PrEP scale-up, successes, and challenges

Rachel Baggaley
team lead for testing, preventions and populations
Global HIV, hepatitis and STI programmes
World Health Organization in Geneva

World Health Organization

HPTN
HIV Prevention Trials Network

World Health Organization

Global PrEP scale up

Evolution of WHO PrEP recommendations and guidance

World Health Organization

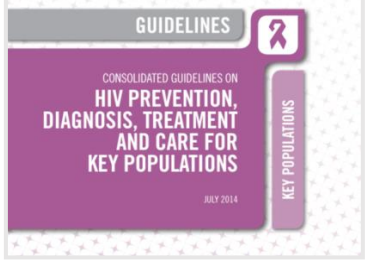
2010
Iprex
PrEP 44% ↓ (MSM)

2012
PrEP
FDA approval

PrEP for SDC, MSM & TG (**conditional** rec in the context of demo projects)

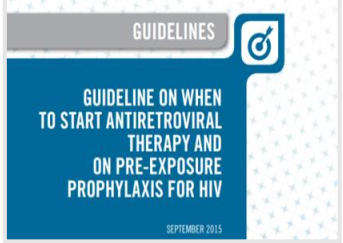
2012

PrEP for MSM (**strong** rec)
Other KP (**conditional** rec) no recommendation for PWID



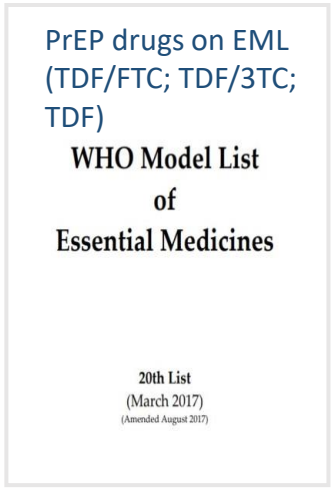
2014

PrEP for people at substantial HIV risk (≈3 per 100PY) (**strong** rec)

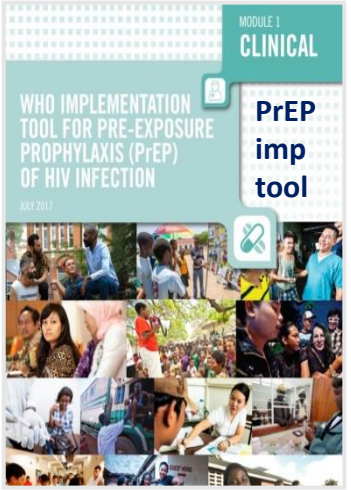


2015

PrEP drugs on EML (TDF/FTC; TDF/3TC; TDF)



2017

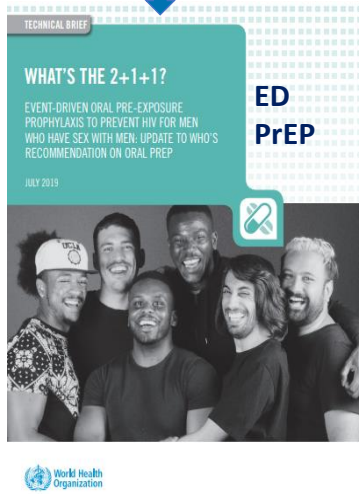


PrEP imp tool

2017

Additional modules on
- M&E
- Adolescents
- PBFW
- STIs and PrEP

2018/19



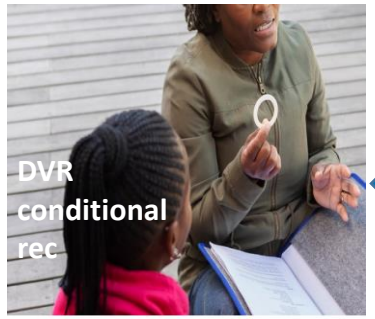
ED PrEP

2019

Dapivirine vaginal ring prequalified

2020
EMA
Article 58 positive opinion

2020



WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women at substantial risk of HIV infection

2021

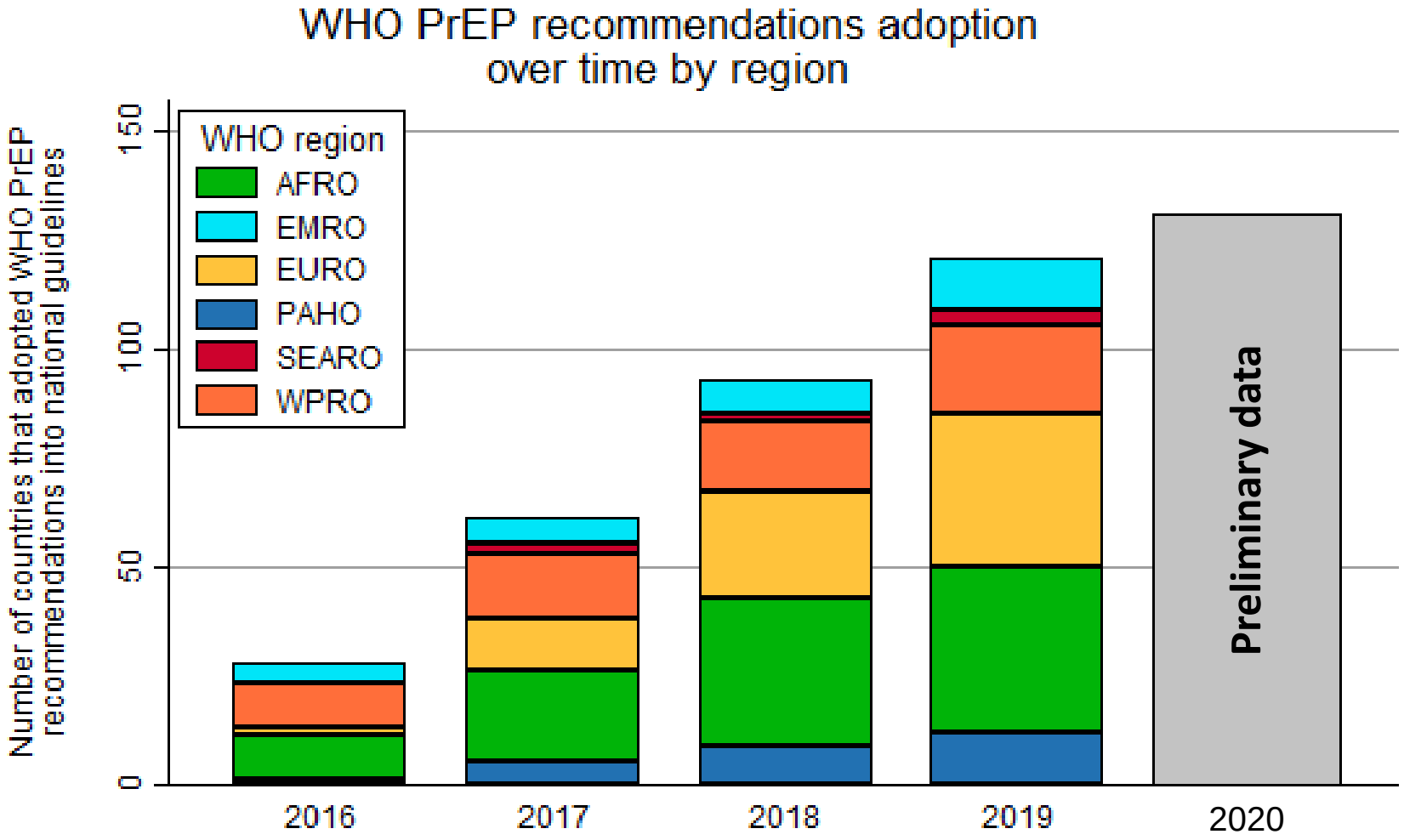
Simplifying PrEP

2021/2

Increase in countries with PrEP policies, by regions, since WHO 2015 recommendation

2020:

- 129 WHO member states adopted WHO PrEP recommendations into national guidelines
- 16 states pending
- But: Guideline adoption does not necessarily translate into implementation and meaningful coverage and access



Source: GAM and WHO regional/country offices. Data for 2020 are preliminary.

Countries with PrEP policies

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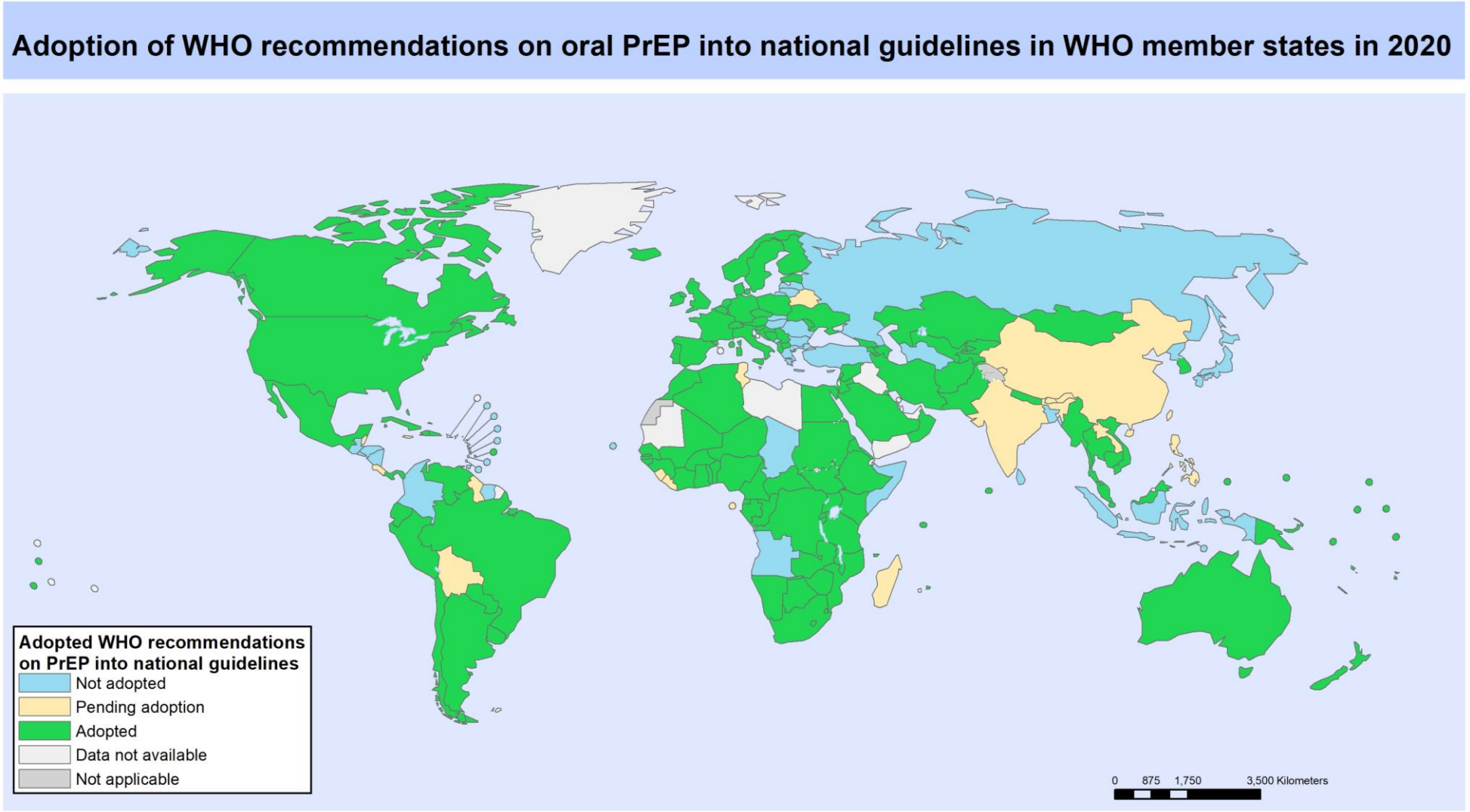
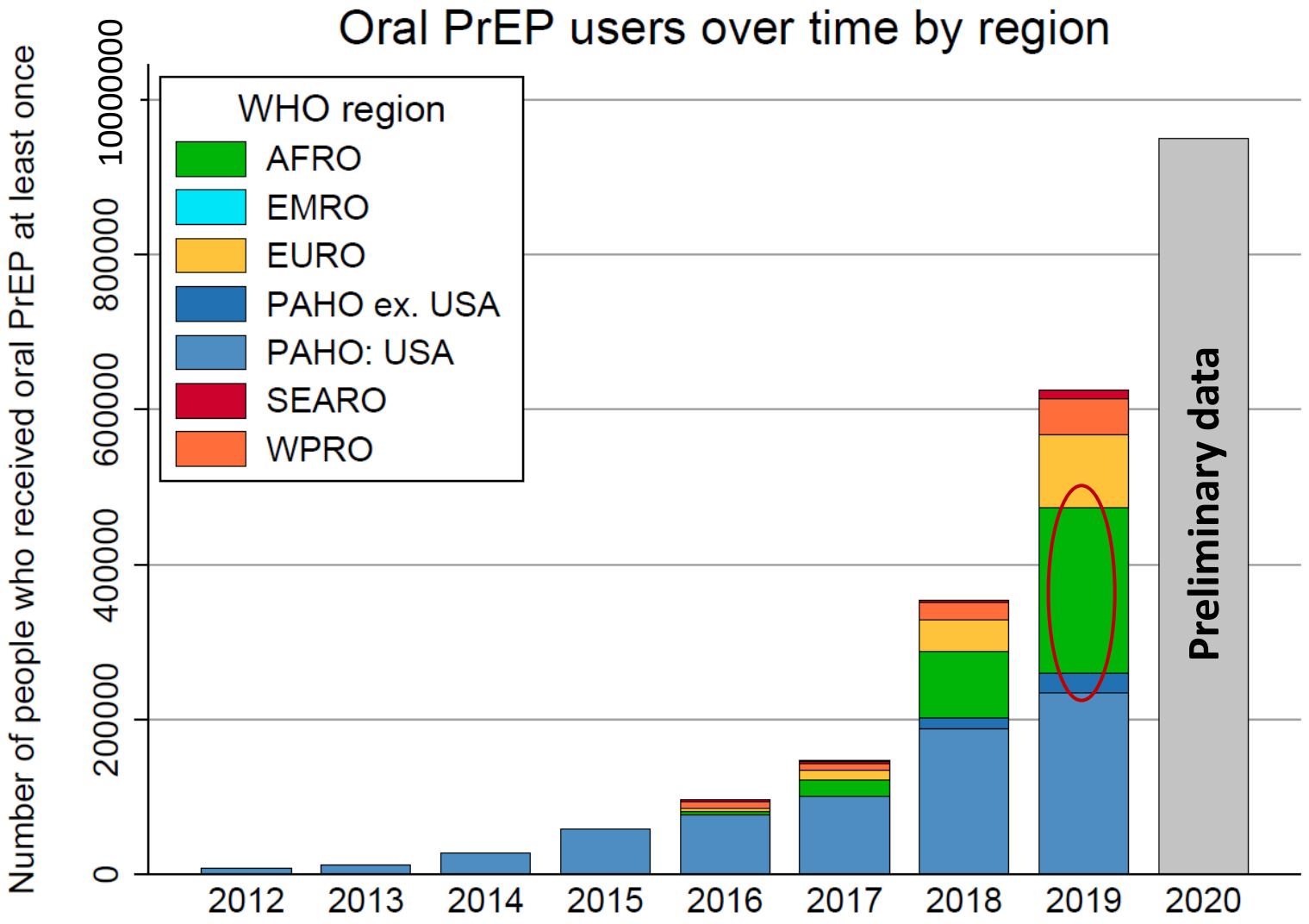


