MRC-NIHR Trials Methodology Research Partnership: Webinar recording

The ILANA Study: using study recruitment targets to promote equity in clinical care for women, racially minoritised people and older people living with HIV in the UK

Presented, on behalf of the UKTMN, by:

Rosalie Hayes and Nishat Halim (Queen Mary University London)

17 April 2024

The slides are available below.

For any queries, please contact uktmn@nottingham.ac.uk

https://www.youtube.com/watch?v=DfBZrt5qwsk&feature=youtu.be

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The ILANA study: using study recruitment targets to promote equity in clinical care for women, racially minoritised people and older people living with HIV in the UK

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Clinical Trial Managers Network Seminar, 17 April 2024

Queen Mary University of London

NHS Barts Health NHS Trust

ViiV Healthcare

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PI - Prof Julie Fox

Statistician – Yuk Lam Wong

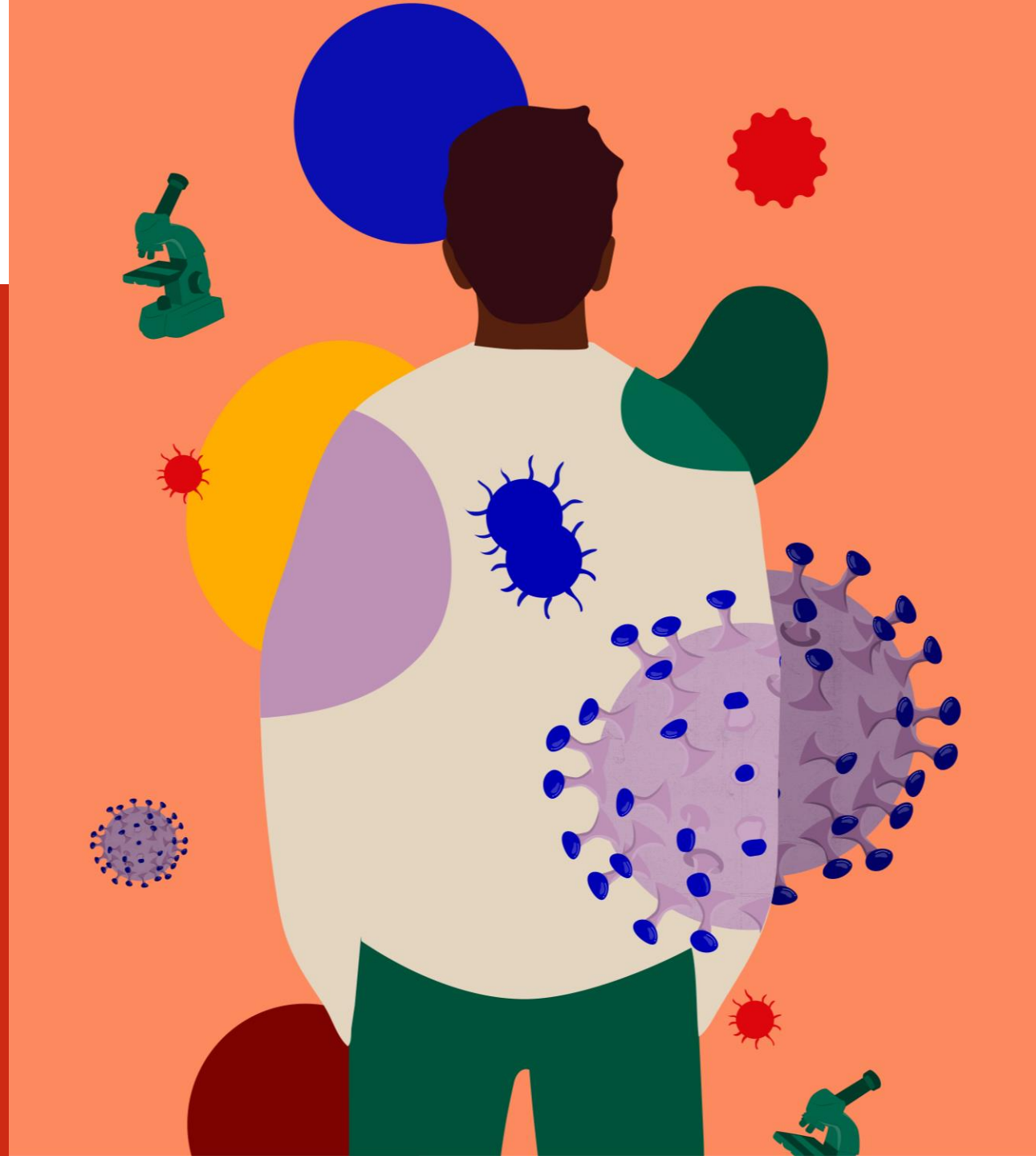
Statistician – Jo Haviland

ILANA Implementing Long-Acting Novel Antiretrovirals

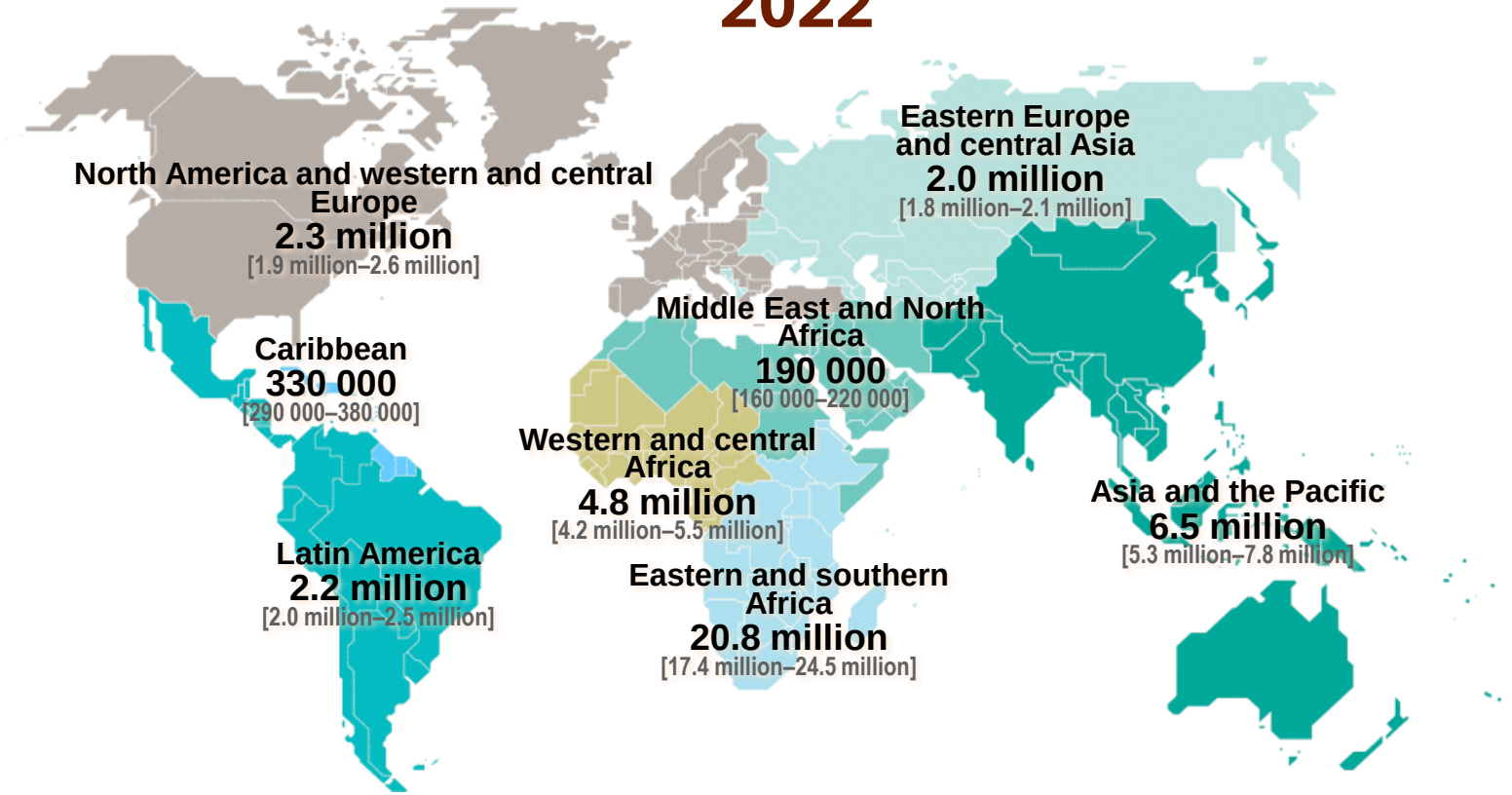
Plan for today's talk

- Background to HIV treatment
- Why inclusion matters for clinical studies
- Introducing the ILANA study
- Putting recruitment targets into practice
- Responding to challenges
- What we've achieved so far

Background to HIV treatment



Adults and children estimated to be living with HIV 2022



Total: 39.0 million [33.1 million–45.7 million]

UNAIDS (2023).

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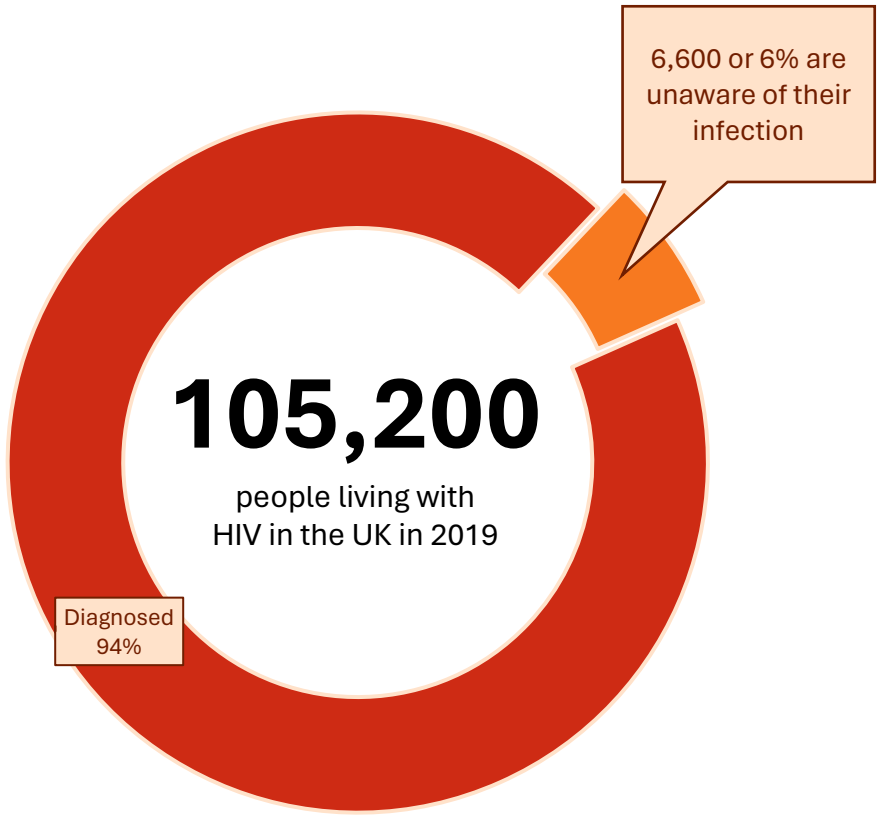
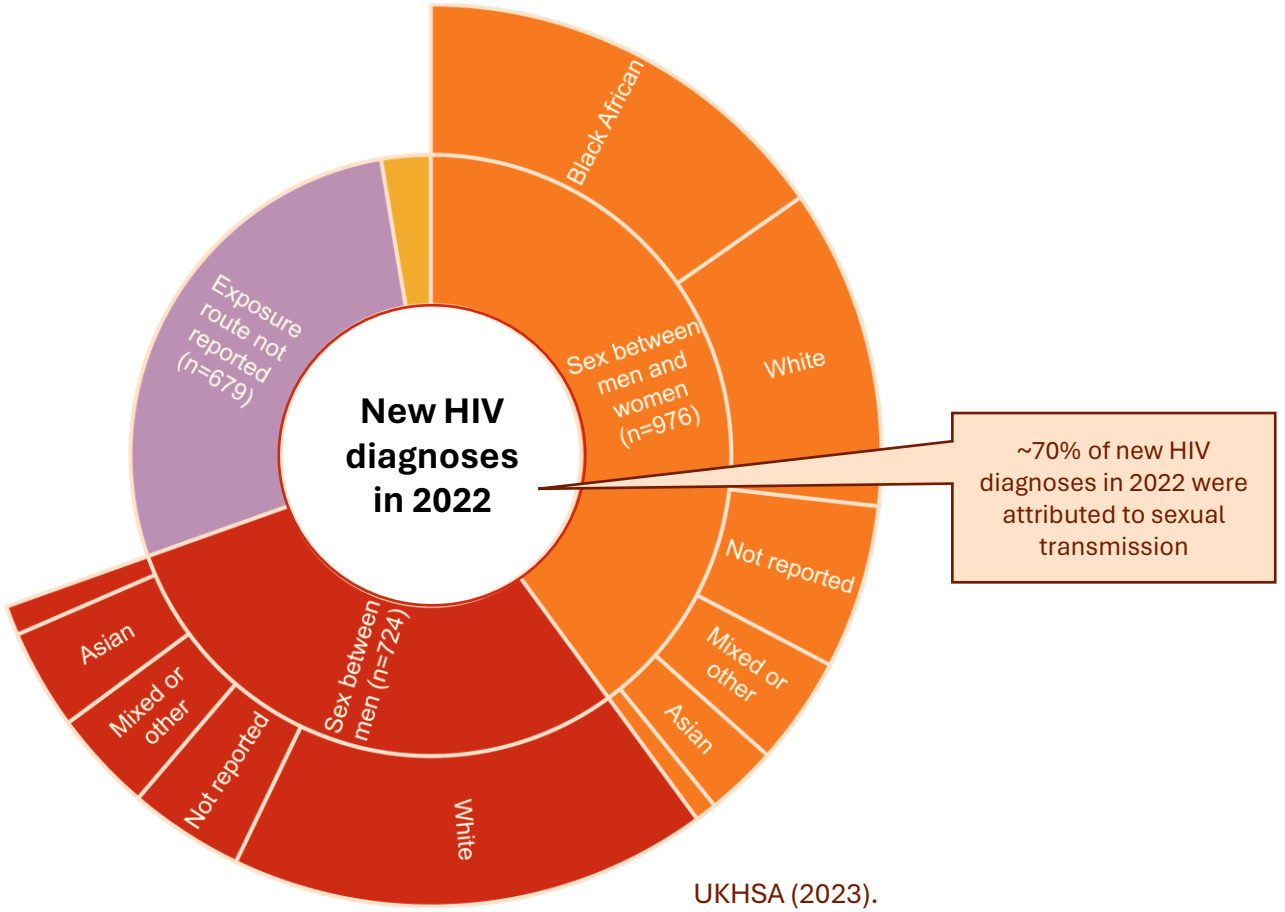
HIV in the UK today



UKHSA (2020).



