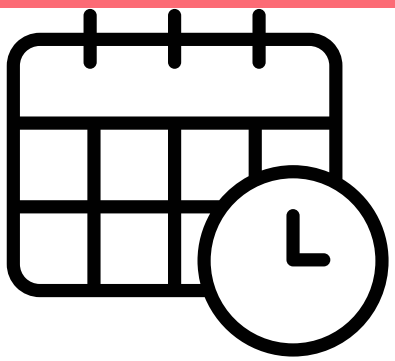
FESTMIH-NEWSLETTER 2025 Q3

WHAT TO EXPECT

November 18th-24th
World AMR Awareness Week

December 1st
World AIDS Day



Dear Readers,

Welcome to our new edition, arriving with the first days of autumn. This issue is a touch more compact than previous ones, perfect for a coffee break between conferences or a quiet evening indoors, yet we hope it remains a rewarding read.

Once again, this newsletter is only possible thanks to the collaboration of scientists and medical professionals across our community, who have helped shape and enrich its contents. This edition follows the UN Days of the fourth quarter, beginning in October. As you explore the articles, we also invite you to look ahead to our next issue, which will spotlight fresh UN Days in Q1 that we haven't featured yet.

We're especially keen on pieces that bring practice to the page: accessibility in clinics and research for World **Braille** Day (4 Jan); making care truly inclusive for **Zero Discrimination Day** (1 Mar).

Short commentaries, field notes, case vignettes, data briefs, and photo essays are all welcome—especially those that showcase concrete tools, lessons learned, or collaboration opportunities across the FESTMIH community.

If you would like to propose a piece or share news from your team, please email our secretariat at any time or feel free to reach out to me directly.

Wishing you a reflective and inspiring autumn and a strong finish to the year.

Warm regards,
Your FESTMIH Newsletter Team

CELEBRATING GLOBAL HEALTH AND EQUITY

For your convenience, please find below a brief **overview** of the International days. Should you be interested in **reading more** on the topic, you are welcome to **follow the link** (Click on the titel) to the corresponding article.

World AMR Awareness Week – 18–24 November

From reserve antibiotics to real-world stewardship

AMR is already costing lives and money at scale—an estimated 1.27 million deaths directly (4.95 million associated) in 2019, with ~1 in 6 bacteremic infections resistant globally and hotspots far higher. Our interview with Dr Ahmad Hussen Tareq turns statistics into bedside rules: when CRE/CRAB sepsis is likely and shock or organ dysfunction criteria are met, start a Reserve agent only after drawing cultures/rapid panels, with ID pre-authorisation, weight-based dosing/TDM, and a hard 48–72 h stop/de-escalation review; no prophylaxis or use in stable, uncomplicated infections. Ward-level levers from Ethiopia—pre-authorisation, "cultures-first," narrower empiric menus, and documentation/audit—worked despite limited lab capacity; sensitive indicators included blood-culture yield, carbapenem DOT and DDD/1,000 patient-days. A UN pilot showed how local co-financing + uptime SLAs and in-country production of discs/media can 2–5× AST throughput and feed dashboards that link use to de-escalation. Education matters: a WHO pilot in four Ethiopian medical schools found audit tasks best predicted better prescribing, with a clear AFRO scale-up path. Economics seal the case: a modest stewardship/diagnostics bundle outperforms uncontrolled Reserve access over 1–10 years; biggest cost drivers are ICU days, drug/diagnostic spend, and mortality, arguing for tiered pooled procurement, ID consults, audit-feedback, stop-orders, and multi-year financing. Finally, One-Health signals (wastewater/abattoir) remain underused—adding antibiotic-residue monitoring could move policy and formularies.

World AIDS Day – 1 December

Twice-yearly PrEP to close the prevention gap

HIV remains unevenly controlled: 40.8 million people live with HIV, 1.3 million were newly infected in 2024, and young women shoulder a disproportionate burden—4,000 AGYW infected each week (≈3,300 in sub-Saharan Africa). PURPOSE-1, a phase-3 trial in 5,338 AGYW in South Africa/Uganda, compared twice-yearly lenacapavir with daily oral F/TAF and F/TDF, using a WHO-endorsed background-incidence counterfactual. Result: 0 infections on lenacapavir (IRR 0.00 vs background and vs F/TDF; P<0.001), while pill-based arms tracked background—an adherence story, not a drug-efficacy failure. Safety was reassuring; injection-site nodules were common but mild, and >500 pregnancies showed no new signals. Programmatically, the message is choice and equity: integrate twice-yearly PrEP into SRH/FP/antenatal services, pair with STI screening, counsel for ISRs, and design financing so marginalised AGYW can actually access it. Data to dignity: two injections a year can convert "possible" prevention into practical prevention for those at highest risk.

WORLD AMR AWARENESS WEEK 2025

NOVEMBER 18TH-24TH

This issue we speak with Dr. Ahmad Hussen Tareq, a gold-medalist Pharm.D and PhD in antimicrobial resistance whose career bridges discovery science and health-system delivery. Our guest has led projects from bench to bedside—co-developing platforms for next-generation antibiotics (including teixobactin candidates) and engineering ultra-potent glycopeptide derivatives of vancomycin—while also advancing rapid mass-spectrometric workflows for microbial diagnostics, pharmacokinetics and pharmacodynamics. He advises a low- and middle-income country health ministry on AMR, communicable diseases and International Health Regulations, and has contributed to Clinical and Laboratory Standards Institute (CLSI) module development.

Beyond the lab, he has collaborated with MIT and Singapore's innovation ecosystem, trained clinicians and researchers across Africa and Asia, and convened international networks connecting thousands of scientists. His recent work focuses on practical stewardship in constrained settings—linking diagnostics to prescribing, building curricula that shift bedside decisions, and designing financing/procurement models that make stewardship stick. In the conversation that follows, he shares field-tested decision rules for Reserve antibiotics, ward-level levers that changed practice in Ethiopia, which competencies truly predict better prescribing, and how economics and One Health signals can steer formularies toward safer, more sustainable use.

