Why do we need PrEP?

Gus Cairns
Editor, NAM / www.aidsmap.com
Prevention coordinator, EATG
Co-chair, PROUD Study
We are winning the fight against HIV
Life expectancy in treated PWHIV is becoming normal

Margaret May et al. BMJ 2011;343:bmj.d6016
How have we managed the global epidemic?

We wouldn’t have done it without price reductions...
And with condoms...

Condom use among MSM in selected countries, 2007 vs 2011

<table>
<thead>
<tr>
<th>Country</th>
<th>2007</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ukraine</td>
<td>38.0</td>
<td>69.0</td>
</tr>
<tr>
<td>Vietnam</td>
<td>58.0</td>
<td>75.0</td>
</tr>
<tr>
<td>Senegal</td>
<td>54.0</td>
<td>77.0</td>
</tr>
<tr>
<td>Bahamas</td>
<td>69.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Cote d'Ivoire</td>
<td>97.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Australia</td>
<td>93.0</td>
<td>93.0</td>
</tr>
<tr>
<td>Thailand</td>
<td>93.0</td>
<td>93.0</td>
</tr>
<tr>
<td>USA</td>
<td>51.0</td>
<td>51.0</td>
</tr>
</tbody>
</table>

Source: www.unaids.org
And with behavior change…


http://127.0.0.1:8081/plosmedicine/article?id=info:doi/10.1371/journal.pmed.1000414
And treatment access...The Cascades
But HIV is on the increase in at least one group


And more so elsewhere...

HIV MSM diagnoses: Poland 2000-11, east Asia 2002-2007


Why? Transmission vulnerability

Estimated number of exposures needed to HIV (average viral load off-treatment) for one infection to occur

- BASHH High
- BASHH Low
- BASHH Average
- CDC

- URAI
- UIAI
- URVI
- UIVI
- UROI
- UIOI
- Transf
- Needle
- Sharing
- Mucous
Why? ‘Condom ceiling’
Why? Because gay men have to make complex choices.
Why? TasP is not enough

- Even in UNAIDS 90/90/90 target, ART will only produce 60% of targeted reduction in incidence.
- As more diagnosed, in concentrated epidemics, most infections come from undiagnosed. Incidence in some groups runs ahead of even frequent testing.

Distribution of infectives* among HIV-infected MSM, UK: 2010, Brown et al

Extending ART to all MSM with CD4 counts <500 cells/mm³ would reduce infectivity from an estimated 35% to 29% and, in combination with halving the undiagnosed, to 21%.
Ergo: Pre-exposure prophylaxis

• Idea of medicines to prevent conditions not new:
  o Antimalarial prophylaxis (‘tonic water’)
  o Isoniazid prophylaxis for TB
  o Co-trimoxazole for PJP (PCP)
  o Statins for heart attacks

• And of course:
  o The contraceptive pill
PrEP history

- First animal study: 1995¹
- First study in infants: 2003²
- First adult study (terminated): Cambodia, 2004³
- First result (65% reduction in infections, but not significant): Ghana, 2006⁴
- First significant result (44% effectiveness): iPrEx, 2010⁵

Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

http://www.proud.mrc.ac.uk/
GMSM reporting UAI last/next 90 days; 18+; and willing to take a pill every day

Randomize HIV negative MSM (exclude if treatment for HBV/Truvada contra-indicated)

Risk reduction includes Truvada **NOW**

Risk reduction includes Truvada **AFTER 12M**

Follow **3 monthly** for up to 24 months

Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months
Individual incident HIV infections

Immediate PrEP  N=3

Deferred PrEP  N=19

Weeks since enrolment

N=19

N=3
Behaviour

- Marginally significant increase (p=0.04) in proportion of men in immediate PrEP arm who had >8 condomless sex partners in last 3 months, compared with delayed arm
- This does not tell us who they were having condomless sex with
On Demand PrEP with Oral TDF/FTC in MSM: Results of the ANRS Ipergay Trial