UKHSA (2023).

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How has living with HIV changed?

Life expectancy for people living with HIV

Rosalie Hayes | July 2023 | Estimated reading time 10 minutes

Mareike Günsche | www.aspect-us.com

Key points

- With the right treatment and care, people with HIV can live a normal lifespan.
- People who have a good response to HIV treatment have excellent long-term prospects.
- You can increase your life expectancy by not smoking and having a healthy lifestyle.

NAM Aidsmap (2023).

Image credit: Terrence Higgins Trust.

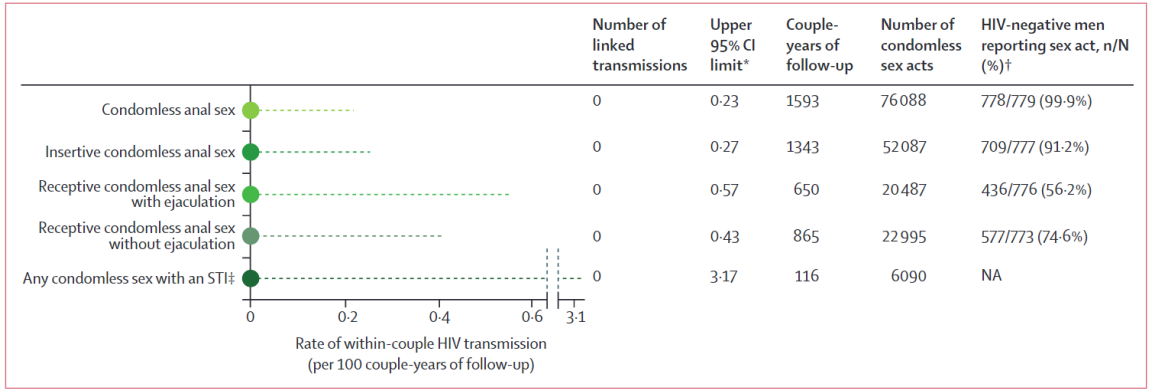

Figure 1: **Rate of within-couple HIV transmission through condomless sex according to sexual behaviour reported by the HIV-negative partner**
STI=sexually transmitted infection. NA=not applicable. *Estimated using the exact Poisson method. †Numerator is the number of HIV-negative men within the eligible couples ever reporting that specific sexual act and denominator is the group-specific number of HIV-negative participants who contributed eligible couple-years of follow-up. ‡Refers to STIs (excluding HIV) self-reported by the HIV-negative partner.

Rodger et al (2019).

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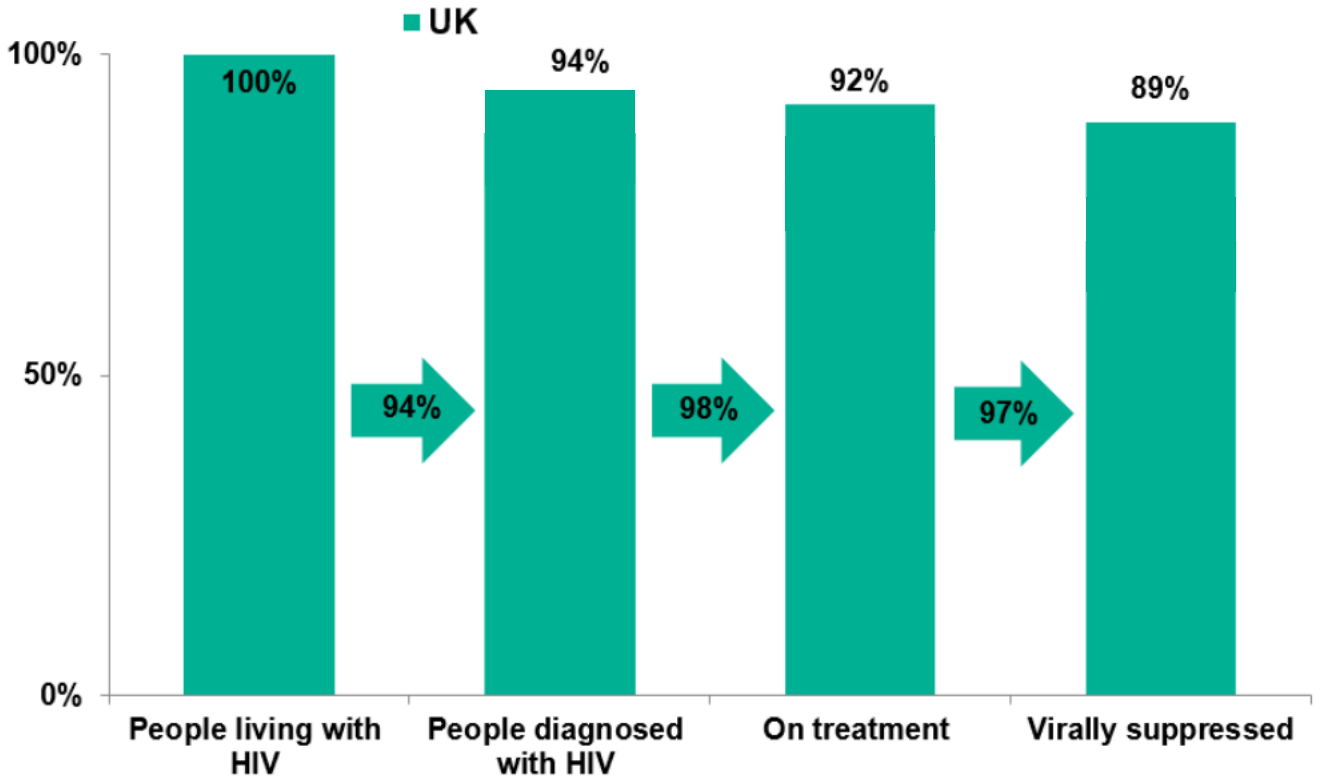
...HIV treatment has a lot to do with it

Figure 4: Continuum of HIV care in the UK, 2019



UKHSA (2020).

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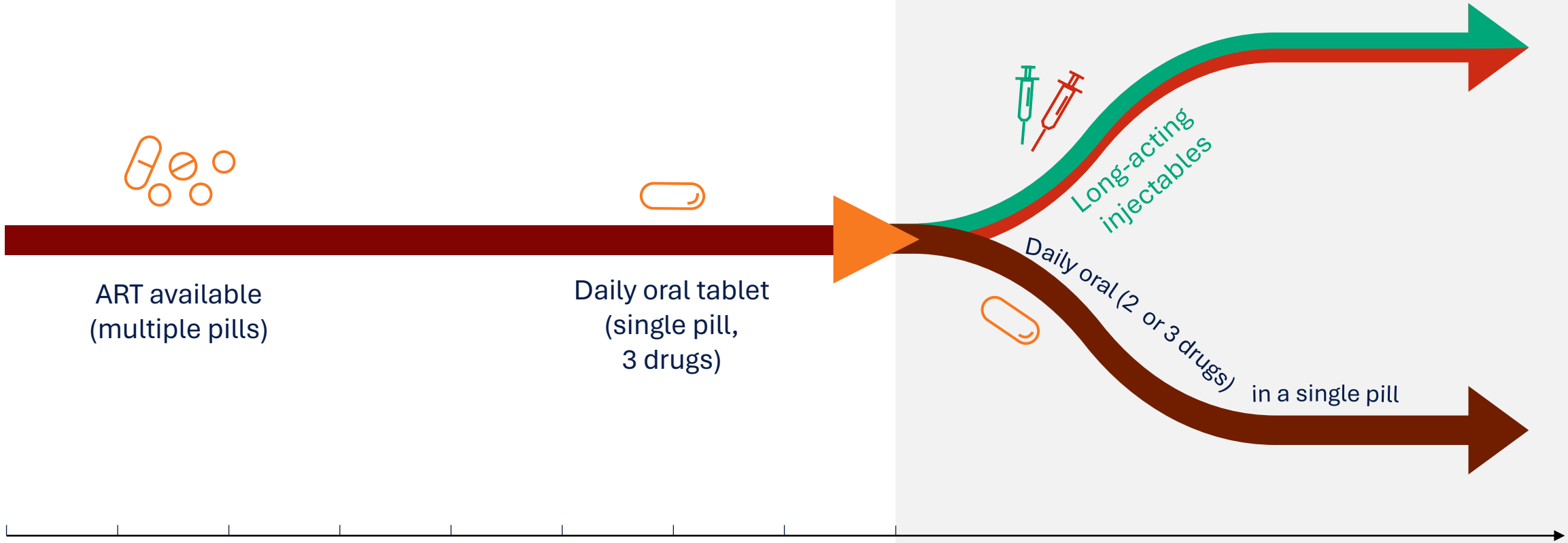
Treatment evolution: Addressing needs beyond viral suppression



