Pre-Exposure Prophylaxis

ECDC comment on the release of CDC guidance on PrEP

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ECDC
Luxembourg, 9 July 2014

Outline

- What is PrEP?
- Clinical research trials
- Cost-effectiveness analysis of PrEP
- U.S. guidelines on PrEP
- ECDC comment on the release of CDC guidelines
- Important considerations for policy makers
- WHO guidelines on PrEP

What is PrEP?

- "PrEP" stands for **Pr**e-**E**xposure **P**rophylaxis
- PrEP is a relatively new HIV prevention method in which an HIV negative person takes a pill daily to reduce their risk of becoming infected
- Taken daily, PrEP stops HIV from taking hold and spreading in your body
- The pill contains two medicines that are also used to treat HIV (tenofovir and emtricitabine)
- Truvada® is the only licenced product currently used for PrEP

Four biomedical interventions are available in the 'HIV prevention toolbox'

- Pre-exposure prophylaxis (PrEP)
- Medical male circumcision
- Post-exposure prophylaxis (PEP) following sexual exposure
- Early treatment of the HIV positive partner (treatment as prevention)

iPrEx study*

- iPrEx was the first randomised controlled trial of PrEP in humans to produce a statistically significant result
- The iPrEx study started in June of 2007 and concluded in Feb of 2011
- iPrEx compared Truvada with a placebo pill in nearly 2,500 gay and bisexual men in six countries (Peru, Ecuador, Brazil, South Africa, Thailand and the U.S.)
- Those who were given PrEP were 44% less likely overall to get HIV than those who were given a placebo
- The efficacy in subjects who took the drugs more than 90% of the time was between 73%-92% (adherence critically important)

*Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010;363:2587-2599.

Overview of clinical research results

- Data from the iPrEx, Partners PrEP and TDF2 studies shows that daily oral PrEP is safe and effective to reduce risk of infection in:
  - heterosexual men and women
  - gay men and other men who have sex with men
  - transgender women
- **The estimates of effectiveness vary in each trial depending on the level of adherence** (iPrEx=42%-92%)
- Two trials of PrEP in women, the FEM-PrEP and VOICE trials, found no effect
- Results from a study in Thailand showed that PrEP was effective at reducing HIV risk in PWID

PrEP Works...If You Take It

Trial	Efficacy	Adherence
CAPRISA 004[6]	1% tenofovir gel: 39%	51%
iPrEx[7]	Oral daily Truvada: 42%	51%
Partners PrEP[8]	Oral daily tenofovir: 67% Oral daily Truvada: 75%	83% 81%
TDF2[9]	Oral daily Truvada: 62%	81%
FEM-PrEP[10]	Oral daily Truvada: No Protection	24%
VOICE[2]	TFV gel: No protection Oral daily tenofovir: No protection Oral daily Truvada: No protection	23% 28% 29%

The point estimate of efficacy for each study is listed and adherence estimates were determined by measuring drug levels from participant samples collected at varying time points.

BOTTOM LINE: PrEP WORKS WHEN TAKEN CORRECTLY AND CONSISTENTLY

Cost-effectiveness analysis of PrEP for MSM in the U.S.* (2012)

Benefits and Costs of PrEP Strategies Over 20 Years – High-risk MSM

Strategy*	New HIV infections	HIV infections prevented	HIV prevalence at 20 years	Total costs of PrEP (billions)	Total costs (billions)	Incremental costs (billions)
100% of High-Risk Start PrEP	155,728	167,143 (52%)	17%	$85	$272	$75
50% of High-Risk Start PrEP	227,686	95,185 (29%)	23%	$42	$233	$36
20% of High-Risk Start PrEP	281,809	41,061 (13%)	28%	$17	$210	$14
Status Quo (No PrEP)	322,871		31%		$196	

Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of preexposure prophylaxis for HIV prevention in the United States in men who have sex with men. Ann Intern Med. 2012 Apr 17;156(8):541-50.

