The role of public health units in the delivery of HIV pre-exposure prophylaxis (PrEP)

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Abstract

Pre-exposure prophylaxis (PrEP) is an HIV prevention strategy involving the use of once daily antiretroviral medications to prevent HIV infection. Available research supports that PrEP, when used as prescribed, can prevent HIV transmission by upwards of 96%. Such findings have led to the development of research publications and guidelines supporting PrEP for individuals at high risk for HIV acquisition, such as men who have sex with men (MSM). Despite its benefit, current use of PrEP in clinical settings has been undermined by false impressions of poor efficacy of PrEP and concerns about increased risk-taking among MSM should PrEP be readily available. Furthermore, guidance for the role of public health units in PrEP access has not been well defined. While we maintain that PrEP should be available to any person who requests it, we feel that public health units should focus on those at highest risk for HIV acquisition, and, in doing so, possibly reduce local HIV rates.

Résumé

La prophylaxie pré-exposition (PrEP) est une stratégie de prévention fondée sur la prise quotidienne de médicaments antirétroviraux pour prévenir le VIH. Selon les recherches disponibles, la PrEP, lorsqu'elle est prise telle que prescrite, peut prévenir la transmission du VIH dans une proportion de plus de 96%. Ces conclusions ont mené à l'élaboration de plusieurs publications et de lignes directrices à l'appui de la PrEP pour les personnes risquant fortement de contracter le VIH, comme les hommes ayant des relations sexuelles avec des hommes (HARSAH). Malgré ses avantages, l'utilisation de la PrEP en milieu clinique a été compromise par de fausses impressions quant à la faible efficacité de la PrEP et les inquiétudes concernant la prise de risque accrue chez les HARSAH si la PrEP était facilement accessible. De plus, les directives sur le rôle des unités de santé publique dans l'accès à la PrEP n'ont pas été bien définies. Bien que nous maintenions que la PrEP devrait être accessible à toute personne qui en fait la demande, nous pensons que les unités de santé publique devraient se concentrer sur les personnes les plus à risque, ce qui pourrait permettre de réduire l'incidence des cas de VIH au niveau local.

Keywords HIV · Pre-exposure prophylaxis · Men who have sex with men

Mots-clés VIH · Prophylaxie pré-exposition · Hommes ayant des relations sexuelles avec des hommes

Introduction

In Canada, the rate of new HIV infections has remained relatively stable over the last 10 years at approximately 2750 (range 1940–3200) infections per year (Public Health

Agency of Canada [PHAC], 2015). Among those affected by HIV, men who have sex with men (MSM) accounted for 49.3% of new diagnoses up to 2014 (PHAC 2015). Reasons for increased rates among MSM come from known correlates of HIV, as identified through biomedical and epidemiological research. These include condomless receptive and insertive anal sex, sex with HIV-positive partners whose viral load is unsuppressed, anonymous and/or multiple sex partners, and recreational substance use (PHAC 2016).

These unchanging rates of HIV infection among MSM in Canada over the last decade highlight the need for new HIV prevention interventions for this group. HIV pre-exposure

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prophylaxis (PrEP) is one such strategy, which involves HIV-negative persons taking HIV medication (fixed dose emtricitabine-tenofovir DF [FTC/TDF] 200/300 mg) once daily to prevent HIV seroconversion (Tan et al. 2017). While the uptake of PrEP has increased in clinical settings, to date, the role of public health units in PrEP delivery has not been well articulated (Hull & Tan 2017). To facilitate understanding among public health professionals, herein we overview key studies about PrEP effectiveness and some common misconceptions about PrEP, and then use this background information to describe one approach public health units can use to scale up PrEP delivery, i.e., focus on persons at highest risk for HIV.

Addressing misconceptions

Despite strong evidence supporting PrEP efficacy, its acceptance as a strategy in the HIV prevention armamentarium is impeded by claims about the unknown long-term effects of PrEP, and the potential negative outcomes on sexual behaviour. To address these concerns, we present the findings of four main PrEP studies, focusing on (1) PrEP efficacy, (2) the potential for behavioural risk compensation with PrEP use, and (3) concerns that PrEP use may contribute to increasing rates of sexually transmitted infections (STIs).

