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Saturday, June 22, 2019 (Room 3)

8:30 - 9:25 WS #108: Prescribing HIV Pre-Exposure Prophylaxis (PrEP) – a Panel Discussion

9:35 - 10:30 WS #120: Prescribing HIV Pre-Exposure Prophylaxis (PrEP) – a Panel Discussion (Repeated)

PREP: ANGEL OR DEMON?

Or, how not to turn a success story into a public health disaster

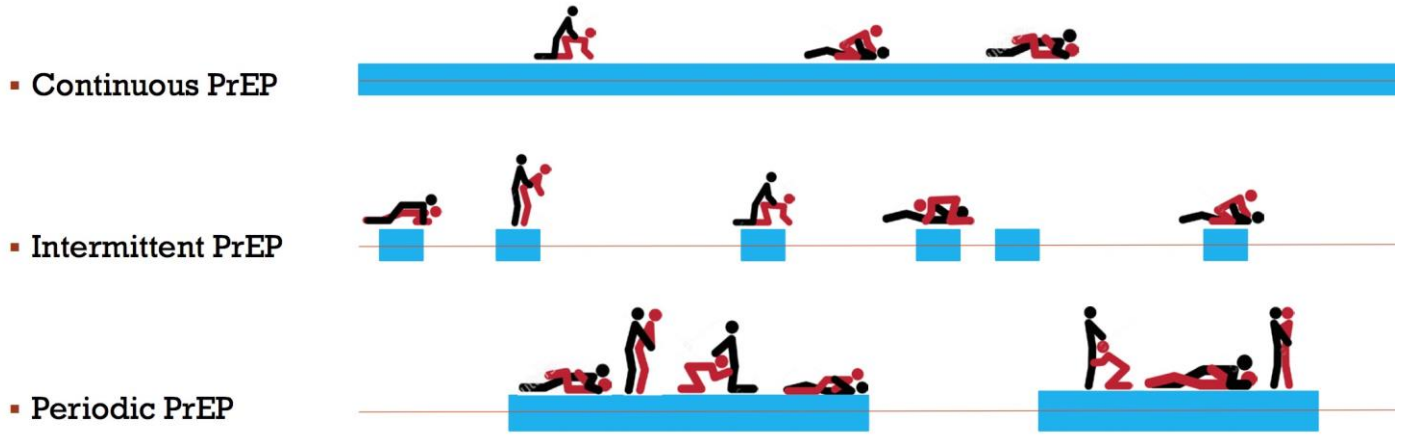
Massimo Giola, FRACP, FAChSHM
Consultant Physician
Clinical Lead of the Sexual Health Services for Bay of Plenty DHB

Contents of my presentation

- Disclaimer: I will only talk about continuous PrEP => although I will be happy to comment about the additional challenges of event-based PrEP during the panel discussion
  - How are we getting on with PrEP in NZ?
  - Is PrEP working at a community level?
  - How we compare to some selected Countries we like to compare ourselves to
  - PrEP failures – are we calling and measuring them in the right way?
  - STIs
  - Peer pressure to PrEP & ditch condoms => is it what we really wanted?