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- If **20%** of the high-risk MSM population were to initiate PrEP, more than **40,000** new HIV infections could be prevented over the next 20 years, at an **incremental cost of $14 billion**
- The **impact on HIV prevalence** among MSM would be **limited**

- If **100%** of the high-risk MSM population were to initiate PrEP, more than **160,000** new HIV infections could be prevented over the next 20 years, at an **incremental cost of $75 billion**
- The **impact on HIV prevalence** among MSM would be **significant**

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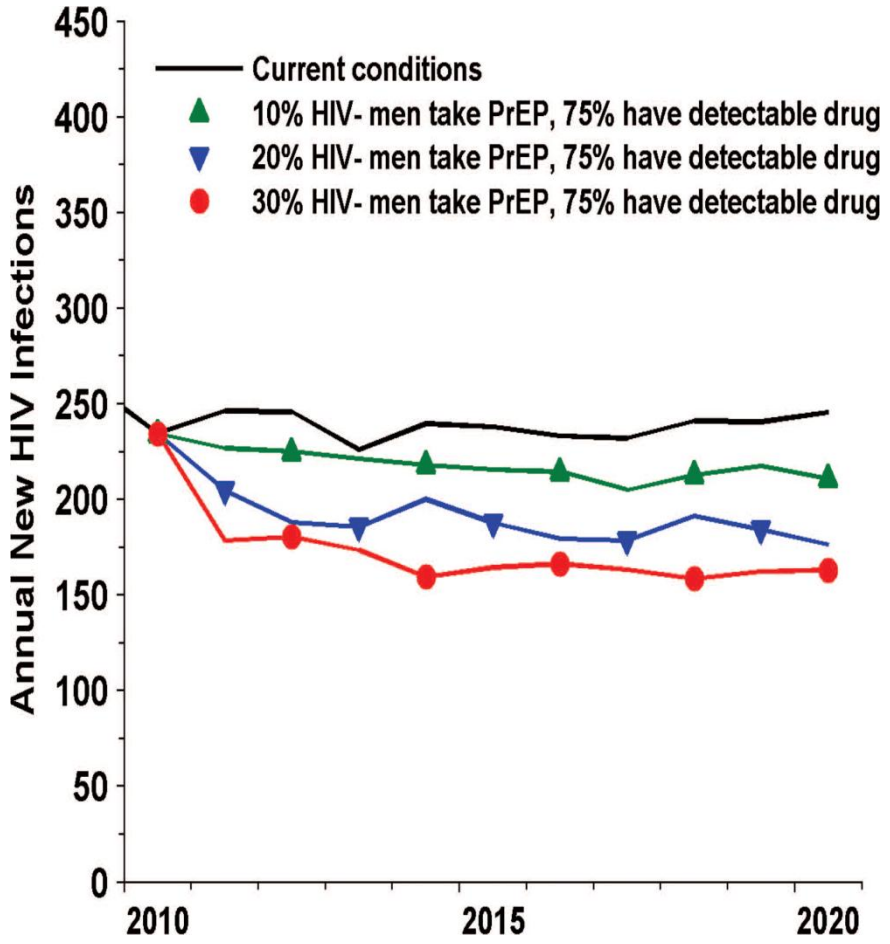
Cost-effectiveness analysis of PrEP for MSM in Australia* (2014)