Hospital Saint-Louis and University of Paris 7, Inserm SC10-US019 Villejuif, Hospital Tenon, Paris, Hospital Croix-Rousse, Lyon, UMR912 SEAS Marseille, France, CHUM, Montreal, Canada and ANRS, Paris, France
Study Design

Double-Blinded Randomized Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with $\geq 2$ partners within 6 m
- eGFR $> 60$ mL/mn

Full prevention services* TDF/FTC before and after sex

Full prevention services* Placebo before and after sex

* Counseling, condoms and gels, testing and treatment for STIs, vaccination for HBV and HAV, PEP

- End-point driven study: with 64 HIV-1 infections, 80% power to detect a 50% relative decrease in HIV-1 incidence with TDF/FTC (expected incidence: 3/100 PY with placebo)
- Follow-up visits: month 1, 2 and every two months thereafter
Ipergay : Event-Driven iPrEP

- 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- 1 tablet (TDF/FTC or placebo) 24 hours later
- 1 tablet (TDF/FTC or placebo) 48 hours after first intake
Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 per 100 PY), 2 in TDF/FTC arm (incidence: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, p=0.002)

NNT for one year to prevent one infection: 18
Adherence by Pill Count

TDF/FTC
Nb pills/month

Placebo
Nb pills/month
PrEP as a bridge to ART

• For couples initiating ART at enrollment, PrEP is offered through 6 months, then stopped:

  ![Diagram](image1)

  ART
  PrEP
  Stop

• For couples in which the infected partner delays or declines ART, PrEP is continued until 6 months after ART initiation:

  ![Diagram](image2)

  ART delayed……………..
  ART
  PrEP
  Stop

• This strategy is supported by mathematical modeling as potentially highly effective and cost-effective (Hallett et al. PLoS Med 2011; Ying et al. CROI 2015, abstract #1106)
The counterfactual expected HIV incidence of 5.2% per year is substantially greater than the 2% seen in prior studies of couples (Partners PrEP, HPTN 052) and is comparable to the ~4-5% seen in high-risk PrEP study cohorts (VOICE, FEM-PrEP, FACTS 001, iPrEx).
Is PrEP for HIV prevention cost-effective in MSM in the UK?

Valentina Cambiano, Alec Miners, David Dunn, Sheena McCormack, KohJun Ong, Noel Gill, Anthony Nardone, Monica Desai, Gus Cairns, Alison Rodger, Andrew Phillips
PrEP scenarios to be considered

PrEP eligibility criteria:
1. had **condomless sex (CLS)** in past 3 months*
2. had **CLS with ≥1 short-term partner (STP)** in past 3 months
3. had **CLS with ≥5 STP** in a 3 month period in the last year
4. had an **STI** in past 3 months

Assuming:
- PrEP is introduced in 2016
- those willing to use PrEP (50% of men if 1 or 2; 80% of men if 3 or 4) actively seek an HIV test when eligible and, if negative, start PrEP
- 25% of the population have an increased probability of having condomless sex and actively seek an HIV test when eligible and if negative start PrEP (this only applies for 1 and 2).

*except if the only partner they have is a long-term partner who is virologically suppressed on ART.
PrEP scenarios to be considered

PrEP eligibility criteria:

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- those willing to use PrEP (50% if (1) or (2); 80% if (3) or (4)) actively seek an HIV test when eligible and if negative start PrEP
- 25% of the population increase condomless sex (if the option is (1) or (2)) and actively seek an HIV test when eligible and if negative start PrEP

*except if the only partner they have is a long-term partner who is virologically suppressed on ART.