Source: GAM and WHO regional/country offices. Data for 2020 are preliminary.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO; GAM
Map Production: HQ UCN/HHS/TPP
World Health Organization

Number of people receiving pre-exposure prophylaxis globally over time



Preliminary data suggests significant growth in global PrEP use in 2020 despite COVID-19 disruptions

Source: GAM and WHO regional/country offices. Data for 2020 are preliminary.

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PrEP successes

2

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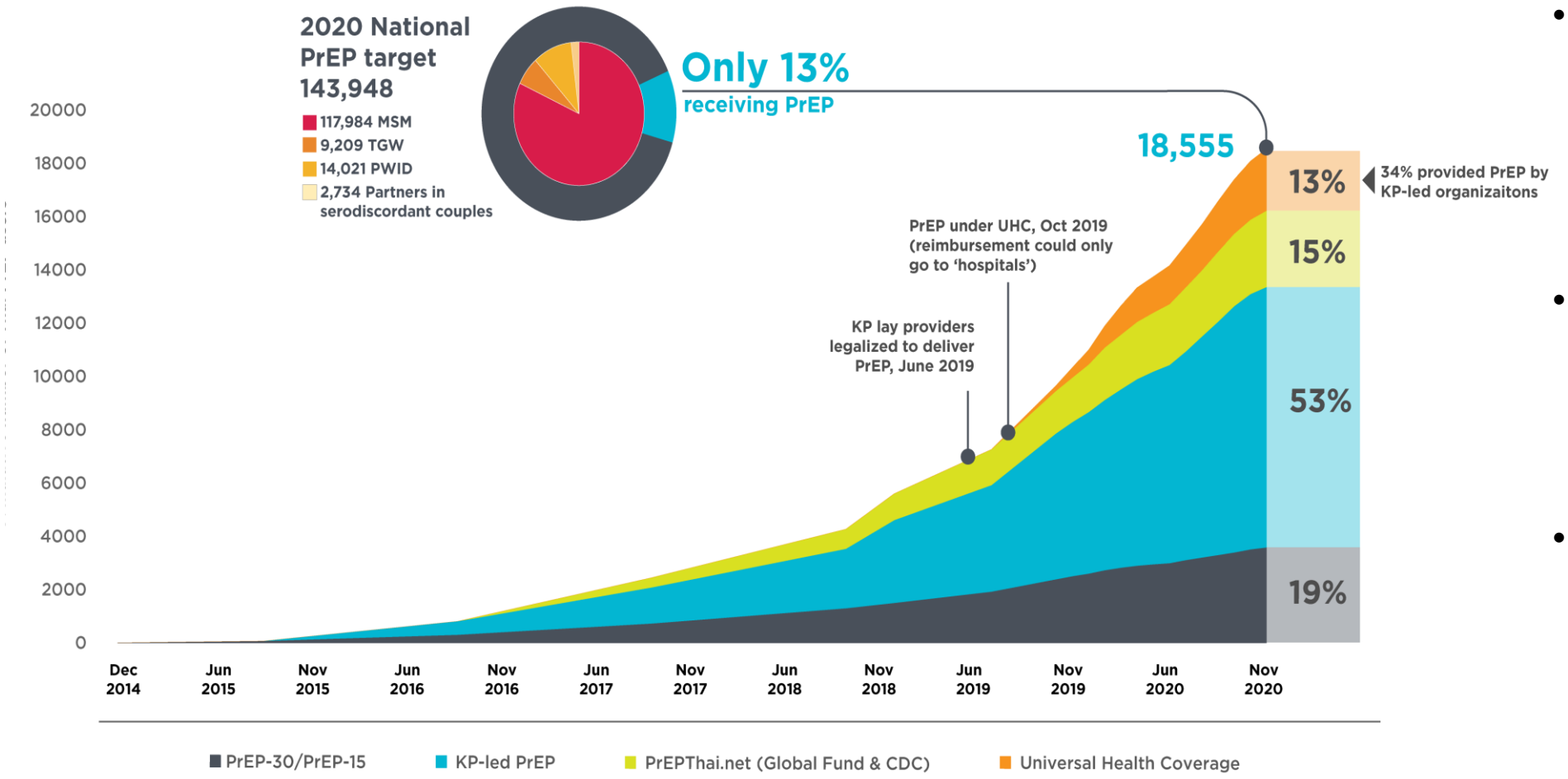
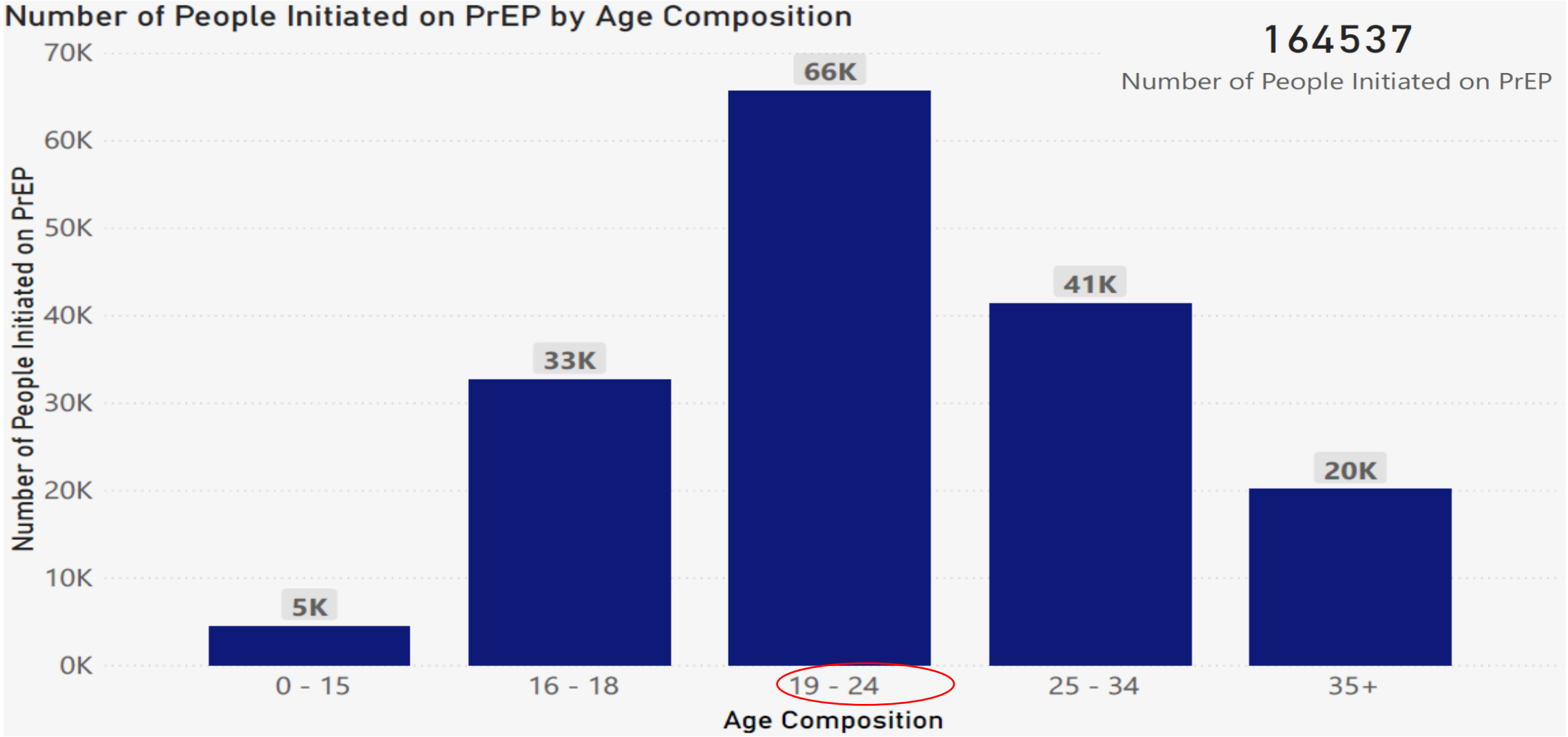
Key population-led PrEP
scale-up and sustainability in Thailand



- Services are identified by the community itself and are, therefore, **needs-based, demand-driven, and client-centered**
- A set of services, focusing on specific health priorities, **designed by key populations**
- Delivered by trained and **qualified lay providers**, who are often members of the key populations

