VHHITAL

VICTORIAN HIV AND HEPATITIS INTEGRATED TRAINING AND LEARNING

HIV Prevention Strategies

phn NORTH WESTERN MELBOURNE

ashm

AlfredHealth

Doherty Institute

VICTORIA State Government

phn VICTORIAN ALLIANCE

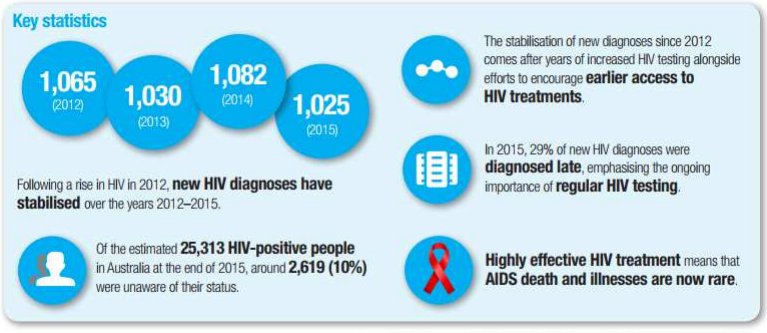
Conflicts of Interest

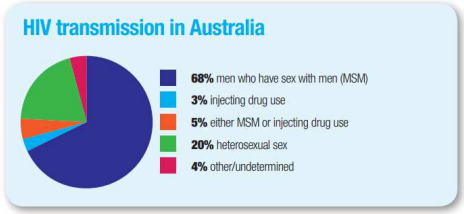
Treatment as Prevention (TasP)

Post Exposure Prophylaxis (PEP)

Pre Exposure Prophylaxis (PrEP)

HIV nationally





Newly-diagnosed HIV is becoming higher among the **Aboriginal and Torres Strait Islander people** than non-Indigenous people (6.8 v 3.1 per 100,000).

https://www.afao.org.au/

90-90-90

An ambitious treatment target to help end the AIDS epidemic

UNAIDS
2014

What does 90-90-90 mean?

By 2020, **90%** of people with HIV will be diagnosed

90% of those diagnosed will be on treatment

90% of those on treatment will have an undetectable viral load

Victoria:

- 90% diagnosed
- 94% treated
- 93% undetectable viral load

Treatment as Prevention (TasP)

Good evidence now available that effective ART (undetectable viral load) is the single most powerful intervention to prevent transmission

The most important factor that increases the risk of sexual transmission of HIV-1 is the viral load (number of copies per millilitre of plasma HIV-1 RNA)

- 2.4x increase risk for every 1log10 increase
- A reduction in plasma viral load of 0.7log10 is estimated to reduce HIV-1 transmission by 50%

Viral load and transmission: a recent seroconverter will be highly infectious

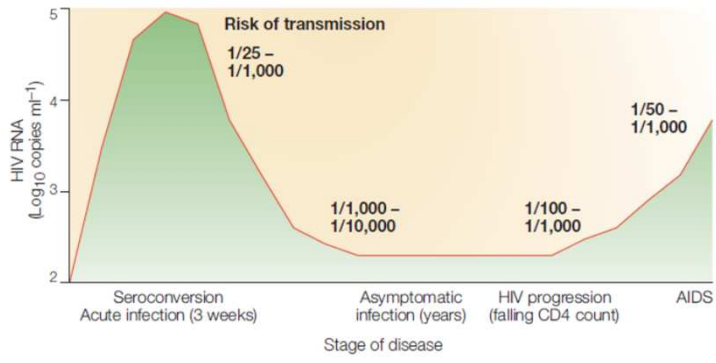
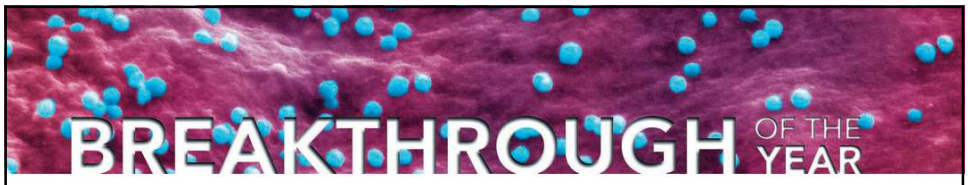


Figure 1 | **The changing viral load during the different stages of disease and the effects of viral load on the probability of sexual transmission of HIV.**

Cohen Nat Reviews Micro 2004



HIV Treatment as Prevention

On 1 December, George Washington University in Washington, D.C., hosted "The Beginning of the End of AIDS," a splashy World AIDS Day event that featured three U.S. presidents, business magnates, and rock stars. The catalyst that brought them together was something Anthony Fauci, the top U.S. government HIV/AIDS scientist, told the crowd even 1 year ago would have seemed "wishful thinking": a clinical trial dubbed HPTN 052 and its "astounding" result.