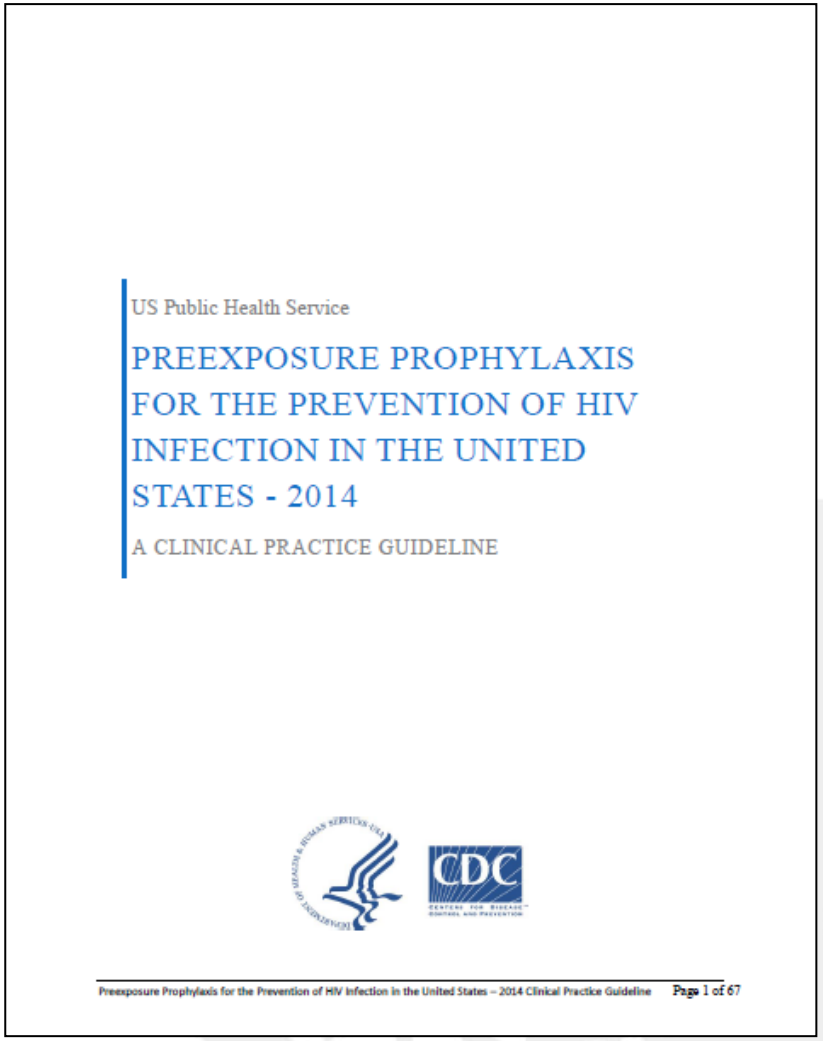
- Providing PrEP to 30% of the total MSM population would account for a 30% reduction in incidence over 10 years (red line)
- Providing PrEP to the general MSM population is not cost-effective
- The most cost-effective strategies targeted HIV-negative men in a discordant regular partnership
- However, this strategy would not have the large population-level impact desired



*Schneider K, Gray RT, Wilson DP. A cost-effectiveness analysis of HIV preexposure prophylaxis for men who have sex with men in Australia. Clin Infect Dis. 2014 Apr;58(7):1027-34.

U.S. guidelines on PrEP

- Based on clinical trials, the U.S. CDC issued interim guidance for PrEP in MSM at high risk for HIV in January 2011
- In July 2012, the U.S. FDA approved the use of Truvada as PrEP
- In May 2014, the U.S. Public Health Service and the CDC issued clinical guidelines formalising and expanding the broad use of PrEP for HIV prevention



PrEP for who?

The CDC guidelines recommend that PrEP be considered for people who are HIV-negative and at substantial risk for HIV infection

For sexual transmission, this includes:

- Anyone who is in an ongoing relationship with an HIV-positive partner
- Gay/bisexual men at risk for contracting HIV (having anal sex without a condom or having been diagnosed with an STI in the past 6 months)
- Heterosexual men or women who do not always use condoms when having sex with partners known to be at risk for HIV

For people who inject drugs, this includes:

- Anyone who has in the past six months injected illicit drugs and shared equipment or has been in a treatment program for injection drug use

ECDC comment on the release of CDC guidance

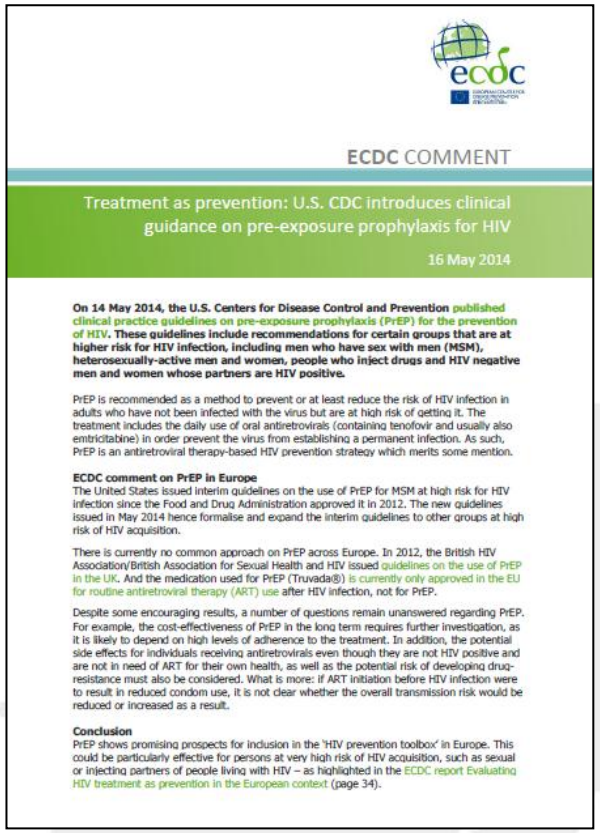
There is currently no common approach on PrEP across Europe

