interview was conducted to assess reasons for uncontrolled HbA1c at baseline. It included questions about appropriate insulin usage, knowledge of diabetes (assessed using Michigan Diabetes Research and Training Centre Brief Diabetes Knowledge Test [MDRTC-DKT] Questionnaire), patient's adherence [assessed using Morisky Medication Adherence Scale (MMAS-8)] and self-care activities [assessed by Summary of Diabetes Self-Care Activities (SDSCA)]. Based on assessment a customized intervention was designed for each patient.

RESULTS Many patients reported issues related to insulin usage such as inappropriate storage, wrong injection technique, infrequent site rotation, multiple use of same syringe, use of wrong syringe, missed doses, inconsistent timing and self dose titration at baseline (16, 8, 9, 21, 4, 28, 12 and 8 respectively). Post intervention these numbers were 1, 0, 1, 4, 0 6, 2, 30 respectively. MDRTC-DKT was poor for all at baseline with a mean score of 9.90 ± 1.788 and it was good at week 12 with a mean MDRTC-DKT score of 20.07 ± 0.907. The mean MMAS-8 at baseline, week 6 and week 12 were 4.33 ± 0.994, 1.6 ± 0.498 and 1 ± 0 respectively. SDSCA questionnaire covering diet, exercise, blood sugar testing, foot care and smoking also showed consistent improvement. HbA1c value at baseline was 8.91 ± 0.207 and at week 12 it was 7.857 ± 0.366 ($P < 0.001$). The mean Fasting Blood Sugar values (mg/dl) at baseline, week six and week twelve were 180 ± 7.895, 167.6 ± 12.653 and 139.7 ± 7.415 respectively (inter group $P < 0.001$).

CONCLUSIONS At baseline the patients had poor knowledge of diabetes and its complications, patients were not following recommendations for appropriate insulin usage, and the compliance to pharmacotherapy and lifestyle changes was poor. Extensive education about diabetes and its complications, insistence on adherence and emphasizing the importance of self-care activities led to improved glycemic control in all the patients. Frequent follow up of the patients after every 3 weeks led to optimisation of both the pharmacological management as well as the lifestyle changes.

DISCLOSURE Nothing to disclose.

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The role of night clubs in urban Dar es Salaam for tuberculosis transmission: using carbon dioxide levels and re-breathed shared air to estimate airborne transmission in Tanzania

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BACKGROUND Tuberculosis (TB) caused by *Mycobacterium tuberculosis*, is an airborne disease. For transmission to occur, an uninfected individual must inhale the previously exhaled breath from an infected individual. Carbon dioxide (CO_2) as a natural tracer gas has been previously proposed to estimate the potential of airborne transmission. Dar es Salaam is one of the fastest growing cities in sub-Saharan Africa, with a rapidly growing entertainment scene of night clubs. By law, they are required to be sound proof with complete closure of all windows, and thus relying on closed air conditioning systems. We describe the risk of TB transmission in night clubs in Dar es Salaam using CO_2 levels and shared, or re-breathed air.

METHODS We used CO_2 monitors developed by the University of Cape Town, South Africa. The portable monitors measure CO_2 levels in parts per million (ppm). Volunteers (18 years and above) carried the monitors for 3–4 h, and recorded the total number of people inside the club. We calculated indoor CO_2

levels (mean and range), volumes of re-breathed air and the proportion of time spent with poor ventilation (≥1000 ppm). We also estimated the risk of TB transmission using modified Wells-Riley equations.

RESULTS There were a total of approximately 25 h of data collection inside the night clubs with approximately 1530 observations. The mean indoor CO_2 level was 2358.4 ppm, ranging from 466 to 8538 ppm while the mean outdoor CO_2 level was 431.1 ppm ranging from 382 to 496 ppm. Poor ventilation conditions were observed during a total of 19.8 (77.6%) hours of observation, with a mean re-breathed air of 0.4 l/min. The mean re-breathed air was significantly higher during Friday night than Saturday night (0.52 l/min vs. 0.28 l/min, *P*-value < 0.0001). Assuming one infectious case per 100 people and a quanta of contagion rate of 8.2/hour, we estimated the risk of TB transmission to range from 0.8% (2 h) to 1.62 % (4 h inside a night club) at mean CO_2 level of 2358.4 ppm.

CONCLUSION The high indoor CO_2 levels and high volumes of re-breathed air suggest a high TB transmission potential in night clubs in Dar es Salaam. Further studies are urgently needed which will provide the basis for evidence-based public interventions to improve the ventilation conditions in such high-risk locations.

DISCLOSURE Nothing to disclose.