

Amplifying the Population Health Benefits of PrEP for HIV Prevention

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(See the Major Article by Volz et al, on pages 1522–9.)

Pre-exposure prophylaxis (PrEP) prevents HIV infection. Robust evidence—first from pivotal clinical trials [1, 2], then rigorous studies testing best-practice models of implementation [3–6], and most recently real-world case studies of clinical delivery [7]—demonstrate that PrEP is highly effective, indeed incredibly so, at providing individual protection against HIV acquisition for men and women from diverse populations worldwide. Regulatory review and normative guidance from the US Food and Drug Administration in 2012 and from the US Centers for Disease Control and Prevention (CDC) in 2014 have been followed by World Health Organization recommendations in 2015, and thereafter by endorsements by more than two dozen countries (www.prepwatch.org). PrEP is thus a central part of global, evidence-based, gold-standard HIV prevention for at-risk individuals.

Nevertheless, for PrEP to have an important impact on the HIV epidemic, it needs to have not just benefits for individuals but at the population level, synergizing with other prevention and treatment interventions to achieve substantive reductions in new infections and resultant morbidity and mortality from

HIV. By 2020, the US National HIV/AIDS Strategy calls for a 25% reduction in new diagnoses [8] and UNAIDS has set a global goal of <500 000 new infections, a 75% reduction compared to 2010 [9]. These are ambitious targets, for any setting, and achieving them will require the best strategy and science to guide interventions and measure impact.

In this issue of the *Journal of Infectious Diseases* [in press], Volz and colleagues present an innovative set of analyses, using molecular sequence data from HIV infections among men who have sex with men (MSM) in the United Kingdom, combined with mathematical modeling, which together provide one potential strategy to maximize population health benefits of PrEP. Specifically, the authors analyzed publicly collected HIV sequence data from nearly 7000 MSM (linked to basic demographic data), used phylogenetic and phylodynamic methods to characterize transmission-associated subgroups with greater risk for HIV acquisition and onward virus spread, and then estimated the population-level benefits that would occur from different scenarios under which a limited amount of PrEP (enough for 15 000 individuals) would be available. Their principal finding (ie, that young MSM, aged < 25 years, had greater HIV risk) seems on first pass to be not particularly surprising, as adolescent and young adult men and women in countries around the world have been repeatedly called out as a high-risk population. However, the Volz and colleagues' results go further than simply documenting younger age as a risk factor for HIV,

demonstrating that young MSM are also more likely to transmit to other young MSM if they do acquire the virus (75% of infections in this group attributed to other young MSM), multiplying the HIV risk within this age group. As a result, prioritized introduction of PrEP to younger MSM would have multiplied benefits, blocking both first-generation infections as well as large numbers of onward transmissions in this group. Thus, high levels of transmission, combined with high connectivity among similarly aged men, in the words of the authors “amplifies incidence ... and PrEP effectiveness” in young MSM.

Amplified effectiveness is what is needed at this time for PrEP and for the total toolbox of effective HIV prevention strategies. The findings of Volz and colleagues remind us that HIV prevention is about a best prevention plan for an individual, but must also be about prevention for his or her current and future partners and, ultimately, about the population more generally. HIV, like other infectious diseases, can benefit from interventions that limit transmission cascades, as seen most dramatically in the last few years in the public health response to the outbreak in Scott County, Indiana linked to injection drug use [10]. As done by Volz and colleagues and by others [11, 12], phylodynamic analyses of viral sequences from that outbreak have been used to characterize opportunities for strategic prevention efforts [13]. This innovative use of molecular epidemiology and mathematical modeling offers exciting new opportunities to use complex science

Received 19 January 2018; editorial decision 19 January 2018; accepted 20 January 2018; published online February 26, 2018

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The Journal of Infectious Diseases® 2018;217:1509–11
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to guide public health decision making in real time. The approach is arguably a continued evolution of the “know your epidemic, know your response” rallying cry from UNAIDS a decade ago, backed up by cutting-edge data analytics.

For PrEP, population health benefits can only occur with enough coverage of the population accessing it to result in those key infections prevented to avert subsequent generations of transmissions. We are not there yet. In the United States, PrEP uptake has skyrocketed, with >120 000 individuals estimated to have initiated PrEP since 2012 [14]; still, CDC estimates that 1.2 million persons, including MSM, people who inject drugs, and heterosexual adults, have indications for considering PrEP use [15]. Some geographies are beginning to see PrEP use at levels that should result in population benefits—for example, Seattle and King County, Washington recently reported that one-third of high-risk MSM there are estimated to be on PrEP currently and there are now more people on PrEP in that locality than are taking antiretroviral treatment (and that is in the context of that locality also achieving the UNAIDS goal of 90% of individuals diagnosed, linked to care, and on suppressive antiretroviral therapy) [16]. New initiatives related to access to PrEP (as well as treatment and other prevention interventions) in Florida and elsewhere in the southern United States offer encouragement that population benefits may be on the horizon for a part of this country that faces substantial disparity in new HIV infections [17]. The United States accounts for most PrEP use in the world at this time, although the vast majority of new infections occur in low and middle income countries; UNAIDS has called for 3 million persons to be on PrEP by 2020 [9]. Ambitious programs like the DREAMS initiative (<https://www.pepfar.gov/partnerships/ppp/dreams/>), supported by the US President’s Emergency Plan for AIDS Relief (PEPFAR), is prioritizing prevention for adolescent girls and young women in 10 African countries

with a multifaceted prevention program, which includes PrEP. In Kenya, a national roll-out program for PrEP is prioritizing delivery to highest-burden counties, bringing services to populations most at risk, and using messaging that is simultaneously entertaining, appealing, and informative [18]; this is a new way to do public health.

The results from Volz and colleagues touch on an important, but potentially sensitive, topic for prioritizing prevention interventions. The idea of “targeting” prevention, to an individual or to a group, may be off-putting, both to those targeted (who wants to have a target applied to them?) and to others (who may have the impression that PrEP is otherwise denied to them). The best available evidence to date suggests that open access to PrEP results in high uptake and likely diminished stigma and discouragement. Moreover, individuals seeking PrEP appear to be commonly self-selecting for being at risk, with high prevalence and ongoing incidence of curable sexually transmitted infections (harbingers of HIV exposure) and corresponding behavioral risks [3]. Conversely, new HIV infections in PrEP-accessing persons have sometimes been concurrent with loss of PrEP access (eg, because of loss of insurance coverage) [7]. Public health agencies and others working on PrEP outreach may be able to address these areas of challenge by prioritizing access to PrEP for all who want it, with directed messaging and marketing to those for whom PrEP needs and potential for benefit are greatest. Indeed, in the United Kingdom, the setting for the work by Volz and colleagues, privately-sourced PrEP, guided by websites providing instructions on how to access the medication prior to its incorporation into the National Health Service but without public health targeting at all, has been reported to have resulted in a 40% decline in new HIV infections in the last year in London [19].

PrEP is an intervention for an individual, but with enough individuals taking PrEP, particularly if infections among

those most likely to acquire and pass on the virus are blocked, population-level benefits will follow. Bringing together robust public health, cutting-edge molecular science, quality clinical care and behavioral science, innovative community engagement and messaging, and strong political will amplify the prevention benefits of PrEP.

Notes

Financial support. This work was supported by the National Institute of Mental Health of the US National Institutes of Health (grant number R01 MH095587).

Potential conflict of interest. The author has led studies of pre-exposure prophylaxis in which study medication was donated by Gilead Sciences and has served on an advisory committee for Gilead Sciences. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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