Kirby Institute

PrEP in Australasia: an overview

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Disclosures

- Research funding
  - Sequirus, Gilead, Viiv, Hologic
- Honoraria for educational presentations
  - Merck, Gilead, Viiv
- Advisory board
  - Viiv

PrEP in Australasia

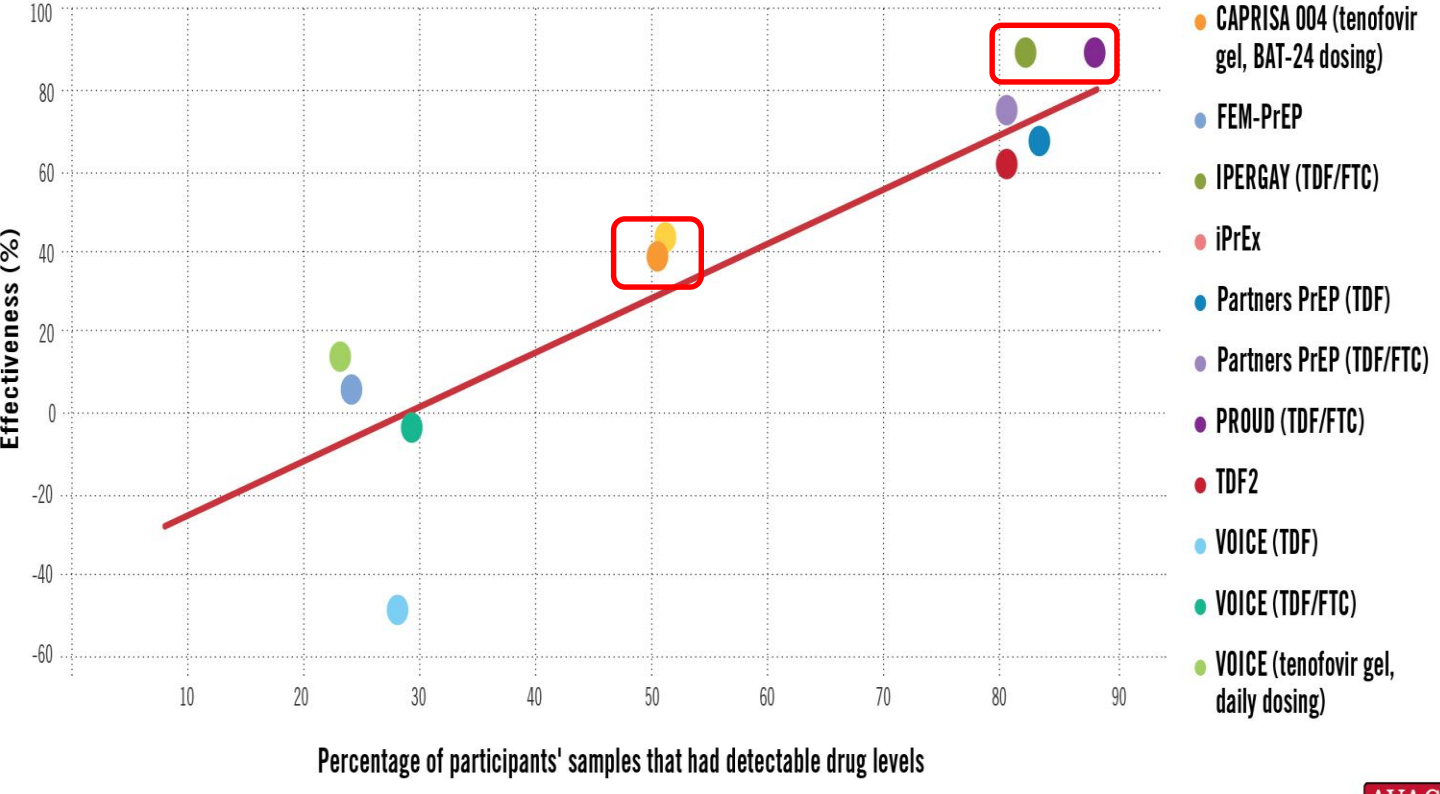
- **The past**
  - The evolution of evidence, policy and practice
- **The present**
  - What demonstration and implementation projects taught us
  - Early PrEP roll-out data
- **The future**
  - Immediate and the next 5 years

The past

PrEP in gay and bisexual men: a gradual evolution of evidence over 5 years

- **2010, iPREX**
  - Daily oral PrEP 44% effective in intent-to-treat analysis
- **2012, iPREX blood level substudy**
  - Non-randomized sub-study
  - PrEP may be 96% effective if >=4 pills taken per week
- **2015, PROUD and iPERGAY**
  - PrEP 86% effective in France and the UK
  - Event-driven/on-demand PreP (2-1-1) also effective
  - Infections occurred only in those not on PrEP

PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



AVAC

February 2016

PrEP efficacy: what we knew by January 2016

- **Oral TDF/FTC PrEP is extremely effective in adherent individuals**

- **Oral TDF/FTC PrEP works best in the rectum**
  - Daily PrEP regimen is forgiving for missing up to 3 pills/week
  - Daily adherence is required for vaginal protection

- **Daily TDF/FTC PrEP is close to 100% effective in adherent gay men**
  - Case reports of failure in adherent individuals are rare (<5)

An evolution of strategy

NSW HIV Strategy 2012–2015
A NEW ERA

Clinical trial results have only recently demonstrated the efficacy of PrEP~. PrEP offers potential as a prevention option for a small number of people who are at very high risk of HIV infection. During the period of this Strategy, NSW Health will consider the application of these trial results to non-trial settings, and the mechanisms to most appropriately and efficiently implement PrEP in line with evidence.