First, for efficacy, in the initial clinical PrEP trial, Grant et al. (2010) found a 44% reduction in HIV incidence among participants who reported using PrEP, whereas subsequent trials demonstrated efficacy up to 96% among study participants who were found to be using PrEP, as confirmed through blood testing (Grant et al. 2014). Within these trials, the long-term protective effect of PrEP was found to be associated with medication adherence, with significant findings for efficacy being demonstrated overall among participants who reported >90% adherence ($p=0.02$) (Grant et al. 2010). Subsequent analyses by Grant et al. (2014), using dried blood spot testing, examined differences in drug concentration among participants using PrEP, and showed that the use of ≥ 4 doses of PrEP per week corresponded with an HIV incidence rate of 0.00 per 100 person-years (95% CI:0.00–1.06), while the use of ≤ 2 doses per week was associated with an HIV incidence of 2.25 per 100 person-years (95% CI:1.19–4.7) (Grant et al. 2014). The main finding here was that PrEP is effective, but only when study participants actually take it.

Second, regarding risk compensation, researchers and healthcare workers have speculated that PrEP use could lead to increased risk-taking among MSM (Grov et al. 2015). To address these assumptions of compensatory behavioural disinhibition among MSM using PrEP, Liu et al. (2013) completed logistic analysis testing to evaluate potential changes in sexual risk behaviour among HIV-negative men receiving PrEP. The overall number of partners among participants receiving PrEP reduced significantly ($p<0.001$) during the study period, as did their number of

sexual partners who were HIV-positive ($p=0.01$) (Liu et al. 2013). This study also found significant decreases in the proportion of MSM engaging in condomless receptive anal sex with all partners ($p=0.003$) (Liu et al. 2013), suggesting no association between PrEP use and increased risk-taking.

Third, researchers have speculated that PrEP use by MSM contributes to increased STI rates (Choudhri et al. 2018). In an analysis of STI rates among MSM using PrEP in the PROUD study, bivariate non-parametric tests (chi-square or Fisher's exact, and Mann-Whitney U) were conducted to assess the differences in STI rates between MSM using PrEP and MSM in the general population accessing STI testing (Dolling et al. 2016). Their analyses demonstrated neither a relationship between MSM using PrEP and number of STI diagnoses, nor a difference in the number of STI diagnoses among MSM using PrEP, compared to MSM in the general population (Dolling et al. 2016). Furthermore, the multivariate regression analyses in Grant et al.'s trial (2010), which assessed STIs at baseline and three-month intervals, showed "no significant between-group differences in the numbers of subjects with syphilis ($p=.49$), gonorrhea ($p=.74$), [and] chlamydia ($p=.43$)..." p. 2593. In these studies, PrEP thus does not contribute to STI transmission among MSM.

Public health approach to PrEP delivery

Given the high efficacy of PrEP to prevent HIV transmission (up to 96%), researchers and clinicians who support PrEP advocate that it should be broadly accessible (Arkell 2018). While we agree with such an approach generally, for PrEP delivery by public health units, our proposal is to target those at highest risk for HIV acquisition. While one way to do this would be to target PrEP at populations most affected by HIV (e.g., MSM, people from endemic countries, and people who use injection drugs (IDU)), belonging to these groups does not denote risk (PHAC 2016). As such, we propose using the Canadian PrEP guidelines (Tan et al. 2017) as a framework, and recommend that public health units help deliver PrEP to the following groups: (1) persons diagnosed with ≥ 2 STIs in the past 12 months, specifically gonorrhoea, chlamydia, or lymphogranuloma venereum (LGV), with a consideration of this being only one diagnosis if rectal; (2) persons diagnosed with infectious syphilis, (3) persons named as HIV contacts (irrespective of whether the contact occurred sexually or through the sharing of drug paraphernalia), and (4) persons who use HIV post-exposure prophylaxis (PEP) (Fig. 1). As part of this, we feel that, during their follow-up for these reportable infections, public health units should add reflex referrals to PrEP for anyone fulfilling the above criteria. In this approach, persons who use injection drugs are not listed as a target population due to a paucity of research, and

Fig. 1 Targeted approaches to PrEP delivery

consequential weak recommendations in the Canadian PrEP guidelines to provide PrEP to these persons (Tan et al. 2017).