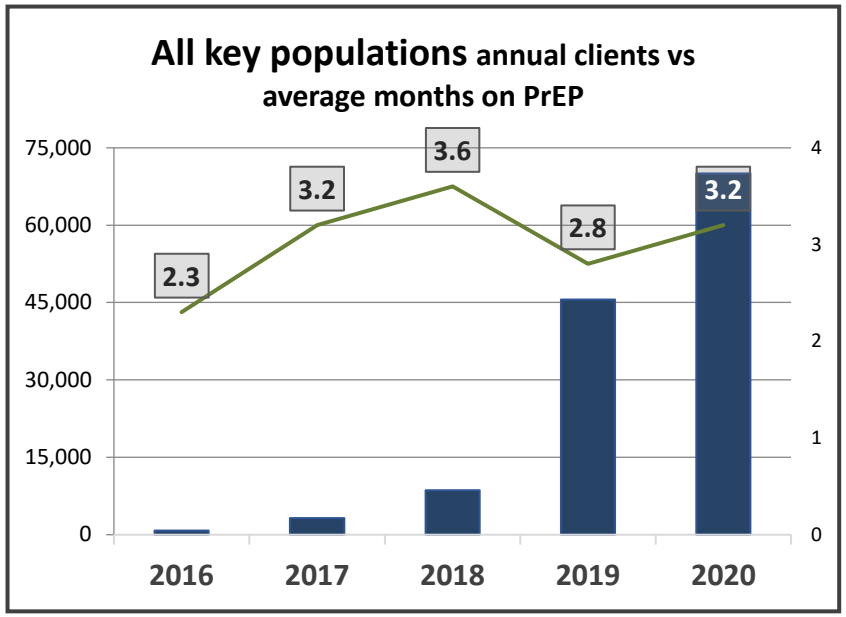
Nittaya Phanuphak, Institute of HIV Research and Innovative (IHRI), Bangkok, Thailand

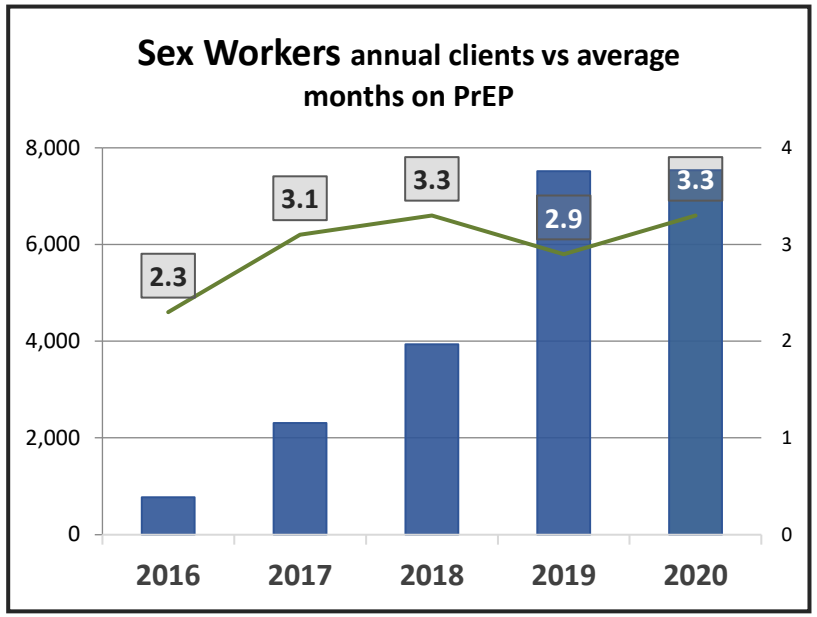
PrEP scale up in South Africa
Initiations by Age

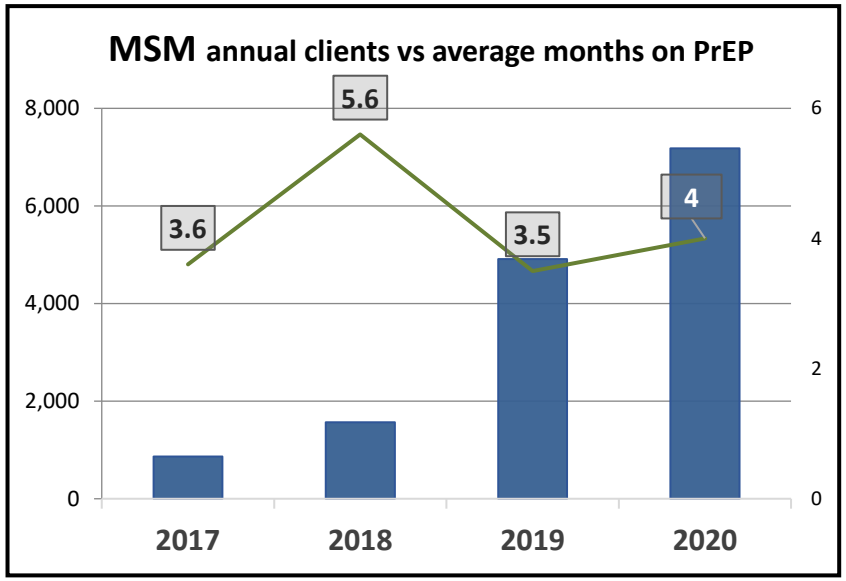


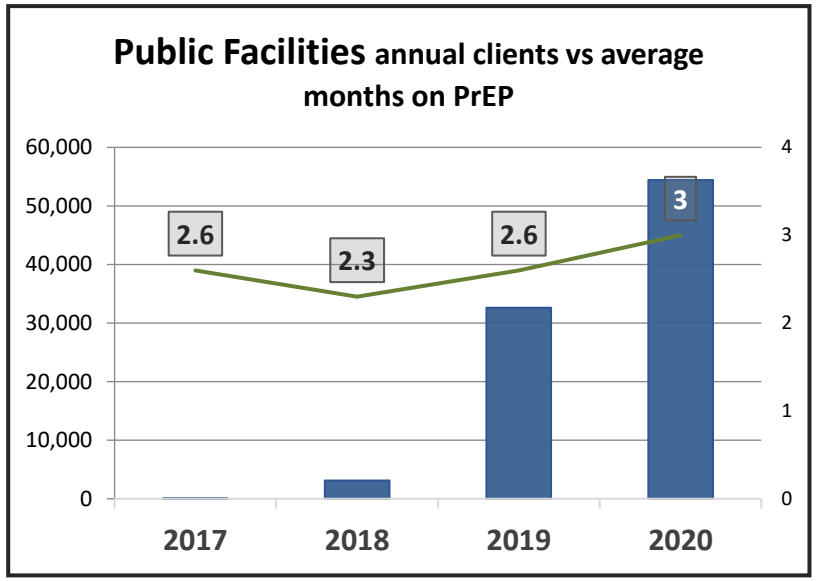
Hasina Subedar, NDoH, South Africa. Data as of Dec 2020

PrEP clients across all populations staying on PrEP for an average of ~3 months per year.







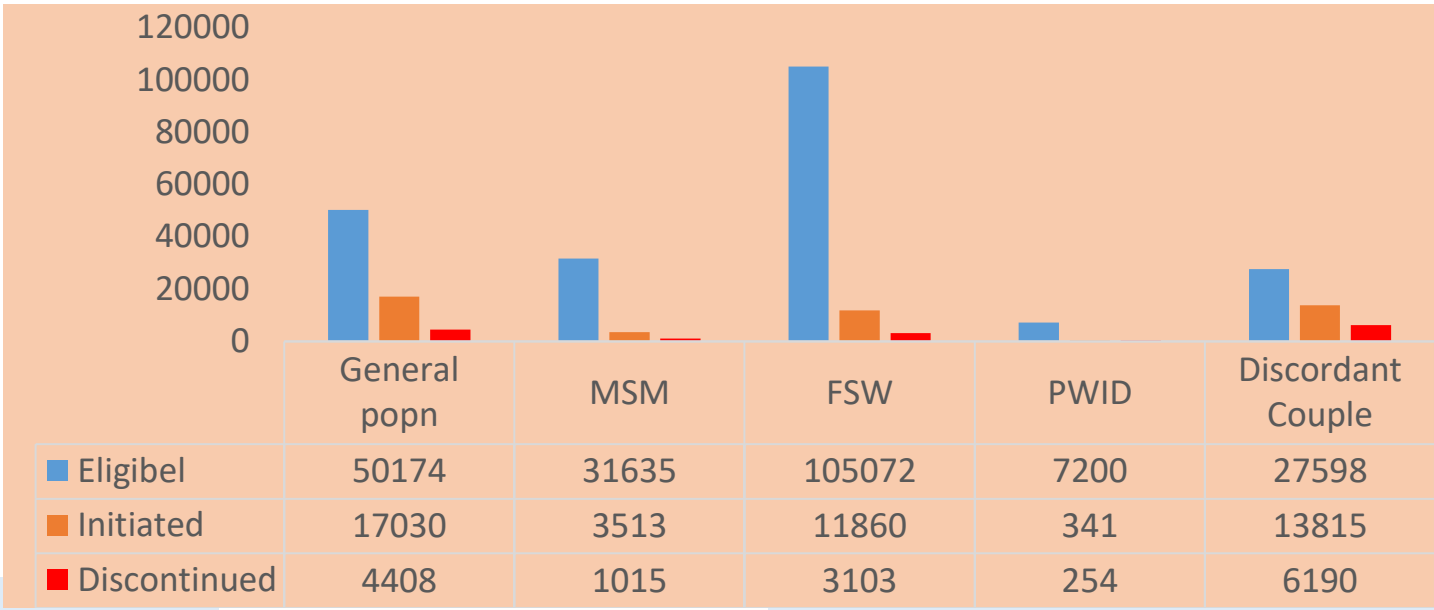


Note: Data as of Dec 2020

Hasina Subedar, NDoH, South Africa. Data as of Dec 2020

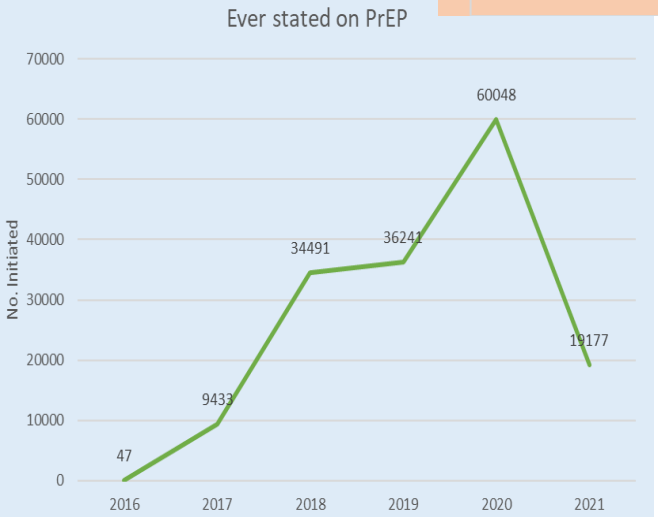
PrEP scale up in Kenya Africa

One of the biggest programmes in Africa

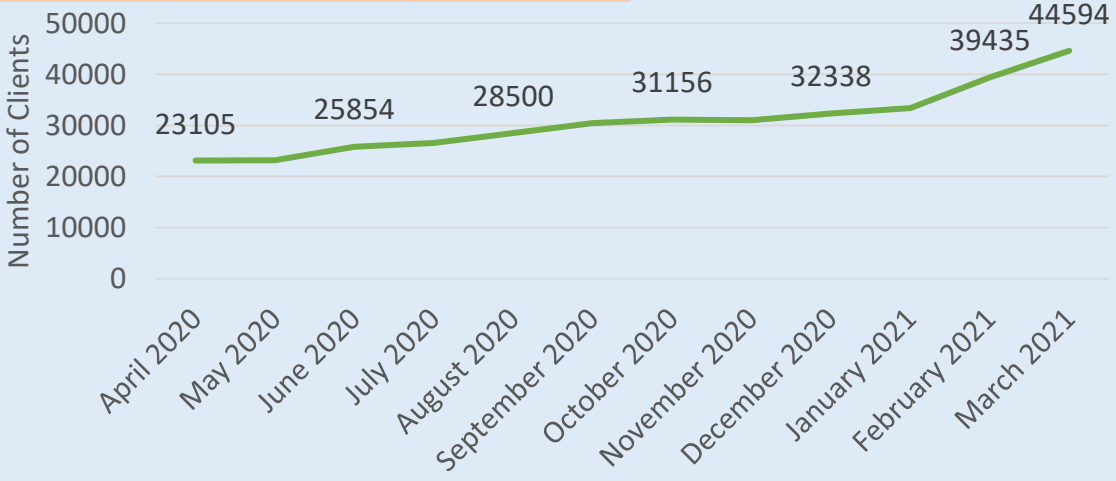


	General popn	MSM	FSW	PWID	Discordant Couple
Eligibel	50174	31635	105072	7200	27598
Initiated	17030	3513	11860	341	13815
Discontinued	4408	1015	3103	254	6190