OUR GOAL

TO WORK TOWARDS THE VIRTUAL ELIMINATION OF HIV TRANSMISSION IN NSW BY 2020

POLICY BRIEF

PRE-EXPOSURE PROPHYLAXIS (PrEP)

WHO EXPANDS RECOMMENDATION ON ORAL PRE-EXPOSURE PROPHYLAXIS OF HIV INFECTION (PrEP)

World Health Organization

NOVEMBER 2015

New recommendation

Oral PrEP containing tenofovir disoproxil fumarate (TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

STRONG RECOMMENDATION, HIGH-QUALITY EVIDENCE

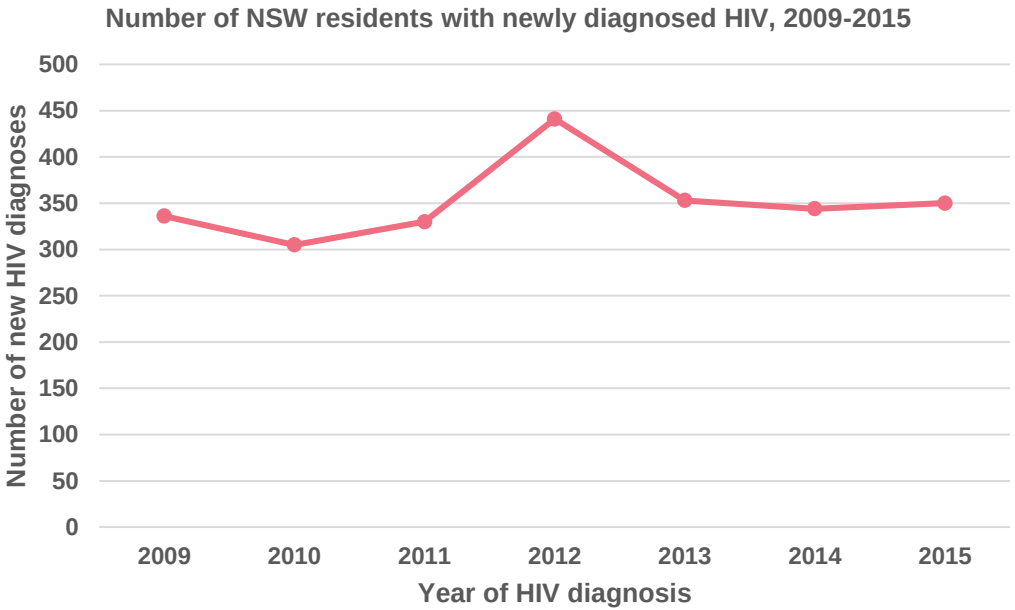
Key evidence

High-quality evidence strongly supports use of PrEP by any person at substantial risk of acquiring HIV infection.

- Twelve trials of the effectiveness of oral PrEP have been conducted among serodiscordant couples, heterosexual men, women, MSM, people who inject drugs and transgender women. These trials took place in Africa, Asia, Europe, South America and the United States.
- PrEP works, when taken.

HIV in New South Wales (NSW) at the end of the 2012-15 strategy

UNAIDS 90/90/90 goals met, but HIV diagnoses stable



Data source: Notifiable Conditions Information Management System, extracted 11 February 2016

Adapted from NSW annual HIV update 2015

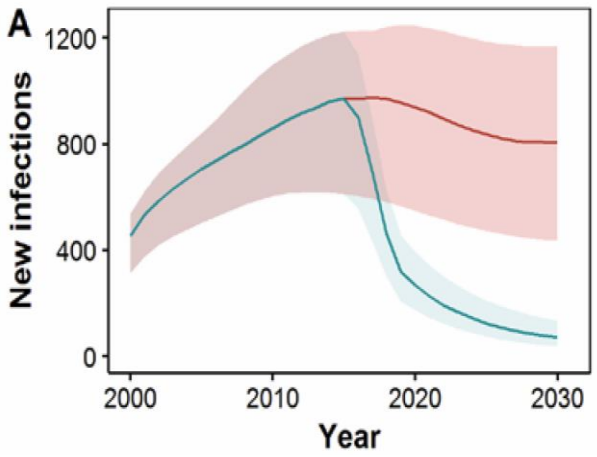
How should PrEP be rolled out? Evidence from mathematical modelling

Impact and cost effectiveness maximised if…

- PrEP targeted to ***high-risk*** gay men
- With ***high coverage*** (90%)
- Rolled out ***quickly*** (1-2 years)

• Lower levels of roll out lead to much lower reductions in incidence

• Herd protection is a critical part of the population effect



R Gray et al, unpublished

NSW HIV STRATEGY 2016-2020

NSW GOVERNMENT Health

To virtually eliminate HIV transmission in NSW by 2020

PrEP is the next critical addition to HIV prevention in NSW.

Expanding PrEP access to people at a high risk for HIV infection, in the context of existing HIV prevention strategies and continuing high levels of HIV and STI testing and treatment, will allow NSW to harness the public health benefits of PrEP and prevent a significant number of new HIV infections

What we will do

Develop robust and sustainable systems to support the expansion of access to PrEP to all people who are at a high risk of HIV infection in line with current evidence and the *PrEP of HIV with Antiretroviral Medications NSW Guidelines*.