The rationale for this targeting follows the impact fraction model, which highlights that an intervention's population-level effects are the outcome of interventions being efficacious, being used by the target population, and that the selected target population is affected by the health condition being addressed (Fig. 2). In other words, for an intervention to achieve intended public health effects, it must be both beneficial and used by an affected population. A few points support our assertion that the above target groups for PrEP fulfil these criteria.

First, bacterial STIs (chlamydia, gonorrhoea, LGV, and infectious syphilis) in the genital and rectal mucosa can affect HIV transmission from viral shedding in ulcerative lesions, greater concentration of virus in inflamed tissue, and higher HIV replication in the presence of STIs (Galvin and Cohen 2004). These infections also compromise mucosal integrity and facilitate HIV acquisition (Galvin and Cohen 2004). Second, persons named as HIV contacts of a partner newly diagnosed with HIV are at higher risk of HIV acquisition due to greater likelihood of HIV infectivity among partners who are not virally suppressed (Cohen et al. 2013); also, such persons have established serodiscordant contacts. Third, recent data from a Canadian PEP program demonstrated ongoing risk of HIV acquisition after PEP use. Of the MSM in this study who initiated PEP, 13.1% were diagnosed with HIV either at the time of PEP initiation or within 1 year of taking PEP, thus providing support for PrEP initiation immediately after completion of PEP to reduce the risk of HIV infection

among these men (O'Byrne et al. 2018). Notably, our assertion that one PEP use warrants PrEP deviates from the Canadian PrEP guidelines (Tan et al. 2017), but we feel that the published literature supports this lower threshold for PrEP initiation.

Ancillary public health benefits

Having identified the target population for PrEP, public health units could ensure that qualifying patients are seen for PrEP assessment and prescription (up to 90 days) by a licenced prescriber or authorized delegate (e.g., nurses working under directive) (Tan et al. 2017). Patients would be seen every 3 months for ongoing PrEP monitoring, including STI/HIV screening, safer sex/medication counselling, and condom distribution, and to obtain their prescription. By having public health units involved in PrEP delivery, not only could this intervention potentially reduce local rates of HIV infection (due to its protective effects and because routine screening as part of PrEP delivery may facilitate timely HIV diagnoses), but also this strategy could facilitate bacterial STI management, particularly considering observed increases in rates in Canada from 2010 to 2015 for gonorrhoea (57.4%), chlamydia (16.7%), and infectious syphilis (85.6%) (Choudhri et al. 2018). Performing STI screening every 3 months—as required for PrEP—is also a strategy to ensure patients who have been diagnosed with infectious syphilis complete post-treatment serology at 3, 6, and 12 months following diagnosis to ensure appropriate treatment response (PHAC 2016). This is particularly important because syphilis treatment failure rates are 5–10% (Singh & Romanowski 1999), and follow-up rates for post-treatment serology are only about 65% in Ottawa.

It is important to consider these benefits in light of certain limitations to PrEP delivery by public health units, which mainly relate to access and retention in care. In its simplest form, access relates to competent prescribers and persons' ability to afford PrEP. In this regard, some steps have been made with the release of the Canadian PrEP guidelines and the inclusion of TDF/FTC on public drug registries in many Canadian provinces. Nevertheless, long wait times and limited access for those without medication coverage persist. Regarding retention in care, implementation and ethical concerns relate to people not attending appointments and how much effort should be made to ensure these highest risk persons use PrEP. This is a balance between public health mandate of disease prevention and patient autonomy over health and risk-taking decisions. We also acknowledge that the

Fig. 2 Impact fraction model

$$[Impact] = [Intervention Effectiveness] \times [Intervention Uptake] \times [Burden of Target Population]$$

narrowness of our categories may exclude many people who need PrEP and reiterate that our categories do not exclude other groups, rather, they aim to specify the highest risk target groups.

Conclusion

In summary, we feel PrEP is an efficacious prevention intervention for MSM and should be made available through public health units. The use of four or more FTC/TDF pills per week yielded detectable study drug concentrations in serum, which corresponded with a 96% reduction in HIV acquisition among MSM using this intervention. Concerns about potential behavioural risk compensation and increased STI incidence were not identified based on analyses of the seminal clinical trials evaluated. Providing PrEP services to those at highest risk for infection may help public health units reach their intended aims of reducing STI/HIV rates, particularly among those most affected by HIV, and may help to facilitate timely STI/HIV diagnoses, treatment, and/or referrals among persons using PrEP.

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