Position Paper:

Considerations for Pre-Exposure Prophylaxis (PrEP) as an HIV prevention tool for gay men in British Columbia

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STATEMENT OF THE ISSUE

Lively discussions of new HIV prevention technologies, including treatment as prevention, have been taking place among researchers, policy makers and HIV/AIDS advocates. One of these new technologies is Pre-Exposure Prophylaxis (known as PrEP), a biomedical intervention which involves taking HIV medications in advance of a potential exposure event to reduce the likelihood of infection. PrEP is not to be confused with Post-Exposure Prophylaxis (PEP), a different biomedical intervention which involves taking HIV medications within 72 hours after exposure to prevent infection. Unlike PEP, PrEP remains a controversial method for reducing risk of infection, with many unanswered questions regarding effectiveness and implementation.

PrEP remains a controversial method for reducing risks ...

To date, only one study has shown PrEP to be effective for gay men and other men who have sex with men. In November 2010, the National Institutes of Health (NIH) released the findings of the iPrEx trial, a research study investigating PrEP's effectiveness in men who have sex with men (MSM) and male transgender populations.[1] A total of 2,441 study subjects were randomized to receive Truvada (a combination antiretroviral tablet containing emtricitabine 200 mg and tenofovir 300 mg) or placebo once daily for a median of 1.2 years. Over the study period, 100 HIV seroconversions were observed: 36 in subjects taking Truvada and 64 in those taking placebo. These results are widely reported as a 44% reduction in HIV seroconversion for people taking Truvada. While the data appears encouraging, the numbers are expressed as a "relative risk reduction", which may lead to a misunderstanding about the true magnitude of the effect. In absolute terms, treatment with Truvada accounts for a 2.4% reduction in HIV seroconversions over the entire study population. To put it another way, according to iPrEx, 42 people would have to be treated with Truvada for one year to prevent one HIV seroconversion (see Table 1). It is important to note that participants in the study were counselled on risk reduction and provided with condoms every 12 weeks.

Truvada # of patients		Placebo # of patients		Relative Risk	Relative Risk Reduction	Absolute Risk Reduction	Number Needed to Treat
Total	HIV +	Total	HIV +				
1224	36	1217	64	36/1224 ÷ 64/1217 = 0.56	1– 0.56 x 100 = 44%	(64/1217) x 100 – (36/1224) x 100 = 5.3 – 2.9 = 2.4%	100/2.4 = 42

The response to the iPrEx findings is mixed. The AIDS Vaccine Advocacy Coalition (AVAC), and the Global Forum on MSM and HIV (MSMGF), two organizations dedicated to HIV prevention and advocacy, both support further research and protocol development related to PrEP. However, the AIDS Healthcare Foundation worked to block the FDA review of PrEP, claiming that it is an ineffective HIV prevention tool.

Given that Truvada is already approved for HIV treatment and is therefore available with a prescription in Canada and the US, the US Centre for Disease Control produced interim guidelines for physicians directing the use of Truvada as PrEP.[2] In these guidelines, they recognize iPrex's demonstrated effectiveness but outline five limitations of the study, perhaps most important being that future results may be different from what was observed in this study.

Health Initiative for Men (HIM) is dedicated to strengthening the health and well-being of gay men. The organization recognises its role in health promotion and the creation of beneficial relationships between gay men and other men who have sex with men and health professionals. HIM also plays a role in communicating the benefits and limitations of emerging HIV prevention technologies through knowledge transfer and exchange.

REVIEW OF CURRENT POLICIES IN CANADA

Health Canada and the Public Health Agency of Canada have not released policies or guidelines for the use of PrEP as a method of prevention for HIV (nor have any provincial or territorial governments).

The majority of discussion has taken place in community-based settings, generally among AIDS service organizations and gay men's health advocates. Forums and committees to discuss PrEP and possible implementation have been created by Canadians AIDS Treatment Information Exchange (CATIE), the Public Health Agency (PHAC) and the Canadian AIDS Society (CAS).

Several Canadian AIDS service organizations have issued responses or information pieces on PrEP. The Canadian AIDS Treatment Information Exchange (CATIE) calls primarily for more research, raising concerns about the efficacy of the drugs, side-effects, adherence, and barriers to availability.[3] They also stress the importance of using PrEP as a part of a larger prevention strategy including condoms, microbicides, PEP, testing, and counselling.

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CATIE has three major concerns about future implementation of PrEP, cited in their Fact Sheet.[4] First, there is concern that people may develop resistance to the drugs used in PrEP, especially if they do not adhere to the medication regimen, or if they become HIV-positive while taking PrEP. Second, while immediate side effects from the drugs used in PrEP are mild, there is significant concern about possible long-term side effects associated with tenofovir, including reduced kidney function and decreased bone density. Finally, the use of PrEP may lead some people to an increase in higher risk activities or diminished condom use.

