PrEP in Future Australia: How will it look?

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Australasian HIV & AIDS Conference, Canberra

2017

Burnet Institute
Medical Research. Practical Action.

Doherty Institute

MONASH University

TheAlfred

Disclosures

None in the past 12 months

Previously

- **Study drug provided VicPrEP Study**
  - Gilead
- **Receipt of unrestricted research funds**
  - Gilead, Abbott, Janssen Cilag, Boehringer Ingelheim
- **Receipt of funding for consultancy, lectures & developing educational resources**
  - ViiV, Merck, Gilead and Abbott
- ***All funds used for research purposes only***

PrEP availability[1]. Guidelines. Approvals November

Guidelines/Programs
- WHO
- CDC/DHHS
- ***Australia****
- South Africa
- Kenya
- Botswana
- Zambia
- Zimbabwe
- Thailand
- Brazil

Licensed
- Canada
- France
- Israel
- Kenya
- South Africa
- USA
- Norway
- Australia
- Europe

GUIDELINES

Journal of Virus Eradication 2017; 3: 168-184

Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine HIV pre-exposure prophylaxis: clinical guidelines

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Abstract

Daily use of coformulated tenofovir and emtricitabine for HIV pre-exposure prophylaxis (PrEP) by populations at high risk of HIV infection is now recommended in guidelines from the United States, Europe and Australia and globally through the 2015 WHO guidelines. These 2017 Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine's (ASHM) PrEP Guidelines are an updated adaptation of the 2014 US Centers for Disease Control's PrEP guidelines and are designed to:

- Support the prescription of PrEP using forms of coformulated tenofovir and emtricitabine that have been registered in Australia by the Therapeutic Goods Administration and other bioequivalent generic drugs that are available in Australia through self-importation, private prescription or Australian PrEP clinical trials
- Assist clinicians in the evaluation of patients who are seeking PrEP
- Assist clinicians in commencing and monitoring patients on PrEP including PrEP dosing schedules, management of side-effects and toxicity, use of PrEP in pregnancy and in chronic hepatitis B infection and how to cease PrEP

Daily PrEP with co-formulated tenofovir and emtricitabine, used continuously or for shorter periods of time, is recommended in these guidelines as a key HIV-prevention option for men who have sex with men (MSM), transgender men and women, heterosexual men and women, and people who inject drugs (PWID) at substantial risk of HIV acquisition.

Keywords: pre-exposure prophylaxis, PrEP, TDF/FTC

Introduction

Co-formulated tenofovir and emtricitabine for use as HIV pre-exposure prophylaxis (PrEP) by populations at high risk of HIV infection is now recommended in guidelines in the United States, Europe and Australia [2–4], as well as globally through the WHO guidelines [5].

These clinical PrEP guidelines update the 2015 Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine's (ASHM) PrEP guidelines and they represent an adaptation and update of the 2014 United States Centers for Disease Control's PrEP guidelines [3].

Between May 2016 and January 2017, the Australian Therapeutic Goods Administration (TGA) approved tenofovir disoproxil fumarate and emtricitabine (TDF/FTC, Truvada), tenofovir disoproxil maleate and emtricitabine (TDM/FTC, Truvada®) and tenofovir disoproxil phosphate and emtricitabine (TDP/FTC, Tenofovir EMT Lupin) for entry onto the Australian Register of Therapeutic Goods (ARTG). These medications are registered for daily use in individuals aged 18 years and over. However, these medications are not yet subsidised by the Pharmaceutical Benefits Scheme for use as HIV PrEP [6]. Other drugs used for PrEP but not registered in Australia can be legally imported into Australia using the TGA Personal Importation Scheme (PIS) [7]. For simplicity, the form TD* is used to denote the tenofovir disoproxil component present in the three registered drugs.

The recommendations included here are designed to:

- support the prescription of PrEP using the ARTG-listed drugs and other bioequivalent generic drugs that are available in Australia, or are being used in Australian PrEP trials
- assist clinicians in their evaluation of patients who are seeking PrEP
- to assist clinicians in commencing and monitoring their patients on PrEP by providing information on PrEP dosing schedules, management of side-effects and toxicity, use of PrEP in pregnancy and in chronic hepatitis B infection and how to cease PrEP.