EIGHTH

National HIV Strategy

2018–2022

Australian Government
Department of Health

Targets

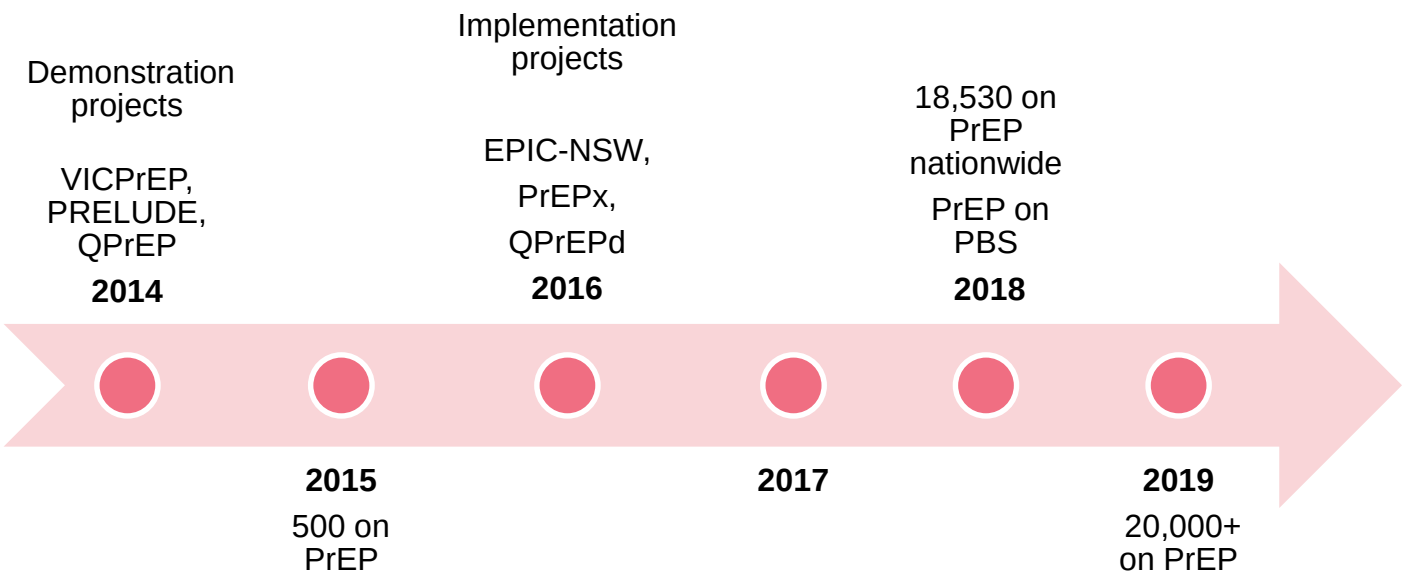
By the end of 2022:

7. Increase the proportion of eligible people who are on PrEP, in combination with STI prevention and testing to 75 per cent

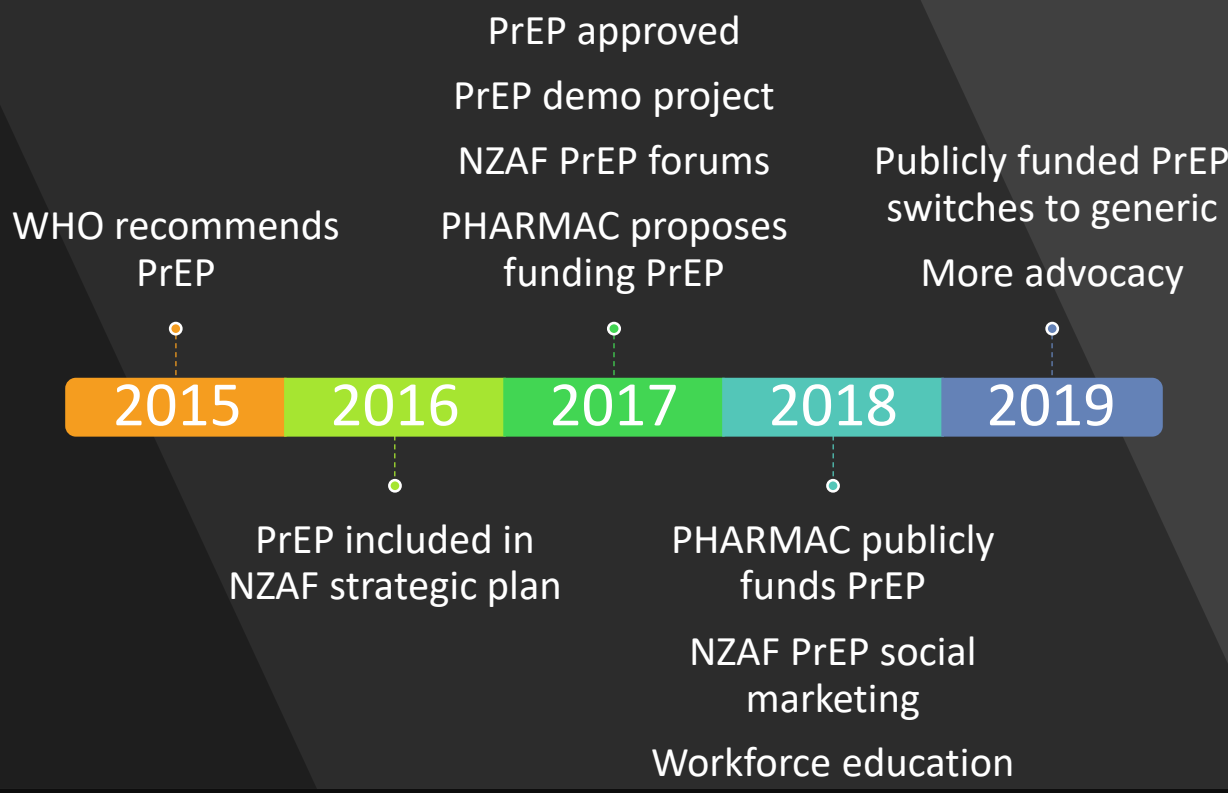
KEY AREAS FOR ACTION

2. Promote the availability and effectiveness of PEP and PrEP and facilitate rapid, widespread and equitable access to PEP and PrEP across the country