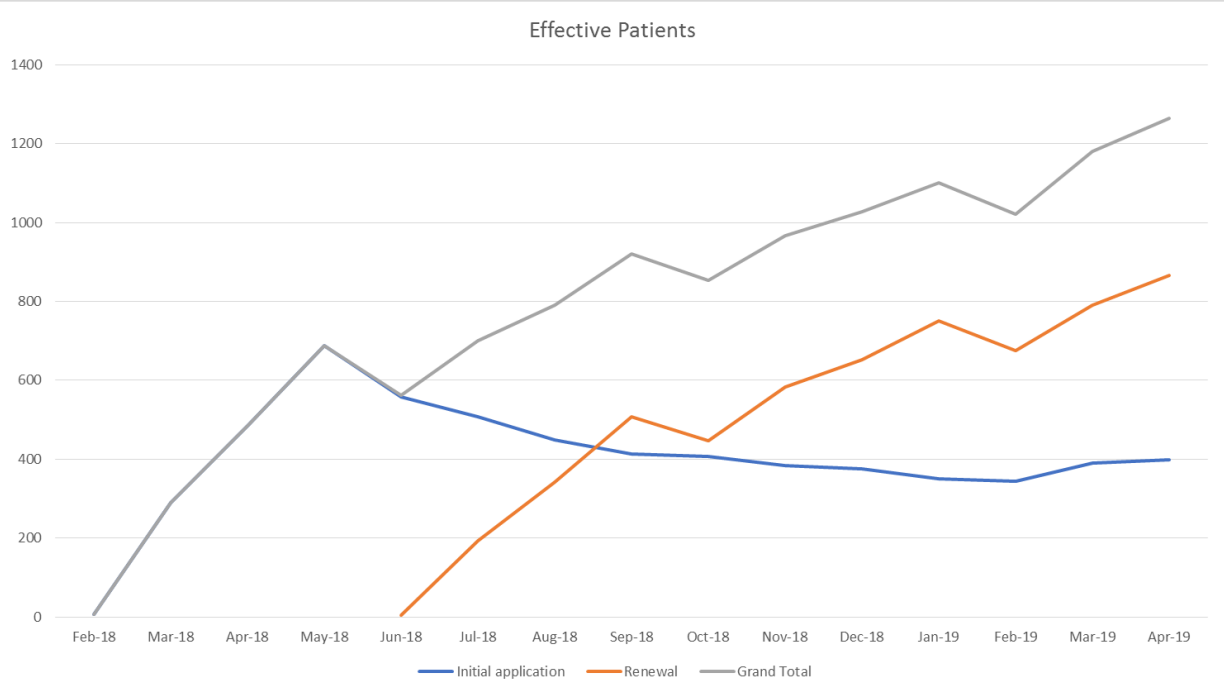
Ways to PrEP

- Continuous PrEP – 1 tablet/day
- Event-triggered PrEP – Ipergay-like
- Periodic PrEP – for the “seasons of risk”



Picture by Vincent Cornelisse, FAChSHM

PrEP uptake in NZ Mar 18 – Apr 19



As at Date	Initial application	Renewal	Grand Total
Feb-18	7		7
Mar-18	290		290
Apr-18	485		485
May-18	688		688
Jun-18	557	5	562
Jul-18	507	193	700
Aug-18	449	342	791
Sep-18	414	507	921
Oct-18	407	447	854
Nov-18	384	583	967
Dec-18	375	653	1028
Jan-19	351	750	1101
Feb-19	345	676	1021
Mar-19	391	790	1181
Apr-19	398	867	1265

Source: PHARMAC

PrEP uptake in NZ Mar 18 – Apr 19

Row Labels	Count of master_encrypted_hcu_id
Auckland	740
Bay of Plenty	45
Canterbury	190
Capital and Coast	230
Counties Manukau	107
Hawkes Bay	27
Hutt Valley	33
Lakes	13
MidCentral	34
Nelson Marlborough	17
Northland	17
South Canterbury	4
Southern	116
Tairawhiti	1
Taranaki	15
Waikato	81
Wairarapa	3
Waitemata	242
West Coast	4
Whanganui	14
Grand Total	1933

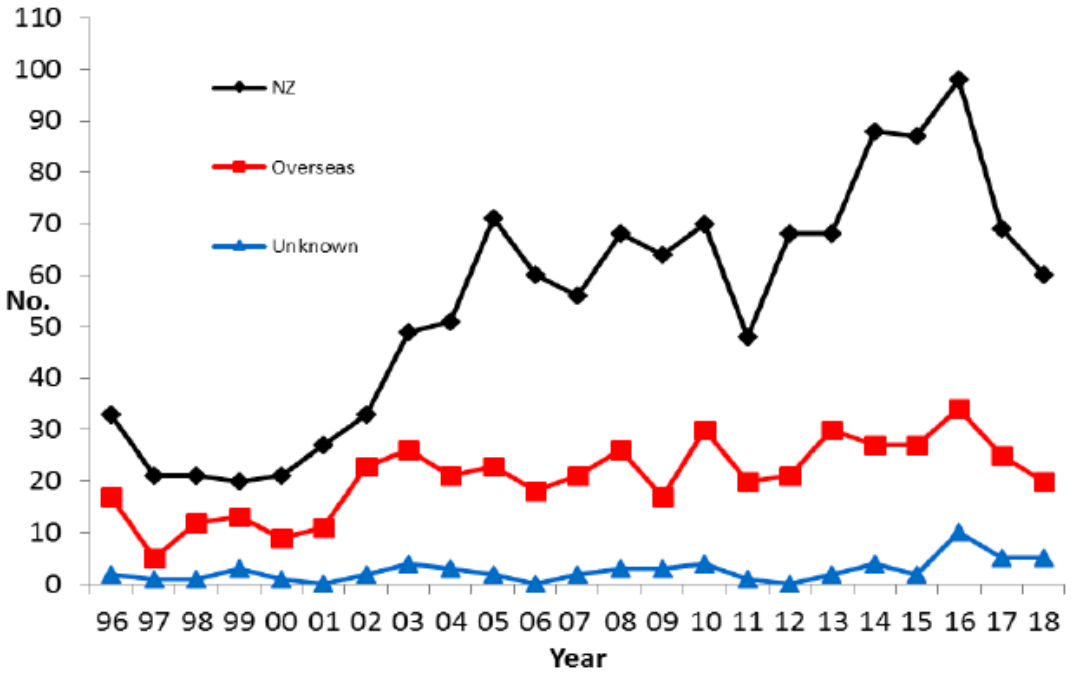
Row Labels	Count of master_encrypted_hcu_id
Maori	176
Other	1691
Pacific Island	66
Grand Total	1933

Row Labels	Count of master_encrypted_hcu_id
16-20	56
21-25	305
26-30	409
31-35	351
36-40	232
41-45	157
46-50	133
51-55	132
56-60	87
61-65	43
66-70	20
71-75	6
76-80	2
Grand Total	1933

Source: PHARMAC

Is PrEP working in NZ?