Daily PrEP with TD*/FTC is recommended in CDC, WHO and earlier Australian guidelines as a key HIV-prevention option for men who have sex with men (MSM), transgender men and women, heterosexual men and women, and people who inject drugs (PWID) at substantial risk of HIV acquisition. Based on available evidence, this guideline does not recommend the coitally timed use of PrEP. Such use can be considered only for patients at risk of HIV infection who are unable to take daily PrEP, and it is contraindicated for people with chronic hepatitis B infection.

The intended users of this guideline include:

- general practitioners who provide care to persons at risk of acquiring HIV infection

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QPrEP
VicPrEP
PRELUDE
EPIC NSW
EPIC ACT
QPrEP'D
PrEPX
PrEPX-SA
PrEPX-TAS

onstration study

New clinical trial

Map: freeworldmaps.net

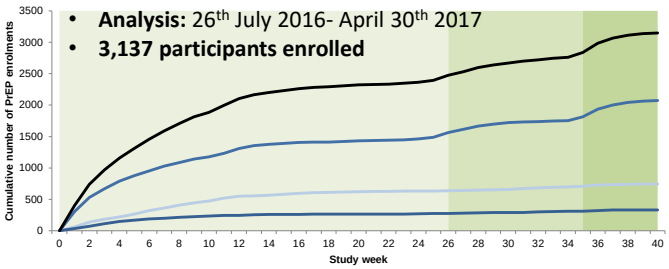
Studies closed- futility

1. Avaac, 2017

Access

- **Assume PBS listing in 2018**
  - **Comment: Otherwise expect community and healthcare activism with ongoing inequity of PrEP provision throughout Australia**
- **Need to start preparing for PBS listing now**
- **Modeling => rapid scale up is requisite** *(Gray, ASHM 2017)*
  - Capacity for scale up will vary by States & Territories
    - NSW: 18 Sexual Health Clinics in EPIC vs 2 Sexual Health clinics in PrEPX
    - Easier for States & Territories where PrEP is already in situ
  - States will need to work with PHNs, Sexual Health Centres, low and high caseload general practices, Pharmacies and Public Hospitals
  - Plan for saturation of clinics if PrEP will be delivered mostly via general practices vs Sexual Health Centres *(Ryan et al, IAS 2017)*

Results- enrolment sites



- **Analysis:** 26th July 2016- April 30th 2017
- **3,137 participants enrolled**

TOTAL= 7 sites

GP Clinics = 4

Sexual Health Clinics= 2

Hospital = 1

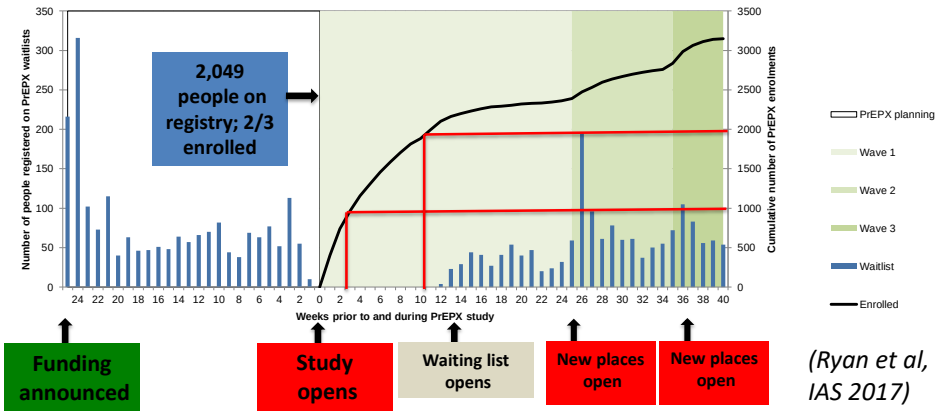
Melbourne Sexual Health Centre
Previously: a free, walk-in-service only
- **PrEPX**: Established appointment model with Medicare rebates to create two all-day clinics/week