PrEP roll-out in Australia: timeline



PrEP Milestones New Zealand



Slide courtesy of Joe Rich, NZAF

The present – what we learned from the demonstration and implementation projects

Adherence is good in Australian gay and bisexual men

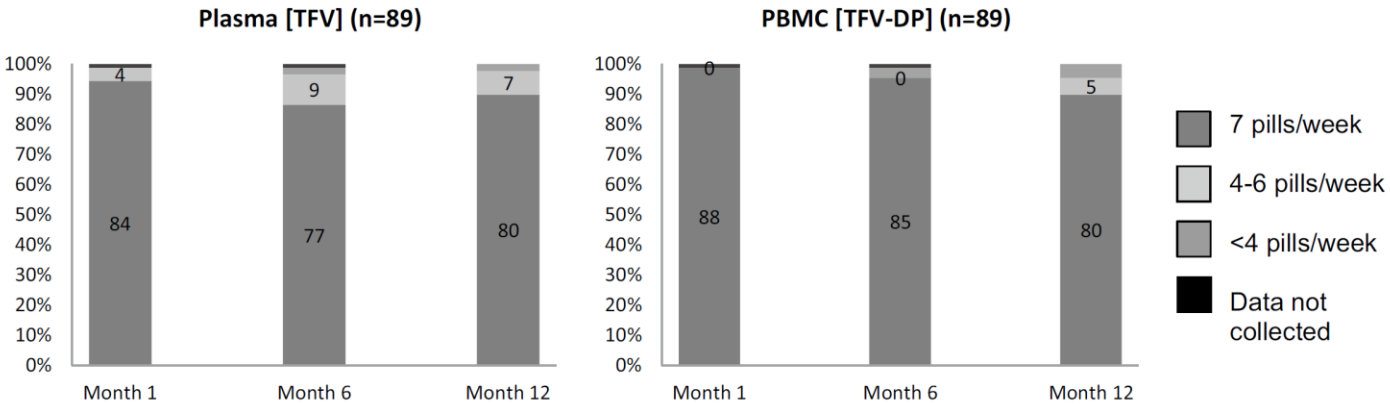
- **VicPrEP study (114 participants, 99% cisgender male)**

Variable	Baseline	Months 0–3	Months 3–6	Months 6–9	Months 9–12
Self-report at clinic visit					
<50% of daily doses taken (%, *n*)	–	0	0	1.9 (2)	0
50–90% of daily doses taken (%, *n*)	–	5.5 (6)	1.9 (2)	3.8 (4)	5.7 (6)
>90% of daily doses taken (%, *n*)	–	94.5 (103)	98.1 (103)	94.2 (98)	94.3 (99)
Refill-based assessment					
% days drug available[c], median (IQR)	–	114 (105–117)	99 (95–107.5)	99 (97–107)	97 (87–100.5)
Online self-report survey	–				
Any missed PrEP doses [% (y/n)]		51.7/48.3	59.8/40.2	61.6/38.4	58.9/41.1
Number missed PrEP doses[d] [mean (SD)]		3.95 (6.00)	4.93 (12.08)	3.41 (1.85)	4.45 (5.91)
Dried blood spot testing (n = 78) (month 6 sample only)					
Evidence of recent dosing (FTC-TP) (%, *n*)	–	–	94.87 (74)	–	–

L Lal et al, AIDS 2017

Adherence is good in Australian GBM (2)

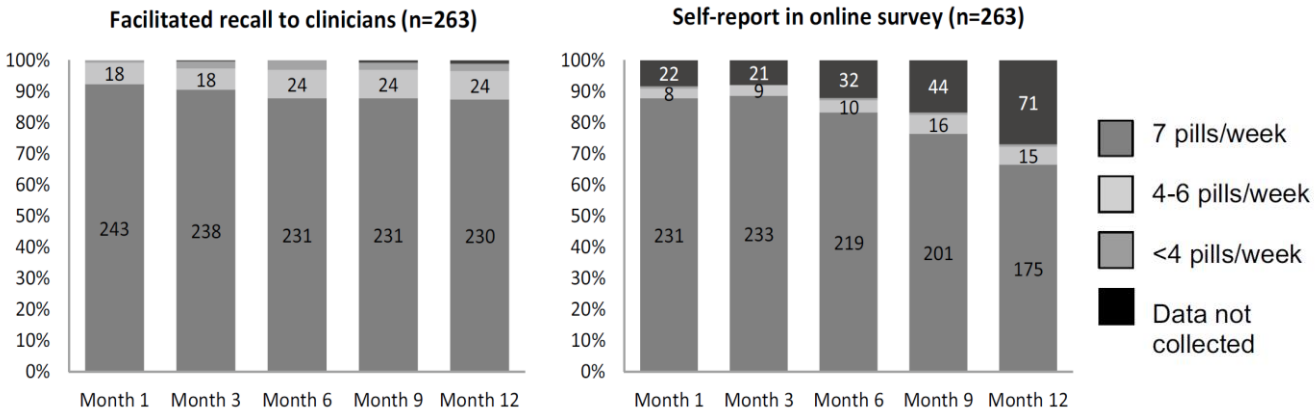
- **PRELUDE study (NSW), 327 participants**