Eligible, initiated & discontinuation April 2020 – March 2021



Ever started on PrEP – till March 2021

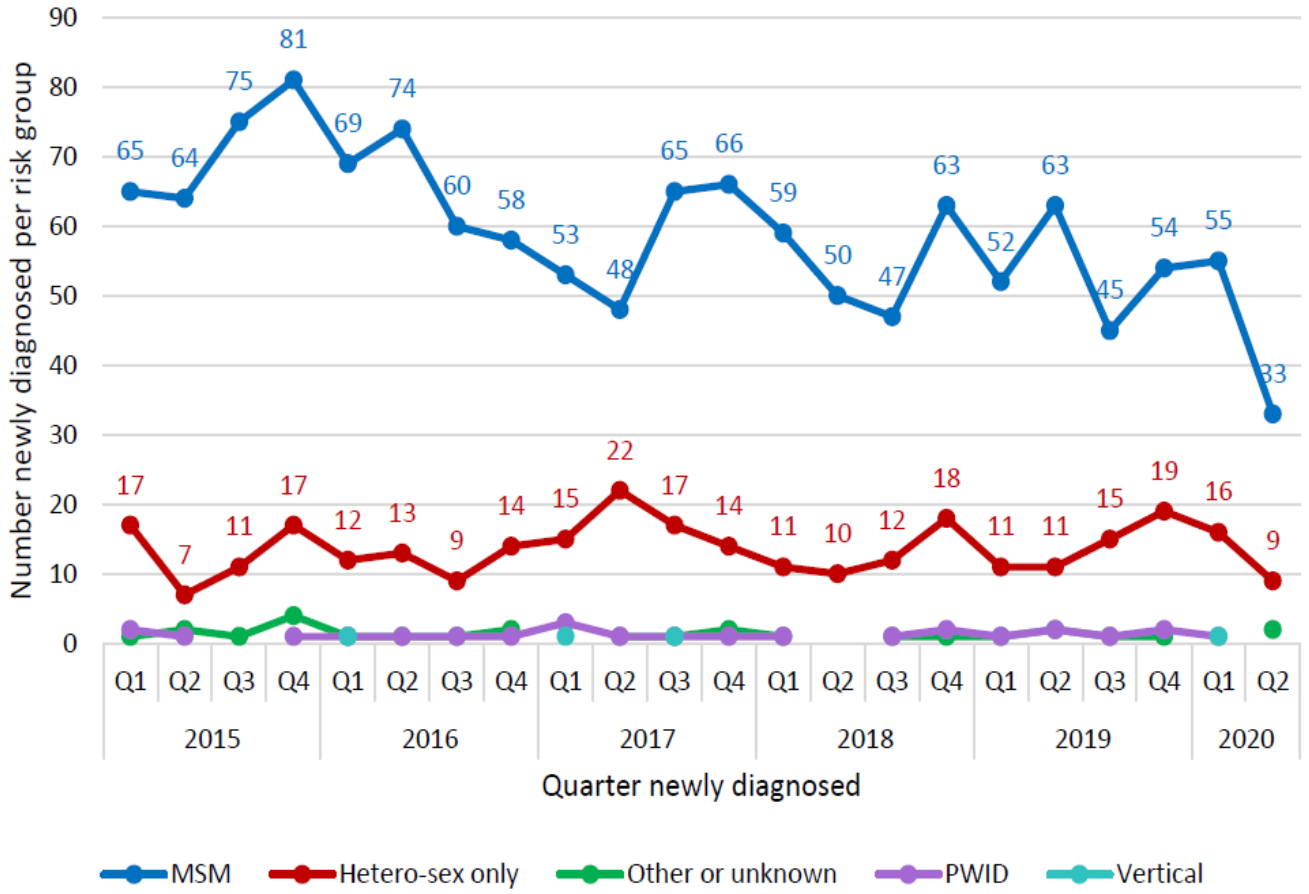


Current on PrEP – One Year Trend

PrEP impact in Australia
declining HIV in NSW, 2015-2020

- 24% decline in HIV diagnoses in MSM
- 42% decline in HIV diagnoses in Australian-born MSM
- 11% reduction in overseas-born MSM
- Declines also smaller in
  - MSM living outside the inner city and
  - MSM aged <25
- *75% decline* in Australian-born men living in the inner city

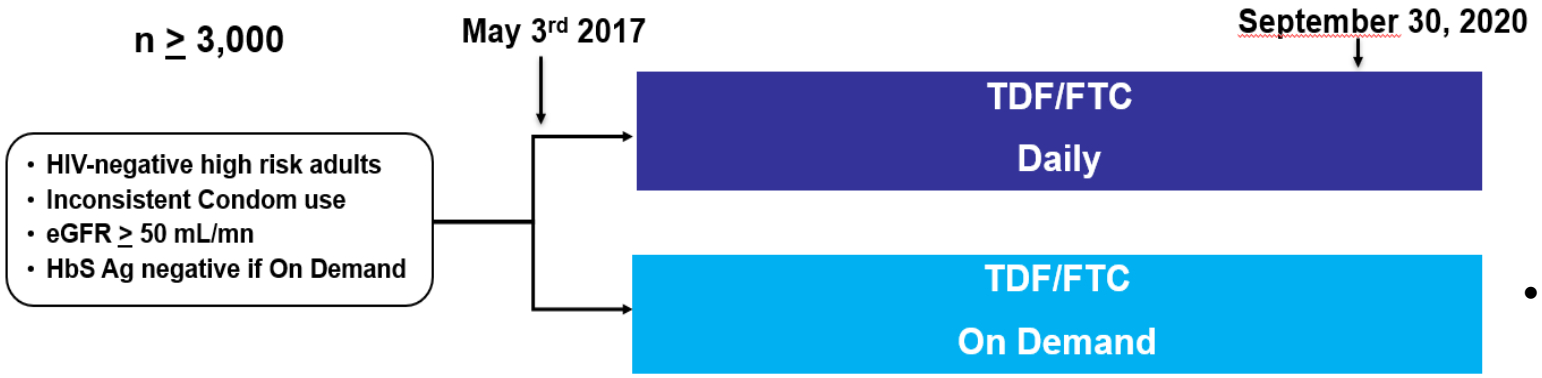
Figure 4: New HIV diagnoses by reported risk exposure, January 2015 to June 2020



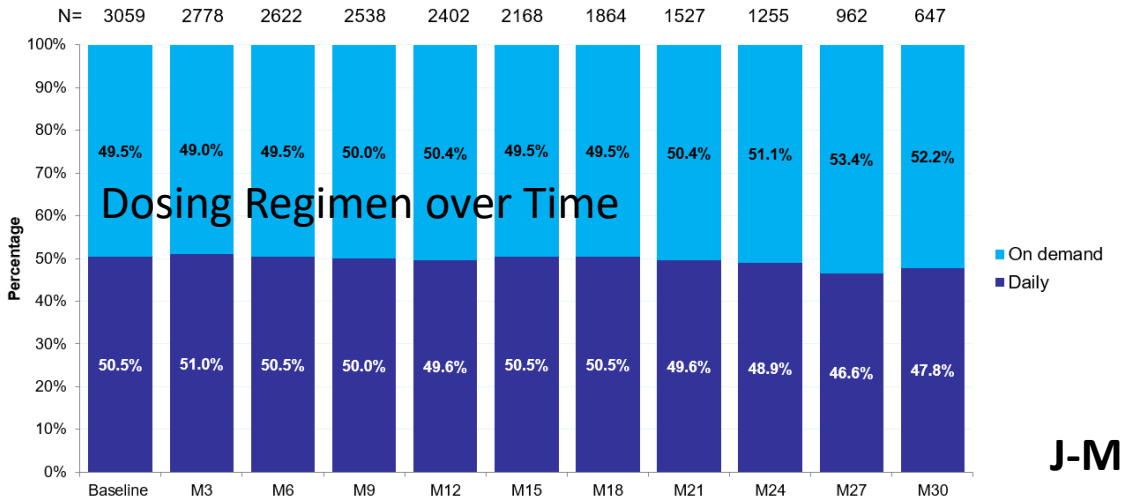
Andrew Grulich, Kirby Institute, UNSW, Australia

- https://www.health.nsw.gov.au/endinghiv/Publications/q2-2020-nsw-hiv-data-report.pdf

Open-Label Prospective Cohort Study in the Paris Region



Treatment	Follow-Up Pts-years	HIV Incidence per 100 Pts-years (95% CI)	IRR (95%CI)
TDF/FTC Daily	2583.25	0.12 (0.02 – 0.34)	**0.99** (0.13-7.38)
TDF/FTC On Demand	2553.68	0.12 (0.02 – 0.34)	



Dosing Regimen over Time

- **HIV Incidence**: 0.11/100 PY (95% CI: 0.04-0.23) (6 seroconversions – all in people who discontinued PrEP)
- **Mean Follow-up** of 22.1 months and 5633 Person-Years
- **Rate of study discontinuation**: 14.4/100 PY
- **Estimated 361 cases averted** (assuming 6.6/100 PY incidence observes un placebo group of the ANRS Ipergay study

J-M Molina and ANRS Prevenir study group, Paris France

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Organization

PrEP challenges

3

PrEP challenges

Global challenges

- How does PrEP fit on overall prevention strategy
- Demonstrating cost effectiveness and impact
- How to address STIs in the global syndemic

Policy challenges

- Inclusion in national guidelines
  - Inc stipulations on who can deliver, populations eligible/allowed
- Regulatory approval**, including for pregnant and breast feeding women**
- KP issues

Programme challenges

- Demand creation and messaging
- **Focus and targeting**
- Where to implement
- **What to include**
  - **Simplification vs. comprehensive services**
- How to monitor
- Who will fund
- **PrEP during COVID-19**
- Drug resistance

Client challenges

- **HIV diagnosis** – initiation, continuation and re-starting
- **Effective use and continuation**
- **STIs**
- **HCV**
- Safety and AEs
- Drug-drug interaction
- Stigma, misinformation
- Managing PEP→PrEP and PrEP→ART

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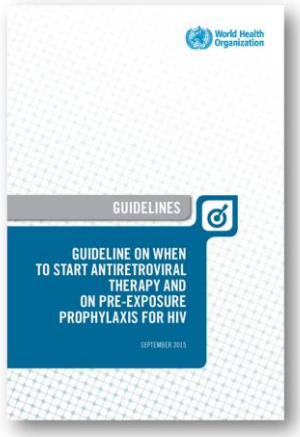
Challenge #1 Focus and prioritization

WHO recommends offer of PrEP for people at 'substantial risk'