Alfred Hospital
Previously: free weekly HIV prevention clinic
- **PrEPX**: Established free nurse-led clinics that ran five day per week
- Now running two days/week

(Ryan et al, IAS 2017)

Results- Enrolment

- **Analysis:** 26th July 2016- April 30th 2017
- **3,137 participants enrolled**
  - 1,000 enrolled during first 3 weeks
  - 2,000 enrolled during first 10 weeks



(Ryan et al, IAS 2017)

Access

- **Inequity of access**
  - MSM vs MSM
    - Gay connected vs less gay connected *(Prestage, ASHM 2017)*
    - Australian vs non-Australian born *(Guy, ASHM 2017)*
    - Educated vs non-educated *(Holt, ASHM 2017)*
    - Employed vs non-employed *(Holt, ASHM 2017)*
  - Rural vs Urban
  - MSM vs CALD, ATSI, PWID
  - Wealthy vs Less Wealthy vs Poor
  - Medicare vs non-Medicare Eligible

Prescribing & Monitoring

- **Prescriber**
  - **Unknown if PrEP will be prescribed under Section 85 or Section 100 of the Health Act**
  - **Will there be requirements for training?**
    - **Comment**: Australian PrEP Guidelines in place
    - States and territories may develop their own training requirements/guidelines
  - **Will there be different requirements GP vs Specialist vs Nurse vs Dentist?**
    - **Comment**: will need as many clinicians and peer workers on board as possible
    - In San Francisco one nurse can monitor 650 people on PrEP
  - **Need education and clear referral pathways for people diagnosed as HIV+ at baseline or whilst on PrEP**

Prescribing & Monitoring

- **Person seeking PrEP**
  - Streamlined Authority Listing requested by Pharma
    - Patient HIV negative and have eGFR > 60mls/min and > 18 years ???
- **Frequency of HIV and STI testing**
  - Current guidelines say 3 monthly for both
  - ? Push back to 6 monthly HIV tests for stable PrEP patients
  - Won't always need to see a doctor for each script
    - Future role of HIV and STI home testing in PrEP setting *(Jamil et al, Lancet HIV 2017; Klausner, ASHM 2017)*
    - PrEP associated with delayed seroconversion & low HIV VL *(Donnell et al, AIDS 2017)* therefore good tests needed
    - Clinics will need good systems in place to monitor testing frequency
- **Comment**: Downside of less visits is less opportunity for broader health evaluations (being evaluated in PrEPX)

Cost

- **Current situation**
  - EPIC : medication is free
  - PrEPX:
    - $38.30/ $6.30 co-payments, 3/12 supply x 4= $153
    - Doctor's visit at GP practice: $30 x 4 = $120
    - STI x 1 per annum: $30 plus $38.30
  - **Out of pocket in Victoria/Tas/NSW: $311 per annum**
- **Post PBS listing**
  - Section 85: ($38.30 x 3) x four times per annum=$460
  - Doctor's visit at GP practice: $30 x 4 = $120
  - STI x 1 per annum: $30 plus $38.30
  - **Out of pocket in Australia: $650 per annum**

Cost

- **IPERGAY versus daily dosing cheaper**
  - DAILY DOSING
    - 7 tablets/wk x 52 weeks= 364 tablets = 4 scripts of 90 tablets/yr
  - IPERGAY REGULAR SEX[1]
    - 3.75 tablets/wk x 52 weeks = 195 tablets = 2.2 scripts of 90 tablets/yr
  - IPERGAY INFREQUENT SEX[2]
    - 2.25 tablets/wk x 52 weeks = 117 tablets =1.3 scripts of 90 tablets/yr
- **Comment**: Cost may drive down doses of PrEP used and/or promote sharing: efficacy concerns with inappropriately low dosing

1. Molina et al, NEJM 2015 2. Antoni et al. ISAS 2017

Dosing

- **IPERGAY data on event-based PrEP dosing for *people having infrequent sex highly effective*** *(Antoni et al IAS 2017)*
  - TGA listing currently for daily dosing only- needs to change
  - PrEP guidelines need to change
- **Daily dosing**
  - 4 doses/wk ≅ 7 doses/wk for efficacy in GBM
  - Watch for bracket creep where people starting using 4 tablets per week, *then* less than 4 tablets /wk
  - **Comment**: Will need to keep message clear that 7 doses/wk needed for vaginal sex
  - Community organisations critical