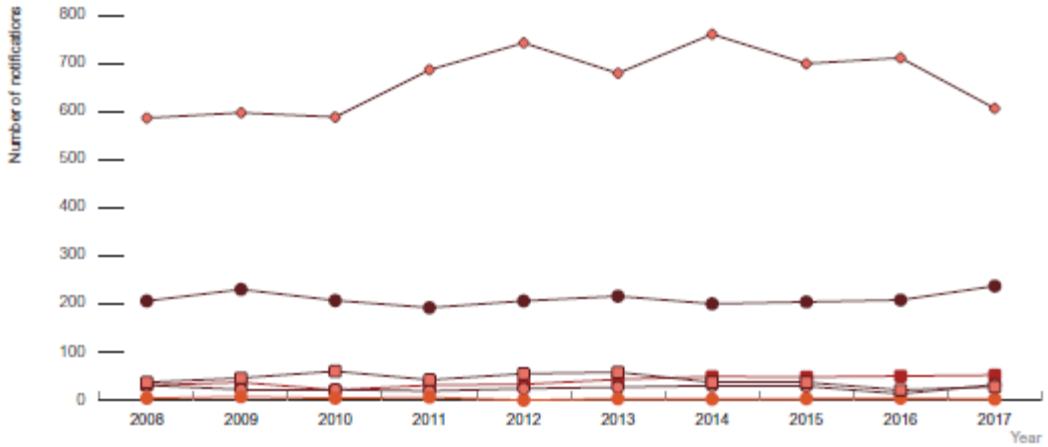
Place of infection of MSM first diagnosed in New Zealand by antibody test annually since 1996 and including those reported by viral load testing since 2002



AEG, AIDS in NZ newsletter, issue 78 – May 2019

Is PrEP working in Australia?

Number of HIV notifications, 2008–2017, by exposure category:

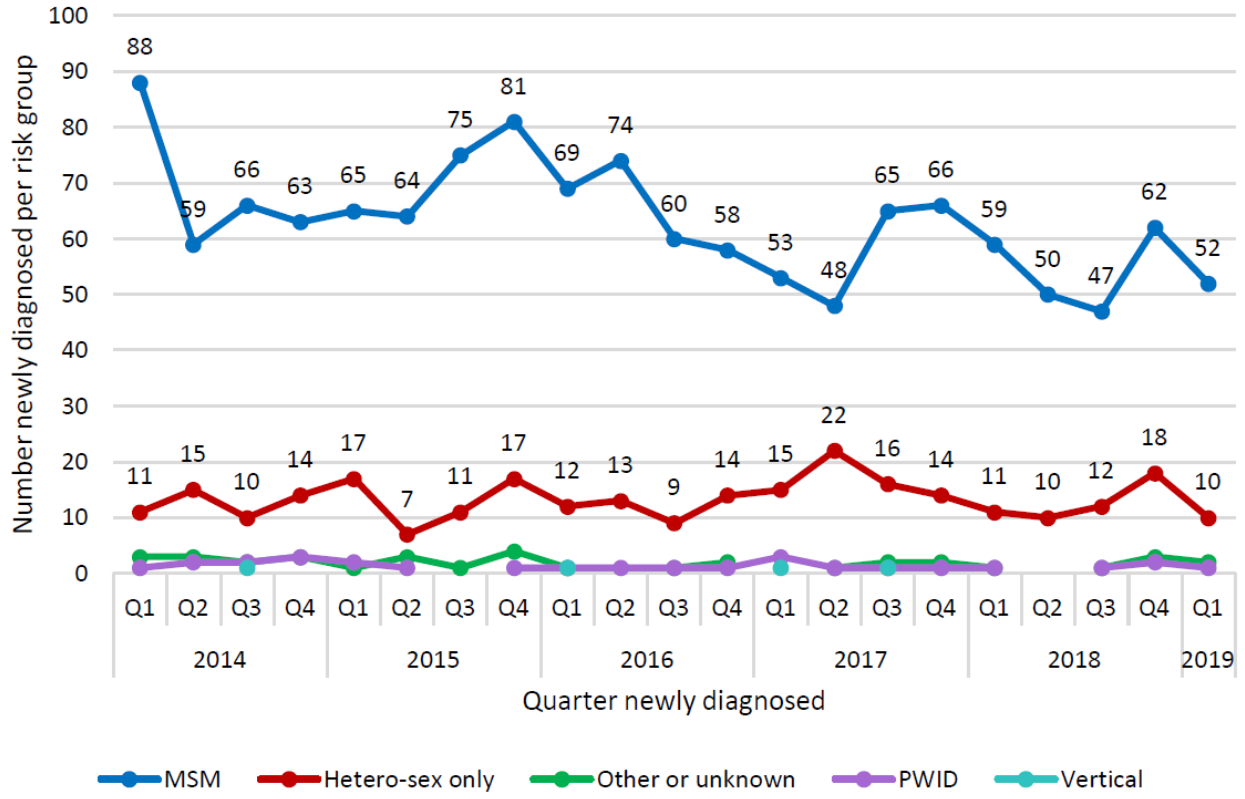


	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male-to-male sex	587	598	589	687	743	680	761	700	712	607
Male-to-male sex and injecting drug use	32	38	22	32	34	44	50	49	51	53
Injecting drug use	32	23	23	20	25	28	31	30	14	33
Heterosexual sex	207	231	208	193	207	217	201	205	209	238
Mother with/at risk of HIV infection	5	8	5	7	1	4	3	4	5	3
Other/undetermined	38	47	61	43	56	59	38	38	22	29