The Canadian AIDS Society (CAS) issued a Community Mobilization Kit which identifies the communities which would benefit from PrEP before the iPrEX study was released.[5] They highlight the risk that HIV poses to youth, serodiscordant couples, men who have sex with men, and drug users, as these communities are more susceptible to social and cultural barriers which could 'undermine other forms of prevention'. There were several possible advantages of PrEP listed in their Mobilization Kit. Unlike condoms (which may not be used during every sexual encounter for various reasons), PrEP would provide a certain level of effectiveness provided proper adherence was maintained. Cost of PrEP drugs are projected to be less than ARV treatment if that person were to seroconvert. The use of the drugs has favourable safety data with HIV-positive people. Finally, doctors who prescribe PrEP are given the opportunity to intervene and recommend other prevention strategies in conjunction with PrEP. However, in addition to the concerns of other ASO's, the CAS is concerned with the effects of poor adherence and the possibility of more resistant strains of HIV being spread.

There are currently no clinical trials on PrEP in Canada.

REVIEW OF OTHER JURISDICTIONS

U.S. Response - Interim Guidance from CDC

As a result of the iPrEX study, the U.S. Centre for Disease Control and Prevention has started to develop guidelines for the distribution and administration of PrEP.[6] The guidelines aim to prevent ineffective or dangerous practices when prescribing PrEP since the medication will not be used for its labelled purpose. The efficacy, toxicity, and possible development of resistance to the components of Truvada were highlighted as chief concerns during the development of these interim guidelines.

The findings of the iPrEX study are subject to limitation. First, the sample size within the United States was not large enough to properly evaluate the efficacy of the drugs. Second, measurement of drug levels in study subjects who seroconverted may not be reflective of actual drug levels at the time of seroconversion. Third, the report doesn't provide information about the long-term health effects of Truvada in HIV-negative men or those that seroconvert while on PrEP. Fourth, results of drug level testing showed that study subjects may not have adhered to the medication as much as they said they did. Finally, adherence measurements in this controlled study may not be reflective of adherence in people who are not part of a clinical trial.

To address some of these concerns, the CDC issued a procedure which includes testing for HIV antibodies before, during, and after PrEP treatment, and includes counselling to ensure adherence and the promotion of other prevention techniques. The prescriptions are to be issued in no more than 90-day supplies and only to be renewed after an HIV-negative diagnosis.

These guidelines are in place for gay men and other men who have sex with men at a high risk of HIV seroconversion, and are to be delivered in conjunction with other prevention services. They are accompanied by the monitoring of HIV-status, side effects, adherence and risk behaviours at regular intervals.

In September 2011, it was announced that the National Institutes of Health and public health organizations in San Francisco were close to finalizing an agreement to launch a PrEP demonstration project.[7] Up to 300 men who have sex with men who are high risk for contracting HIV would be enrolled in the pilot study. City Clinic would administer the program while Magnet, the gay men's health center in The Castro, would help identify suitable participants for the study.

On May 10th, 2012 a panel of experts recommended to the FDA that Truvada be approved for pre-exposure prophylaxis. The FDA has not yet acted on the recommendation, but it is expected to side with the panel.

Australian Response

The Australian Government has not implemented policies or guidelines for the use of PrEP as a method of prevention for HIV, but does show interest in further research into microbicides and vaccines as a prevention tool.[8]

Some community-based organizations have expressed cautious optimisim about PrEP

Some community-based organizations (such as ACON) have expressed cautious optimism about PrEP. Currently, Truvada is licensed for use in Australia as HIV treatment, but is not licensed for use by HIV-negative persons.

There are currently no clinical trials being undertaken in Australia.

United Kingdom Response

The United Kingdom has not issued policies or guidelines for the use of PrEP as a method of prevention for HIV.

The National AIDS Trust welcomed the iPrEx result, not only as a prevention method but also as a step toward a more robust HIV prevention strategy. The Terrence Higgins Trust also welcomed the results, but highlighted the importance of further clinical trials, while also stressing that PrEP would ideally be used in conjunction with other risk reduction strategies.

In April 2011, it was reported in the British media that the British HIV Association and the British Health Protection Agency were submitting a research proposal that would create a PrEP pilot program which would allow between 3,600 and 6,000 "high risk" gay men to partake in the study, half of those being given PrEP.[9]

FDA Approval Controversy

AIDS Healthcare Foundation (AHF) has expressed concern about the iPrEx study by launching an advocacy campaign, claiming that "Gilead is pushing to gain FDA approval to market this ineffective HIV prevention pill". They maintain that further study is needed to ensure patient safety and the public's health, and are urging the FDA to re-consider approval.[10]

In February 2011, The Global Forum on MSM & HIV welcomed the CDC's interim PrEP guidelines for MSM in the United States.[11] In March 2011, the organization issued a press release supporting the FDA's review of pre-exposure prophylaxis, calling the AIDS Healthcare Foundation campaign to block the PrEP review "misguided and counterproductive".

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HIM'S POSITION

Given the controversial nature and disputed efficacy of Pre-Exposure Prophylaxis (PrEP), HIM has adopted the following position:

- Gay men should have more HIV prevention options. HIV/AIDS continues to disproportionally affect gay men. In B.C., gay men and OMSM represented 45.5% of total new HIV infections in 2009, and 50.5% in 2010.