- Burden: In 2019, bacterial AMR caused an estimated 1.27 million deaths and was associated with 4.95 million deaths worldwide.
- Current trend: WHO's latest GLASS analysis indicates ~1 in 6 lab-confirmed bacterial infections are now resistant; in SE Asia and the Eastern Mediterranean it's ~1 in 3. Some African settings report >70% resistance to first-line therapy for selected bloodstream infections.
- Economics: Unchecked AMR could trim up to 3.8% of global GDP annually by 2050 and push ~28 million people into poverty.
- Drug pipeline: Innovation remains thin—of 32 antibiotics aimed at WHO priority pathogens, only 12 are considered innovative; just 4 target at least one WHO "critical" pathogen.
- Environment matters: The UNEP One-Health review shows polluted wastewater, pharmaceutical effluents, agriculture, and poor waste management are key environmental drivers of AMR spread.
- Vaccines help: Better use of existing and new vaccines could avert ~2.5 billion antibiotic daily doses each year (≈22% reduction).
- Stewardship target (AWaRe): WHO's goal is ≥60% of national antibiotic use from Access antibiotics to curb resistance and preserve Watch/Reserve options.

AMR-INTERVIEW

Reserve antibiotics in systems without stewardship (decision rule)
A district hospital without routine AST and with a nascent stewardship team presents with a patient likely to have CRE/CRAB bacteraemia. Under what specific conditions would you prescribe an AWaRe Reserve agent (e.g., colistin, cefiderocol, ceftazidime–avibactam)? Please indicate the minimum safeguards you consider mandatory—blood cultures ± rapid panels, pre-authorisation with ID consult, dosing/TDM, and a 48–72-hour stop/de-escalation review—as well as your red lines given selection risks (e.g., mcr-1, carbapenemases).

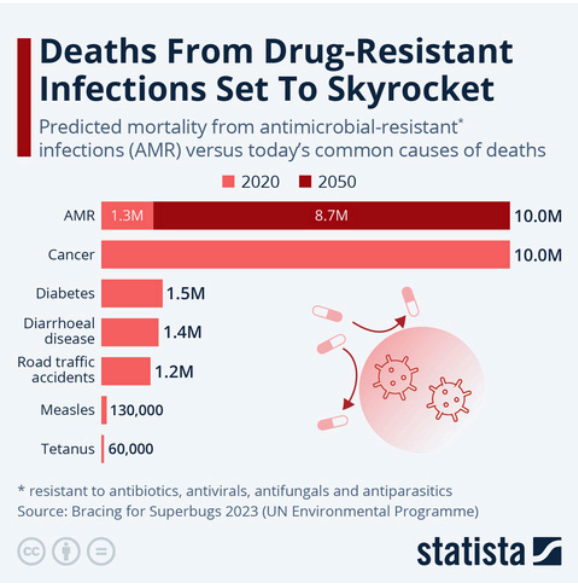
Patient likely to have CRE/CRAB bacteraemia, it could be life threatening situation, most likely the AWaRe Reserve agent will be used, the clinician along with team of experts, including the senior expert share notes and believes that

1. high probably of CRE/CRAB bacteraemia with high grade fever, previous history of CRE/CRAB or any indication that carbapenem is not working.
2. the criteria for sepsis shock/clinical sepsis syndrome or organ dysfunction is met that includes BP, blood lactate condition, oxygen saturation deranged numbers.
3. Patient is resistant to tertracylines and carbanpenem and decides to proceed with Reserve agent as time is short and patient can die.

In this situation the minimum safeguard to consider includes

1. Getting blood culture samples or other culture samples before starting the antibiotic therapy from the patient.
2. The decision is taken with group of physicians including the senior most physician and include the nascent stewardship team in the process, ensuring detailed documentation of all steps
3. Having a clear dose, duration and de-escalation plan that starting the Reserve agent now, once the patient situation improves can it be moved to narrow spectrum antibiotic, for this decision, ideally culture tests and other lab test results are important.

Generally the red line involves using Reserve agents for prophylaxis resistant infection treatment or the scenario where patient is stable, no risk of sepsis or hemodynamic crash and patient is having uncomplicated infection which can be managed with antibiotic other than reserve category antibiotics.



Antimicrobial resistance (AMR) could rival today's top killers by 2050.

Global deaths linked to drug-resistant infections are projected to rise from ~1.3 million (2020) to ~10 million per year by 2050, approaching current annual cancer deaths. For context, today's deaths from diabetes (~1.5M), diarrhoeal disease (~1.4M) and road traffic injuries (~1.2M) are lower.

AMR-INTERVIEW

AMR integrated into emergency response and primary care (Ethiopia)
Ethiopia has integrated AMR into sepsis bundles, outbreak guidelines, and primary health-care protocols. Which ward-level changes mattered most (order sets, “cultures-first” routines, narrow empiric menus, automatic stop orders)? Which indicators proved most sensitive during surge periods—time-to-first-antibiotic, blood-culture yield, carbapenem DOT per 1,000 patient-days, total antibacterial DDD per 1,000 patient-days, de-escalation rate—and what changed once these protocols were introduced?

