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COMMENTARY

Pre-exposure Prophylaxis for HIV Infection: Preventing Disease or Promoting Sexual Health?

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Practitioners of public health recognize that disease prevention and health promotion occupy the same continuum of activities that are aimed at improving individual and population health. Closely related as they are, however, these two domains are not identical—either in concept or in practice. Their differences owe to the widely-accepted definition of health as a state of "complete physical, mental and social well-being and not merely the absence of disease or infirmity" [1]. Namely, while the absence of disease brought about by prevention activities is a laudable goal and an important component of health, it may not be the only condition necessary to achieve and sustain overall health.

This observation is especially pertinent when considering the domain of sexual health. Admittedly, definitions of sexual health have evolved over time and will continue to develop as our understanding of human sexuality grows [2]. Nevertheless, the following elements are currently recognized as essential determinants of sexual health [3]:

- Overall well-being, not just the absence of diseases related to sexual activity;
- Respect, safety and freedom from discrimination and violence;
- Assurance of certain human rights as they pertain to sexuality, gender and gender expression;
- Recognition of diverse sexualities
- Relevant across the lifespan and not limited to the function of reproduction; and
- Influenced by gender norms, roles, expectations and power dynamics.

These elements illustrate that many of the factors shaping individual sexual health outcomes are not directly controlled by individuals. Gender power imbalances, cultural attitudes about gender expression and same sex behavior, lack of access to competent and culturally-sensitive services—all of these circumstances can influence an individual's ability to achieve and maintain a state of sexual health [4]. Recognizing that social norms, organizational dynamics, laws, policies, and economics can all influence health—in this instance, sexual health—is more than an academic observation. Instead, this awareness serves as a powerful reminder to public health practitioners that our interventions to improve sexual health outcomes cannot be limited to the provision of individual health services but must also address the broader social, legal and economic circumstances that can foster, or impede, healthy sexual outcomes. Consider the example of pre-exposure prophylaxis (PrEP) for the prevention of human immunodeficiency virus (HIV) infection as a case in point.

Soon after the Preexposure Prophylaxis Initiative (iPrEx) trial demonstrated that daily oral antiretrovirals (tenofovir disoproxil fumarate and emtricitabine) could effectively prevent the acquisition of HIV among sexually active, at-risk men who have sex with men [5], the Centers for Disease Control and Prevention (CDC) released interim guidance for HIV preexposure prophylaxis in men who have sex with men [6]. Following the results of other randomized controlled trials, CDC issued interim guidances for the use of HIV preexposure prophylaxis in heterosexually active adults [7] and in injecting drug users [8]. Other important PrEP milestones include FDA's 2012 approval of emtricitabine/tenofovir disoproxil fumarate for the prevention of sexually acquired HIV infection in high-risk adults [9], the 2014 release of U.S. Public Health Service's (USPHS) first clinical practice guidelines on antiretroviral preexposure prophylaxis

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to prevent HIV [10], and the FDA's expanded approval, in May 2018, of emtricitabine/tenofovir disoproxil fumarate to reduce HIV acquisition in high risk adolescents [11].

In short order, advocates and practitioners alike recognized PrEP as a momentous enhancement to existing HIV prevention strategies and a substantial step forward toward ending the HIV/AIDS epidemic. When the U.S. government released the 2020 update to the National HIV/AIDS Strategy in July 2015, it contained language advising federal and local agencies to expand access to PrEP by educating and training health care providers about its benefits and increasing PrEP awareness among potential consumers [12]. Some analysts estimated that even if less than half of the MSM for whom PrEP was indicated began to use the regimen, the U.S. would see a 33% decrease in expected HIV infections over the coming decade [13].

Recent analyses have shown a 56% increase from 2012 to 2017 in the annual prevalence of PrEP use in the United States [14]. But despite these trending increases, a mere 7% of the estimated 1.1 million persons in the U.S. who could benefit from PrEP were prescribed the regimen in 2016, including a scant 2.1% of women with indications for PrEP use [15]. Furthermore, substantial disparities in PrEP uptake have been noted by race/ethnicity. An examination of PrEP use among enrollees in California's Medicaid program found dramatic increases throughout the state during the period of study (2012–2016); yet, rates of PrEP uptake were "consistently lower" for Hispanics and Blacks compared to Whites [16]. Analyzing antiretroviral prescriptions dispensed during 2014–2016 within a database that captures prescriptions from all payers, the CDC found that "nearly six times as many white men and women were prescribed PrEP as were black men and women" [15]. In addition to disparities by gender and race/ethnicity, rates of PrEP uptake are noted to be especially low among persons younger than 25 years of age [14, 16].