In the early days

success was defined as prolonging life

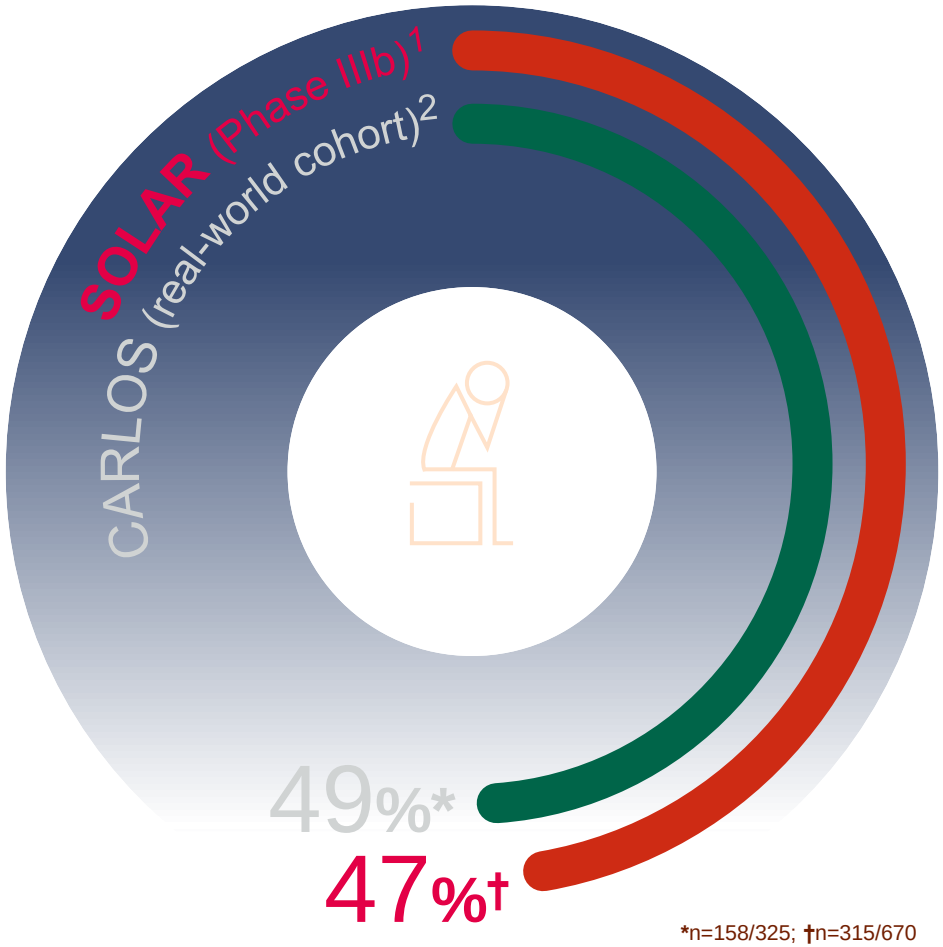
As treatment evolved

success became achieving near normal life expectancy with fewer short- and long-term side effects and more convenient dosing

Today

More emphasis on QoL and patient reported outcomes, engagement is integral to success

Why is treatment evolution important for people with HIV?



*n=158/325; †n=315/670

…reported always/often experiencing one or more of the following psychosocial challenges with daily oral HIV treatment

Fear of disclosure

“ *Worried about people unintentionally discovering their HIV status*

Adherence anxiety

“ *Worried about forgetting to take their HIV medication*

Daily reminder of HIV

“ *Felt that their HIV medication was a reminder of their HIV status*

1. Ramgopal MN, et al. Lancet HIV 2023 (online ahead of print)
2. Scherzer J, et al. IAS 2023. Poster EPE0863

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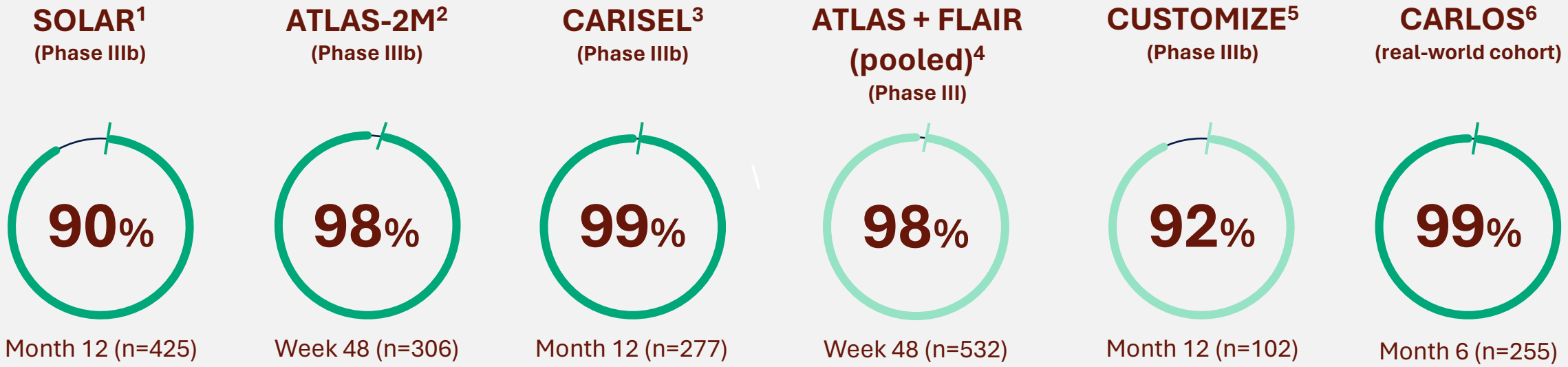
What injectable HIV treatments are now available?

- Currently only one injectable HIV treatment approved in UK – **long-acting cabotegravir and rilpivirine** (CAB+RPV LA)
- CAB+RPV LA is **effective** and **safe** (three large phase III clinical trials).
- Approved dosing period is **every 8 weeks**.
- Ventrogluteal, intramuscular injection which must be administered by a qualified clinician.