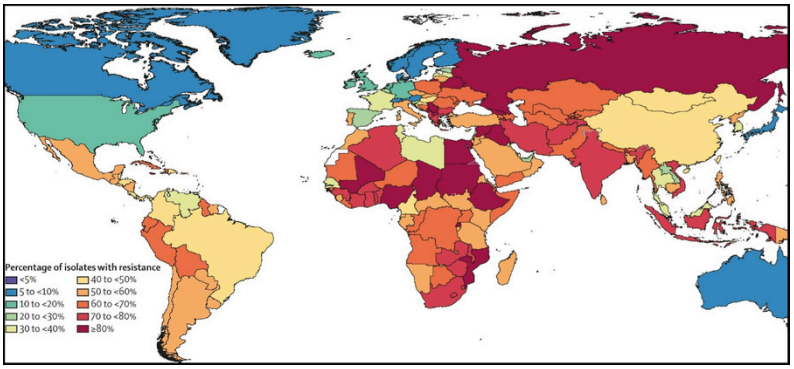
Ethiopia has integrated AMR in health sector transformation plan (national guidelines), health emergency response, primary healthcare response plan and their guidelines. Some hospital has prepared hospital antimicrobial use policy at health facility level to support ward level changes.
Ward level changes focus on preauthorization(infancy stage) for reserve category antibiotics, sometime retrospective feedback(infancy stage), usually narrow empiric therapy utilization, culture first and utilization of antibiogram. However there are many practical challenges, Ethiopia has more than 480 health facilities hardly twenty five health facilities has functional or partially functional microbiology laboratory capacity that can perform AST culture, even fewer can perform blood culture testing capacity with no sustainable supply chain of diagnostics supplies.
Ward level changes that mattered most are the implementation of preauthorization(infancy) in yekatit-12 hospitals, documentation of case discussion post consultation with ID and retrospective audit approach with an trained pharmacist team though at infancy but starting at major tertiary hospitals. They create more impact specially when they are sync with regular IPC standards as conducted in yekatit-12 hospital. The severe limitation of diagnostics supplies and limited medication options often force physicians to rapidly adapt and make the best use of available antimicrobial supplies with minimum and sometime without diagnostic support.
There are some indicators are more sensitive during surge period. Blood culture yield is one of the sensitive indicators but due to limited resources it’s a challenge. Recently health facilities in Ethiopia started capacity building to measure carbapenem DOT per 1,000 patient-days and total antibacterial DDD per 1,000 patient-days. As it is not contingent on supplies rather then record keeping, and it is considered more feasible, at this moment around 80 health facilities were trained in measuring their antibacterial DDD/1000 patient days. Two of them started to report their DDD/1000 patient days data more actively. Once these changes were introduced, the will to practically implement stewardship became more active. For routine treatment WATCH category antimicrobials were use, trend to use culture test more actively and documentation with preauthorization for Reserve category antibiotics. This trend was observed in two pilot hopsitals (yekatit-12 hospital and Jimma university hospital).

AMR-INTERVIEW

Workforce and curriculum: from pilot to measurable competence
You led the WHO pilot embedding AMR in undergraduate and in-service curricula. One year post-completion, which competencies and assessments (e.g., OSCE items, case-based prescribing, audit tasks) best predict improved antibiotic decisions? What is your scale-up plan for WHO African Region (AFRO) Member States, including governance, faculty development, and outcome measurement?

I lead WHO first global pilot of AMR medical education tool in the undergraduate curricula of four medical universities in Ethiopia. The pilot was conducted to allow both onsite and online implementation. In first stage, the medical teaching institute conducts their existing curricula review against the given checklist, identify gaps indicated by the tool. Address those gaps in lieu of national government medical council regulation, either those missing topics can be introduced as part of revised/updated undergraduate medical curricula or it could be attached with existing curricula as an additional trainings/webinars/workshops. For In-service training, the professional health associations will utilized to incorporate more advanced skill based training a part of their continuous professional development.
In terms of competencies and assessments best predicted to improve antibiotic decision, audit tasks were found to be more impactful followed by case based prescribing.
The scale-up plan for WHO AFRO (African Region member states) including engaging the teaching medical universities in AFRO region through WHO AFRO regional office as first step, encourage them to conduct their local curricula evaluation using WHO AMR education tool. The self explanatory tool can be utilized well by institutes. Then national WHO country office can support them in its implementation; and simultaneously universities in Ethiopia which were part of first global pilot can be connected to other universities through WHO offices to help them in implementation of AMR education pilot tool, including gap identification and deploying right interventions that suit local context.

This world map shows the estimated share of K. pneumoniae isolates that were resistant to third-generation cephalosporins (3GCs, e.g., ceftriaxone/cefotaxime/ceftazidime). High values (red–purple, ≥70–80%) cluster across parts of South Asia and West/Central Africa and extend through some countries of Eastern Europe/Russia; lower values (<10–20%, blue–teal) are seen in Scandinavia, Canada, Australia and Japan.Why it matters: 3GC resistance in K. pneumoniae is a practical proxy for ESBL/AmpC producers—pathogens that drive neonatal sepsis and hospital outbreaks and force escalation to carbapenems, accelerating CRE pressure. Where map colors are orange–purple (≥40%), empiric therapy for severe sepsis often needs carbapenem-sparing strategies plus rapid cultures and early de-escalation;



Where colors are blue–green, narrow empiric menus remain feasible.
Caveats: These are 2019 estimates compiled from heterogeneous datasets (sentinel hospitals, surveillance systems). Several LMICs have sparse microbiology capacity; case mix and sampling differ by country. Always interpret alongside your local antibiogram and GLASS data.

Source: *Lancet/GRAM analysis; "Third-generation cephalosporin-resistant K. pneumoniae (2019)".*

AMR-INTERVIEW

Diagnostics sustainability: maintaining services post-pilot
Your UN innovation pilot in Ethiopia focused on diagnostic sustainability. Which procurement/financing model actually maintained service (reagent rental vs. local co-financing, service-level agreements with uptime clauses)? How did you link utilisation data to stewardship (dashboards, antibiotic time-outs), and what was the effect on empiric broad-spectrum starts and 72-hour de-escalation?