HIV/AIDS researchers have long debated whether antiretroviral drugs (ARVs) used to treat HIV-infected people might have a double benefit and cut transmission rates. [illegible] to which the viral load in blood predicts the risk of HIV transmission," they cautioned.

Then in May of this year, the 052 clinical trial conducted by the HIV Prevention Trials Network reported that ARVs reduced the risk of heterosexual transmission by 96%. "Now we have absolute, confirmed data," said Fauci at an AIDS conference this summer in Rome where researchers first presented the HPTN 052 data in detail. Fauci, who heads the U.S. National Institute of Allergy and Infectious Diseases—the main funder of the $73 million trial—said the challenge now was to apply the results.

The researchers planned to compare the groups until 2015. But on 28 April, an independent monitoring board that periodically reviewed the data stunned Cohen and his collaborators when it recommended that the results of the trial be made public as soon as possible. Of the 28 people who become infected with HIV that genetically matched the viruses in their long-term partners, only one was in the early treatment group—which also experienced 41% fewer serious health problems associated with HIV. Infected people in the delayed arm of the study were offered ARVs immediately.

The HPTN 052 results and other recent successes have raised hopes that combining such inter-

Online
sciencemag.org
For an expanded version of this section, with podcast, video, links, and more, see

Science, 2011; 334:1628

HPTN 052: Immediate vs Delayed ART for HIV Prevention in Serodiscordant Couples

HIV-infected, sexually active serodiscordant couples; CD4+ cell count of the infected partner: 350-550 cells/mm^3 (N = 1763 couples)

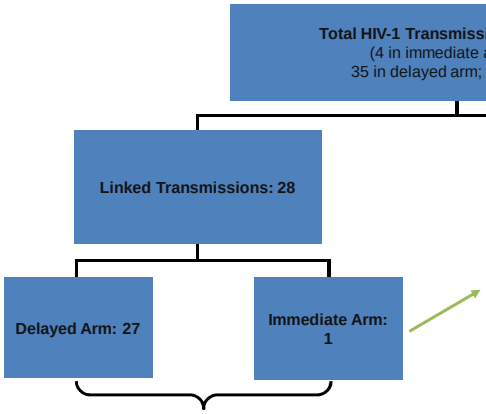
Immediate ART
Initiate ART at CD4+ cell count 350-550 cells/mm^3
(n = 886 couples)

Delayed ART
Initiate ART at CD4+ cell count ≤ 250 cells/mm^3*
(n = 877 couples)

- Primary efficacy endpoint: virologically linked HIV transmission
- Primary clinical endpoints: WHO stage IV events, pulmonary TB, severe bacterial infection and/or death
- Couples received intensive counseling on risk reduction and use of condoms

Cohen MS, et al. N Engl J Med. 2011;365:493-505.

HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples, 2011

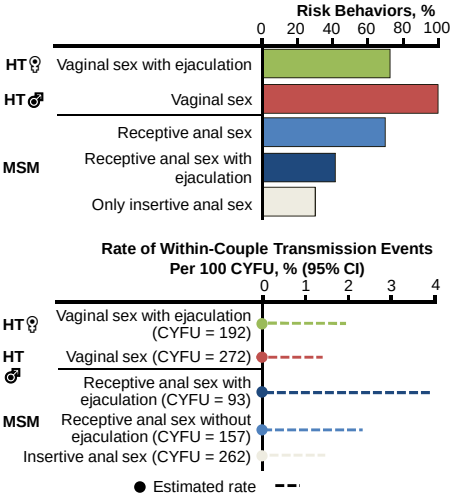


Single transmission in patient in immediate ART arm believed to have occurred close to time therapy began and prior to suppression of genital tract HIV

Cohen MS, et al. N Engl J Med. 2011;365:493-505.

