Editorial

HIV Prevention: The Promise of Pre-Exposure Prophylaxis in Singapore

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Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) remains a global health problem, with 2.1 million new infections globally in 2015[1] and 455 newly diagnosed cases in Singapore in the same year.[2] It is increasingly evident that novel strategies are needed to achieve significant reductions in new HIV infections. These include the use of treatment as prevention (TasP), wherein highly active antiretroviral therapy (HAART) is initiated early after the diagnosis of HIV infection to suppress viral load and reduce infectivity;[3] as well as post-exposure prophylaxis (PEP), where a 4-week course of HAART is administered after high risk exposures to reduce the likelihood of infection.[4]

HIV pre-exposure prophylaxis, or PrEP, is a new and promising addition to the HIV prevention armamentarium, which has heretofore been focused on behavioural risk reduction, and which may have plateaued in effectiveness—as evidenced by the relatively stable incidence of HIV infections despite ongoing prevention efforts.

PrEP involves the use of anti-retroviral drugs (primarily the co-formulation of tenofovir disoproxil fumarate [TDF] and emtricitabine [FTC] known by its trade name Truvada) by HIV-negative individuals who are at high risk of contracting HIV to prevent infection. These populations include men who have sex with men (MSM) that report high risk sexual behaviour, HIV-negative partners in serodiscordant couples and women at-risk.

The evidence underpinning the use of PrEP is derived from numerous large, randomised controlled trials demonstrating its efficacy in preventing HIV infection. Of note is that none of the major trials were led or initiated by pharmaceutical companies. Amongst MSM and transgender women, the iPrEx trial of daily-administered PrEP demonstrated an overall reduction of HIV transmission risk of 44%; those with detectable plasma levels of Truvada had a 92% reduction in risk compared to those with undetectable drug levels, underlining the efficacy of PrEP when therapy was adhered to.[5] The French and Canadian iPERGAY trial of on-demand PrEP (taken before, then 24 and 48 hours after each sexual act) showed that MSM randomised to receive Truvada had a 85% risk reduction of HIV infection compared to the comparator group; again, this was dependent on adherence to the recommended regimen.[6] The Partners PrEP trial, carried out amongst 4758 heterosexual serodiscordant couples in Uganda and Kenya, showed a risk reduction of HIV transmission of 84% in men and 66% in women taking Truvada.[7] The Botswanan TDF2 trial, which enrolled 1219 heterosexual men and women, showed an overall efficacy of 62%.[8] There is some evidence to suggest that PrEP is cost-effective, especially when compared to the high healthcare costs incurred in lifelong HIV treatment for those who are infected,[9] however, more research is needed in this area.

Numerous concerns have surfaced since the introduction of PrEP, including the development of genotypic and phenotypic resistance to TDF and FTC, which are also widely used for HIV treatment; and the concern of risk compensation, where individuals on PrEP may behave more riskily due to the misconceptions of immunity proffered by PrEP. While worrying, these have not been borne out by the evidence.

In the Partners PrEP trial, drug resistance was detected in only 1 of 3 individuals taking Truvada who became HIV-infected during the study period; no resistant virus was detected in the 33 participants of both sexes who seroconverted after enrolment in the TDF2 trial.[7,8] A meta-analysis of 6 large randomised trials failed to find a statistically significant increased risk of developing TDF resistance in subjects who seroconverted following randomisation to PrEP in their respective studies.[10] With regard to risk compensation, the same meta-analysis found no reduction in the reported use of condoms in sex amongst study participants enrolled. The number of sexual partners reported by study subjects was also not found to be higher following enrolment. The incidence of non-HIV sexually transmitted infections (STIs) has been found to be high in a number of PrEP studies—however, this may not necessarily point to increased risk-taking behaviour as pre-implementation STI rates were often not determined. The incidence of bacterial STIs like gonorrhoea and syphilis have shown a rising trend in recent years, and further emphasises the need for effective biomedical prevention of HIV transmission in light of shifts in sexual risk behaviour

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in at-risk populations. Modelling studies suggest that without PrEP, HIV incidence is unlikely to decrease substantially.[11]

The success of PrEP as a means of HIV prevention is dependent on how effectively it can be implemented in the communities where it is needed. An effective PrEP delivery model includes regular monitoring for adverse drug reactions (nephropathy and reduced bone mineral density are of concern, but are uncommon in PrEP trials); regular HIV testing; STI screening and treatment; and behavioural counselling on sexual risk reduction.

Data from demonstration projects and open-label extension studies evaluating the provision of PrEP outside of clinical trial settings is needed to guide PrEP implementation. These studies, many of which are underway in both resource-rich and resource-limited settings, seek to determine the feasibility of PrEP delivery models, patient service delivery preferences (including site of provision of PrEP services), as well as barriers to and motivators of adherence to PrEP.[12]

Such studies are needed in the local setting to inform the implementation of PrEP in Singapore. PrEP is already available in several clinics and restructured hospitals, but efforts are still much needed to increase awareness and educate the public, as well as elucidate the unique care preferences of local at-risk populations. In addition, developing a system of financing PrEP for those who need it most (but who may be ill-equipped to afford it at its current price) is an important short-term goal for healthcare providers and policymakers. Such efforts, whether for research, clinical or programmatic purposes, must be multidisciplinary and involve clinicians, patient advocates, community stakeholders and representatives from healthcare leadership.

PrEP is already strongly recommended by the World Health Organisation and the United Nations Programme on HIV/AIDS (UNAIDS) as part of a holistic strategy internationally to reduce HIV infection, which includes encouraging early testing and treating, advocating safer sex practices, and an emphasis on retention in care and adherence to treatment for HIV-infected individuals.[13,14] The UNAIDS Prevention Gap Report, published in July 2016, specifically names PrEP as one of the 5 pillars of HIV prevention, alongside providing HIV prevention services to key at-risk populations and increasing condom availability.[15] Sustainable and affordable provision of PrEP in Singapore should be made a priority in the local HIV/AIDS response on the basis of its efficacy, cost-effectiveness, and synergism with existing prevention methods.

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