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
Global PrEP scale up
Evolution of WHO PrEP recommendations and guidance

- **2010**: Iprex PrEP 44% ↓ (MSM)
- **2012**: PrEP FDA approval

**2012**

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

- **WHO Model List of Essential Medicines**

**2018/19**

- **WHO Prequalification of medical products and health technologies**

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

**2020**

- **EMA Article 58 positive opinion**

**2021/2**

- **Simplifying PrEP**

**2021**

- **Dapivirine vaginal ring prequalified**

**2020**

- **Dapivirine vaginal ring prequalified**

**2019**

- **EMA Article 58 positive opinion**
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.
2020:
- 129 WHO member states adopted WHO PrEP recommendations into national guidelines
- 16 states pending
- But: Guideline adoption does not necessarily translate into implementation

Source: GAM and WHO regional/country offices. Data for 2020 are preliminary.
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.
PrEP successes 2
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
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.

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

Note: Data as of Dec 2020
PrEP scale up in Kenya Africa
One of the biggest programmes in Africa

Eligible, initiated & discontinuation
April 2020 – March 2021

Eligible
Initiated
Discontinued

General popn
MSM
FSW
PWID
Discordant Couple

50174
31635
105072
7200
27598
17030
3513
11860
341
13815
4408
1015
3103
254
6190

Current on PrEP – One Year Trend

Ever started on PrEP – till March 2021

Number of Clients
• 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

Andrew Grulich, Kirby Institute, UNSW, Australia

**Open-Label Prospective Cohort Study in the Paris Region**

- **n ≥ 3,000**
- **May 3rd 2017**
- **September 30, 2020**

**Treatment**

**Follow-Up Pts-years**

- **TDF/FTC Daily**
  - 2583.25
- **TDF/FTC On Demand**
  - 2553.68

**HIV Incidence per 100 Pts-years (95% CI)**

- **TDF/FTC Daily**
  - 0.12 (0.02 – 0.34)
- **TDF/FTC On Demand**
  - 0.12 (0.02 – 0.34)

**IRR (95% CI)**

- **TDF/FTC Daily**
  - 0.99 (0.13-7.38)

- **HIV Incidence**: 0.11/100 PY (95% CI: 0.04-0.23) (6 seroconversions – all in people who discontinued PrEP)
- **Mean Follow-up**: 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 unplacebo group of the ANRS Ipergay study)

**Dosing Regimen over Time**

J-M Molina and ANRS Prevenir study group, Paris France
PrEP challenges
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
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 $\geq 3$ per 100 person–years in the absence of PrEP. HIV incidence $\geq 3$ 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.

---

**Challenge #1 Focus and prioritization**

Why do we need to focus

PrEP offer: PrEP for AGYW in South Africa

AGYW 15-24 yrs

$\approx 7$ million

$\approx 5$ million HIV-ve

$\approx 4$ million sexually active

Huge heterogeneity

- HIV prevalence $>20\%$ (12-$>25\%$ according to province)
- Incidence overall $0.7$-$1\%$
  (ECHO sites $<3$-$>6\%$)

STI

HIV prevalence $>25\%$

Sex work

SW PSE

131-182K SW
(0.76-$1\%$ adult female pop
HIV prevalence $>50\%$ (30-70% according to region)
Incidence $>5\%$)
Challenge #1 Focus and prioritization

**Screening tools**

- 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”

**Epidemiology**
- geography
- Pop density

**Population group**
- SDC - everywhere
- MSM, transgender women - everywhere
- SW – ESA
- AGYW - some ESA
- ?others

**Individual risk**
- Self-perception
- Risk score
- Who wants PrEP

? do away with risk assessment entirely or modify them to a less prescriptive approach – as PrEP conversation tool ... or something else
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
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.
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 [1]
  - China (MSM), Zhang et al [2]
  - Uganda (TGW), Mujugira et al [3]
  - Uganda (SW), Mujugira et al [4]
- March 2020 WHO suggested use of HIVST to aid PrEP continuation during C-19
  - Numerous programme examples of using HIVST during PrEP C19-adaptions

What about HIV self-testing for PrEP?

- 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 availability low for PBFW in high incidence settings


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)
### PrEP services are an opportunity for STI prevention and control

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Weighted average per 100 PY (95% CI)</th>
<th>I² statistic (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>22.8 (19.0-27.4)</td>
<td>94% (&lt;0.001)</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>19.9 (16.6-23.9)</td>
<td>93% (&lt;0.001)</td>
</tr>
<tr>
<td>Early syphilis</td>
<td>2.0 (1.3-3.1)</td>
<td>97% (&lt;0.001)</td>
</tr>
<tr>
<td>Any Ct/Ng/Tp</td>
<td>71.9 (60.1-86.1)</td>
<td>95% (&lt;0.001)</td>
</tr>
</tbody>
</table>

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

---

**Challenge (and opportunity) #6 STIs**

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

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Weighted average per 100 PY (95% CI)</th>
<th>I² statistic (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>22.8 (19.0-27.4)</td>
<td>94% (&lt;0.001)</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>19.9 (16.6-23.9)</td>
<td>93% (&lt;0.001)</td>
</tr>
<tr>
<td>Early syphilis</td>
<td>2.0 (1.3-3.1)</td>
<td>97% (&lt;0.001)</td>
</tr>
<tr>
<td>Any Ct/Ng/Tp</td>
<td>71.9 (60.1-86.1)</td>
<td>95% (&lt;0.001)</td>
</tr>
</tbody>
</table>
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

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
What next
The biomedical prevention technologies pipeline

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 .........

TDF/FTC

PrEP

Potential future prevention technologies

TAF, islatravir implant

Injectable cabotegravir lenacapavir

Other oral preparation F/TAF Islatravir

Dapivirine Vaginal Ring

BNAbs

Multi-purpose technologies HIV

MPTs Other STIs pregnancy

Micobiome modulating products
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, HIts RH

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


Telehealth consultation


Photo credit: PrEP1519
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

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


New for PrEP
WHO guidance on simplifying PrEP – coming end 2021

• Starting and stopping rules “time to protection”
  • “effective use”

• Behavioural screening/ eligibility

• 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


- 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

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

How to make safe?

How to measure?

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

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.

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

- **WHO colleagues** Michelle Rodolph, Robin Schaefer, Heather-Marie Schmidt, Niklas Luhmann, Maeve de Mello, Silvia Bertagnolio, Annette Verster
- Andrew Grulich, Kirby Institute, UNSW, Australia
- Dvora L Joseph Davey, University of California Los Angeles
- Jean-Michel Molina, University of Paris
- Hasina Subedar, NDoH, South Africa
- Elizabeth M Irungu, , Jomo Kenyatta University, Kenya
- Ruth Kamau, NASCOP, Kenya
- Mary Mugambi, NASCOP, Kenya
- Kimberly Green, PATH, Vietnam
- Kristine Torjesen, FHI360
- Nittaya Phanuphak, Institute of HIV Research and Innovative (IHRI), Bangkok, Thailand
- Heather Ingold, Unitaid
- Siobhan Malone, BMGF
- Ioannis Mameletzis-Hodges