The sexual behaviour refers to the last 3 months if not indicated.
Health benefits and costs over 80 years

PrEP in men having:
- CLS
- CLS with ≥1 STP
- CLS with ≥5 STP
- CLS with STIs
- CLS (no increase in CLS or testing)

Cost-effectiveness threshold range

<table>
<thead>
<tr>
<th>Change in Cost (£ million) compared to no PrEP</th>
<th>Change in QALYs* compared to no PrEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>£57,145</td>
<td>150,000</td>
</tr>
<tr>
<td>£39,314</td>
<td>100,000</td>
</tr>
<tr>
<td>£9,466</td>
<td>50,000</td>
</tr>
<tr>
<td>£9,290</td>
<td>0</td>
</tr>
<tr>
<td>£1,522 m saved</td>
<td>-25,000</td>
</tr>
</tbody>
</table>

*discounted at 3.5% rate
Health benefits and costs over 80 years

50% reduction in cost of ARVs

80% reduction in cost of ARVs

Cost-effectiveness threshold range;

PrEP in men having:
- CLS
- CLS with ≥1 STP
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Extra

• PrEP advocacy and agitation
PrEP advocacy

– Kicked off by HIV+ treatment activists and allies

• But by definition, these are not the ‘end users’ of PrEP
  – The HIV negative-at-risk population has to adopt and champion PrEP

• But they often do not have the scientific background and biomedical perspective of treatment activists
  – HIV prevention has largely been seen as the community’s own endeavour/area of expertise

• Can lead to conservatism/ignorance of prevention science
US: provocation

Giving up on Gay Men

By Michael W养任，President, AIDS Healthcare Foundation

Recent headlines appeared taking medication as ‘pre-exposure prophylaxis’ to prevent transmission of HIV among gay men. The news came in a study of nearly 5,500 men in six countries that found that an average man taking the medication was 44% less likely to become infected than a control group taking a placebo.

How very sad that we have come to this point. The appoach for this approach shows just how disposable we consider the lives of gay men.

If we were talking about protecting the general population with a treatment that was only 44% effective, would we be celebrating? The 44% who receive a benefit from the medication were intensively counseled monthly, with frequent blood draws and tests for sexual infections. This is in no way representative of any real world situation.

In the real world, why would anyone subject himself to drug therapy—with the potential of very serious side effects—every day if they had any intention of using condoms? If someone tells almost any man that it is safe to have sex without a condom, they will likely do so.

Kevin Fenton, chief of HIV/AIDS for the Centers for Disease Control and Prevention said “Some studies suggest that even a small increase in risk behavior due to a false sense of security about the pill’s effectiveness could actually increase HIV infections, an outcome we cannot afford.”

A large percentage of patients already infected with HIV do not take their medication. How likely are unaffected men to take pills every day for the rest of their lives to prevent an HIV infection? If the pre-exposure HIV medication is not at the therapeutic levels in their systems below they have sex, they will not be protected.

The potential use of drugs to prevent HIV infection is based on the premise that we cannot succeed in getting gay men to use condoms. Has an effective effort really been made to market condoms in gay-friendly ways? Are condoms readily available in bars, bathhouses and other meeting spots? Advertised on TV? Do our political, religious and community leaders speak out forcefully for preventing gay men from HIV infection?

Another question: who will pay for this $10,000 per person, per year pre-exposure treatment?

I commend research into HIV prevention. But, our communities must consider these points if we are going to offer hundreds of thousands of gay men for an unproven experiment.

For more information or to send a letter to Gilead CEO John C. Martin, Please visit nomagicpills.org.

The FDA has approved Truvada, an HIV treatment medication, to be taken by uninfected people as a pre-exposure prophylaxis, or “PrEP” -- that is, to protect against HIV. The PrEP drug is intended for those individuals who engage in high-risk sexual behavior and is prescribed to be used in conjunction with safe sex practices. So are these “high-risk” folks actually using the drug as the doctor prescribed?
US: reaction
US: initiatives

We feature real stories from people who have chosen to use PrEP as one way to protect themselves from HIV. We invite you to share your PrEP experience via audio, video, or in writing. Send video or audio links and/or text we will post them here. You can include your name, or you may contribute your story anonymously. This blog is for users, potential users, and providers. Look for the links in the sidebar.

We have not heard of any insurance company or any Medicaid program outright denying coverage of Truvada, however, which requires paperwork to be filled out. And the cost of prescription drug benefits, will determine the cost to you as the consumer. To date, we have seen from providers who are unwilling to write a prescription.