S Vaccher et al, AIDS & Behavior, 2019

Adherence is good in Australian GBM (3)

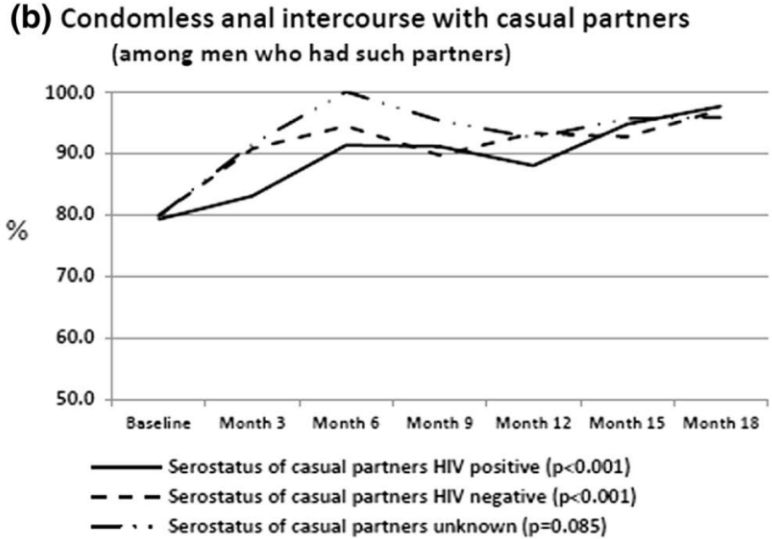
- **PRELUDE study (NSW), self report**



S Vaccher et al, AIDS & Behavior, 2019

Increasing condomless intercourse, but zero HIV infections

- **PRELUDE study (NSW)**

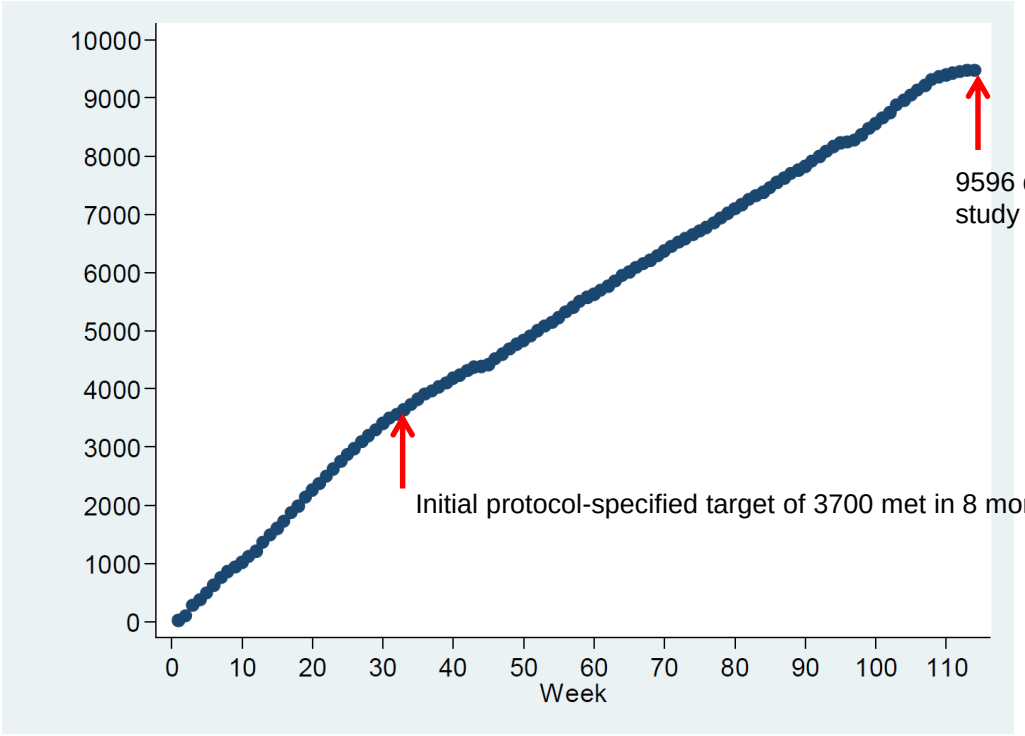


Not risk compensation
But “increasing CLAI”