- Regular condom use with partners whose status are different than theirs or unknown remains the most effective HIV prevention method.

More research is needed before gay men should adopt PrEP as an HIV prevention tool.

- In their pursuit of pleasure and intimacy, some gay men do not use condoms. With this in mind, any research into new prevention technologies is welcome.

- iPrex is one study of Pre-Exposure Prophylaxis, using one HIV medication. More research is needed before gay men should adopt PrEP as an HIV prevention tool.

HIM recognizes that:

- The iPrEx study has demonstrated some effectiveness of Truvada as PrEP. However, according to iPrEx, 42 people would have to be treated with PrEP for one year to prevent one HIV seroconversion.

- PrEP offers population-level benefits. That is, if widely implemented, health authorities may see a decrease in sero-conversions. At an individual level, however, using PrEP is not a guarantee against HIV infection.

- PrEP could be used as a complementary harm-reduction strategy for individuals at a high-risk of exposure to HIV infection. These may include (but are not limited to) serodiscordant couples, sex workers, and those who may be regularly exposed to HIV through high-risk sexual behaviour such as condomless anal intercourse with a partner whose status is different or unknown.

CONSIDERATIONS

HIM recognizes the potential of PrEP at a population level, but there are important considerations for individuals and health care providers regarding the use of PrEP as a prevention technique.

Considerations for Individuals

- Access – In British Columbia, Truvada is currently approved only for the treatment of HIV, and is distributed through the BC Centre for Excellence in HIV/AIDS. HIV-negative individuals seeking to use Truvada would be required to find a physician willing to prescribe Truvada as PrEP (an "off label" prescription).

- Cost – In British Columbia, HIV medications (such as Truvada) are funded by the provincial government through the BC Centre for Excellence in HIV/AIDS. Individuals using Truvada for PrEP would be required to pay for the treatment (some extended health plans may cover the cost). Since the cost of Truvada in Canada is approximately $800 per month, this could pose a significant barrier to persons lacking the ability to pay.

- Risk Compensation – Participants in the iPrEx study received counselling, and were encouraged to use additional prevention techniques. If PrEP is introduced and risky behaviours increase as a result, the risk of HIV infection may also increase, offsetting any benefit of PrEP. "If people using PrEP stop using condoms or clean needles, their risk for HIV infection may actually increase because PrEP is less effective than other prevention methods."[4]

- Management of STI's – PrEP is only designed to prevent HIV infections. It does not provide protection against other STI's. If individuals using PrEP reduce condom use (see: Risk Compensation) or engage in higher- risk sexual behaviours, they could be at a higher risk of contracting sexually transmitted infections. Some STI's increase the likelihood of HIV infection, which could offset prevention benefits provided by PrEP.

- Adherence – The CDC stresses the importance of taking PrEP daily: "PrEP provided a high level of protection only to those who took the pills regularly […]".[2] Some individuals are unable to follow a daily pill regimen consistently, which impacts the effectiveness of PrEP.

- HIV testing – Prior to starting PrEP, individuals must first test negative for HIV. They must also undergo consistent, scheduled HIV tests while on PrEP. PrEP should not be used by those who sero-convert (see: Drug Resistance).

- Drug resistance – "A person could develop drug resistance if they are HIV-positive (and don't know it) when starting PrEP or they become HIV-positive while taking PrEP. Once a person's HIV becomes resistant to the drugs used in PrEP, those same anti-HIV drugs may not work for treating their HIV infection."[4]

- Side Effects – Common side effects from Truvada include diarrhea, headache, nausea, and fatigue. Other side effects associated with longer-term use include the loss of kidney function and reduced bone density.

Considerations for Health Care Providers and Community-Based Agencies

- Awareness - "For a technology to be adopted for use, individuals must be aware of its existence as well as its efficacy and characteristics […]. Awareness of post-exposure prophylaxis (PEP) tends to be low among men who have sex with men […]. Levels of awareness of vaccines, microbicides and pre-exposure prophylaxis (PrEP) vary."[13]

- Social Marketing Barriers – While the concept of an anti-HIV pill taken regularly to avoid new infection is extremely marketable, this sort of narrative does not tell the entire story, which is much more complex.

- It would be difficult to accurately promote the benefits of PrEP on an individual level.

- Medicalization – "There is a concern that the introduction of biomedical prevention strategies, such as PrEP, will lead to the "medicalization" of prevention – that is, shift the focus of HIV/AIDS prevention to medical solutions and away from effective behavioural, structural and community-based interventions."[4]

- Medical Monitoring – The use of PrEP requires close medical monitoring, such as bone density scans, liver and kidney tests, and regular HIV testing. For some individuals, access to health care providers is limited, thus rendering the required medical monitoring unachievable.

- Cost Effectiveness – To prevent one HIV seroconversion, iPrEx data suggests 42 people would have to be treated with Truvada for one year at an approximate cost of $9,500 per person.

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