Oral PrEP should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches

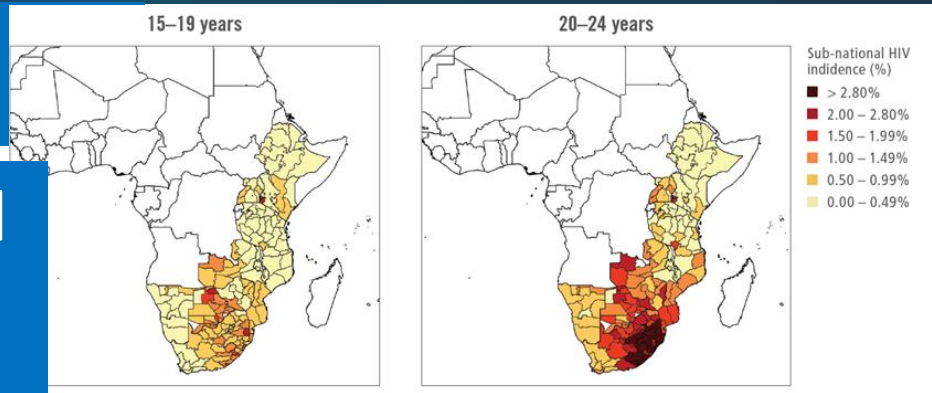


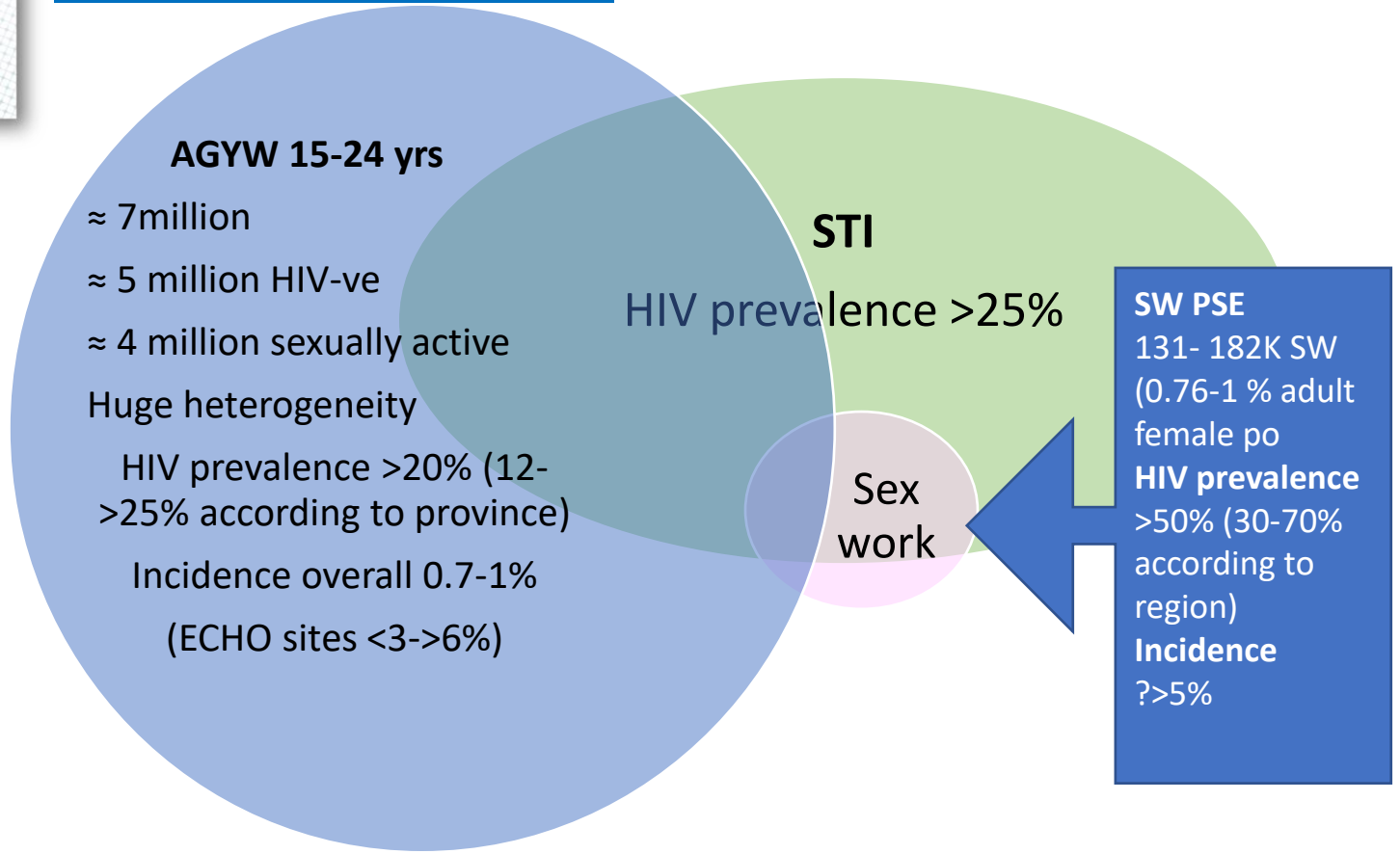
Rationale – approximation of when PrEP might be cost-effective

Defining "substantial risk": *Substantial risk of HIV infection is provisionally defined as HIV* ***incidence ≥3 per 100 person–years*** *in the absence of PrEP. HIV incidence ≥3 per 100 person–years identified among some groups of MSM, transgender women in many settings and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection.*

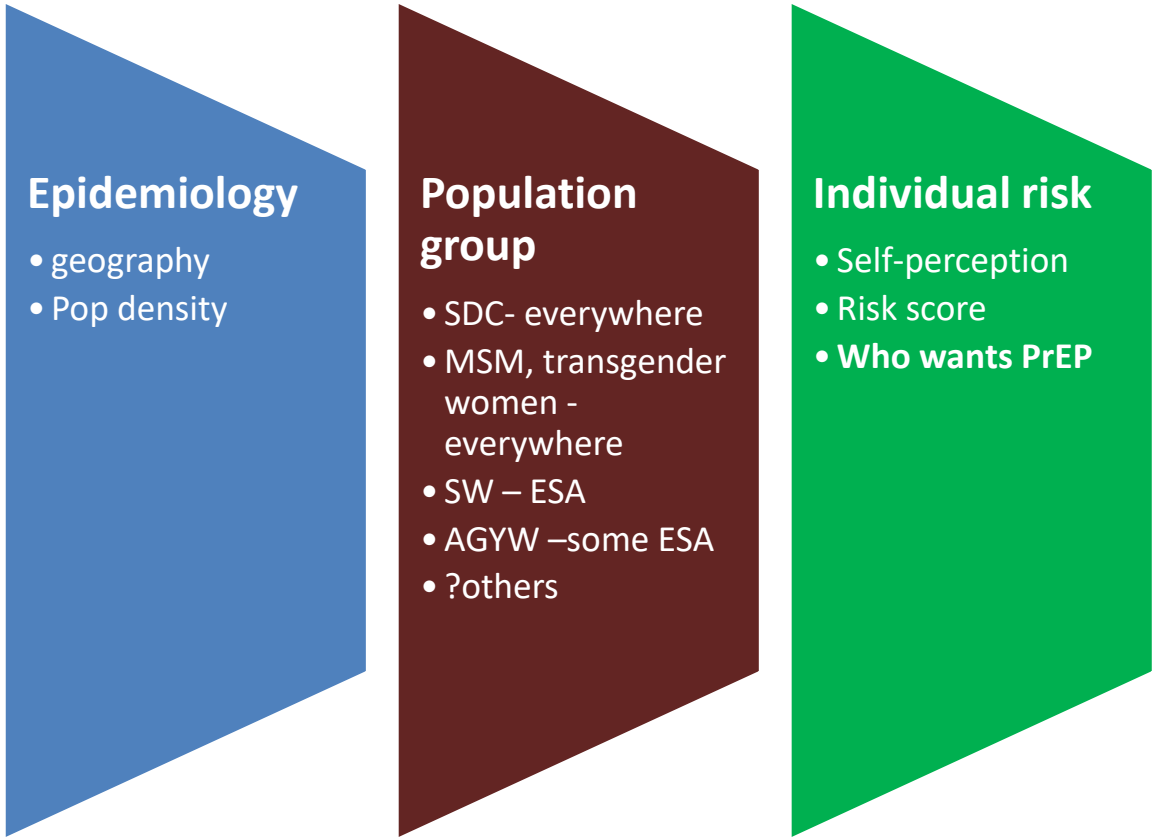
Why do we need to focus

PrEP offer: PrEP for AGYW in South Africa





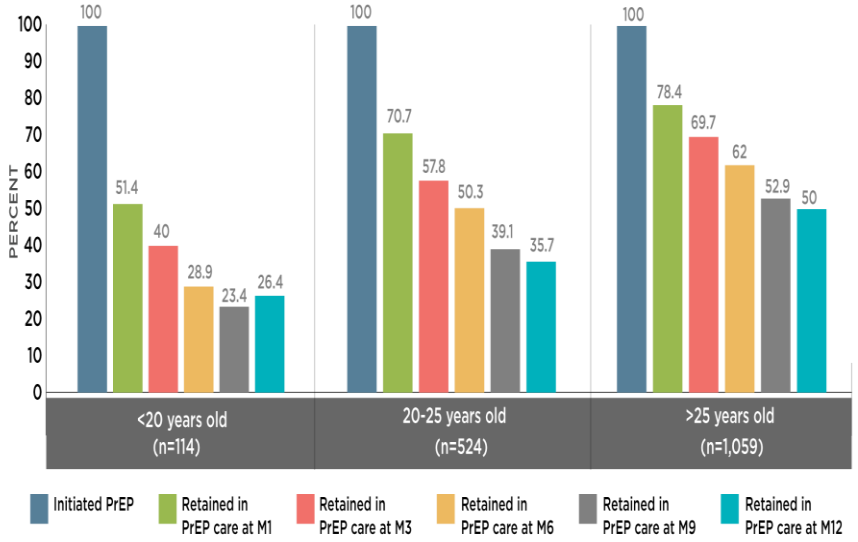
Challenge #1 Focus and prioritization ? screening tools



? do away with risk assessment entirely or modify them to a less prescriptive approach – as PrEP conversation tool … or something else

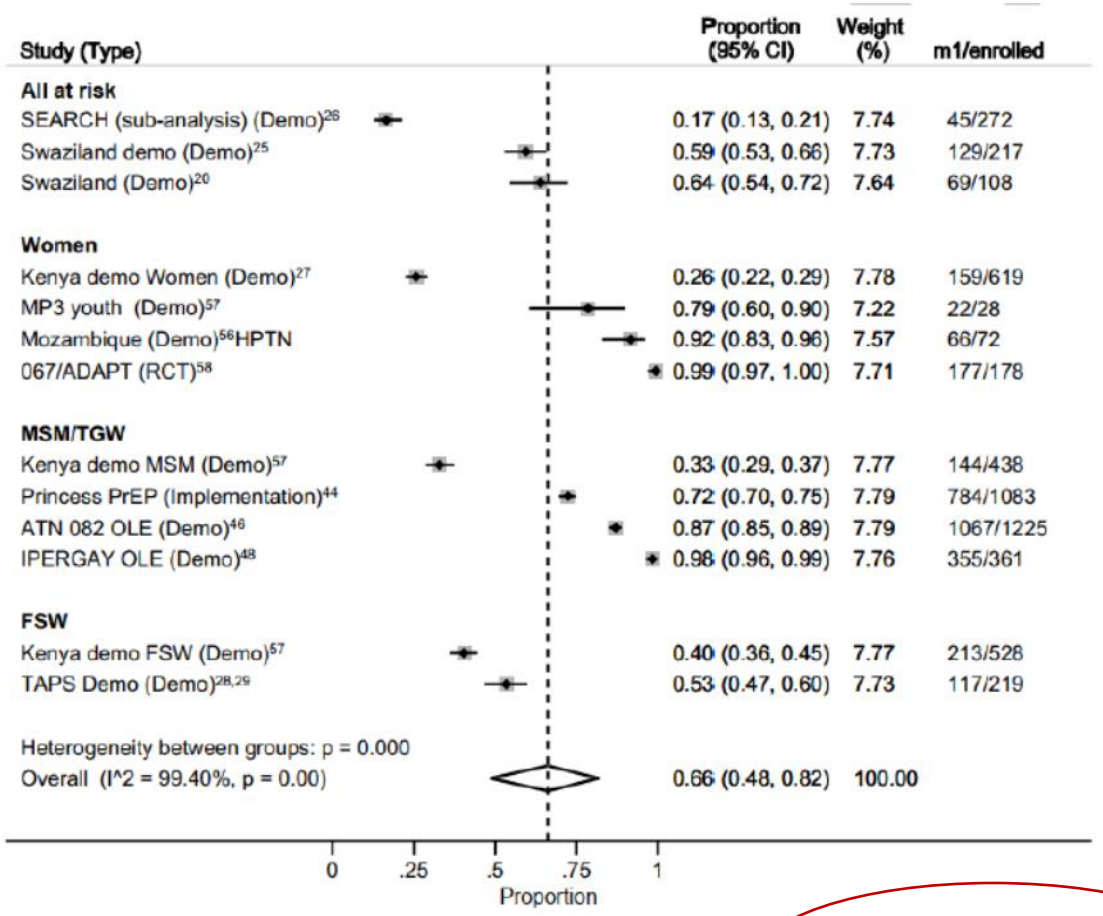
- **Mixed evidence of the utility of risk screening tools**
- **Screening not to screen people out of PrEP**, but identify those most at risk and open a conversation around risk between provider and client
  - Difference between "risk assessments" and "eligibility"
  - **People who request PrEP should be offered it** – counselling and support more important than risk screening for PrEP
- **Move from screening tools to community and conversation approach** (about HIV risk, PrEP and if and how it could be a suitable or acceptable prevention method)
  - part of a PrEP conversation - discuss apprehension/barriers and overall willingness/readiness to use PrEP
- **"Risk screening" may reinforce a barrier, especially for AGYW**
- **Caution about language**
  - "risk" – interpreted as a pejorative, morality issues
  - ? better to say "PrEP conversation tool" or "PrEP counseling tool"