- **HIV incidence 0 (95% CI 0-0.93/100py)**

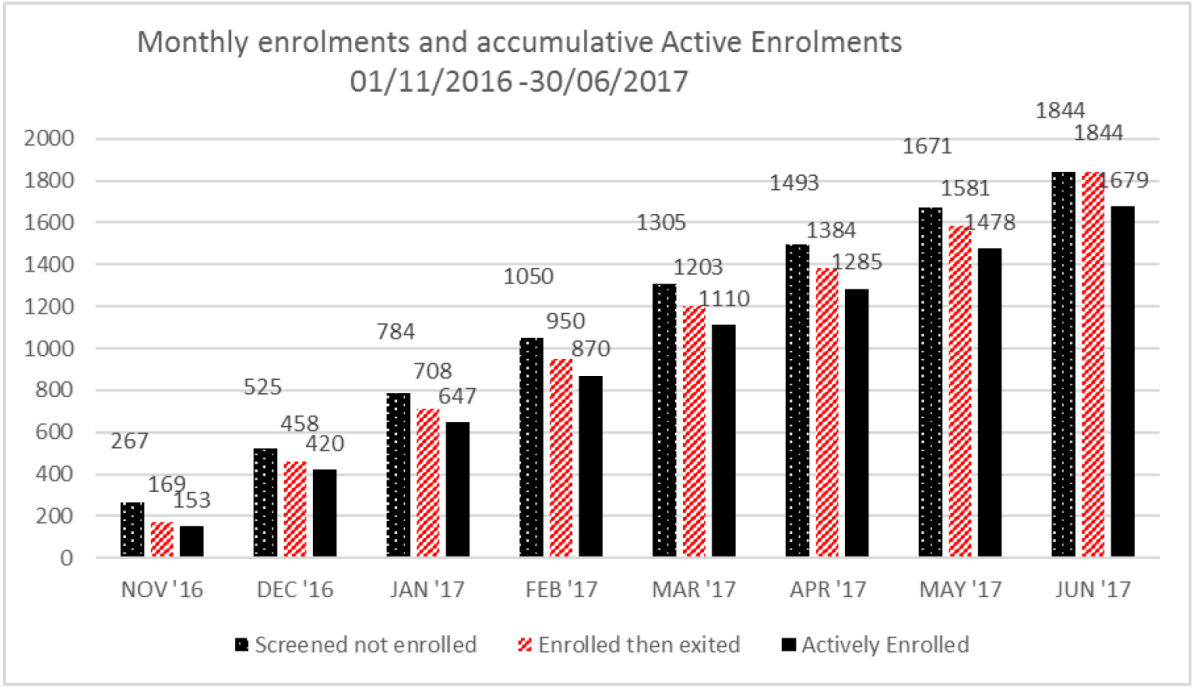
I Zablotska et al, AIDS & Behavior, 2019

Implementation: PrEP demand is high
EPIC-NSW final enrolment curve (to April 30 2018)



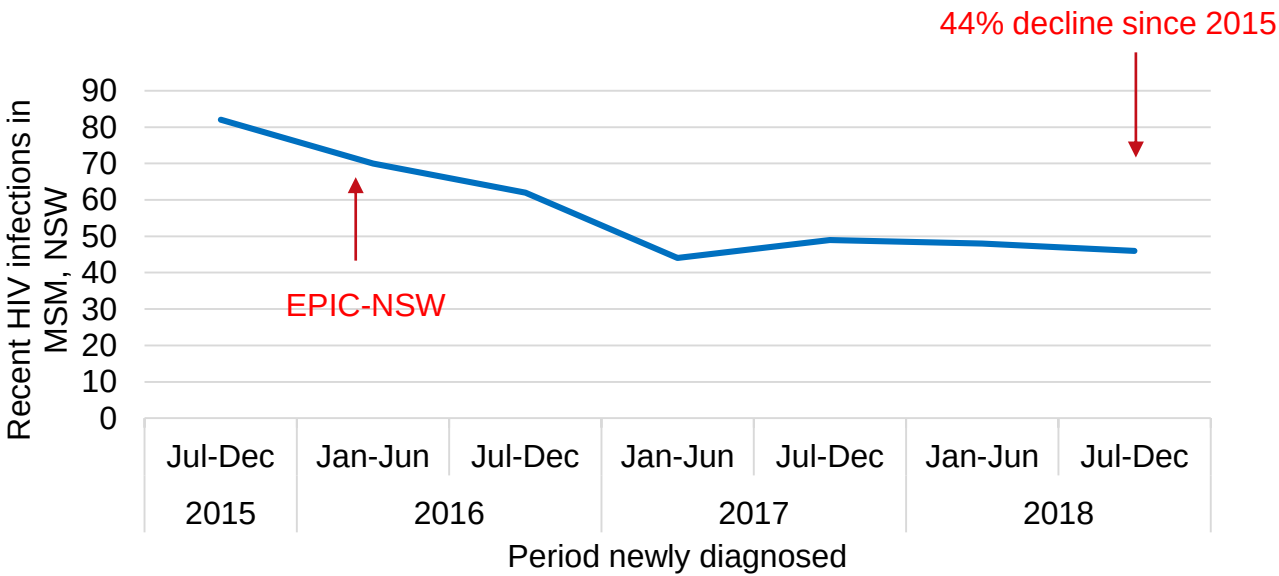
High PrEP demand: QPREP'd

Figure 8 Cumulative Screening and Enrolment Numbers



Impact: rapid targeted implementation leads to rapidly declining HIV

State-wide recent HIV infections in MSM in NSW



A Grulich et al, IAS Mexico, July 2019

Impact: in-cohort HIV incidence is greatly decreased

	Published data Lancet HIV 2018	End-of-study
Person years follow up	4100	19690
New HIV infections	2	30
HIV incidence/CI	0.48/1000py (95%CI 0·12–1.95/1000py)	1.52/1000py (95% CI 1.07-2.18/1000py)