PARTNER: Risk of HIV Transmission With Condomless Sex on Suppressive ART

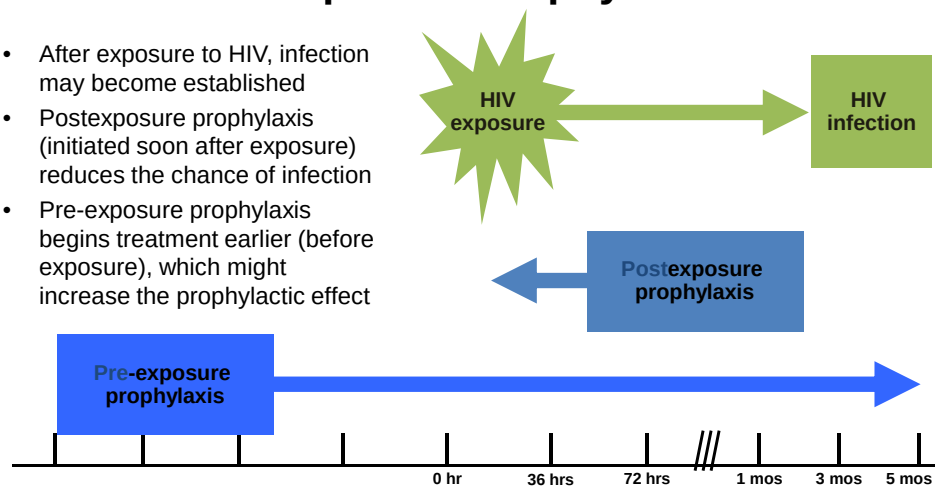
- Observational study of rate of HIV transmission in heterosexual and MSM serodiscordant couples (N = 767 couples)
  - HIV+ partner on suppressive ART
  - Condoms not used
- Analyses: 6-monthly risk behavior questionnaire, HIV-1 RNA (HIV+ persons), HIV test (HIV-negative persons)
- Endpoint: phylogenetically linked transmissions
- No linked transmissions recorded in any couple during study period



Rodger A, et al. CROI 2014. Abstract 153LB.

Pre- vs Postexposure Prophylaxis

- After exposure to HIV, infection may become established
- Postexposure prophylaxis (initiated soon after exposure) reduces the chance of infection
- Pre-exposure prophylaxis begins treatment earlier (before exposure), which might increase the prophylactic effect



What is PEP?

- Use of antiretroviral drugs after exposure to reduce the likelihood of HIV infection
- Evidence – no RCT. Based on animal data, case control, occupational exposure,MTCT prevention data
- 2-3 drugs given for 28 days
- < 72 hours post-exposure (preferably as soon as possible)
- Non s100 indication
- Available on ASHM website (www.ashm.org.au/pep-guidelines) for:
  - National guidelines on Non-occupational exposure (NPEP) and Occupational exposure
  - Links to State and Territory guidelines
  - refer to local guidelines for specific protocol/drugs

Common presentations for NPEP

- Male-to-male sex
  - Anal
  - Oral
- Heterosexual sex
  - Vaginal
  - Oral
- Sexual assault
  - Heterosexual
  - Male-to-male
- Needle sharing/needle assault
- Needle stick injury (park, beach etc)
- Other - Trauma, dermatitis, broken skin exposure

Factors that may increase the risk of HIV transmission include:

- A high plasma viral load (a high VL when seroconverting or with advanced disease)
- A sexually transmissible infection in the source or exposed individual.
- A breach in genital mucosal integrity (e.g. trauma, genital piercing or genital tract infection)
- A breach in oral mucosal integrity when performing oral sex
- Penetrating, percutaneous injuries with a hollow bore needle, direct intravenous or intra-arterial injection with a needle or syringe containing HIV infected blood
- The uncircumcised status of the insertive HIV negative partner practising IAI or IVI.

PEP recommendations after NON-OCCUPATIONAL exposure to a KNOWN HIV status source

Type of exposure with known HIV positive source	Estimated risk of HIV transmission per exposure if source NOT on antiretroviral treatment	PEP recommendation	
		Source not on treatment or on treatment with detectable or UNKNOWN viral load	Source viral load KNOWN to be undetectable
Receptive anal intercourse (RAI) - ejaculation - withdrawal	 1/70 1/155	3 drugs	Not recommended*
Shared needles and other injecting equipment	1/125	3 drugs	Not recommended*
Insertive anal intercourse (IAI) (uncircumcised)	1/160	3 drugs	Not recommended*
Insertive anal intercourse (IAI) (circumcised)	1/900	3 drugs	Not recommended*
Receptive vaginal intercourse (RVI)	1/1250	3 drugs	Not recommended*
Insertive vaginal intercourse (IVI)	1/2500	3 drugs	Not recommended*
Receptive or insertive oral intercourse	Not measurable	Not recommended†	Not recommended
Mucous membrane and non-intact skin exposure	< 1/1000	3 drugs	Not recommended