The UN innovation pilot in Ethiopia was focused on locally producing antibiotic disc, specialized media at the research labs in medical university, deploying requisite quality control measures to ensure accuracy and standardization, and encourage its utilization at clinical labs in the hospitals to increase the local AST and culture test capacity atleast 2X to 5X. It will enable clinical labs to conduct culture tests as per patient need.
The model was based on local co-financing with service level agreements with suppliers in local currency ONLY. In many cases, previous failures in Ethiopia and other Low middle income country have this limitation of foreign exchange to avail services. In this arrangement, focused is to work with partners where the maintaining services or supplies is not dependent on USD/Euro/GBP and actively work with local pharmaceutical industry who imports their pharmaceutical raw material in bulk. Moreover, this approach will support sustainability in supply chain of raw material.
The utilization data to stewardship is related first with generating the required surveillance information, including preparing antibiogram specific to health facilities. Majority of health facilities across Ethiopia, including those trained with implementation of Antimicrobial stewardship response, often have limited or no diagnostic capacity. One of the hospital with functional AMR surveillance response also enrolled with AMS program has developed a dashboard synching surveillance and stewardship data. The plan is to further refine that dashboard to improve empiric broad spectrum start and 72 hours de-escalation which is done manually with limited information. Usually the biggest limitation in health facilities is implementing AMS without microbiology lab infrastructure.
UN innovation pilot core was to empower health facilities to conduct diagnostics test on their own as per patient need. Create local antibiograms, enable narrower empirical treatment and improve the surveillance quality, capacity and coverage leading to utilization of surveillance data and then its synchronization with stewardship data.

AMR-INTERVIEW

Economics to steer procurement and stewardship (Pakistan + tool)
Using only published ranges and your Pakistan costing tool at a high level: how does the 1-, 5-, and 10-year budget picture compare between

1. uncontrolled access to AWaRe Reserve agents (no pre-authorisation, limited AST) and
2. a modest stewardship/diagnostics bundle (ID consults, audit-feedback, blood cultures/rapid tests, stop orders)?

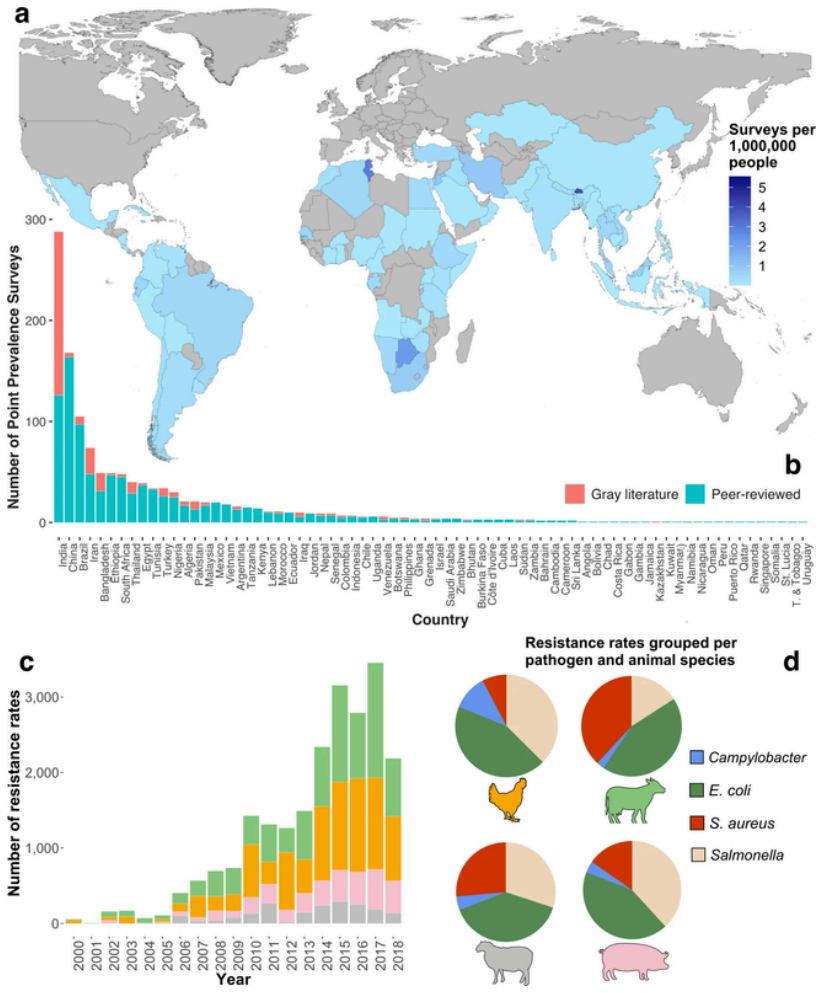
Which cost drivers dominate (LOS, ICU days, drug spend, mortality/DALYs), under what assumptions does (B) become cost-saving or at least cost-effective, and how should that translate into procurement/formulary decisions (tiered access, conditional tenders) and multi-year financing?

The tool we developed to measure the economic burden of AMR reveals that often the economic burden of AMR at national level is massive, sometime equivalent to national health budget of the low middle income country. Many countries are in the process to revise their national action plans with proposed budget. As most countries are unaware about their AMR economic burden, their NAP proposed budget could be understated from 1/100 to 1/1000 of their AMR economic burden.
If we compare the budget picture from today to next 10 years considering two scenarios, in lieu of our study

1. first scenario where business is as usual with uncontrolled access to AWaRe Reserve agent (no pre-authorisation, limited AST, no audit-feedback),
2. the second scenario with modest stewardship/diagnostic bundle (ID consults, audit-feedback, blood culture/rapid test, stop orders)

due to lot of variable factors its difficult to determine the precise cost and impact for above given scenario, considering extremely insufficient data, in WHO GLASS Pakistan reports AMR surveillance data from around 2% of 1280 public sectors hospitals. Generally we found that an infection treatable with 1st and 2nd line antibiotics, termed it as susceptible infection could cost between (50-150$), the AMR infection could be moderate (non-ICU case) or severe (ICU case) and it can cost between (200$ to 3000$) or more. If we look at the direct cost due to AMR in context of Pakistan, presently assuming 1 million non-fatal AMR infections in-patient cases, it burdens the national exchequers with an additional US$770 million, if the 2nd scenario that involves modest stewardship/diagnostic bundle would be in practice in 1280 public and other private health facilities, this additional cost of US$770 million would be close to negligible.
While analyzing cost drivers that dominate the cost. While considering direct cost in context of public and private sector, ICU days, cost of diagnostics and medicine play a leading role. In Pakistan, the out of pocket expenditure is around 60% of total healthcare expenditure, cost of medicine and diagnostics is long term factor burdening household for moderate infections and number of days in ICU in addition to medicine and diagnostics that became the leading cost factor for severe infection, often straining households to catastrophic healthcare expenditures. While looking at Indirect cost, premature mortality is the leading cost driver for indirect cost.