Injectable therapy was preferred vs daily oral therapy

Phase III and Real-world Cohorts:

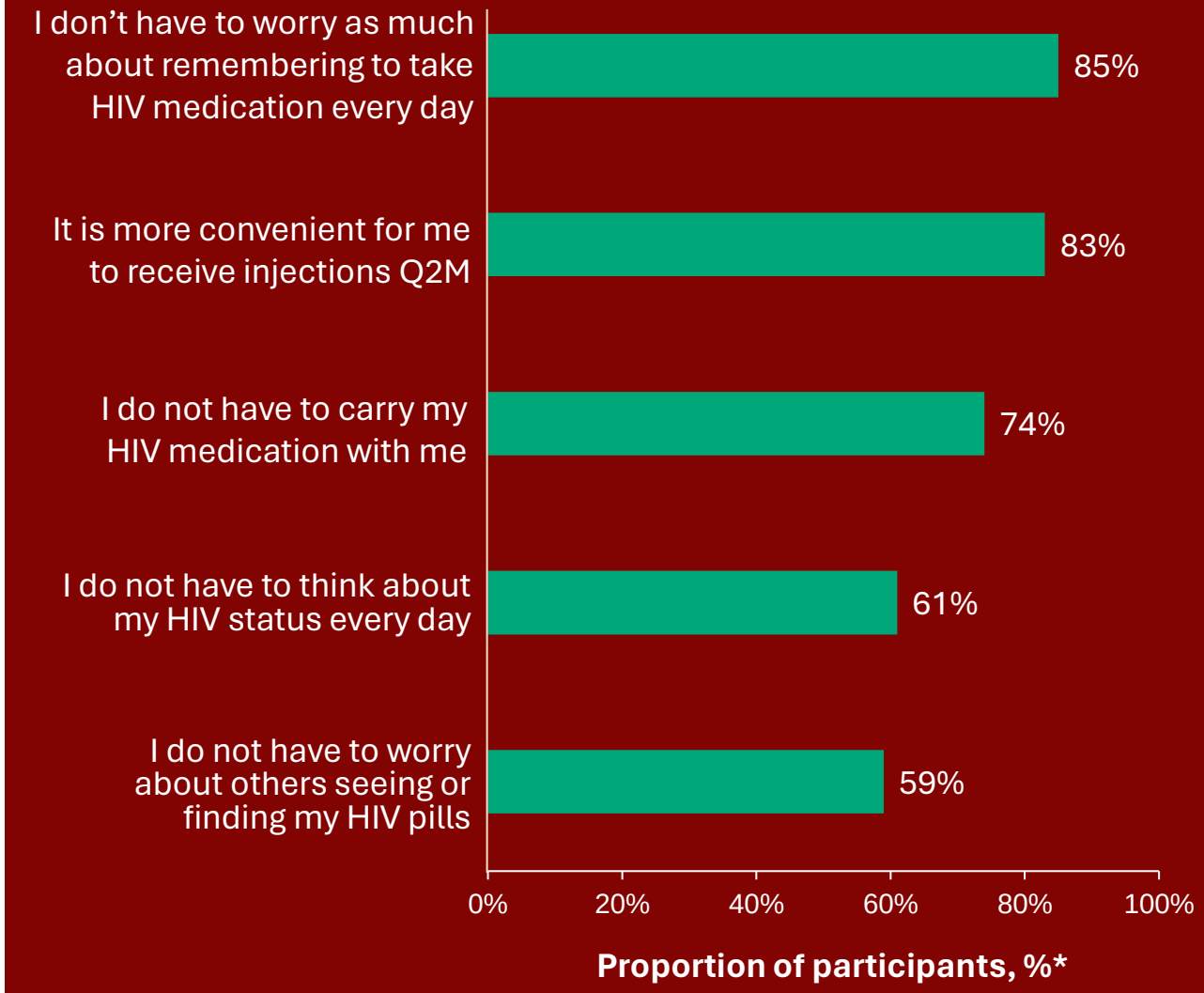


1. Ramgopal MN, et al. Lancet HIV 2023;10(9):e566–577 (and suppl. appendix)
2. Chounta V, et al. Patient 2021;14:849–62 **3.** Lutz T, et al. HIV Glasgow 2022. Poster P123
4. Murray M, et al. AIDS Behav 2020;24:3533–44
5. Garris CP, et al. J Int AIDS Soc 2022;25:e26006; **6.** Scherzer J, et al. IAS 2023. Poster EPE0863

Which therapy do you prefer?

(n=425)

Why? (n=382)



Ramgopal MN, et al. Lancet HIV 2023;10(9):e566–577 (and suppl. appendix)

Inclusion in clinical studies and why it matters

CAB + RPV LA: Inclusion across phase III studies

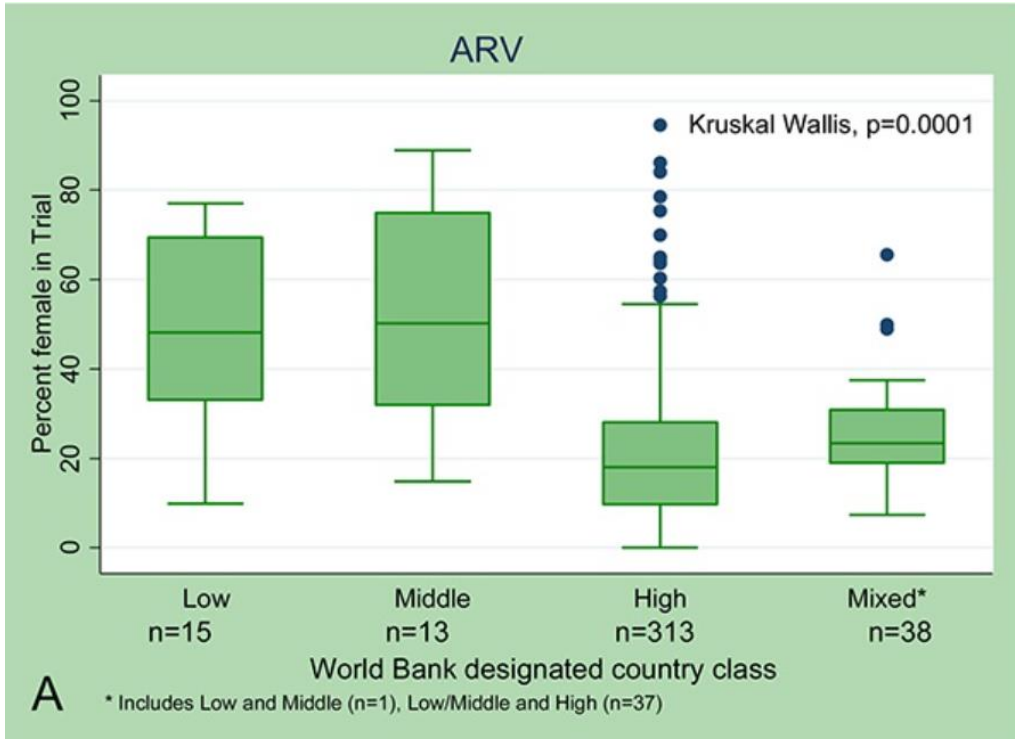
In total : Phase III LA treatment trials:

Female 25%

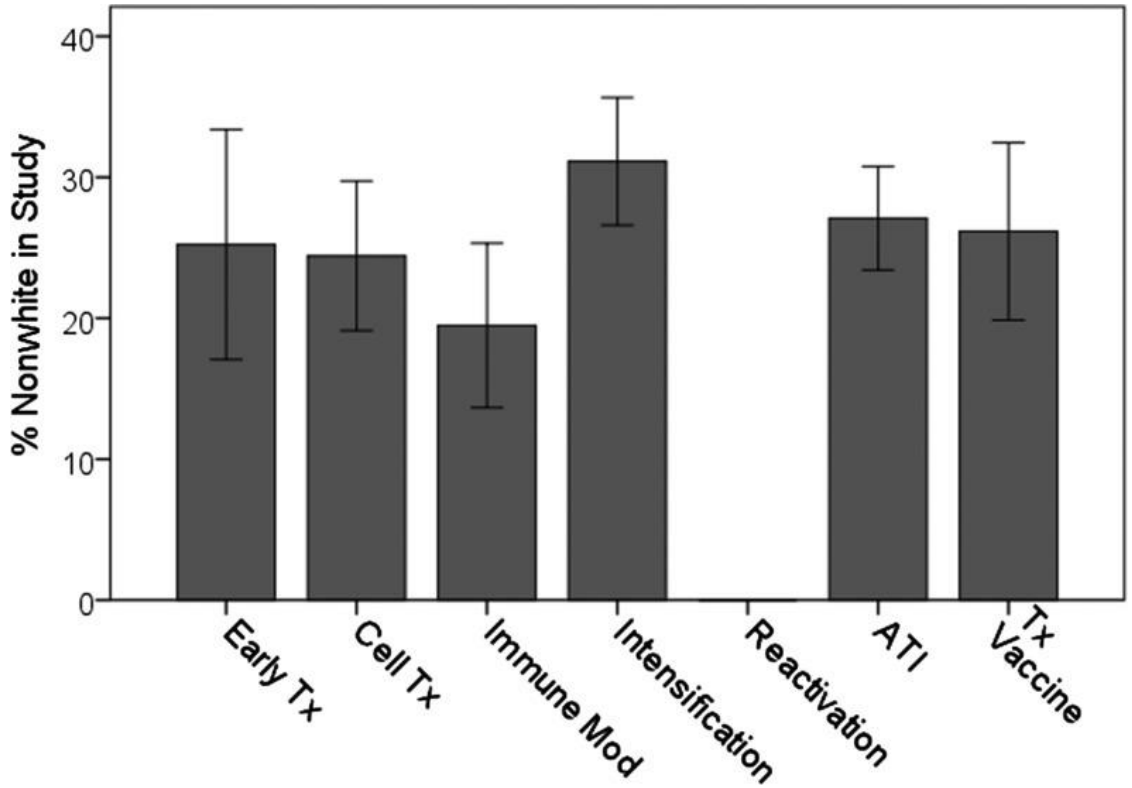
Racialised minorities 28%

Adults ≥ 50 years 18%.

And it isn't just a problem in injectable HIV treatment studies…



Curno et al (2016)



Johnston et al (2015)

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Why does this all matter?

Building trust in medical research and institutions

Promoting fairness for potential participants and their communities

Generating biomedical *and social* knowledge

Adapted from Schwartz AL, et al (2023)

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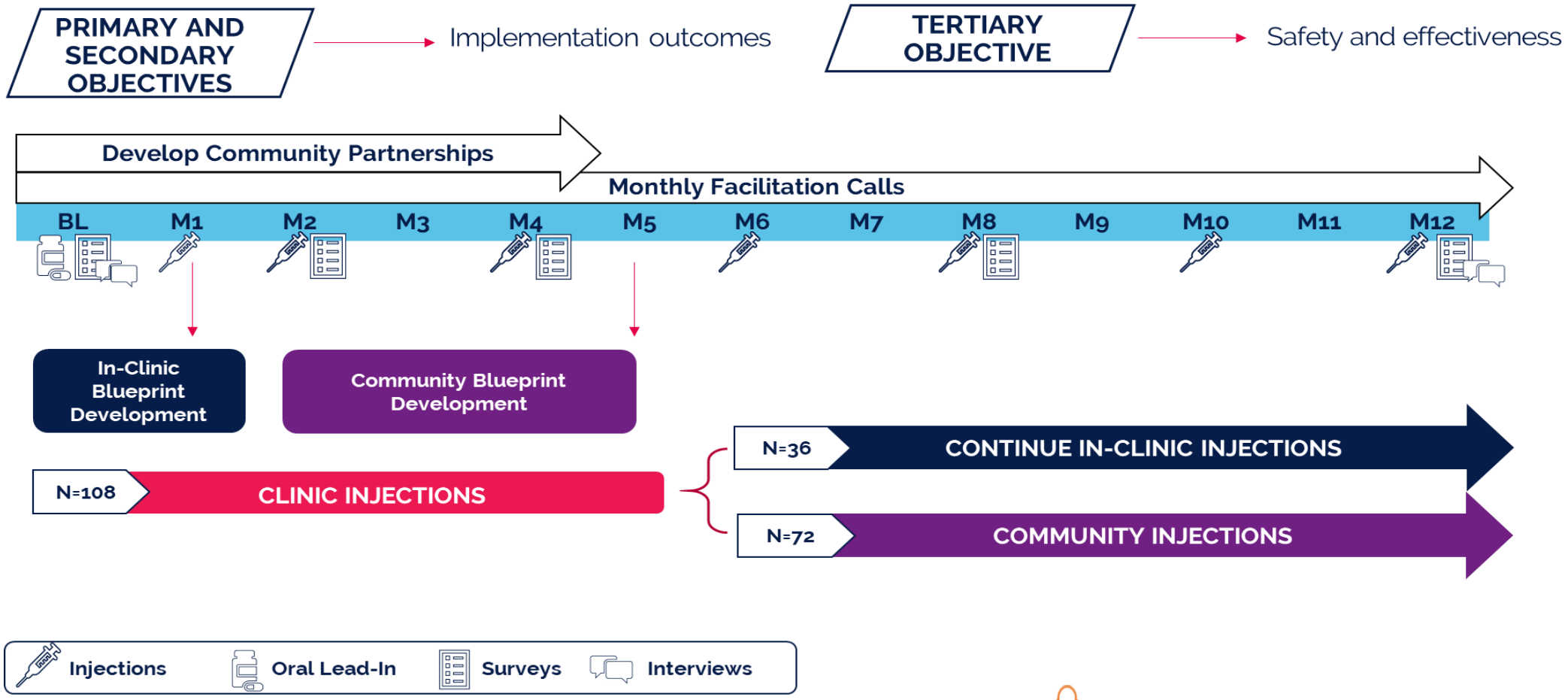
Introducing ILANA

The ILANA study

- ILANA (Implementing Long Acting Novel Antiretrovirals) is a pragmatic real-world implementation study.
- This study explores implementation of injectable CAB+RPV LA in two settings per site – one in the clinic and one in the community.
- Conducted in six large clinic sites both in London and outside of London.
- Sites chose the community site based on their local needs and resources. These were: patients' homes (n=3), HIV charitable organisations (n=2), and community satellite clinic (n=1).
- All PWH participants will be receiving CAB+RPV LA as part of their routine care, regardless of the study arm.
- Any patient who does not wish to participate in this study, will still receive the treatment if they wish as part of their routine care.

Study design

ILANA STUDY – DESIGN



Inclusion and exclusion criteria

Inclusion

- Able and willing to complete informed consent prior to inclusion
- ≥ 18 years of age
- Documented HIV-1 infection
- Will receive CAB+ RPV as part of their routine clinical care
- In accordance with SmPC and NICE guidance:
  - Virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen
  - Without present or past evidence of viral resistance to, and no prior virological failure with agents of the NNRTI or INI class
  - Not co-infected with hepatitis B

Exclusion

- Prior exposure to CAB + RPV LA
- Based on contraindication for CAB LA, RPV LA, in accordance with EU license, MHRA license and NICE guidance:
  - Prior virologic failure on drugs of the NNRTI or INI class
  - Resistance mutations to any drugs of the NNRTI or INI class
  - Pregnancy

What is special about ILANA?