* **Provided the source history is reliable, they are compliant with medication, attend regular follow-up and have no intercurrent STI.**

† PEP may be recommended for receptive oral intercourse with ejaculation if the exposed person has a breach in their oral mucous membrane.

PEP recommendations after NON-OCCUPATIONAL exposure to a source with UNKNOWN HIV status

Type of exposure to source with unknown HIV status	Estimated risk of HIV transmission per exposure	PEP recommendation
Receptive anal intercourse (RAI) - ejaculation - withdrawal	1/700* 1/1550*	2 drugs if source MSM or from high prevalence country (HPC)
Shared needles and other injecting equipment	1/12,500† (1/1250 – 1/415‡ if source MSM)	2 drugs if source MSM or from HPC
Insertive anal intercourse (IAI) (uncircumcised)	1/1600*	2 drugs if source MSM or from HPC
Insertive anal intercourse (IAI) (circumcised)	1/9000*	Consider 2 drugs if source MSM or from HPC, particularly if concurrent STI, trauma or blood
Receptive vaginal intercourse (RVI)	1/1,250,000^	Not recommended Consider 2 drugs if source MSM or from HPC
Insertive vaginal intercourse (IVI)	1/2,500,000^	Not recommended Consider 2 drugs if source from HPC
Receptive or insertive oral intercourse	Not measurable	Not recommended
Mucous membrane and non-intact skin exposure	< 1/10,000* (MSM exposure)	Not recommended
Needlestick injury (NSI) from a discarded needle in community	Not measurable	Not recommended

* Based on estimated seroprevalence 10% (9.6%) in MSM.
† Based on estimated seroprevalence 1.0%.
‡ Based on estimated seroprevalence of 29%.
^ Based on estimated seroprevalence 0.1%.

PEP recommendations after <u>OCCUPATIONAL</u> exposure to a known HIV-positive source

Type of exposure with known HIV-positive source	Estimated risk of HIV transmission per exposure if source not on antiretroviral treatment	PEP recommendation	
		Source not on treatment or on treatment with detectable or UNKNOWN viral load	Source viral load KNOWN to be undetectable
NSI or other sharps exposure	1/440	3 drugs	Consider 2 drugs
Mucous membrane and non-intact skin exposure	< 1/1000	3 drugs	Consider 2 drugs

* PEP may be recommended if needle and syringe contained fresh blood and sufficiently penetrated the skin.

Which regimen?

2-drug regimens^:

Tenofovir 300mg with lamivudine 300mg (Daily)*

OR

Tenofovir disoproxil fumarate/emtricitabine 300mg/200mg (Daily)

3-drug regimens:

Your preferred 2-drug regimen **PLUS**

dolutegravir 50mg (Daily)

OR

raltegravir 400mg (BD)

OR

rilpivirine 25mg (Daily)

Dolutegravir, raltegravir or rilpivirine as the 3rd drug:

The current guidelines recommend dolutegravir or raltegravir or rilpivirine as the 3rd drug in PEP. Using three drugs for PEP increases the likelihood of an adverse event e.g. drug-drug interactions and the potential for rhabdomyolysis with raltegravir.

PEP in Shepparton

- NPEP Service based at Alfred (hub and spoke model)
- Suzanne Wallis. Sexual Health Nurse
  - Goulburn Valley Community Health
  - 0427 564 512
- Phone advice line Victorian NPEP line 1800 889 887
- Accident and Emergency Department after hours

Pre exposure prophylaxis (PrEP)

- Pre-exposure prophylaxis (PrEP) involves the use of **antiretroviral drugs** by HIV uninfected individuals to **reduce HIV acquisition risk**.
- Effective in preventing sexual transmission of HIV in high risk groups
- Tenofovir / emtricitabine (FDC) has the most evidence base
- Licensed by the TGA, but not subsidized in Australia at present
- There are demonstration projects running in Australia:
  - EPIC-NSW (NSW)
  - PrEPX (Victoria)
  - QPrEP (QLD)