If we look from the perspective of procurement/formulary decision and health financing, a tiered pooled procurement of medicine (ACCESS and WATCH category antibiotics and diagnostics), synced with social health protection system/multilayered financing, combined with requirement for hospitals to implement IPC/AMS program, audit-feedback/preauthorization, ID team consultation can make whole program cost effective and can reduce the excess AMR cost significantly. Taking similar measure is the only viable sustainable solution to address AMR, else the health system and economic impact in case of AMR outbreak would be more far devastating then COVID-19. As per reports, incase the AMR response donot improves the AMR economic burden could easily double in coming 5 to 10 years, further straining health system and economy.
Further more, if we look at the capacity of private healthcare sector, some of the health facilities have effectively implemented stewardship-diagnostic bundle, ID consultation, audit/feedback, blood and AST cultures in routine practice, and have acquired international JCI accreditation certifications. Some health facilities routinely conduct DDD/1000 patient day calculation very often and its part of their practice as well. Some of the health facilities have implemented pooled procurement system for medicine and diagnostics, synced with multiyear financing system that has an additional angle of charity based sponsorship to reduce the out of pocket expenditure impact on households.



Criscuolo, N. G., Pires, J., Zhao, C. & Van Boeckel, T. P. resistancebank.org, an open-access repository for surveys of antimicrobial resistance in animals. Sci Data 8, 189 (2021).

This four-panel graphic from the resistancebank.org paper visualizes the evidence base behind antimicrobial resistance (AMR) in animals across low- and middle-income countries (LMICs), 2000–2019. Panel a maps where point-prevalence surveys were done—dense activity in South Asia and parts of Africa, but large data gaps elsewhere. Panel b shows that just a handful of countries (e.g., India, China, Brazil, Iran) contribute most surveys, with a notable share coming from grey literature. Panel c charts a sharp rise in reported resistance rates over the last decade, driven mainly by poultry and cattle studies. Panel d highlights which pathogens dominate the dataset—chiefly E. coli and Salmonella, with fewer data for Campylobacter. The takeaway: AMR surveillance in livestock is growing but uneven; resistancebank.org helps centralize these scattered data to guide one-health policy and targeted stewardship.

AMR-INTERVIEW

One Health signals that change human prescribing
Please cite two instances where non-human surveillance (animal colistin use, abattoir/wastewater resistome data, residue monitoring) directly led to changes in human clinical guidance or national formulary decisions. What data cadence, attribution approach, and accountability mechanisms were required for clinicians and policymakers to act on those signals?

Non-human surveillance of waste water is conducted at national level to identify the presence of polio strain virus, at this moment the environmental samples are not analysed for colistin, other antibiotics in Pakistan as part of government response. The environmental samples are analyzed, wastewater resistome data is also collected to a limited extent as a part of research activity by academia. However there is a very strong need for it, as colistin and other reserve category antibiotics are easily available in pharmacies and often used without involvement of certified practitioner.

As of now, there is hardly an example of non-human surveillance leading to change in human clinical guidance or national formulary decision.
First the sensitization of the government is required to drive change in the direction of reducing the consumption of colistin and other reserve category antibiotics. To sensitize the government at highest level, the economic burden of AMR in Pakistan report is compiled and policy brief will be shared to trigger that change.
One of the thing in consideration is to include the analysis of antibiotics among the environmental samples collected, to have baseline of those signals for policy makers and clinicians to respond.
So far, the accountability mechanism is proposing to strengthen the capacity of health facilities and public health labs across the country to actively report AMR surveillance and stewardship data. Another approach closely synced with supply chain that are the public health labs and health facilities have minimum supplies to measure antibiotic traces in various samples, and how to ensure sustainable supply of these necessary items for continuity of standardized response.

Be Part of the Next FESTMIH Newsletter!
Celebrate global health by contributing to our Q4 2025 Edition!

Choose a **UN Day topic** in Q1 and send articles, project summaries, or inspiring stories to our E-Mail.

Deadline: 30.11.2025

WORLD AIDS DAY

A detailed analysis of twice-yearly Lenacapavir for PrEP, its context within the global HIV epidemic, and its implications for frontline health programs.

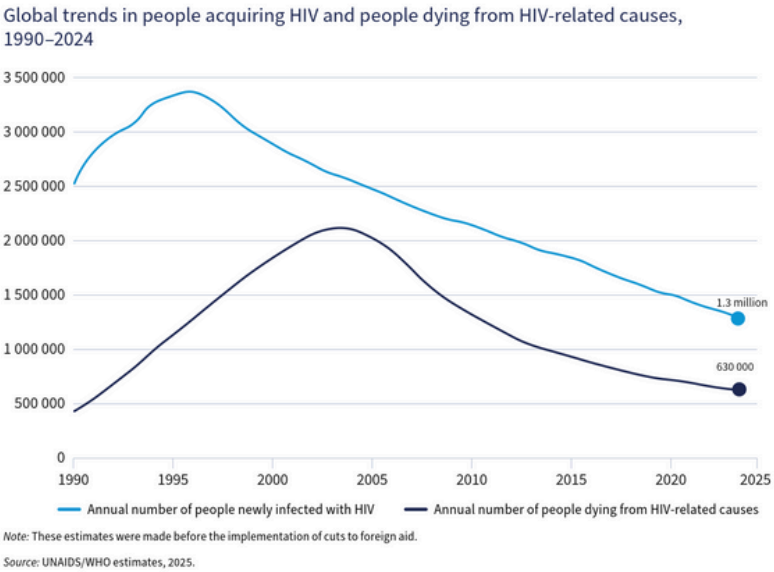
The Global Context: A Persistent Epidemic and a Critical Prevention Gap