The Kirby Institute: HIV, viral hepatitis and sexually transmissible infections in Australia, Annual surveillance report 2018

Is PrEP working in NSW?

New diagnoses January 2014 to March 2019 by reported HIV risk exposure:



NSW HIV STRATEGY 2016-2020: DATA REPORT Quarter 1 2019

Is PrEP working at a community level?

- Similar data to what we are seeing in NZ and Australia are being reported around the world
- They suggest PrEP is working at a community level – to some extent, but it has not been so far the “silver bullet” killing the HIV epidemic
  - also, the decline in new HIV infections is for now limited to MSM…
  - … and particularly to “privileged” MSM => born in the Country vs immigrant, white/caucasians vs other ethnicities, living in big cities vs rural/remote…

Do we need to widen the criteria to access PrEP in NZ?

- How do we compare?
- Scotland, Wales, Northern Ireland: PrEP funded in the public sexual health clinics (SHCs), risk criteria apply (see https://www.hps.scot.nhs.uk/web-resources-container/implementation-of-hiv-prep-in-scotland-first-year-report/)
- England: PrEP available as a capped "implementation trial" (PrEP IMPACT, 10,000 people) through the SHCs
  - 56 Dean Street Clinic in London Soho sells generic PrEP to people left out of the trial:

Buy	Cost	Equivalent per pack
1 pack x 30	£30	£30
3 packs x 30	£60	£20
6 packs x 30	£105	£17.50

Do we need to widen the criteria to access PrEP in NZ?

- How do we compare?
- Canada:
  - PrEP funded through the government HIV &SHCs
  - they have developed a risk-scoring system (HIRI-MSM) => people scoring > 11 are offered PrEP
    http://www.cmaj.ca/content/189/47/E1448#sec-4
- France:
  - closest to NZ: initiation only in HIV & SHCs, repeats for up to 1 year by GPs, back to the specialist clinic once a year to confirm eligibility & absence of contraindications
    https://www.aides.org/prep

Do we need to widen the criteria to access PrEP in NZ?

- How do we compare to the billing systems?
- USA:
  - any Doctor can prescribe PrEP
  - most insurance plans reimburse it
  - otherwise, Gilead Inc. (the manufacturer of Truvada) will help in finding one that does
  - there are still significant out-of-pocket co-payments even when the insurance plan funds it
- Australia:
  - funded through the PBS, any Doctor can prescribe it *https://www.afao.org.au/about-hiv/hiv-prevention/prep/*

Do we need to widen the criteria to access PrEP in NZ?

Yeah nah

- I personally believe we are more comparable to UK/Canada/France than to Australia/USA
- I particularly like the French model and would love to introduce in NZ the requirement for Specialist review (face-to-face or virtual) every 1-2 years to endorse the GP to continue prescribing
- The “virtual” endorsement gives us the flexibility to address the shortage of PrEP Specialist prescribers in Auckland
- Re the risk criteria, we could adopt the Scottish ones, which are a bit wider than our current criteria:

https://www.hps.scot.nhs.uk/web-resources-container/implementation-of-hiv-prep-in-scotland-first-year-report/

RISK BEHAVIOUR ELIGIBILITY CRITERIA

An individual who is:

- A current sexual health partner, irrespective of gender, of people who are HIV positive and have a detectable viral load

OR

- An MSM or transgender women with a documented bacterial rectal STI in the last 12 months

OR

- An MSM or transgender women reporting condomless penetrative anal sex with two or more partners in the last 12 months, and likely to do so again in the next three months

OR

- Irrespective of gender, an equivalent high risk of HIV acquisition, as agreed with another specialist clinician

Do we need to widen the criteria to access PrEP in NZ?

Yeah nah

- My top priority if widening access would be that no one is left behind and that everyone receives gold-standard sexual health care including PrEP if indicated:
  - Regional, rural, and remote people:
    - assess and strengthen the network of the free public sexual health clinics
    - ensure that all DHBs have activated pathways of referral to the HIV prescribers for PrEP initiation
    - ensure that all Doctors and Nurse Practitioners/Prescribers working in the sexual health clinics are able to initiate PrEP under supervision/auditing of the HIV prescribers
    - establish and widen a network of GPs able and willing to do repeat PrEP prescriptions under appropriate supervision/auditing
  - If we genuinely believe PrEP is a public health intervention and not a “personal wellness choice” then it should be free for users as a vaccination
    - including people not otherwise entitled to funded health care in NZ like international students, WHV, seasonal workers, etc.

