

How is PrEP continuation reported and where are we now? A Systematic Review

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BACKGROUND

Oral pre-exposure prophylaxis (PrEP) effectiveness is contingent upon consistent use during periods of high risk for HIV. Continual engagement in care via follow-up visits is important not only to provide refills of the drug, but for ongoing HIV/STI testing, adherence support, risk reduction counseling and support for side effects. Despite growing adoption of PrEP, continuation in care among different PrEP target populations is not well documented.

Furthermore, despite the importance of consistent measurement of PrEP continuation, there is little consensus on how to do this. There is general

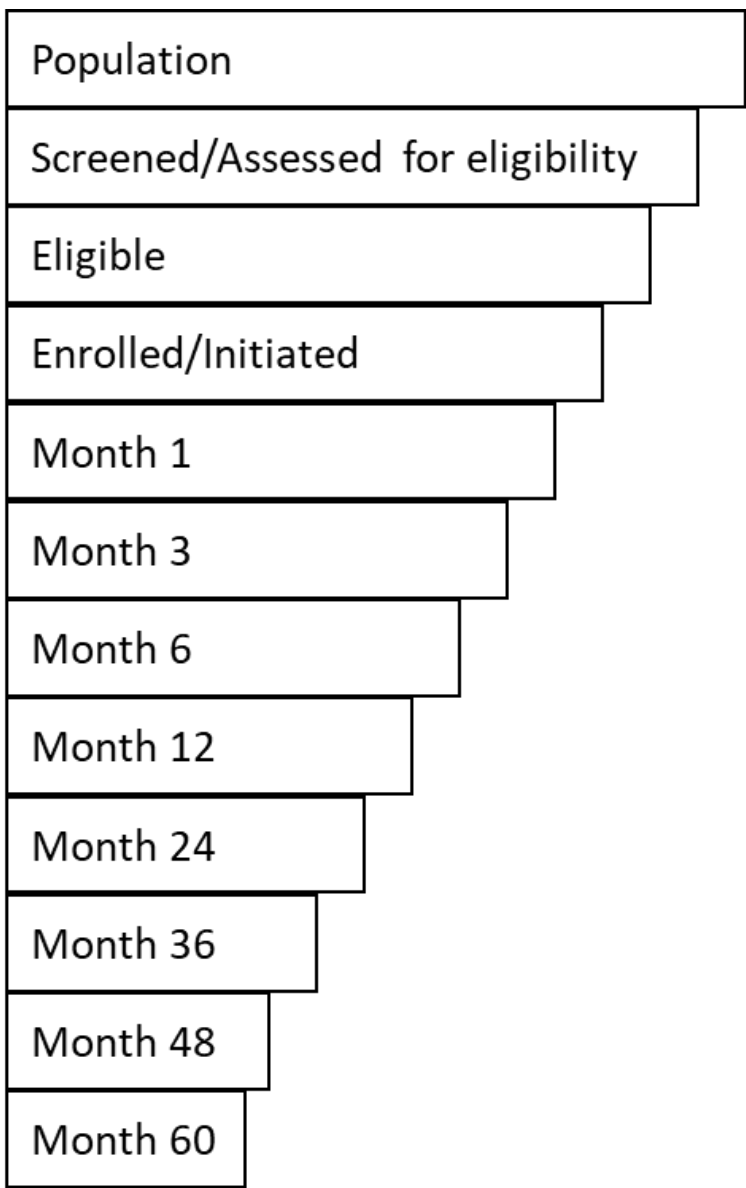
agreement that the use of the word retention is not appropriate for prevention given that, unlike antiretroviral treatment (ART), one does not need to be on PrEP for life, and there will be cycles where clients can safely go on and off PrEP in consultation with their provider. Yet existing PrEP indicators do not account for safe cycling, or varying dosing schedules.

This systematic review aims to contribute to the ongoing conversation around appropriate monitoring of PrEP continuation by identifying and summarizing existing published data on PrEP continuation along a PrEP cascade.

METHODS

We searched MEDLINE, Embase and Global Health; and HIV conference abstracts for studies directly reporting continuation data on oral PrEP. Only those studies reporting on primary data were deemed eligible, with modeling studies and simulations excluded. We mapped data on participants' continued attendance at follow-up visits, i.e. continuation, along a PrEP cascade (**Figure 1**).