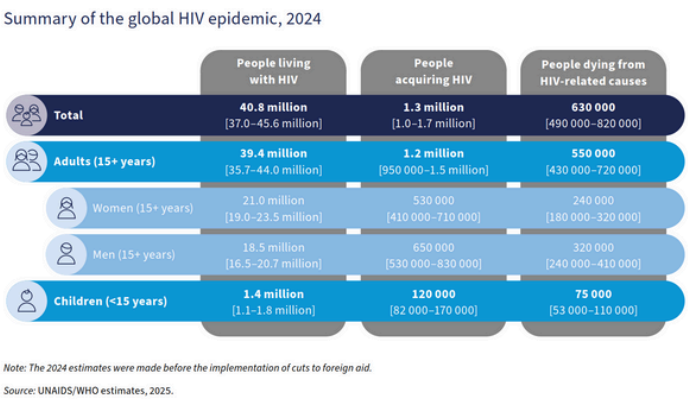
The global HIV landscape in 2024/2025 is a study in stark contrasts. Decades of research have yielded highly effective tools for both treatment and prevention, yet the world is falling short of its targets. The latest UNAIDS Global HIV Statistics paint a sobering picture: despite significant progress, the epidemic remains a formidable public health challenge, with women and girls continuing to bear a disproportionate burden. Understanding this context is essential to appreciating the potential impact of new prevention technologies.

At a Glance: The Global HIV Epidemic in 2024

(Source: UNAIDS Fact Sheet 2025)

- People Living with HIV: 40.8 million people globally are living with HIV.
  - 53% of whom are women and girls.
- New Infections: 1.3 million people were newly infected with HIV in 2024.
  - 45% of all new infections occurred in women and girls.
  - In sub-Saharan Africa, this rises to 63% of all new infections.
- AIDS-Related Deaths: 630,000 people died from AIDS-related illnesses in 2024, a 70% reduction since the peak in 2004, but still a staggering loss of life.
- Treatment Coverage (ART):
  - 77% of all people living with HIV were accessing ART.
  - 83% of adult women (15+) were on ART, compared to 73% of adult men.
  - 84% of pregnant women received ART to prevent vertical transmission.
  - Only 55% of children (0–14 years) were accessing treatment, a critical gap.





HIV data and statistics. Buchholz, Katharina. „Infographic: World Split on Breast vs. Bottle Feeding“. Statista Daily Data, 6. August 2024. https://www.statista.com/chart/32791/infants-aged-0-5-months-exclusively-brestfed.

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Global HIV trends, 1990–2024. New infections have fallen from >3 million in the mid-1990s to ~1.3 million in 2024, and AIDS-related deaths from just over 2 million in the mid-2000s to ~630 000. Yet 40.8 million people were living with HIV in 2024 (39.4 million adults; 1.4 million children). Note: 2024 figures were estimated before recent foreign-aid cuts. Source: UNAIDS/WHO, 2025.

While global ART coverage continues to improve, bringing the world closer to the 95–95–95 targets, prevention remains a persistent weak link, especially for adolescent girls and young women (AGYW). Every week in 2024, 4,000 AGYW aged 15–24 years became infected with HIV, with 3,300 of these infections occurring in sub-Saharan Africa [cite: UNAIDS]. This highlights a crucial programmatic failure: the existing prevention options are not adequately meeting the needs of this key population.

The leading tool for biomedical prevention, daily oral pre-exposure prophylaxis (PrEP), has proven highly effective when taken as prescribed. However, as the introduction to the recent PURPOSE-1 trial in the New England Journal of Medicine states plainly, "women's uptake of, adherence to, and persistence in the use of PrEP remains limited worldwide" [cite: NEJM]. The reasons are multifaceted and include pill fatigue, stigma, privacy concerns, and the simple logistical challenge of maintaining a daily medication regimen.

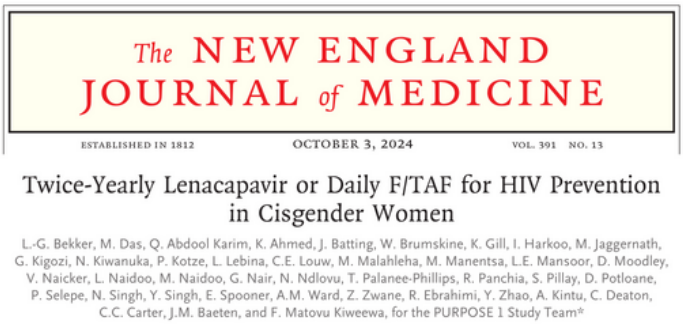
This long-standing adherence challenge is the driving force behind the development of long-acting prevention methods. A truly effective prevention tool must not only be biologically potent but also align with the lived realities of the people it is designed to protect. It is against this backdrop of urgent need that the results of the PURPOSE-1 trial, evaluating the twice-yearly injectable lenacapavir, have been met with such anticipation.

The PURPOSE-1 Trial: Design and Landmark Efficacy Findings

Published in the New England Journal of Medicine, the PURPOSE-1 study was a phase 3, double-blind, randomized, active-controlled trial designed to evaluate the safety and efficacy of a novel HIV prevention option for cisgender women [cite: NEJM].

Trial Design

The trial enrolled 5,338 HIV-negative adolescent girls and young women (ages 16–25) across 28 sites in South Africa and Uganda—regions with high background HIV incidence. The design was innovative and tailored to the ethical complexities of modern PrEP trials:


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 3, 2024 VOL. 391 NO. 13

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. Carter, J.M. Baeten, and F. Matovu Kiweewa, for the PURPOSE 1 Study Team*

- Randomization: Participants were assigned in a 2:2:1 ratio to one of three arms:
  a. Lenacapavir: A subcutaneous injection every 26 weeks.
  b. Daily Oral F/TAF (emtricitabine–tenofovir alafenamide).
  c. Daily Oral F/TDF (emtricitabine–tenofovir disoproxil fumarate), serving as the active control.
- Blinding: To maintain the double-blind design, participants in the injectable arm received daily placebo pills, and those in the oral arms received placebo injections.
- Counterfactual Incidence: Crucially, the trial did not include a true placebo group, as it would be unethical to deny participants access to proven PrEP. Instead, investigators estimated a "background HIV incidence" from the broader population of over 8,000 women screened for the trial. This was achieved using a WHO-endorsed recency-assay method, providing a robust and ethical benchmark to measure the true efficacy of the interventions.