PrEP trials showing efficacy

Trial	Population/Setting	Intervention	HIV Infections, n		Reduction in HIV Infection Rate, % (95% CI)
			PrEP	Placebo	
iPrEX[1] (N = 2499)	MSM, transgender women, 11 sites in US, South America, Africa, Thailand	TDF/FTC	36	64	44 (15-63)
Partners PrEP[2] (N = 4747)	Serodiscordant couples in Africa	TDF	17	52	67 (44-81)
		TDF/FTC	13		75 (55-87)
TDF2[3] (N = 1219)	Heterosexual males and females in Botswana	TDF/FTC	9	24	62 (21-83)
Thai IDU[4] (N = 2413)	Volunteers from 17 drug Thai treatment centers	TDF	17	33	49 (10-72)

Adherence Is a Key Determinant of PrEP Trial Outcomes

Study	Detection of TFV in Plasma, %	
	HIV Seroconverters	HIV Uninfected
iPrEx[1]		51
Partners PrEP[2] (TDF/FTC arm)		81
Thai IDU[3]		67

In the large iPrEx, Partners PrEP, and Thai IDU studies, TFV was detected in blood samples of the majority of subjects who remained HIV uninfected during the study

1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 3. Choopanya K, et al. Lancet. 2013;381:2083-2090.

Adherence Is a Key Determinant of PrEP Trial Outcomes

Study	Detection of TFV in Plasma, %	
	HIV Seroconverters	HIV Uninfected
iPrEx[1]	9	51
Partners PrEP[2] (TDF/FTC arm)	25	81
Thai IDU[3]	39	67

By contrast, TFV was detected in only a minority of subjects who acquired HIV, arguing that adherence to taking the study medication was related to remaining HIV uninfected

1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 3. Choopanya K, et al. Lancet. 2013;381:2083-2090.

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This difference in TFV detection translated into a relative risk reduction of acquiring HIV:
iPrEx: 92% (95% CI: 40% to 99%; *P* < .001)
Partners PrEP TDF/FTC: 90% (95% CI: 56% to 98%; *P* = .002)
Thai IDU: 70% (95% CI: 2% to 91%; *P* = .04)

1. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410. 3. Choopanya K, et al. Lancet. 2013;381:2083-2090.

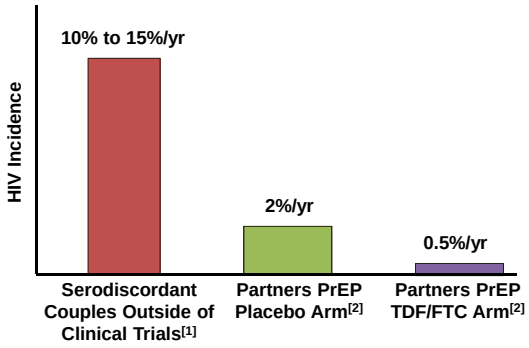
Prescribing PrEP: CDC Interim Guidance for MSM, Heterosexual Couples, IDUs

Component	Recommendation
Risk assessment	• PrEP indicated for those at high HIV risk
Eligibility	• HIV negative, adequate renal function
Dosing	• 1 FDC tablet, once daily
Follow-up	• Testing for HIV every 3 mos • Counseling on risk reduction and testing creatinine at 3 mos and then annually • Testing for STIs every 3 mos, even if asymptomatic
Discontinuation	• PrEP not meant for lifelong administration but rather for periods of highest risk

[3]. CDC. MMWR Morb Mortal Wkly Rep. 2014;63:872-873.

PrEP Works Together With Other HIV Prevention Strategies

- Example from Partners PrEP Study: package of HIV prevention services, including ongoing risk-reduction counseling, HIV testing, ART, treatment of STIs, and other strategies *plus PrEP* synergize to maximally reduce HIV risk



1. Quinn TC, et al. N Engl J Med. 2000;342:921-929. 2. Baeten JM, et al. N Engl J Med. 2012;367:399-410.

Acessing PrEP and PEP in Shepparton

PrEP

Alan Wallace at Princess Park Clinic - PrEPX shared care.

NPEP

Business hours Suzanne Wallis Goulburn Valley Community Health

After hours Emergency Department

The best contact points are the Alfred PrEPX phoneline on 9076 2940 or The Alfred PrEPX email prepx@alfred.org.au

Questions?