Challenge #2 Continuation and 'effective use'



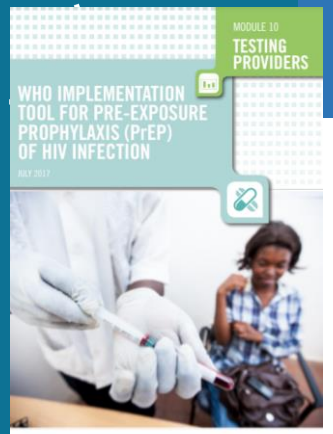
PrEP continuation a challenge in some place especially for younger people, Nittaya Phanuphak, Institute of HIV Research and Innovation in Bangkok, Thailand, MSM

- What is effective use
- Daily and ED for MSM
- Daily for AGYW and transgender populations
- Seasons of risk
- How to measure, monitor and advise



Stankevitz, *AIDS* 2020, Systematic review of 41 programmes → >30% discontinued PrEP by Month 1

Challenge #3 HIV testing



WHO HIV testing in PrEP services recommendation, 2015/2019

- Use WHO **serial testing strategies, within a validated testing algorithm**, using WHO prequalified assays.
- Individuals may be tested at POC following the **national testing algorithm**, usually a combination of 3rd generation RDTs
- If the initial HIV test -ve and no history or signs/ symptoms of an acute viral syndrome, **offer same day initiation**
- Once initiated on PrEP, HIV testing is suggested every 3 months and whenever restarting PrEP after a gap in use.
- Additional HIV testing 1. month after starting or restarting PrEP may also be beneficial

False +ve

- **PrEP use does not increase the rate of false positivity**. As PrEP use increases, and incidence declines, false +ve results will occur and important to addresses these with messaging and testing algorithm. Ideally does not involve stopping PrEP and only transitions to ART when HIV infection is fully established.

False –ve

- **During acute infection,** initiation of PrEP, **may delay seroconversion** by viral suppression, thus altering immune response. Frequent retesting (quarterly) continues to be needed at this time.
- People starting on PrEP during acute infection who are bridged from PrEP to ART soon after infection can be more difficult to establish infection retrospectively.

But note

- **Breakthrough HIV infections among 'adherent' PrEP users extremely rare**
- **HIV diagnosis due to starting PrEP during acute infection uncommon**

What about HIV self-testing for PrEP?

WHO guidance 2015-19

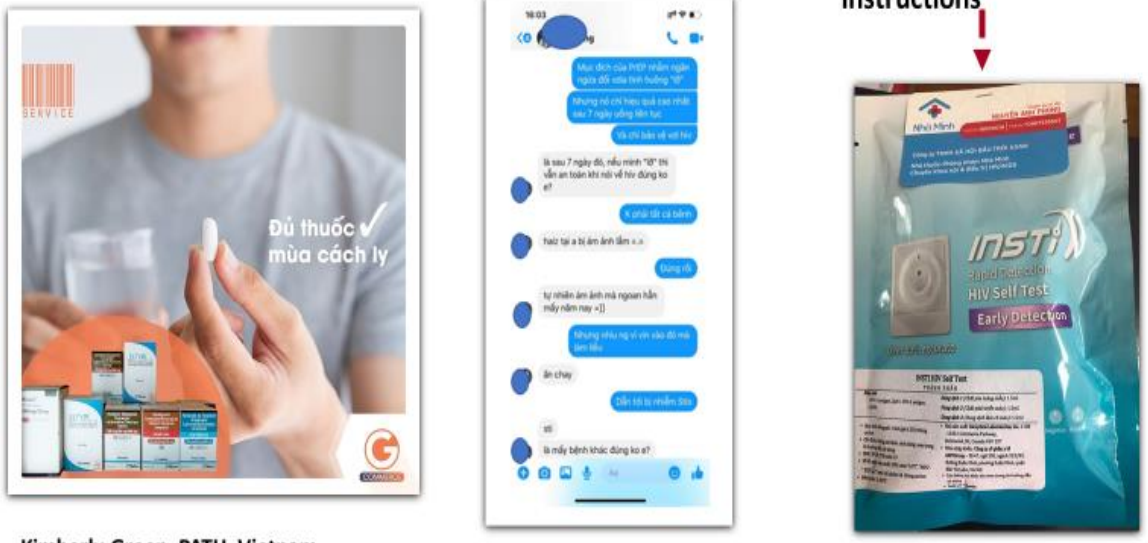
- Current guidance: HIVST suggested for potential demand creation, but not for monitoring during taking PrEP

- 4 trials underway looking at HIVST in PrEP programmes
  - **Kenya, Ortblad et al** https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3521-2 and https://clinicaltrials.gov/ct2/show/NCT03593629
  - **China (MSM), Zhang et al** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7371146
  - **Uganda (TGW), Mujugira et al** https://clinicaltrials.gov/ct2/show/NCT04328025
  - **Uganda (SW), Mujugira et al** https://clinicaltrials.gov/ct2/show/NCT03426670

- March 2020 WHO suggested use of HIVST to aid PrEP continuation during C-19
  - Numerous programme examples of using HIVST during PrEP C19-adaptions

Vietnam (Healthy Markets): Online support and counseling for PrEP clients

Online promotion → Online customized counseling → HIVST kit delivered to client with follow-up instructions

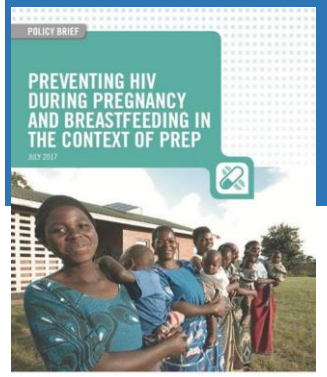


Kimberly Green, PATH, Vietnam

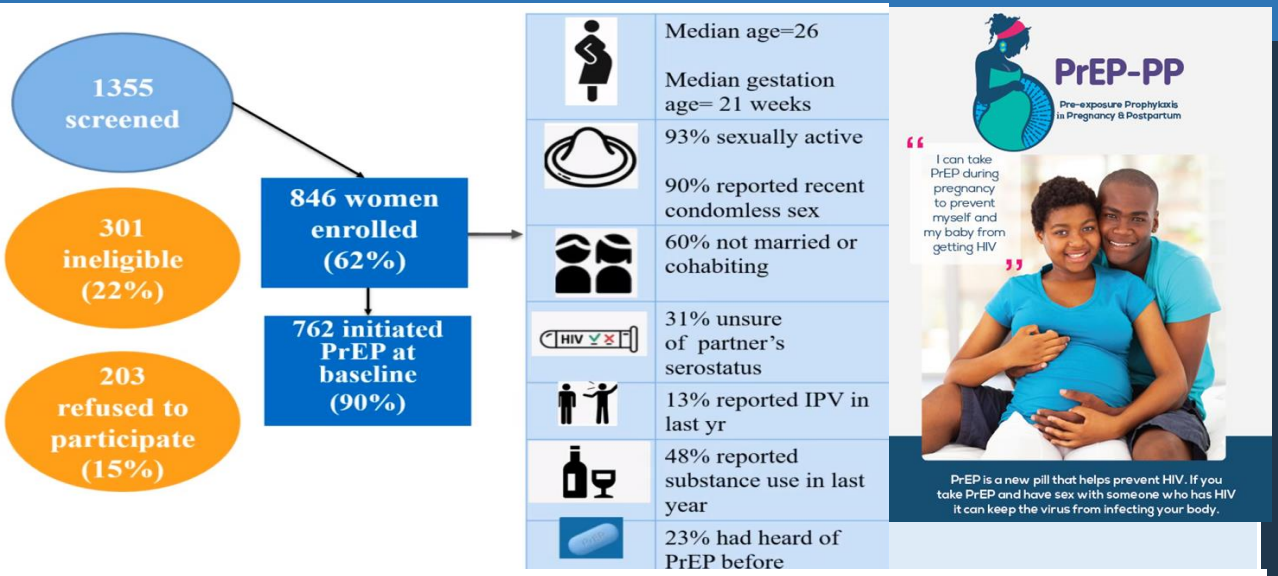
- Oral fluid-based RDTs can be more affected by ARV drugs, so blood-based RDTs may be preferable
- Access, feasibility and uptake need to be considered
- WHO review and new guidance as part of 'simplifying PrEP delivery' guidance end 2021

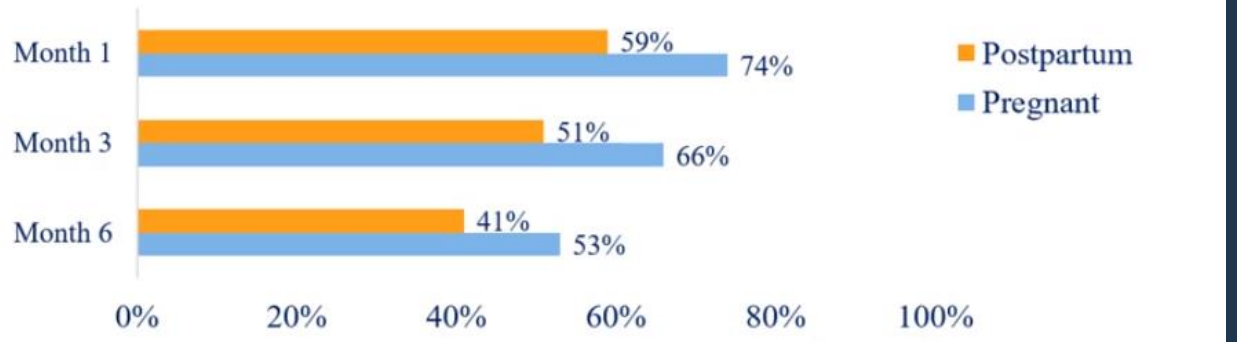
Challenge (and opportunity) #4 PrEP use during pregnancy and breastfeeding

- High HIV incidence in pregnant and breastfeeding women (HIV incidence - a meta-analysis of 37 studies, (Graybill, AIDS, 2020)
  - Pregnancy=3.4/100 PY
  - Breastfeeding=3.1/100 PY
  - Combined=4.6/100 PY
- Risk of vertical transmission high in acutely infected women
- PrEP is safe & effective at reducing HIV acquisition in pregnancy and postpartum (Mofenson, *AIDS*, 2017, Joseph Davey, *JIAS*, 2020)
- Daily PrEP adherence needed in pregnancy when TDF plasma concentrations lower than postpartum