PrEP prescribing needs to be audited regularly

- Study in 15 primary care clinics in the San Francisco area
- All pts receiving PrEP 2013-17 (405 pts, median PrEP duration 11.3 months)
- 85% male, 66% MSM, median age 34 years
- Initial HIV testing: 77%; initial STIs testing: 81%
- Follow-up testing: for HIV, in 68% of 4-month intervals and for STIs in 67% of 6-month intervals
- In MSM, providers ordered extragenital NG/CT screening (pharyngeal or rectal) 70% of the time a urine test was ordered
- 2 cases of incident HIV: 1 after self-discontinuing PrEP, 1 using PrEP intermittently
- The practices that did better were the ones with established protocols/reminders and internal supervision/auditing.

Open Forum Inf Dis DOI: 10.1093/ofid/ofy099

PrEP failures: HIV Infection Despite High Adherence to PrEP

Pt	PrEP Adherence	Seroconversion	Likely Cause of PrEP Failure
43-yr-old MSM[1]	24 mos, supported by pharmacy records, blood concentration analyses, and clinical history	Acquired MDR HIV infection	Exposure to PrEP-resistant, multiclass-resistant HIV strain
MSM in his 20s[2]	Excellent by self-report, supported by blood and hair concentration analyses	Acquired MDR HIV infection after 2 instances of condomless insertive anal intercourse with 2 different partners within 11 wks before diagnosis	Exposure to PrEP-resistant, multiclass-resistant HIV strain
50-yr-old MSM[3]	Excellent by self report, supported by blood analyses	Acquired wild-type HIV infection after 2-5 median condomless anal sex partners per day in each month following PrEP initiation	Chronic rectal inflammation ± trauma
34-yr-old MSM[4]	Excellent during the 3 months preceding HIV infection diagnosis, supported by self-report and hair segmental analysis	Acquired MDR HIV (K103N, K65R, M184V) Given 1 month plus 11 repeats of PrEP, failed to attend appointments for HIV testing, was not chased up	Exposure to NNRTI-R HIV, likely developed MDR mutations while inadvertently treated with 2 drugs
28-yr-old male sex worker[5]	Excellent during the 6 weeks preceding the HIV diagnosis, as supported by hair and plasma analysis	Acquired MDR HIV (A98G, K103N, M184V) Several CLAIs with a foreign male client during the first 1–2 weeks on PrEP	Exposure to MDR HIV or acquisition of NNRTI-R HIV followed by further mutations

1. Knox DC et al. N Engl J Med 2017;376:501-502. 2. Grossman H et al. HIVR4P 2016. Abstract OA03.06LB.
3. Hoornenborg E et al. CROI 2017. Abstract 953. 4.Thaden JT et al. CROI 2018. Abstract 1041 5. Colby DJ et al. CID DOI: 10.1093/cid/ciy321

'In complete shock': Australian man contracts HIV despite taking PrEP drug

Sydney man Steven Spencer contracted HIV despite being on PrEP for years.

https://www.stuff.co.nz/national/health/111501680/in-complete-shock-australian-man-contracts-hiv-despite-taking-prep-drug

- Note that Steven's PrEP was event-based ("on-demand")
- I have heard recently a prominent Australian PrEP researcher trying very hard to convince the audience this was not a PrEP failure, but a "failure to assess correctly when on-demand PrEP was needed" – is this not exactly the whole point, i.e. a failure of on-demand PrEP as a strategy to prevent HIV infection?

IMPACT OF PREP ON DRUG RESISTANCE AND ACUTE HIV INFECTION, NEW YORK CITY, 2015-2017

- 95 (3%) out of 3,721 persons with a recent HIV diagnosis had a report of pre-diagnosis PrEP use
- Median duration of PrEP exposure before diagnosis was 3 months (IQR=7)
- Persons with a history of pre-diagnosis PrEP use were significantly more likely to have resistance mutations to 3TC
- There were no signature TDF mutations (K65R) detected among pre-diagnosis PrEP users.