Adherence

- **Will it decline over longer periods (3-5 years?)**
- **Difficult to measure at population level**
  - Will need Medicare data to derive a sense of the average number of scripts populations are filling per annum
- **Role of pharmacists will be key**
  - Talking with patients who have not picked up a PrEP script for > 3 months
  - Contact prescribing clinician

Toxicity

- **Will not have new PrEP agents until at least 2020**
  - People may spend 5-6 years on TDF/FTC
- **Known reversible bone and renal toxicity in the shorter term[1-4]**
  - Concern re bone growth/recovery in younger people
  - Await research on efficacy of zoledronate for bone health in PrEP setting
- **?Unknown toxicity:** ? fertility in HIV negative people
- **Comment**
  - Need a PrEP Registry to follow toxicity
  - ? CV benefit of PrEP: tenofovir known to lower lipids and it is associated with cardioprotective effect in HIV+ people

1. Liu et al, JAMA Int Med 2016. 2. Gandhi et al, Lancet HIV 2016. 3. Glidden et al. JAIDS, 2017. 4. Havens et al, CID 2017 . 5. Chen et al, JAHA, 2017

STIs

- **Ongoing modelling needed to help us plan our STI services and strategies around PrEP**
- **Need careful analyses in PrEP setting**
  - Determine STI incidence in PrEP & non-PrEP using populations
  - Don't assume STIs are all 2^0 to lack of condom use[1] (saliva and rectal gonorrhoea!)[2]
- **Broader current concerns around STI resurgence and resistance in the community**
  - Don't throw the baby out with the bath water
  - PrEP is the most efficacious HIV prevention tool we have apart from abstinence which is not good for you and may not even be a thing

Image:https://www.phrases.org.uk/. 1. Lal et al, AIDS 2017. 2. Chow et al, Sex Transm Infect 2016

STIs

- **Need new strategies and interventions for testing and treatment**
  - ? PrEP users with recurrent STIs should be tested every 6 weeks
  - Home based testing for STIs
  - ? Offer doxycline to PrEP users with recurrent STIs once more data are available on its effectiveness
  - Engage the community to advise on strategies around STIs in PrEP setting

STIGMA in PrEP Setting

- **Lots of Opportunity for Stigma**
  - PrEP only wanting sex with PrEP
  - On PrEP vs not on PrEP
  - STIs vs no STIs
  - Condoms vs no condoms
  - Assume person is HIV+
- **Partner violence**
- **Stigma in the Healthcare setting**
  - Low caseload GP practices
  - Pharmacies
  - Pathology services
- **Comment**: Educate people, empower PrEP users

The future Future

- **Other PrEP modalities will filter through**
  - Injections; implants; infusions
  - Watch for divide between PrEP options for wealthy and poor Australians
- **Watch out for lesser efficacy of PrEP in people on immunosuppressive therapy**
- **As TasP messages broaden/consolidate**
  - Less PrEP use between serodifferent monogamous couples

The future Future

- **In 3-5 years time if NSW's dramatic decline in new HIV diagnoses in MSM extends to other Australian jurisdictions *plus* we greatly exceed 90-90-90 how much risk of HIV will there be to MSM populations?**
  - How necessary will PrEP be for MSM if the proportion of undiagnosed HIV+ people falls to 1-2% and we achieve >90% viral suppression of all PLHIV??
  - Will it differ between other populations at risk of HIV?
  - How will we monitor whether and when we should change our messaging around PrEP's utility???
- **Comment**: HIV surveillance crucial

The future Future

- **High STIs and low condom use and low community HIV viral load**
  - May see small "outbreaks" of HIV around big international events e.g Olympic games
- **Climate change**
  - May undo huge gains in HIV treatment and prevention
- **Comment**: Activists and healthcare providers: please don't retire yet!!!

Thank You!