Study Population: High Risk, High Relevance

The trial's strength lies in its recruitment of precisely the population most in need of new prevention options. The median age was 21 years. The study confirmed the high-risk environment: during follow-up, the incidence of curable STIs (chlamydia, gonorrhea, or trichomoniasis) was exceptionally high across all arms, at approximately 48–51 cases per 100 person-years. This finding underscores that the risk of HIV exposure in these communities is frequent and real, not merely theoretical.

Group	Participants (n)	HIV Infections (n)	Incidence per 100 Person-Years (95% CI)
Lenacapavir	2,134	**0**	**0.00** (0.00–0.19)
Daily F/TAF	2,136	**39**	**2.02** (1.44–2.76)
Daily F/TDF	1,068	**16**	**1.69** (0.96–2.74)
Background Incidence	*8,094*	*N/A*	*2.41 (1.82–3.19)*

Primary Efficacy Findings: An Unambiguous Result

At a planned interim analysis, the results were so clear that the trial's independent data monitoring committee recommended unblinding the study early. A total of 55 new HIV infections were observed.

The conclusion was unequivocal: zero infections occurred in the lenacapavir group.

Compared to the estimated background incidence of 2.41 cases per 100 person-years, lenacapavir demonstrated 100% efficacy in preventing HIV (Incidence Rate Ratio [IRR] 0.00; P<0.001). It was also statistically superior to the active control, daily oral F/TDF (IRR 0.00; P<0.001).

Interpreting the Results: The Critical Role of Adherence and Safety

The headline result of zero infections with lenacapavir is powerful, but a deeper look at the data from the oral PrEP arms provides an equally important lesson for public health programs: the profound impact of adherence.

The Adherence Story: Why Daily Oral PrEP Underperformed

The HIV incidence rates in the F/TAF and F/TDF arms (2.02 and 1.69 per 100 person-years, respectively) were not significantly different from the background incidence. This was not a failure of the drugs themselves. A pharmacological sub-study of a random 10% of participants revealed that adherence to the daily pills was low and decreased over time.

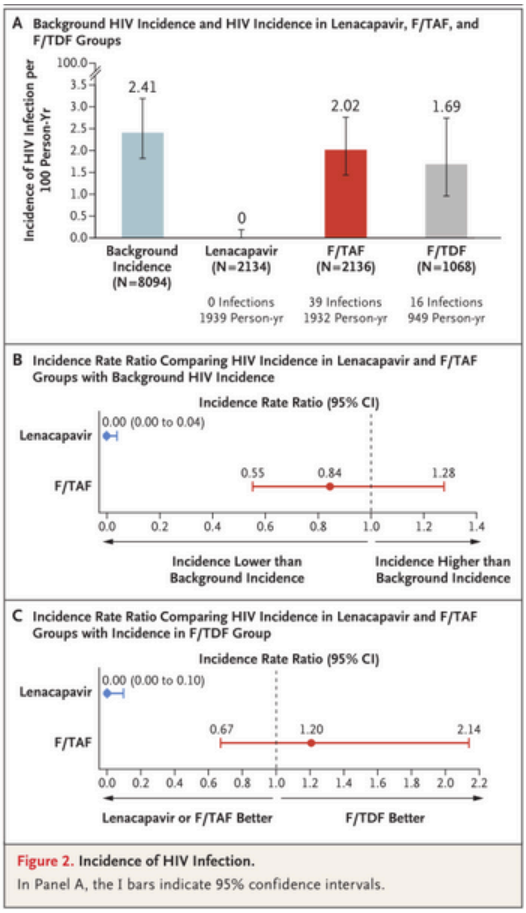


Figure 2. Incidence of HIV Infection.
In Panel A, the I bars indicate 95% confidence intervals.

PURPOSE-1 HIV incidence and relative risk. Panel A visualizes absolute incidence in the screened background cohort versus each trial arm; Panels B–C show incidence-rate ratios with 95% CIs. No infections were observed with twice-yearly lenacapavir, which was significantly lower than both background incidence and F/TDF. F/TAF was not significantly different from background and showed no meaningful difference versus F/TDF. Note: a direct statistical test of F/TDF versus background was not reported; background incidence was estimated from the screened cohort using a recency-assay algorithm.

A matched case-control analysis within the F/TAF arm confirmed this: most women who acquired HIV had low or undetectable levels of tenofovir in their blood. Conversely, medium or high adherence was associated with ~90% lower odds of infection.

This finding is the crux of the matter: daily oral PrEP is highly effective, but only if it is taken consistently. The superior performance of lenacapavir in this trial was not due to greater biological potency but to its long-acting formulation, which removes the burden of daily adherence. The value proposition of lenacapavir is simple: for many, remembering two injections a year is far more achievable than remembering to take a pill every single day.

Safety and Tolerability Profile

The overall safety profile of lenacapavir was favorable, with no new safety concerns identified.

- Adverse Events: The rates of grade ≥3 adverse events were low and similar across all three groups (around 4–5%). No deaths were attributed to any of the study drugs. Notably, nausea and vomiting were less frequent in the lenacapavir group compared to the oral PrEP groups.
- Injection-Site Reactions (ISRs): The most common events associated with lenacapavir were ISRs, reported by 68.8% of participants at some point. These were overwhelmingly mild-to-moderate nodules under the skin that typically decreased in frequency and size with subsequent doses. Crucially, these reactions were well-tolerated, with only 0.2% of participants discontinuing the drug due to an ISR.
- Pregnancy and Breastfeeding: The trial design commendably allowed participants who became pregnant to continue the study. A total of 510 pregnancies occurred during follow-up. Interim analyses showed no safety signals for lenacapavir, with outcomes broadly consistent with expectations for this population. This is a critical piece of data for real-world implementation in women of reproductive age, though dedicated follow-up is ongoing.