Despite some encouraging results, a number of questions remain unanswered regarding PrEP

1. The cost-effectiveness of PrEP in the long term requires further investigation

2. The potential side effects for individuals receiving ART even though they are not HIV positive, as well as the potential risk of developing drug-resistance must be considered

3. If ART initiation before HIV infection were to result in reduced condom use, it is not clear whether the overall transmission risk would be reduced or increased as a result



ECDC COMMENT

Treatment as prevention: U.S. CDC introduces clinical guidance on pre-exposure prophylaxis for HIV

16 May 2014

On 14 May 2014, the U.S. Centers for Disease Control and Prevention published clinical practice guidelines on pre-exposure prophylaxis (PrEP) for the prevention of HIV. These guidelines include recommendations for certain groups that are at higher risk for HIV infection, including men who have sex with men (MSM), heterosexually-active men and women, people who inject drugs and HIV negative men and women whose partners are HIV positive.

PrEP is recommended as a method to prevent or at least reduce the risk of HIV infection in adults who have not been infected with the virus but are at high risk of getting it. The treatment includes the daily use of oral antiretrovirals (containing tenofovir and usually also emtricitabine) in order prevent the virus from establishing a permanent infection. As such, PrEP is an antiretroviral therapy-based HIV prevention strategy which merits some mention.

ECDC comment on PrEP in Europe

The United States issued interim guidelines on the use of PrEP for MSM at high risk for HIV infection since the Food and Drug Administration approved it in 2012. The new guidelines issued in May 2014 hence formalise and expand the interim guidelines to other groups at high risk of HIV acquisition.

There is currently no common approach on PrEP across Europe. In 2012, the British HIV Association/British Association for Sexual Health and HIV issued guidelines on the use of PrEP in the UK. And the medication used for PrEP (Truvada®) is currently only approved in the EU for routine antiretroviral therapy (ART) use after HIV infection, not for PrEP.

Despite some encouraging results, a number of questions remain unanswered regarding PrEP. For example, the cost-effectiveness of PrEP in the long term requires further investigation, as it is likely to depend on high levels of adherence to the treatment. In addition, the potential side effects for individuals receiving antiretrovirals even though they are not HIV positive and are not in need of ART for their own health, as well as the potential risk of developing drug-resistance must also be considered. What is more: if ART initiation before HIV infection were to result in reduced condom use, it is not clear whether the overall transmission risk would be reduced or increased as a result.

Conclusion

PrEP shows promising prospects for inclusion in the 'HIV prevention toolbox' in Europe. This could be particularly effective for persons at very high risk of HIV acquisition, such as sexual or injecting partners of people living with HIV – as highlighted in the ECDC report Evaluating HIV treatment as prevention in the European context (page 34).

ECDC comment on the release of CDC guidance

- PrEP shows promising prospects for inclusion in the 'HIV prevention toolbox' in Europe
- This could be particularly effective for persons at very high risk of HIV acquisition, such as sexual or injecting partners of PLWHA
- However, implementation data and formal licensure and guidelines are still lacking in most EU countries
- This makes it difficult to provide a clear recommendation at present that would apply to the entire European Union
- ECDC will continue to follow this strategy closely in collaboration with sister agencies, Member States and the EU Commission

Important considerations for policy makers

- As people live longer with HIV, the costs of treatment will increase. Can countries afford to invest in PrEP?
- In light of international guidelines moving toward earlier treatment of those that are HIV positive, treatment costs are only going to increase
- Providing ART to HIV negative individuals before having reached sufficient ART coverage among those that are HIV positive is an issue that needs to be considered
- Will PrEP divert resources away from other prevention activities?
- The high costs associated with PrEP will have to be considered in terms of who will be eligible for PrEP
- Adherence to PrEP is a critical factor in determining its efficacy. How will we ensure that adherence is maximised?
- Will the use of PrEP impact on condom use? If so, will overall transmission risk increase or decrease as a result of PrEP?

WHO guidance on PrEP (2012)

PrEP may be considered as an additional intervention among:

- Serodiscordant couples
- Men and transgender women who have sex with men

WHO may develop full implementation guidelines for PrEP in 2015

Acknowledgments

Andrew Amato
Anastasia Pharris