WHO guidance (2017) support PrEP use for PBFW

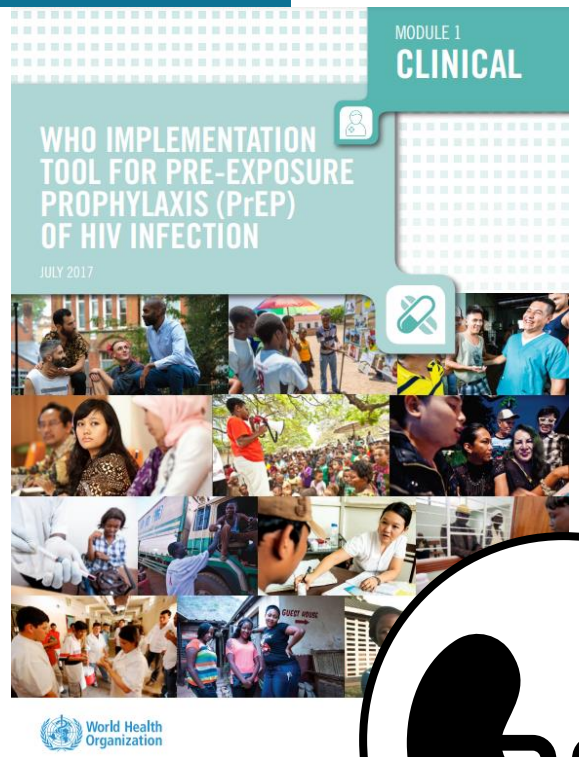




PrEP persistence during PBF, Dvora L Joseph Davey, PrEP-PP study Cape Town, South Africa (CROI 2021)
https://www.croiconference.org/abstract/impact-of-common-side-effects-on-prep-persistence-during-pregnancy-in-south-africa/

- **PrEP availability low for PBFW in high incidence settings**
- **Support needed for adherence and persistence**

Challenge #5 Creatinine screening



Current - WHO *suggested* procedures on monitoring renal function

- Baseline creatinine clearance (to identify pre-existing renal disease)
  - PrEP can be initiated before receiving results
- Monitoring every 6 months (more or less frequently depending on comorbidities, age, weight, and baseline creatinine clearance)
  - Discontinue only after creatinine elevation is confirmed on separate specimen

Ongoing analysis of >18,000 PrEP users from 15 countries

- Baseline prevalence of creatinine clearance <60ml/min (contraindication for PrEP)
- Risk of decline in creatinine clearance after PrEP initiation

Revising guidance on monitoring renal function – can we simply or remove?

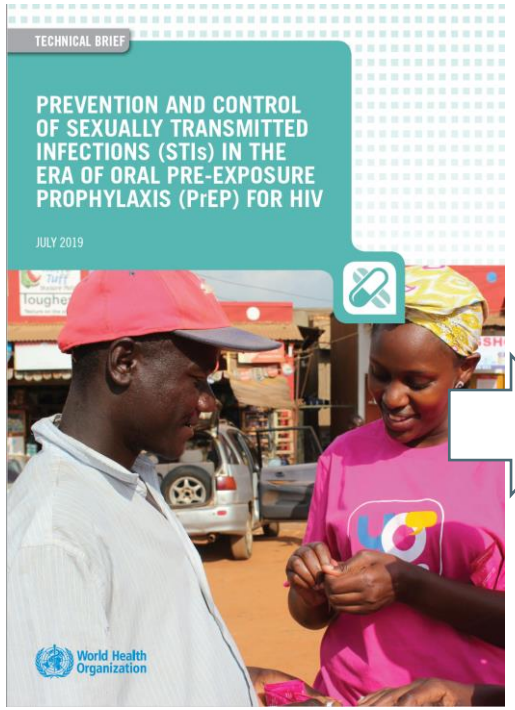
- Consolidated HIV guidelines (July 2021)
- Revised PrEP Implementation Tool (end 2021)

Challenge (and opportunity) #6 STIs

PrEP services are an opportunity for STI prevention and control

	Chlamydia trachomatis	Neisseria gonorrhoeae
MTN-020/ASPIRE (phase III microbicide trial)	Prevalence = 12% Incidence = 27% per year	Prevalence = 4% Incidence = 11% per year
HPTN 082 (PrEP demonstration project)	Prevalence = 29% Incidence = 33% per year	Prevalence = 8% Incidence = 14% per year
POWER (PrEP implementation project)	Prevalence = 26% Incidence = 53% per year	Prevalence = 10% Incidence = 20% per year
PrEP-PP	Any STI - 34% prevalence 65% asymptomatic	

STIs in AGYW PrEP trials in ESA, Connie Celum, Dvora Joseph Davey



Pathogen	Weighted average per 100 PY (95% CI)	I^2 statistic (p value)
Chlamydia	22.8 (19.0-27.4)	94% (<0.001)
Gonorrhoea	19.9 (16.6-23.9)	93% (<0.001)
Early syphilis	2.0 (1.3-3.1)	97% (<0.001)
Any Ct/Ng/Tp	71.9 (60.1-86.1)	95% (<0.001)

STIs in PrEP programmes: weighted average STI incidence, 62 studies from 26 countries. Ong JJ, Baggaley R, Wi TE,. *JAMA Netw Open*. 2019

Initial tests:
HIV test; suggest Cr, HBsAg, STIs screening (e.g. syphilis, gonorrhoea, chlamydia); consider HCV for MSM.
Every 3 months: HIV test, suggest check STIs, assess PrEP indications and use.
Every 6 months: Suggest Cr.'

Special situations:
- Exposure to HIV in the past 72 hours: use PEP for 28 days, then start PrEP.
- Acute viral syndrome: consider re-testing in 1 month before PrEP initiation.
- Pregnancy and breastfeeding: PrEP can be offered and continued.
- If HBsAg *negative*: consider vaccination; if HBsAg *positive*: assess HBV treatment indications; consider risk of flare if PrEP stopped.
- Adolescents: may benefit from more frequent appointments e.g. monthly visits.

#OfferPrEP

More information: http://who.int/hiv/pub/prep/prep-implementation-tool

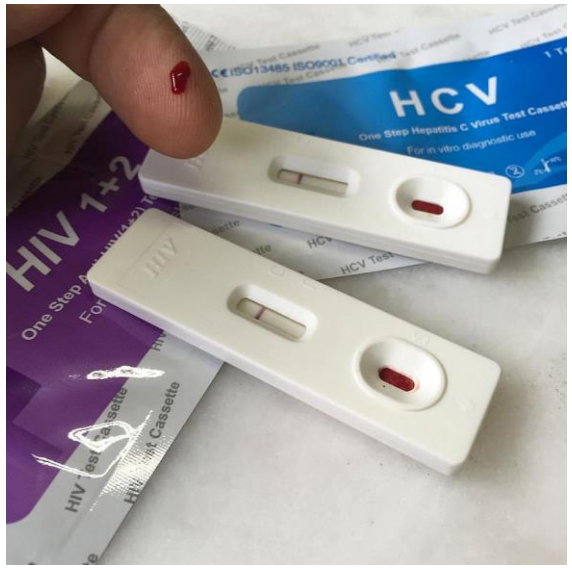
Challenge (and opportunity) #7 HCV

High HCV prevalence and incidence among MSM taking PrEP

Pooled HCV prevalence in MSM - 3.4% (95% CI: 2.8-4.0%)
- 1·5% (1·0–2·1) in HIV-negative MSM
- 6·3% (5·3–7·5) in HIV-positive MSM

highest in Africa and South-East Asia (5.0%, 95% CI: 0.0-16.6).

In HIV-negative MSM, the pooled HCV incidence was:
- 0.12 (95% CI: 0-0.72) per 1,000PY in MSM not on PrEP
- 14.80 (95% CI: 9.65-20.95) per 1,000PY on MSM on PrEP



HCV self-tests - WHO pathways for recommendation and prequalification

Prevalence and incidence of hepatitis C virus infection in men who have sex with men: a systematic review and meta-analysis

Jin F et al *Lancet Gastroenterol Hepatol*. Jan 2021

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World Health
Organization

What next

4

The biomedical prevention technologies pipeline

HPTN HIV Prevention Trials Network

TDF/FTC

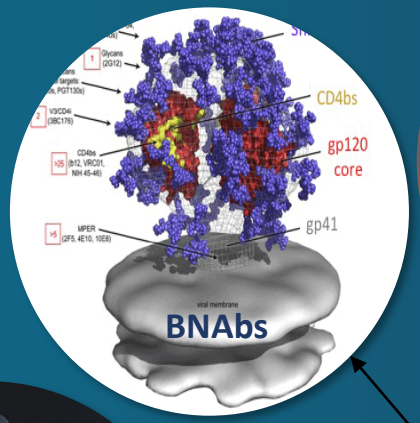
New products
Offer choice and
?↑demand

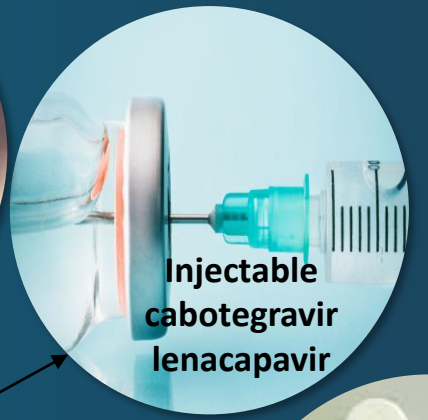
Overcome some oral TDF-FTC issues

- Continuation
- Adherence
- Renal safety

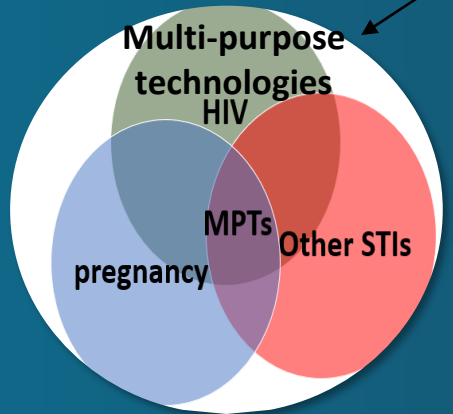
But have new challenges and unknowns

- Efficacy in real world setting
- Testing and DR
- Cost ……





Potential future prevention technologies



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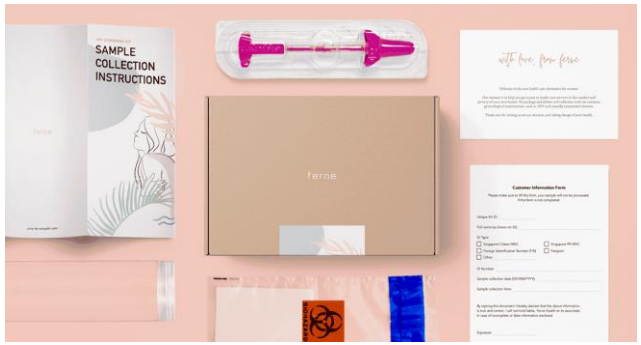
COVID-19: disruptions, adaptations and learning for the future

- self-testing/self-collection – for HIV, HCV and STIs
- community distribution sites, pharmacy models, mobile distribution
- simplification and DSD– longer distribution of PrEP
- virtual space – for info, demand creation, ordering supplies & tests, telemedicine, counselling support, follow-up ….

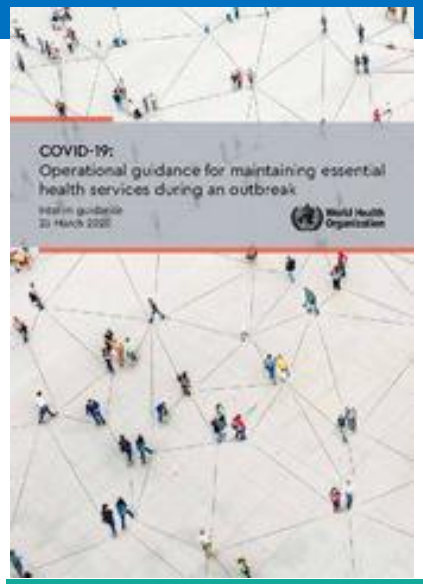


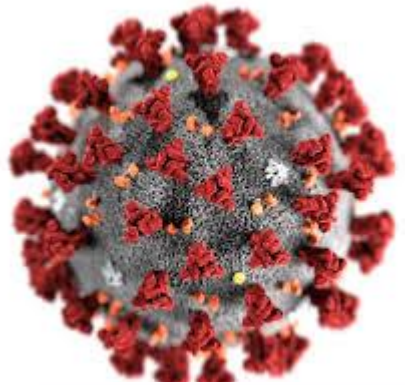
SELF-CARE IS CENTERED ON THE PREMISE OF EMPOWERMENT. WITH COVID-19 LIKELY TO AFFECT OUR LIVES FOR YEARS TO COME, SELF-CARE WILL BECOME MORE IMPORTANT FOR INDIVIDUALS TO BE EMPOWERED TO TAKE THEIR HEALTH AND WELL-BEING INTO THEIR OWN HANDS.