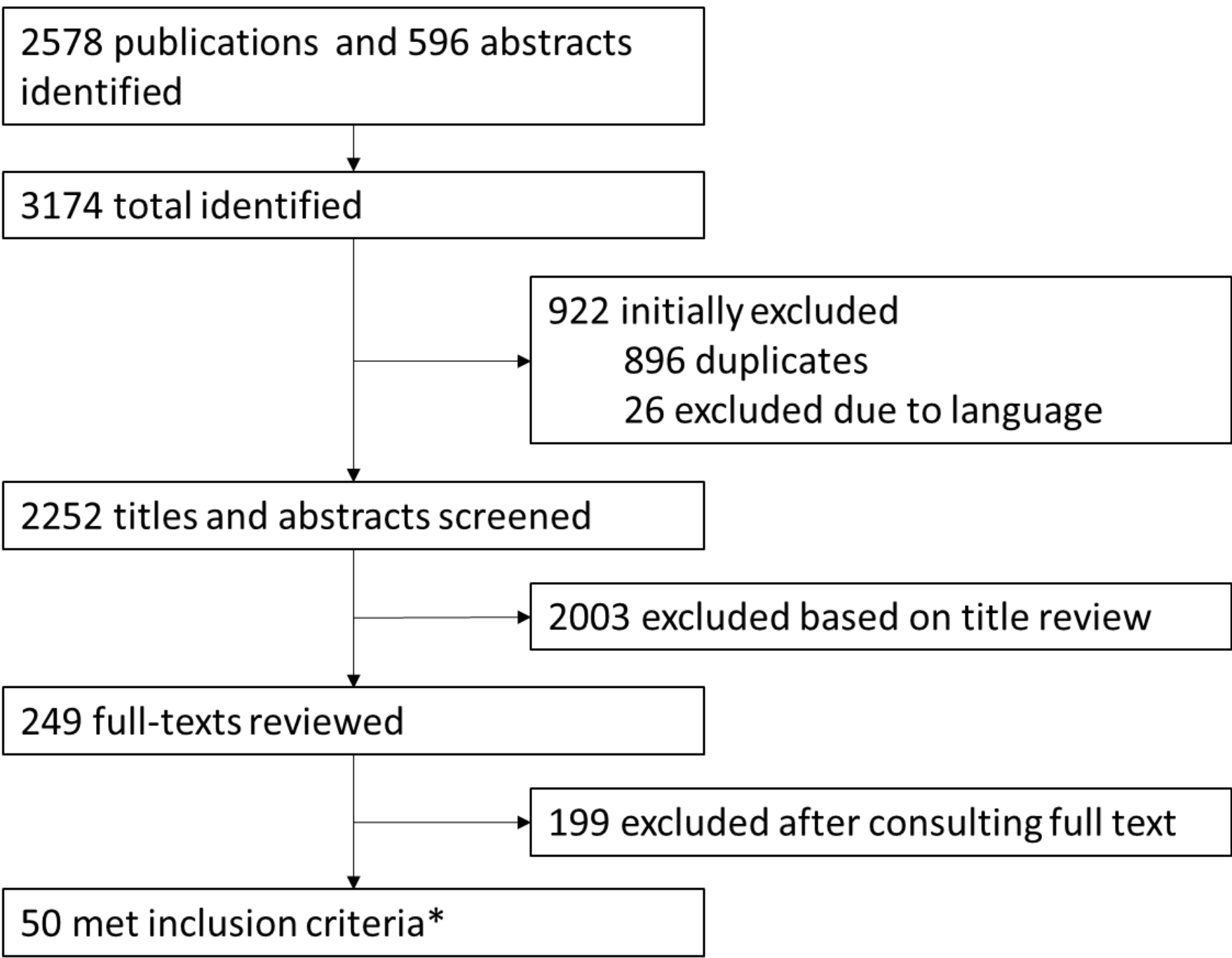
Figure 1. PrEP cascade



RESULTS

Search Results

Figure 2. Study flowchart



The search was conducted November 6, 2018 and yielded 2,578 articles and 596 abstracts, of which 249 were retained for full text review (**Figure 2**). *Fifty records met the inclusion criteria for this review covering 41 individual trials, demonstration projects or routine implementation/clinical programs.

Studies included 24 open label or demonstration projects, 9 routine implementation/clinical programs, and 8 randomized controlled trials (RCTs). Studies were most commonly in Africa (16, 39%) and North America (12, 29%), followed by Europe (4, 10%) or Asia (4, 10%). Client populations were men who have sex with men (MSM)/transgender women (TGW) (18, 44%), all people at risk (9, 22%), and women (6, 15%).

Reporting of PrEP cascade components

Continuation was most commonly reported at month 6, followed by months 3 and 12, and month 1 (**Figure 3**). Some studies reported continuation as total or average length of follow up (in days, months or years). It was not possible to fit these data into the PrEP cascade so these studies were excluded. No studies discussed a retention or continuation definition that suggested continued *need* for PrEP or cycling were considered in the statistics presented.