CROI 2019, Abstract number 107

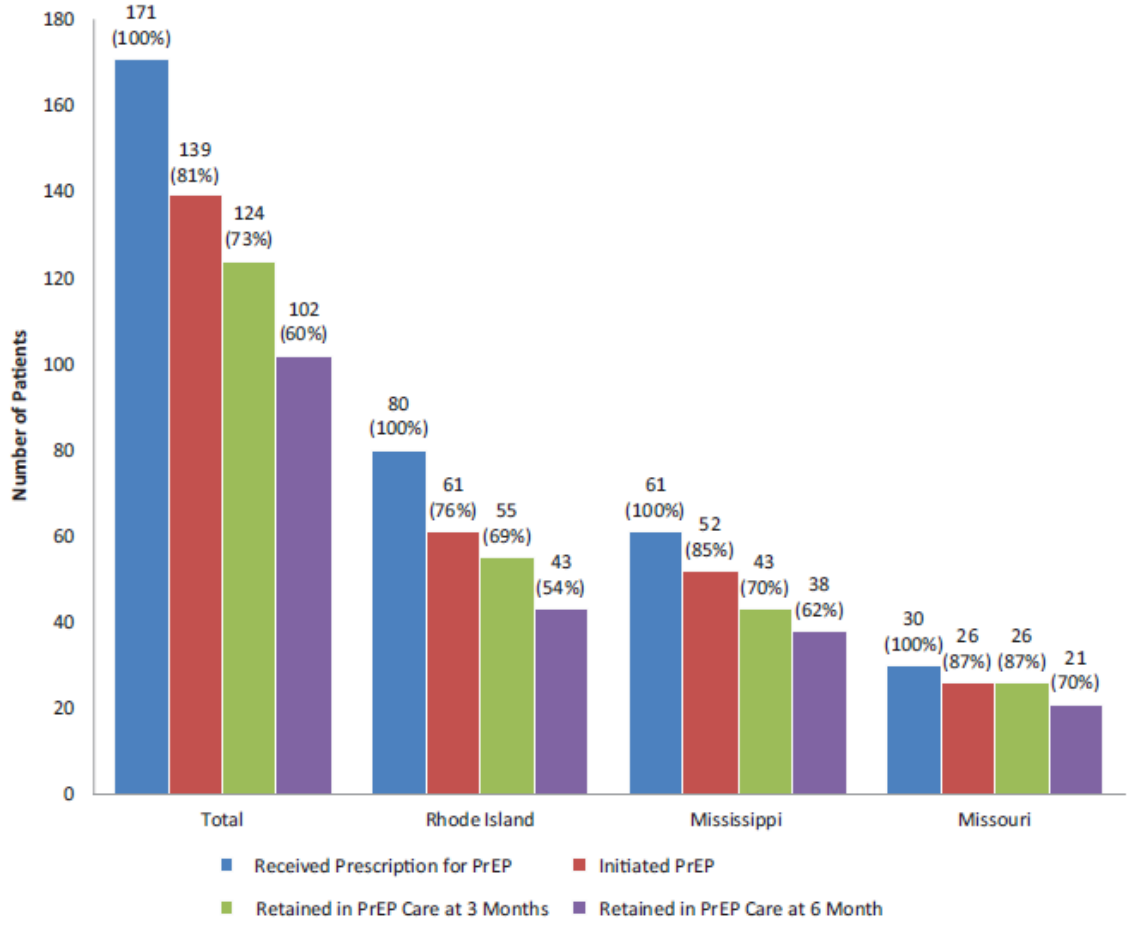
So, how many are the PrEP failures? 7 or >100?

- Depends: intention-to-treat (ITT) or on-treatment (OT)?
- In all other fields of medicine, we say ITT is the most rigorous method to assess the efficacy of an intervention
  - an anti-hypertensive can lower the blood pressure satisfactorily in 100% of the patients who take it consistently (OT), but it's not a great strategy for hypertension management if 40% of the patients stop taking it after 6 months because of side effects/cost/inconvenience related to prescriptions and monitoring (ITT)
- Why then we seem to be so shy in admitting that PrEP efficacy as a strategy (ITT) is much worse than its efficacy when consistently and correctly taken (OT)?

Real-life challenge: retention on PrEP

- Retention in HIV pre-exposure prophylaxis (PrEP) care cascade overall and for Rhode Island, Mississippi and Missouri:

If any of the 40% of PrEP users who have stopped taking it at 6 months contracts HIV, those will be PrEP failures by ITT analysis.



Chan PA et al. Journal of the International AIDS Society 2016, 19:20903

Does PrEP increase STIs or not?

- PrEP users are diagnosed with intercurrent STIs (chlamydia, gonorrhoea and syphilis, mostly) much more frequently than people relying on condoms for HIV prevention
  - is this due to a compensatory decrease in condom use, or just to more frequent STI screenings?
- Systematic meta analysis of 17 studies:
  - PrEP use was associated with a significant increase in rectal CT(OR: 1.59; 95% CI 1.19–2.13) and an increase in any STI (OR, 1.24; 95% CI, .99–1.54)
  - most studies showed evidence of an increase in condomless sex among PrEP users.

Clinical Infectious Diseases 2018;67(5):676–86

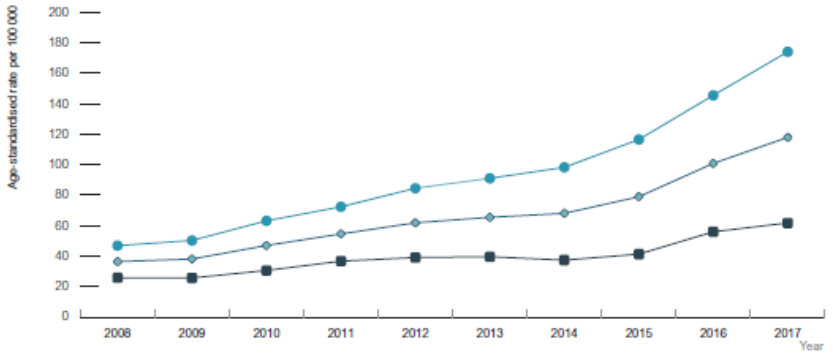
High Rates of Anal HPV Infection in Gay Men Using PrEP in IPERGAY

- More than 90% of the baseline anal samples showed any HPV genotype, with 76% of samples having >1 HPV infection
- Presence of any high-risk genotype was 84% in anal tissue, 25% in genital tissue and 10% in oral tissue
- Overall, 4.5% of cytology results (n=7) were high-grade squamous intraepithelial lesions (HSIL)
- Worryingly, only 38% of the anal HR HPV genotypes were covered by the 9-valent vaccine
- No information yet re longitudinal data and treatment.