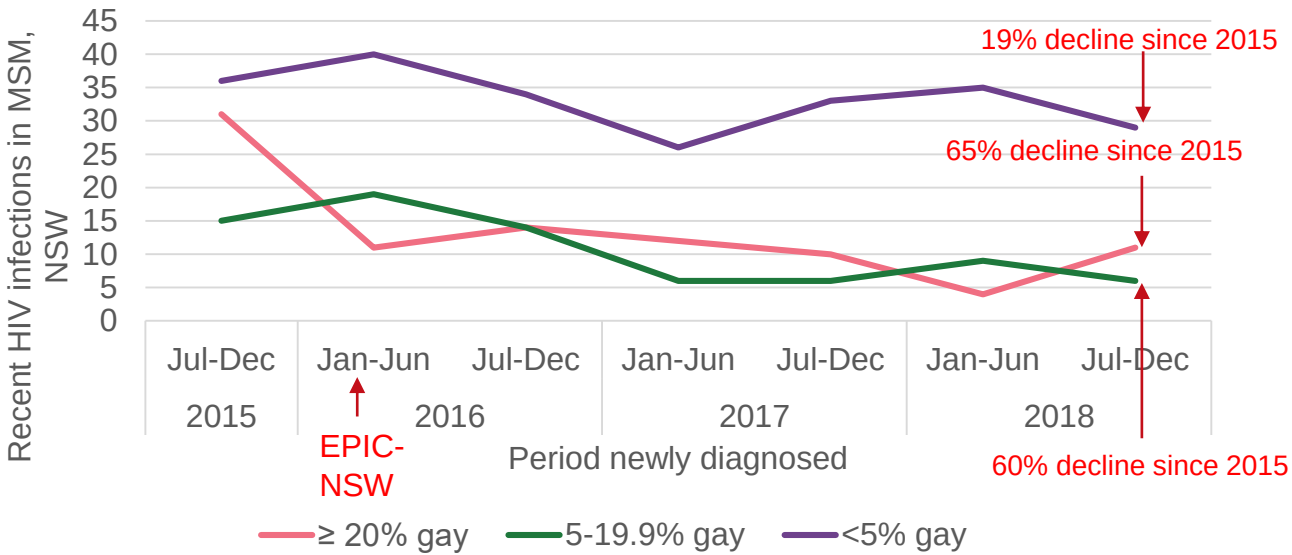
Observed incidence of 1.52/1000 person years (30 cases)

Compares to an expected incidence of >20/1000py (>400 infections)

A Grulich et al, Lancet HIV 2018

Impact: HIV reductions are largest in inner city “gay suburbs”

State-wide recent HIV infections in MSM in NSW by percent of postcode gay



Grulich A et al, IAS Mexico, July 2019

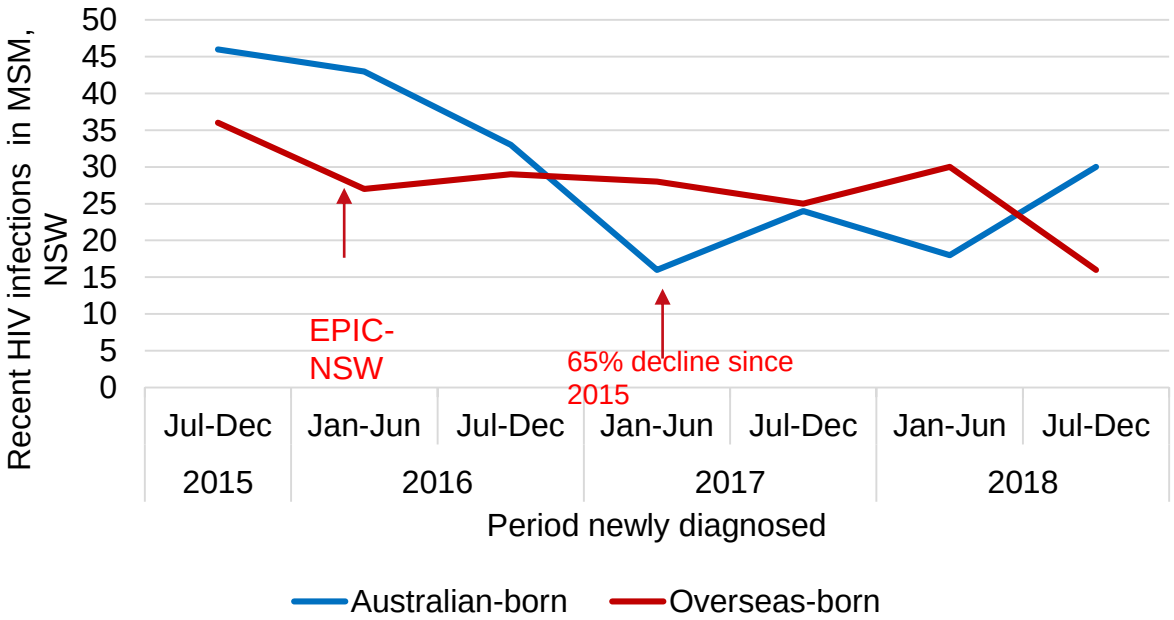
Risk factors for incident HIV: area of residence

- **HIV incidence by percentage of postcode gay**

		n	Incidence per 1000py	Incidence rate ratio	95% CI	p
% of postcode gay	>=20%	6	0.94	1	---	0.069
	10-19%	2	1.10	1.16	0.23-5.75	
	5-9%	1	0.44	0.47	0.06-3.87	
	<5%	20	2.21	2.34	0.94-5.84	

Impact: HIV reductions are largest in the Australian born

State-wide recent HIV infections in MSM in NSW by place born



A Grulich et al, IAS Mexico, July 2019

Risk factors for incident HIV: country of birth

		n	Incidence per 1000py	Incidence rate ratio	95% CI	p
Country of birth	Australia	16	1.52	1	---	0.811
	English, high-income	3	1.33	0.88	0.26-3.01	
	Asia	5	2.05	1.35	0.50-3.69	
	Other	2	0.94	0.62	0.14-2.70	

Characteristics of 30 seroconverters

- **None were adherent to daily PrEP at time of infection**
  - Many had picked up PrEP only once or twice
  - Most stopped PrEP many months or even up to 2 years before