- Anti-racist, anti-sexist, anti-ageist study design
- Recruitment targets:
  - **50%** women
  - **50%** racially minoritised participants
  - **30%** people aged 50+
- People who got pregnant during study were supported to continue if they wished

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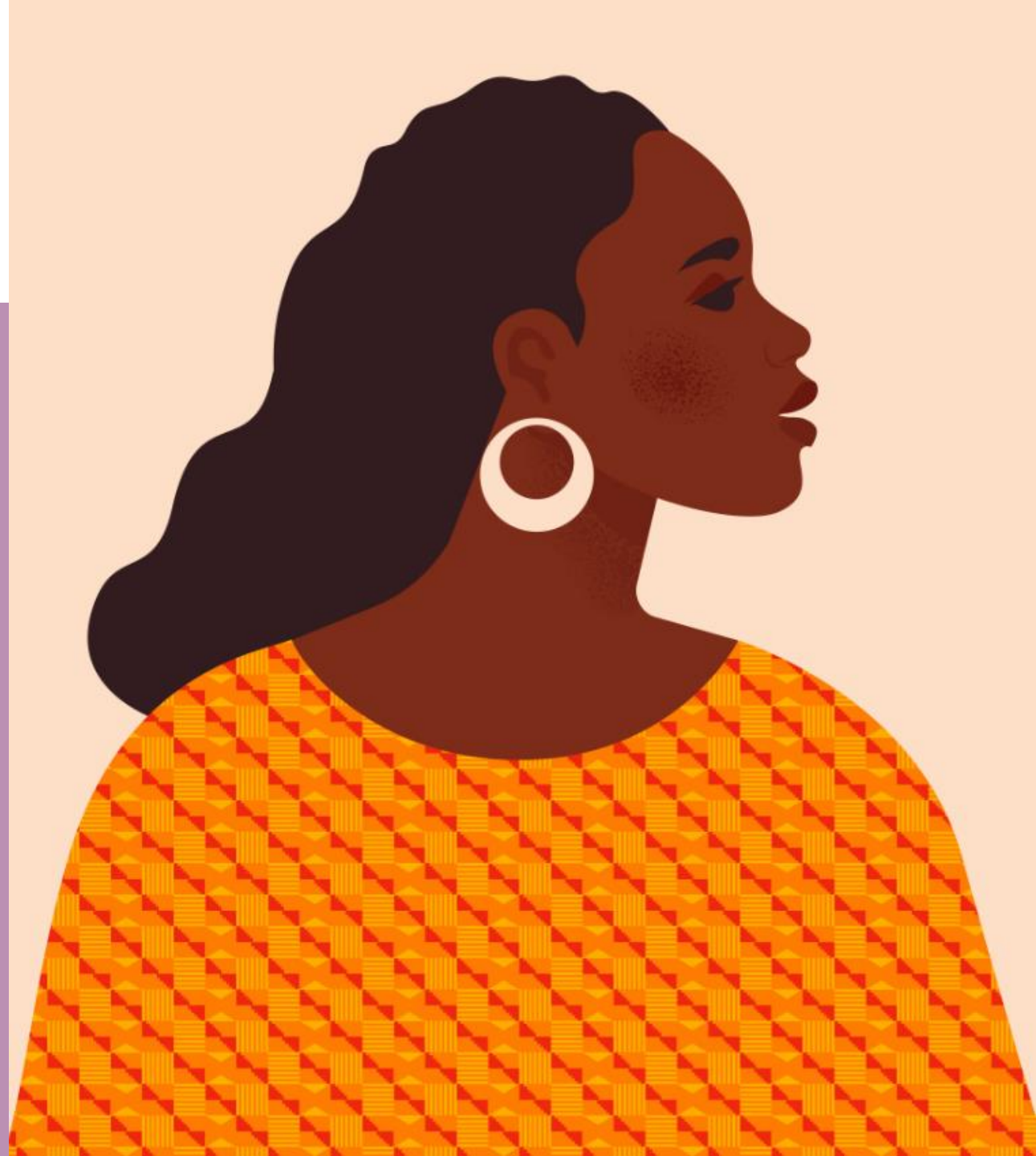
Putting the recruitment targets into practice



Recruitment strategy

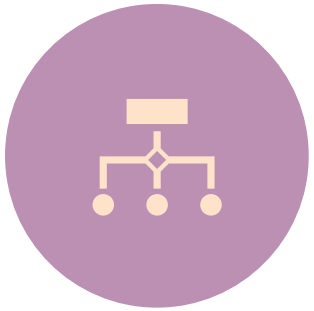
- Each site to recruit 18 participants, at least 9 women and at least 9 from racially minoritised groups.
- Develop list of people who want CAB+RPV LA
  - Willing to have CAB/LA in the community in second half of the study (not a deal-breaker)
  - Willing to consent to interviews and questionnaires
- Need to maintain list so people aren't repeatedly approached
- Explain that this may well be the fastest way to access CAB+RPV LA; it will take time for clinics to offer to everyone via routine provision.
- Identifying a clinic staff member to manage the list, clinicians email them

Name	MRN	gender	ethnicity	Eligible clinically	ILANA yes	ILANA no

Key steps

FEASIBILITY

SITE SELECTION



PROTOCOL WRITE-UP

ENFORCING TARGETS

CONSTANT COMMUNICATION!

Feasibility and Site Selection

- Prior to sites being selected for this study – feasibility forms were sent to enquiring PIs to complete and sign off
- These forms detailed the expectations of the recruitment target and asks sites to confirm that they can meet these targets
- CI Involvement – communication with potential PIs – discussed targets/potential barriers
- Feasibility forms created by team for sites to complete

Trial Population and Recruitment		
What is your anticipated likely recruitment rate, having reviewed inclusion & exclusion criteria?		2-5 patients / week
Are there any circumstances that may be expected to affect recruitment?		☐ Yes ☒ No
Facilities and Equipment		
Does the site have adequate, secure storage for study records (e.g. paper CRFs and Consent Forms)?		☒ Yes ☐ No
Are archiving facilities available to the site?		☒ Yes ☐ No
Electronic Data		
Do site staff have experience with online case report forms?		☒ Yes ☐ No
Are there local policies in place for the storage, transfer and security of data?		☒ Yes ☐ No
Does the site have support for data entry?		☒ Yes ☐ No
Monitoring/Audit		
Are study staff willing to allow the ILANA management team access to the medical records and source documents to ensure compliance with good clinical practice and adherence to the protocol?		☒ Yes ☐ No

Protocol Write-Up

- To ensure our diversity targets were met – the targets were written into the protocol
- This was written into the following sections of the protocol:
    1. Background
    2. Rationale for study design
    3. Study design
    4. Participant allocation
    5. Cohort allocation / sequential allocation

Enforcing targets

- Monitoring recruitment
- Weekly updates emails
- Chasing sites via Teams, Phone or Email
- Constant communication was vital
- Heavy CI Involvement

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Responding to challenges

Challenge 1: Delays in Set-Up

- Delays in set-up leading to rushed recruitment risking targets
  - Experienced substantial delays (R&D, MDT issues)
  - Site did not meet targets
  - Amendment submitted to allow for over-recruitment at other sites

Challenge 2: Initial over-recruitment of Men

- Initial over-recruitment of men
  - Some initial resistance to not just recruiting more men
  - Male recruitment capped
  - Site ended up find overrecruiting women

Challenge 3: Meeting a demographic target

- Concerns around different distributions of demographics between clinical cohorts
  - Concerns over meeting EM recruitment target
  - Careful site selection - redistribute study slots
  - Site ended up meeting target

What made addressing these challenges easier?