AIDS 2018, 23-27 July 2018, Amsterdam. Poster TUPEB056

Gonorrhoea and syphilis in Australia

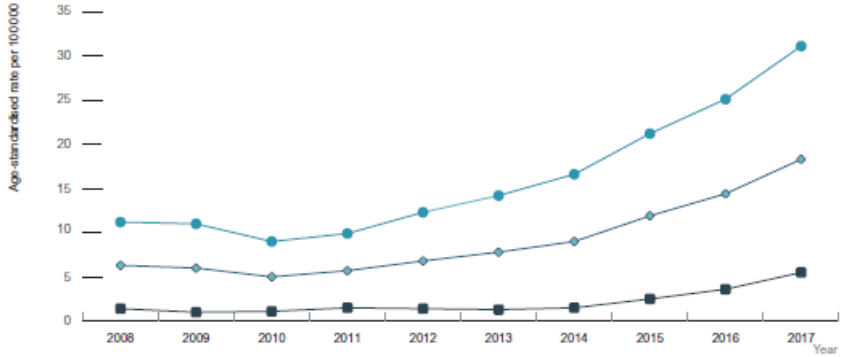
Gonorrhoea notification rate per 100 000 population, 2008–2017, by sex



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Men	46.9	50.3	63.2	72.4	84.6	91.1	98.3	116.6	145.6	174.2
Women	25.8	25.7	30.6	36.7	39.1	39.6	37.4	41.3	56.0	61.8
Total	36.4	38.1	47.0	54.6	61.9	65.5	68.1	79.0	100.9	118.0

Source: Australian National Notifiable Diseases Surveillance System.

Infectious syphilis notification rate per 100 000 population, 2008–2017, by sex

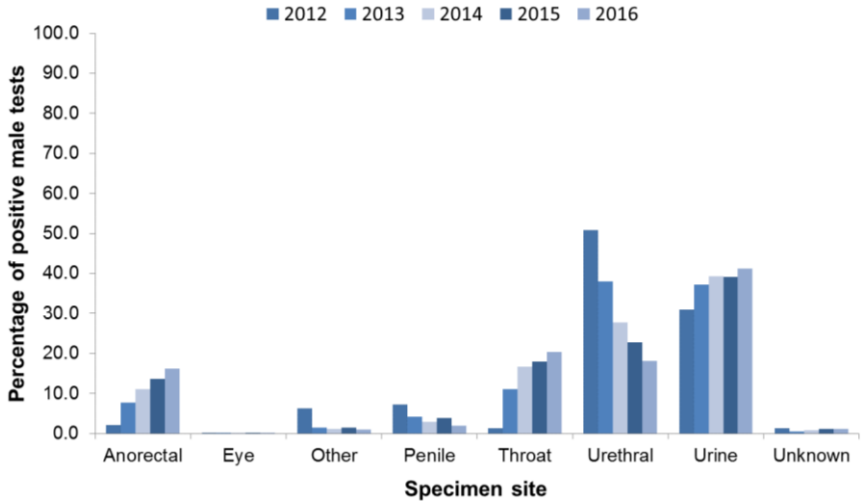


	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male	11.2	11.0	9.0	9.9	12.3	14.2	16.6	21.2	25.1	31.1
Female	1.4	1.0	1.1	1.5	1.4	1.3	1.5	2.5	3.6	5.5
Total	6.3	6.0	5.0	5.7	6.8	7.8	9.0	11.9	14.4	18.3

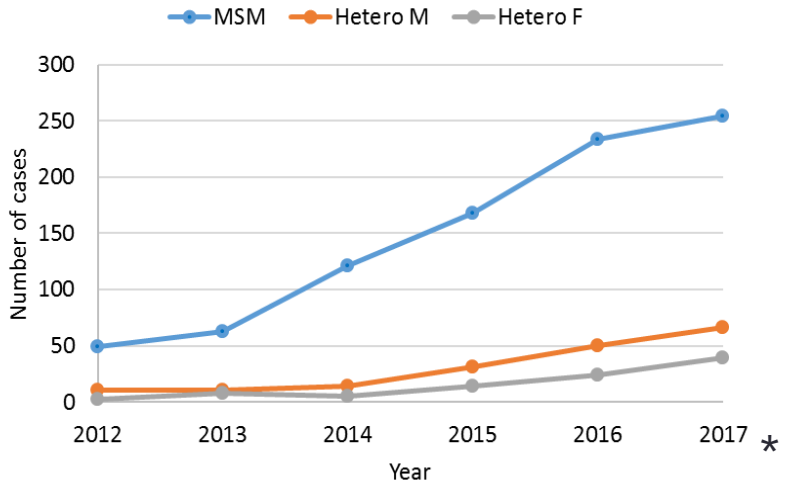
Source: Australian National Notifiable Diseases Surveillance System.