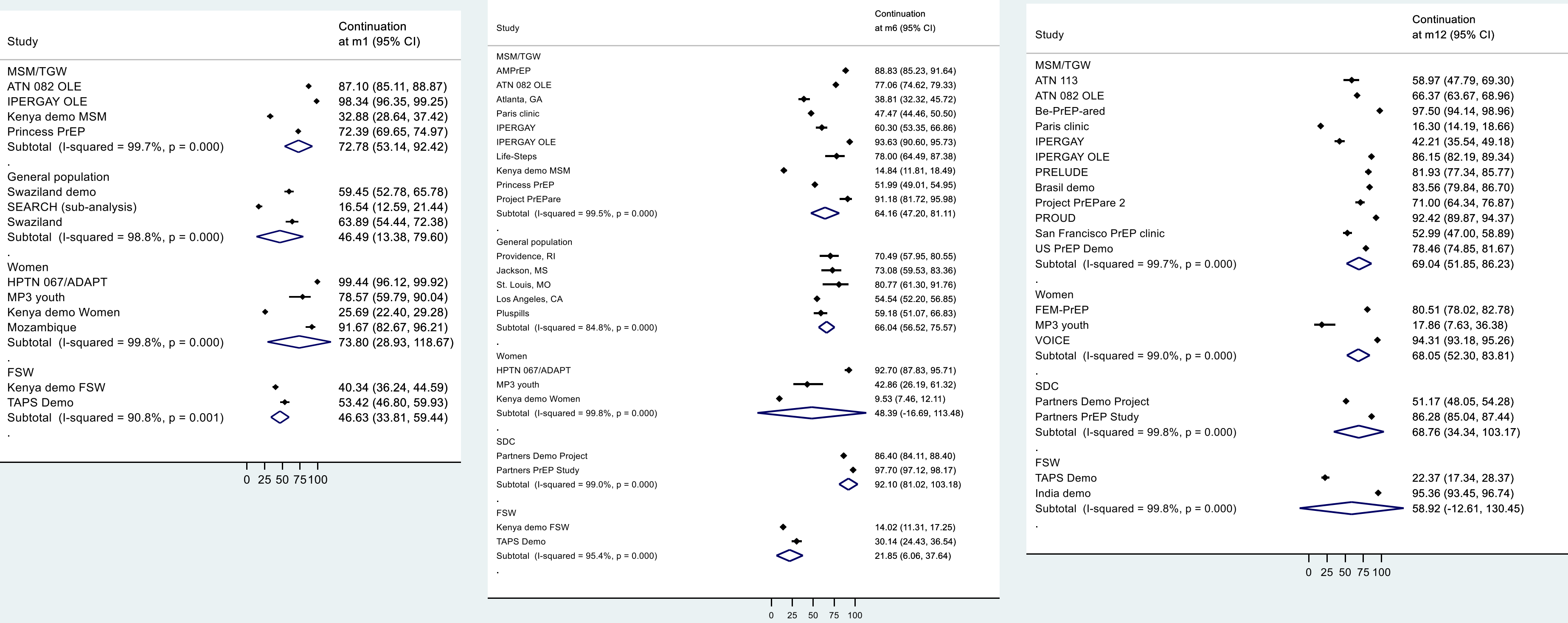
Figure 3. Stages of the PrEP care cascade reported by studies under review (n=41)



Continuation by study type

Pooled estimates of continuation at months 6 and 12 were consistently highest in RCTs, at 82.6% (95% CI: 68.9%, 96.4%) at month 6 and 79.4% (95% CI: 72.3%, 86.5%) at month 12. Pooled estimates for open label/demonstration projects and implementation studies were similar at 6 months (55.6% and 56.4%, respectively), but diverged at 12 months (70.1% and 48.1%, respectively).

Figure 4. Forest plots of pooled continuation by sub-population at months 1 (left), 6 (middle), and 12 (right) after initiation



Continuation by Population

At month 1, pooled continuation was highest among women (73.8%) followed by MSM (72.8%), female sex workers (FSWs) (46.6%) and the general population (46.5%) (Figure 5). Considerable variation was observed across studies and populations. (**Figure 4**).

Continuation at 6 months was highest among serodiscordant couples (SDCs, 92.1%) followed by general population (anyone at risk, 66.0%), MSM (64.2%), women (48.4%) and FSWs (21.9%) (Figure 6). However, continuation among women varied so widely by study that the estimated confidence interval (CI) is too large to give a robust estimate.

Continuation at 12 months was similar across populations, ranging from 69.0% in MSM/TGW and 58.9% in FSWs.

CONCLUSIONS

- **Reporting of continuation at various time points on the PrEP cascade varies widely;** greater consensus is needed on which specific cascade stages are important to track.
- **Discontinuation was high at month one;** this has important implications for the use-effectiveness of PrEP and suggests PrEP initiations may not be a very useful indicator in estimating PrEP effectiveness.
- **The continuation decline was sustained over time** suggesting current guidelines that focus only on reporting continuation at three months may be inadequate.
- **No studies reported on cycling or safe stopping of PrEP.** Likewise, current PrEP indicators do not require differentiation between those stopping due to lack of risk versus those who are still indicated for PrEP.
- **Continuation varied by population, and within populations.** Some of this variation can likely be attributed to varying study type. As more data become available, future studies should examine pooled continuation rates by population and study type.

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