Strong relationships between RTM, CI and PIs

Earlier internal deadlines to hasten recruitment and then allowed for flexibility later without needing an amendment

However, being prepared to swiftly submit amendments when required was also in preventing delays

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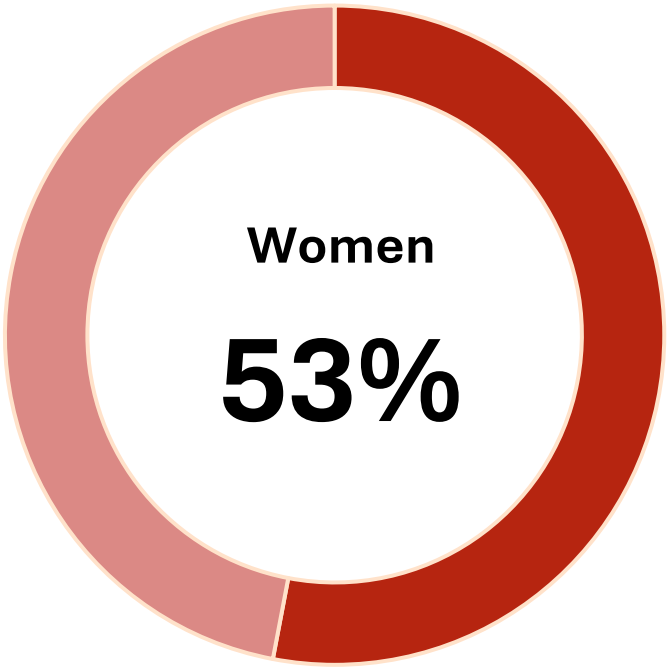
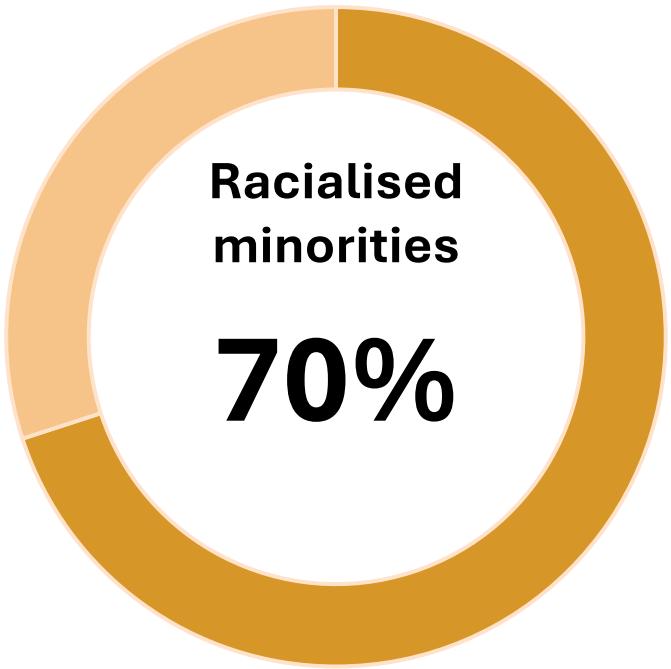
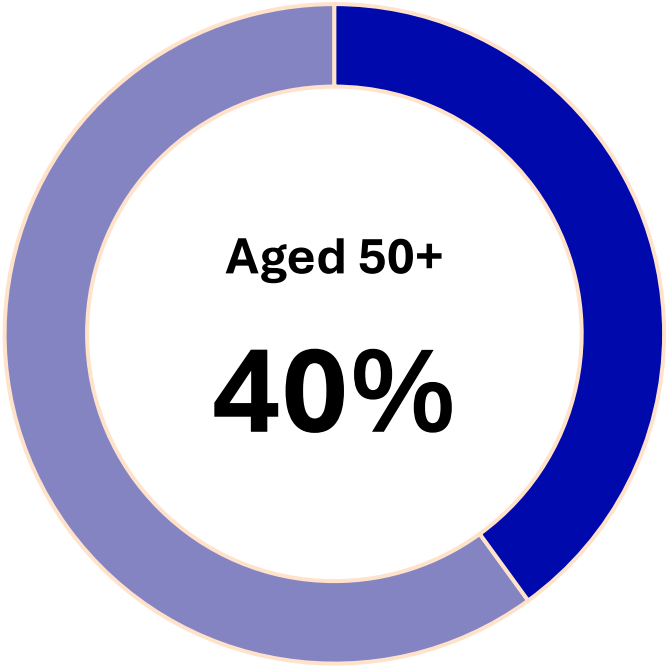
What we've achieved so far

The ILANA study met inclusivity targets







Preliminary quantitative findings…

Mean difference* (SD) in scores		Black N=54	Non-Black N=52	Women (cis/trans) N=60	Men N=46	Total N=106	p-value for change from baseline[1]
Injection: change from baseline to M4	FIM	+0.21 (0.53)	+0.02 (0.51)	+0.16 (0.57)	+0.06 (0.45)	**+0.12 (0.52)**	**0.023**
	AIM	+0.11 (0.67)	+0.04 (0.45)	+0.01 (0.62)	+0.16 (0.49)	+0.08 (0.57)	0.175
	IAM	+0.20 (0.58)	+0.07 (0.50)	+0.17 (0.58)	+0.09 (0.50)	**+0.13 (0.55)**	**0.013**
Community-based location: change from baseline to M4	FIM	-0.23 (1.24)	+0.04 (0.13)	-0.11 (1.08)	-0.08 (1.17)	-0.10 (1.12)	0.359
	AIM	-0.08 (1.35)	+0.13 (1.00)	-0.06 (1.21)	+0.13 (1.17)	+0.02 (1.19)	0.855
	IAM	-0.10 (0.17)	+0.17 (1.02)	-0.06 (1.09)	+0.16 (1.22)	+0.03 (1.15)	0.775
HIV-TSQ12 change from baseline		+5.43 (8.65)	+7.58 (11.85)	+5.32 (8.84)	+8.00 (11.97)	**+6.48 (10.35)**	**<0.001**

FIM (Feasibility of Intervention Measure); AIM (Acceptability of Intervention Measure); IAM (Intervention Appropriateness Measure); HIVTSQ-12 (HIV Treatment Satisfaction Questionnaire)

[1] p-value refers to change from baseline for total group only, not any sub-group.

Preliminary qualitative findings…

Building trust

- “I'm part of this WhatsApp group of women living with HIV in ((area)) and they were like, be careful, they’re experimenting on us. How many women do you know who are on this? This medication is tested on gay men and never on women, which is sort of true but I just said things are changing… So yes, I think I’ve convinced or I’ve encouraged one or two who are struggling because of stigma to go on injectables… And I think one of them has started already.” **Grace** (Black African woman, aged 54, clinic arm).

Promoting fairness

- “At the earliest stages you couldn’t just be put on it you would have to pay like quite a tidy sum to even get it… I said yeah, I’d be happy to trial it and see how it goes… I think it was only [available] through the study at the time.” **Joshua** (Black British man, aged 37, clinic arm)

Generating social knowledge

- “What puts me off about [attending a HIV charity], is that it’s already labelled. If I go to a pharmacy, anyone can go to a pharmacy for a headache or whatever. It’s the fact that it’s HIV-specific that puts me off.” **Abimbola** (Black African woman, aged 55, clinic arm).

Key messages

- Greater inclusion in clinical trials helps to **improve trust**, **promote fairness** and **generate new knowledge.**
- Using **recruitment targets** for underserved populations is an effective way to increase trial diversity
- Assessing **feasibility**, writing targets into the **protocol**, **monitoring** recruitment and **constant communication** were key to ensuring targets were met (and exceeded!)

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Any questions?

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