Gonorrhoea and syphilis in NZ

Gonorrhoea site of infection as a percentage of positive male tests, 2012-2016



Infectious syphilis cases by sexual behaviour, 2012-2017*



*Data for 2017 provisional and based on un-reconciled Enhanced Surveillance data for 369/470 cases with completed questionnaires

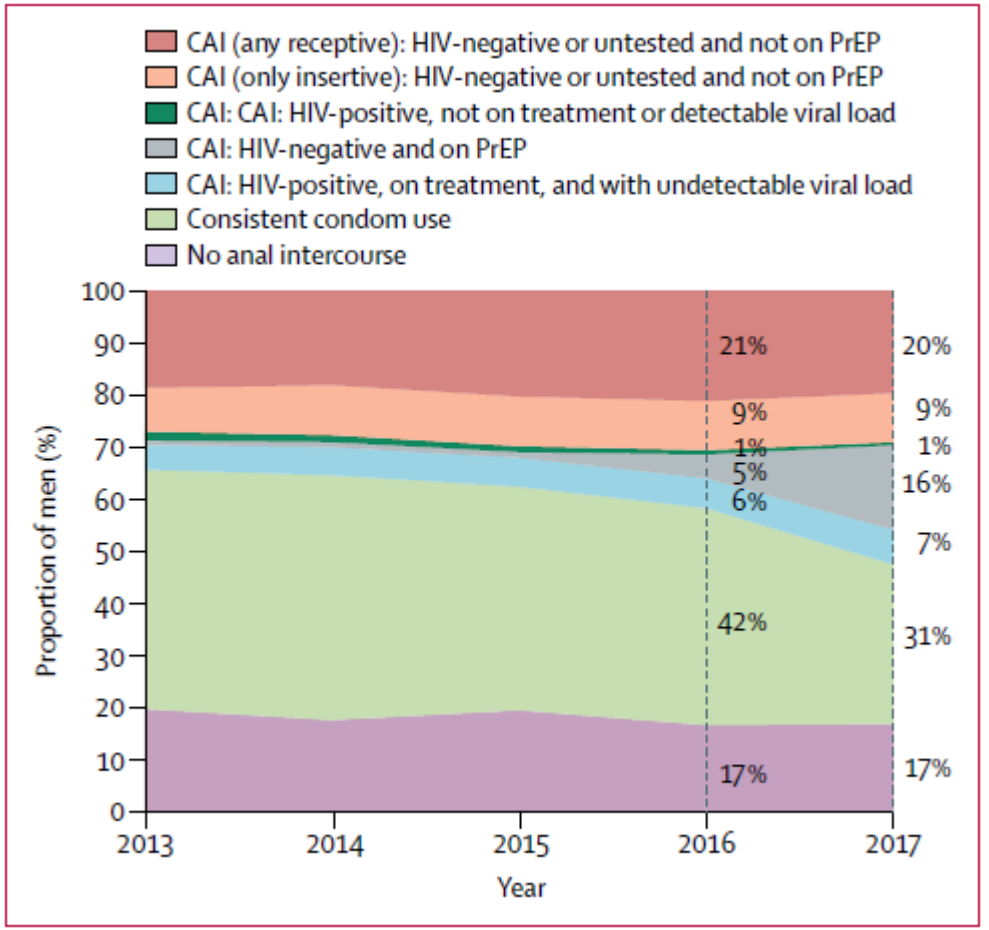
Data source: Laboratory-based STI surveillance, ESR

Inadvertent promotion of condomless sex and peer pressure to ditch condoms

- Behavioural qualitative research and anecdotal first-hand experience tell us that:
  - condomless sex is being seen again as the normal sex and the best, more pleasurable one
  - guys who were consistent condom users are now coming forward for PrEP evaluation, not because they wanted it, but because they are under peer pressure to have condomless sex
- Using or not a condom is for sure an individual choice, but are all the prevention strategies equal from a public health perspective?
  - should there be a holistic approach to sexual health encompassing HIV and STI prevention, or not?
- Finally, we fought for PrEP to be funded for the high-risk people who were refractory to condom use, not for PrEP to become the default HIV prevention strategy at the expense of condom use
  - what would the funders think of the following slide?

Success story or public health disaster in making?

Sex practices with casual male partners in the 6 months before survey in Melbourne and Sydney, 2013–17
CAI=condomless anal intercourse.
PrEP=pre-exposure prophylaxis



Lancet HIV 2018; 5 e448–56 Published Online June 6, 2018 http://dx.doi.org/10.1016/ S2352-3018(18)30072-9