- Mohammed Majam, Head of Medical Technologies, Ezintsha, Wits RHI

INTERNATIONAL SELF-CARE DAY 2020 #better4tomorrow #selfcare4shrh

SELF-CARE TRAILBLAZER GROUP





Maintaining essential health services: operational guidance for the COVID-19 context

Interim guidance
1 June 2020

Maintaining and prioritizing HIV prevention services in the time of COVID-19

Introduction

In the time of coronavirus disease (COVID-19), sex and drug use will continue, regardless of physical distancing orders and policies. People

Preserving momentum and focus on HIV prevention

Several critical actions and temporary modifi

WHO

- monitoring -service disruptions
- working with modelling consortium
- providing guidance on keeping services going
- reviewing C-19 service adaptions

Community-based PrEP delivery during COVID-19

PrEP1519 Brazil: PrEP for young MSM and TGW (15-19) despite COVID-19

Telehealth consultation

Photo credit: PrEP1519

https://www.who.int/news-room/feature-stories/detail/brazil-prep-study-continues-despite-covid-19-disruptions

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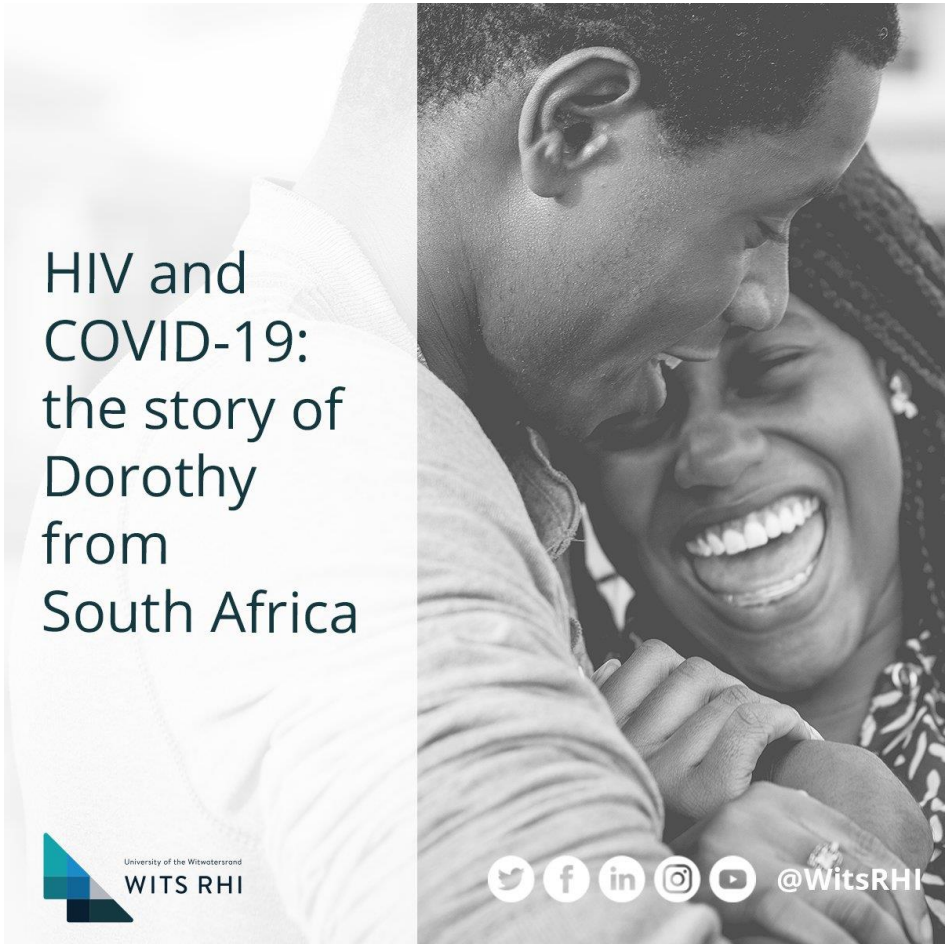
Mobile PrEP delivery during COVID-19

Project PrEP: Mobile PrEP during COVID for AGYW



Mobile sexual and reproductive health clinic

Dorothy: Offered her house as venue for mobile services

Photo credit:
Project PrEP,
WITS RHI

https://www.who.int/news-room/feature-stories/detail/hiv-and-covid-19-the-story-of-dorothy-mokgomotsi

Unitaid
Innovation in Global Health

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Community-based PrEP delivery during COVID-19

Key population-led health services for MSM and TGW in Thailand adapted during COVID-19

PrEP home delivery

Photo credit: Mplus Foundation, Chiang Mai

https://www.who.int/news/item/26-11-2020-pre-exposure-prophylaxis-services-in-thailand-during-covid-19

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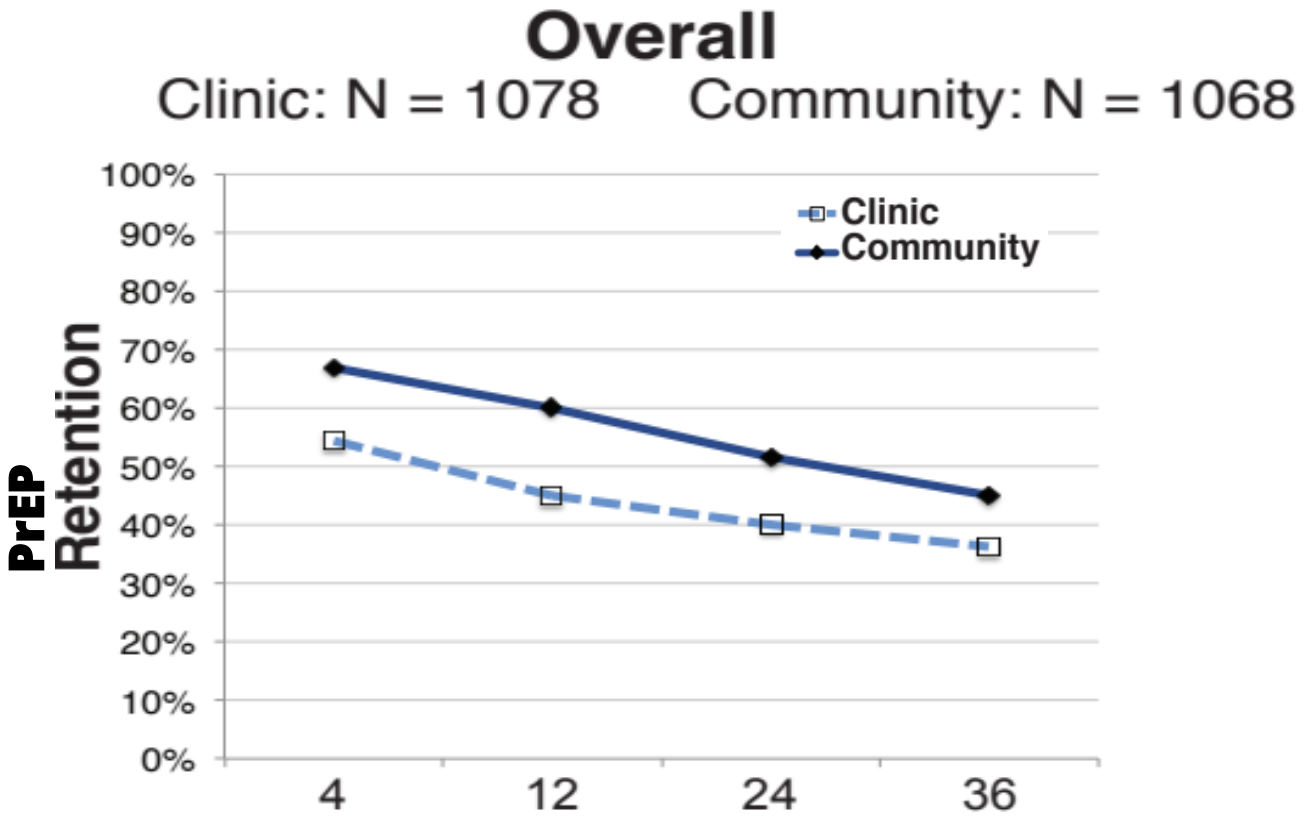
Mobile PrEP delivery before COVID-19

SEARCH Study: RCT on Kenya & Uganda on clinic- vs. community-based PrEP delivery.

Higher PrEP retention in community PrEP group.



SEARCH
SUSTAINABLE EAST AFRICA RESEARCH IN COMMUNITY HEALTH

World Health Organization

Jewell et al. 2018. Community Delivery Increases PrEP Uptake and Retention in SEARCH Study in Uganda and Kenya . AIDS2018. https://programme.aids2018.org//PAGMaterial/eposters/11180.pdf

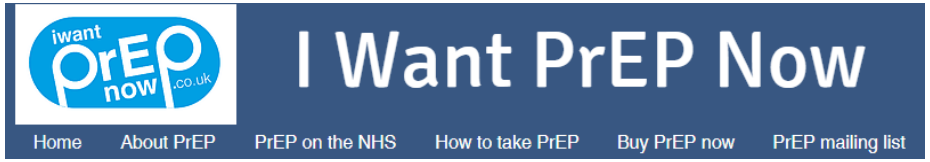
New for PrEP

WHO guidance on simplifying PrEP – coming end 2021

- **Starting and stopping rules "time to protection"**
- "effective use"
- **Behavioural screening/ eligibility**
  - ? risk screening to screen in or out, ?risk assessment/self-assessment/on-line tools ?PrEP conversation
- **Tests before starting and frequency during taking**
  - HIV testing (Ab, 4th gen, NATT) self-testing blood based and oral
  - ?Creatinine
  - HBV testing
  - others (HCV, STI, dual HIV-syphilis)
- **Delivery – staff -** doctors, clinical officers, nurses, trained lay providers, pharmacists
  - Who can screen, initiate, continue, support?
- **Delivery – where**
  - Community
  - ?Telemedicine
  - ?Pharmacy (inc without a prescription)
- **Delivery – entry point**
  - Contraception services
  - ANC/PNC
  - sexual health/STI services
  - post rape care services
  - KP services

- **What's in the essential PrEP package and what needs to have a link for referral?**
  - Contraception
  - Condoms
  - STIs services
  - GBV services
  - Harm reduction for PWID
  - Chem sex 'services'
  - Mental health
  - Referrals for ART and Rx for hepatitis
  - Transitioning hormones for transgender populations
- **Support for 'informal' use**
- **Programme monitoring and indicators**
  - PrEP initiation … do we need anything else
- **Considerations for future products**

Private sector & “informal” PrEP use



Gay men in China pour in to buy anti-HIV drug in Thailand

national July 12, 2017 12:54

By China Daily
Asia News Network
7,911 Viewed

Thailand has been a hot destination for Chinese tourists for years. Yet many now are heading to the Southeast Asian country for a new reason - to buy cheap drugs to prevent HIV.

According to Hornet's Brazilian PrEP Survey, Gay Men Want PrEP But Need More Information

- 7% of respondents currently taking PrEP, prior to the Brazilian rollout, inc through clinical trials and ordering online.
- 36% were likely to use PrEP in the next six months

Blued online survey

- 24 million users in China
- From survey increasing demand and informal use

PrEP increasingly available through on-line platforms (often unregulated)

How to make safe?

How to measure?

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