If you have trouble getting a prescription for Truvada as PrEP from your provider, or getting a PrEP prescription we are happy to troubleshoot with you. Send us an email to myprepexperience@gmail.com.
### US: normalisation? (In SF)

<table>
<thead>
<tr>
<th>Group</th>
<th>People</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV negative at substantial risk:</td>
<td></td>
</tr>
<tr>
<td>MSM with 2+ non-condom anal sex (ncAI) partners¹</td>
<td>12,589</td>
</tr>
<tr>
<td>MSM with 0 ncAI and an STI in the last year²</td>
<td>2,325</td>
</tr>
<tr>
<td>Female partners of HIV+ MSM³</td>
<td>653</td>
</tr>
<tr>
<td>Trans women⁴</td>
<td>522</td>
</tr>
<tr>
<td><strong>TOTAL estimated PrEP eligibility</strong></td>
<td><strong>16,089</strong></td>
</tr>
<tr>
<td><strong>TOTAL reporting any PrEP in past year⁵</strong></td>
<td><strong>5,059</strong></td>
</tr>
<tr>
<td><strong>Percent of eligible people using PrEP in the past year</strong></td>
<td><strong>31%</strong></td>
</tr>
</tbody>
</table>

¹ SFAF Clinic Survey: 16% already n PrEP, 60% want to be
What are the (extra) issues in Europe?

• Cost/affordability
• Arguments from equity: will PrEP take resources away?
• Fear of PrEP being a preferable alternative
• East-versus-west
• Homophobia
• Health systems based on solidarity rather than liberty
• ‘We all have to agree to this’
• Internalised homophobia in gay men: responsible gay men versus Truvada whores
• Alternatives: informal PrEP, PEP-as-PrEP, online generics
Europe

- Strong community engagement in both Ipergay and PROUD
- Activists’ meeting at Melbourne
Some media

NHS to offer tablet which can reduce HIV risk by 90%
“Although an NHS England process to evaluate PrEP is underway, any decision to provide PrEP will probably not be implemented until early 2017, which is too long to wait. We are calling for earlier access to PrEP. The NHS must speed up its evaluation process and make PrEP available as soon as possible. Furthermore, we call for interim arrangements to be agreed now for provision of PrEP to those at the highest risk of acquiring HIV.”
These results are ground-breaking. A European licence for a measure that was approved by the US Food and Drug Administration in 2012, and which is already being used by at least 12,500 people in the US, is overdue... **We call on all stakeholders to make PrEP available and accessible in Europe:** We ask that Gilead, the manufacturers of Truvada®, to immediately file for a PrEP indication for Truvada® to the European Medicines Agency (EMA). We ask the EMA to clarify the regulatory pathway for access to PrEP.

The community turns out to demand PrEP now in the NHS!! With 6,000 diagnoses every year - two years is much too long to wait! Thanks to all our allies at Terrence Higgins Trust Positively UK HIV i-Base and all other orgs who turned up!! (**SEE THE REST OF YOU AT OUR GENERAL MEETING TONIGHT 6:30PM - UNITE Bldg, 33-37 Moreland St. EC1V 8BB**
Film – and Individual testimonies

So Why Are So Many Gay Men Opposed To PrEP?

By The Gay UK, Aug 16 2014 08:23AM

So why are so many gay men adamantly opposed to PrEP, the daily dose of the anti-retroviral drug Truvada, which is at least 90% effective at protecting against HIV? Indeed, according to a recent iPrEx open-label extension (iPrEx OLE), to date the largest demonstration project of HIV Pre-Exposure Prophylaxis, daily taking of Truvada could be as much as 99% effective.

by Greg Mitchell | 16th August 2014
A personal note: 1981

- New to London gay scene 1977
- Syphilis? 1978
- Diagnosed 1985
- Probable seroconversion illness 1984
- If PrEP had been available in 1978 I might not have got HIV
For Paul
Thanks to...

- Sheena McCormack
- Jean–Michel Molina
- Bob Grant
- Jared Baeten
- Damon Jacobs
- Brandyn River Gallagher
- Valentina Cambiano
- Noel Gill
- Nicholas Feustel
- Ben Collins
- ACT–UP London
- Henning and EATG