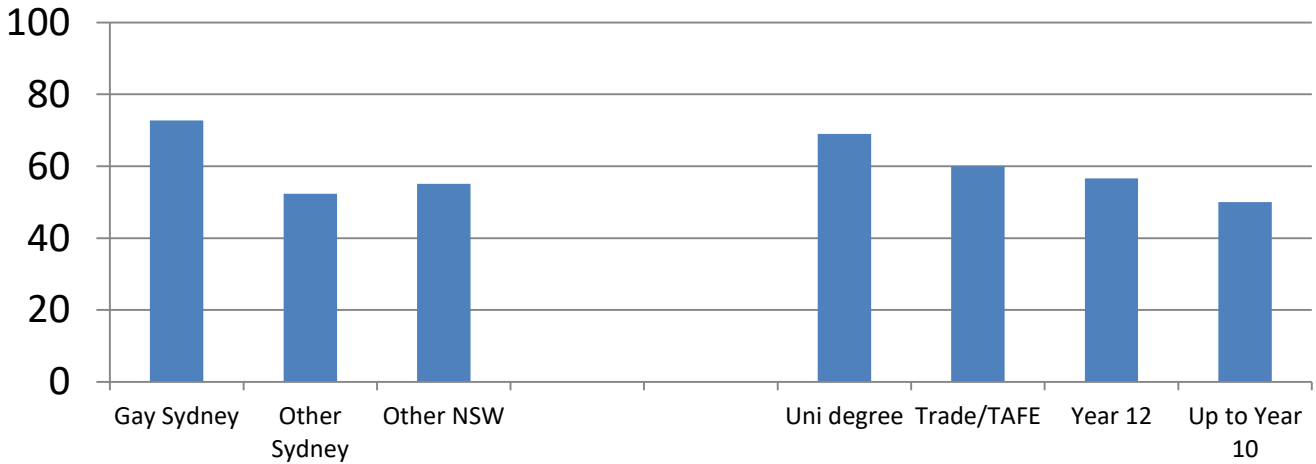
- **Highly varied reasons for stopping PrEP**
  - HIV risk changed (entered relationship, wanting to “calm down”)
  - Mental health issues, recreational drug use, cost, prison
  - Toxicity (early symptoms, 1 case of decreased eGFR)

- **One M184V mutation**
  - Likely acquired, not transmitted, in a man who continued PrEP for at least 2 months while HIV infected

The future

Increasing PrEP coverage

- **The 8th National HIV strategy targets 75% of those eligible on PrEP**
- **Periodic surveys allow tracking of proportion of those eligible taking PrEP**



Sydney Gay Community Periodic Survey 2019

Getting to 75%: challenges ahead

- Close to reaching this in some community-attached inner-city gay community settings
- Achieving equity in coverage (country of birth, non-gay-community attached men, young men)
- Further consultation required on the best surveillance measures of coverage

WHAT'S THE 2+1+1?

EVENT-DRIVEN ORAL PRE-EXPOSURE PROPHYLAXIS TO PREVENT HIV FOR MEN WHO HAVE SEX WITH MEN: UPDATE TO WHO'S RECOMMENDATION ON ORAL PREP

JULY 2019

World Health Organization

CONCLUSIONS AND CONSIDERATIONS FOR IMPLEMENTING ED-PREP FOR MEN WHO HAVE SEX WITH MEN

- "ED-PrEP is safe and highly effective in reducing risk of HIV acquisition through receptive and/or insertive sex between men. It can be offered as an alternative to daily PrEP dosing for men who have sex with men.

- Countries with existing PrEP guidelines, but where ED-PrEP is not recommended, can consider including the option of ED-PrEP (TDF/FTC or TDF/3TC) in the "2+1+1" dose schedule for men who have sex with men when updating national guidelines and protocols.

World Health Organization

Non-daily PrEP: Preferences

- **315 GBM enrolled in the NSW PRELUDE study 2014-16 asked their ideal way to take PrEP**
  - 64% daily
  - 20% event driven
  - 14% periodic

- **970 former PrEPx participants, Nov 2018**
  - 48% were interested in participating in an on-demand PrEP study
  - Those interested in ED PrEP were more likely to report
    - having stopped PrEP,
    - difficulties with adherence,
    - infrequent sex, and
    - toxicity concerns

[35] S Vaccher et al, Frontiers Pub Health 2018; V Cornelisse et al, Open Forum Inf Dis 2019

Injectable PrEP: Cabotegravir

- 8-weekly injectable PrEP
- Two RCTS comparing it to daily oral PrEP underway
- Trial results by 2022

HPTN 083
an HIV prevention clinical trial

HPTN 084
Long-acting Injectable For the Epidemic

PrEP implants

- **Islatravir (nucleoside reverse transcriptase translocation inhibitor)**
- **Potential for an implant inserted annually using existing contraceptive technology**
- **Phase 1 studies encouraging**
- **Phase 2 studies soon**
- **At least 5 years away**

PrEP today: implications for HIV elimination

- **Further increase in PrEP coverage is required**
  - Modelling suggests (at least) > 75%
  - Equity is a fundamental challenge
- **Addressing stopping/re-starting PrEP is critical**
  - 2-1-1 helps make stopping and starting easier
  - Long acting forms of PrEP will help
- **Policy/structural change**
  - Improved PrEP access for non-Medicare card holders (recent migrants/students/visitors) is a critical part of the equation
- **Key affected populations with high HIV incidence throughout Asia need PrEP**
  - and this is critical for Australia's epidemic

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PrEP researchers in Australia and New Zealand