Programmatic Implications and Critical Appraisal

The results of PURPOSE-1 are not just a scientific success; they represent a potential paradigm shift for HIV prevention programs worldwide. Translating this clinical trial efficacy into real-world impact will require careful planning and a commitment to equity.

Implications for HIV Prevention Programs

For health ministries, NGOs, and frontline providers, the key considerations for a future rollout of lenacapavir include:

1. A Focus on Choice: The trial reinforces that a one-size-fits-all approach to PrEP is ineffective. The goal should be to build a "choice architecture" where women can select the method that best fits their life circumstances—be it a daily pill or a twice-yearly injection. Programs should be prepared to offer multiple options, not ultimatums.
2. Integrated Delivery Models: Twice-yearly injections are well-suited for integration into existing health services. Linking PrEP delivery to routine sexual and reproductive health (SRH) clinics, family planning services, and antenatal care could increase uptake, reduce stigma, and minimize travel burdens for clients. Given the high STI rates in the trial, pairing PrEP visits with STI screening and treatment is a clear opportunity for synergistic public health impact.
3. Counseling and Monitoring: While ISRs were well-tolerated, effective counseling will be key to managing patient expectations. Clients should be informed that mild, temporary nodules at the injection site are common and tend to diminish over time. Programs should develop clear protocols for monitoring ISRs to build patient and provider confidence.
4. Equity-Driven Rollout: New, premium health products often exacerbate inequities, becoming available only to those who can afford them or who live in urban centers. As planning for lenacapavir begins, a deliberate focus on equity is paramount. Donors and national programs must ensure that this highly effective option reaches the very populations who were centered in the trial: marginalized adolescent girls and young women in high-burden settings.

From Data to Dignity

The UNAIDS data shows us where HIV prevention is failing. The PURPOSE-1 trial shows us a powerful new tool to address that failure. For the millions of young women who face a substantial risk of acquiring HIV, an option that requires action only twice a year could be the difference between prevention being a theoretical possibility and a practical reality.

The message for our community is clear: we must advocate for and prepare for the introduction of new, user-friendly prevention technologies. By centering patient choice, integrating services, and demanding equitable access, long-acting PrEP options like lenacapavir can become more than just a scientific breakthrough—they can become a cornerstone of a more just and effective global response to HIV.

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A NOTE OF GRATITUDE AND LOOKING AHEAD

Dear FESTMIH Community,

As Europe moves from the last shimmer of summer into windswept, rain-soaked days, this feels like the perfect moment to sit down with a cup of tea or coffee and dive into our new issue. I hope you've found it both engaging and useful. Especially the pieces on antimicrobial resistance (AMR) and evolving approaches to HIV prevention and care. Autumn is a busy bridge between summer leave and the winter holidays, and many of us are pushing projects forward under tight timelines. That spirit shaped this edition too: we aimed for clear, evidence-driven articles that you can put to work immediately.

A heartfelt thank-you to Dr Ahmad Hussen Tareq for a thoughtful interview that brought practice and policy together so well. Contributions like his are exactly what make this newsletter, and the FESTMIH community, so productive.

If you'd like to discuss one of your projects, showcase your expertise, or seek collaborators across borders, we'd love to hear from you. Send us a short note, a lead, or a draft; we're happy to help shape it into a feature. This exchange of ideas is what keeps our network vibrant and impactful.

Thank you for your time, your trust, and your commitment to global health. Wishing you a focused, rewarding stretch between now and December—and we look forward to featuring more of your work in the next issue.

Warm regards,
Maximilian Förster

A Quarterly Commitment to Connection

We are excited to **continue** this journey **with you**. The FESTMIH Newsletter is a **quarterly publication**, and each issue is carefully **curated around** the **United Nations International Days**, celebrating their relevance to global health and cooperation. We aim to foster a **platform** where our **community** can **share**, **learn**, and **inspire** action.

Do you have a story, project, or initiative to share? Or perhaps you know an inspiring individual or organization that deserves the spotlight? We would **love** to **hear from you**! The next edition will focus on the **UN International Days of Q1.**

To explore the **full list** of upcoming observances, visit the **UN International Days page**. If you're ready to contribute, send your ideas, articles, or summaries to our team at this **E-Mail**.

Warm regards,
The FESTMIH Newsletter Team

SOURCES

‘Antimicrobial Resistance’. n.d. Accessed 28 September 2025. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.

Bekker, Linda-Gail, Moupali Das, Quarraisha Abdool Karim, et al. 2024. ‘Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women’. New England Journal of Medicine 391 (13): 1179–92. https://doi.org/10.1056/NEJMoa2407001.

Carruthers, Tom. 2017. ‘What Are Superbugs?’ Curious, December 2. https://www.science.org.au/curious/people-medicine/what-are-superbugs.

Criscuolo, Nicola G., João Pires, Cheng Zhao, and Thomas P. Van Boeckel. 2021. ‘Resistancebank.Org, an Open-Access Repository for Surveys of Antimicrobial Resistance in Animals’. Scientific Data 8 (1): 189. https://doi.org/10.1038/s41597-021-00978-9.

Dinge Erklärt – Kurzgesagt, dir. 2019. Die Antibiotika Apokalypse Erklärt. 7:11. https://www.youtube.com/watch?v=4YsaZQzT7Z8.

‘HIV Data and Statistics’. n.d. Accessed 26 October 2025. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics.

‘Multiresistente Bakterien mit Tarnkappe’. n.d. Accessed 28 September 2025. https://www.mpg.de/12524499/mrsa-bakterien-staphylokokken-immunsystem.

Reardon, Sara. 2015. ‘Spread of Antibiotic-Resistance Gene Does Not Spell Bacterial Apocalypse — Yet’. Nature, ahead of print, December 21. https://doi.org/10.1038/nature.2015.19037.

‘Stop Using Antibiotics in Healthy Animals to Preserve Their Effectiveness’. n.d. Accessed 28 September 2025. https://www.who.int/news/item/07-11-2017-stop-using-antibiotics-in-healthy-animals-to-prevent-the-spread-of-antibiotic-resistance.