Given its promising role in reducing new HIV infections, public health advocates are understandably concerned about the wide gap, described above, between PrEP need and its actual uptake. In part, this disparity can be explained by the well-documented lag between the release of new findings from high-quality biomedical research (in this case, the evidence that daily antiretroviral PrEP can effectively prevent the acquisition of HIV) and the incorporation of these findings into clinical and public health practice [17]. Consistent with this premise is the observation that in 2015, a year following the release of clinical practice guidelines on the use of PrEP, only 22% of a national sample of health care professionals had actually read the guidelines [18]. Additionally, low levels of consumer awareness of PrEP among those for whom the regimen is indicated, also contribute to suboptimal uptake [19]. Clearly, educating both providers and consumers about the role of PrEP in preventing HIV transmission is necessary if we wish to accelerate the uptake of this proven biomedical intervention. However, it would be shortsighted to assume that increased awareness, alone, will result in levels of PrEP uptake and adherence necessary to bring about population-level decreases in HIV incidence. Or to paraphrase Greene and his colleagues, writing on the topic of integrating emerging research findings into public health practice, "use needs to be about shaping the product, not just disseminating or selling it" [17, page 166]. Which brings us back to the issue of sexual health.

We contend that enabling the widespread uptake of PrEP among those at-risk individuals for whom it is indicated will be much more effective within a framework that embraces a comprehensive sexual health perspective as opposed to one that focuses solely on PrEP as a means of preventing the acquisition of HIV. Pursuing conventional disease prevention strategies to promote PrEP can be likened to a product driven enterprise in which the product is fully developed, and the major effort focuses on "selling" said product to receptive markets by promoting its attributes. In contrast, a sexual health promotion approach—one that endorses overall well-being, acceptance and respect for diverse sexual identities—is more aligned with a consumer driven strategy, in that it places the wants, needs and daily circumstances of potential consumers in the forefront of product promotion. Stated more explicitly, promoting PrEP as a component of overall sexual health means that public health practitioners must actively address the social, cultural, economic, legal and other structural circumstances that impact its uptake and continued use and should not limit their efforts to solely raising awareness about the regimen's effectiveness.

Support for the assertion that a sexual health approach to the scaling-up of PrEP would be superior to one that concentrates exclusively on disease prevention can be found by scrutinizing those factors, beyond awareness, that influence its uptake, beginning with the issue of stigma. Researchers have found that for both men [20] and women [21], stigmatizing attitudes that associate PrEP use with promiscuity are strongly associated with a lack of interest in using PrEP and/or discussing potential PrEP use with a provider. Twenty-three percent of 264 men who were surveyed at a 2015 gay pride community festival in Atlanta, Georgia believed that PrEP was for "promiscuous" persons and this belief was associated with an expressed lack of interest in using PrEP [20]. A 2017 online survey of nearly 600 female Planned Parenthood clients from 3 cities in Connecticut found that over one-third (37%) believed that people would think that they "slept around" if they were to use PrEP; endorsement of these stigmatizing attitudes was significantly associated with less interest in discussing PrEP with a provider [21].

Undoubtedly, stigma has many layers. In addition to stigmatizing perceptions of "promiscuity" and "sexual irresponsibility" that have been associated with PrEP use, stigma

associated with male same sex behavior has been identified as a disincentive to using PrEP—especially when gay and bisexual men anticipate negative judgements from health care providers and, as such, are fearful to raise the subject of PrEP use with them [22–24]. This is especially troubling given that the most recent estimates of adults with indications for HIV PrEP use in the U.S. indicate that nearly three-quarters (71.1%) are men who have sex with men [25].

An interesting perspective on the impact of negative attitudes about male same sex behavior on PrEP use can be found in a survey of 115 U.S. medical students [26]. Students were recruited via email from two medical schools in northeastern U.S. Those who chose to participate were provided background information about PrEP and then presented with a clinical vignette describing a hypothetical patient seeking PrEP. The hypothetical patient was described as a 31-year-old male in a monogamous relationship with an HIV positive male partner who was not virally suppressed; further description stated that the patient used condoms "inconsistently" during anal sex with his partner. The race of the hypothetical patient was described as either white or black, based on random assignment. While "minimal evidence for racism affecting clinical decision-making emerged," participants who expressed greater heterosexism (as measured by five items that assessed participants' attitudes about male homosexuality) "more strongly anticipated increased risk behavior and adherence problems…associated with lower prescribing intention" [26]. Thus, suggesting that social biases and negative attitudes about homosexuality held by providers can interfere with the appropriate prescription of PrEP.

In addition to stigma, organizational and other structural barriers can also impede the scaling-up of PrEP services. A study of men who have sex with men attending public sexually transmitted disease (STD) clinics in New York City between the years of 2007 and 2012 found that the annual incidence of HIV acquisition was 2.4 per 100 person-years and was highest among Black and young (< 20 years) MSM [27]. Furthermore, having any incident STD was associated with a higher risk of HIV acquisition [27]. Findings such as these give rise to an obvious point: STD clinics are ideal settings in which to provide PrEP services for clients who are at high-risk of becoming infected with HIV [28]. Also, because STD clinics serve large numbers of racial and ethnic minority patients, implementing PrEP services in these settings could help to reduce current racial and ethnic disparities in rates of HIV acquisition [29]. Unfortunately, the current infrastructure of most STD clinics presents barriers to taking advantage of this critical opportunity.

As noted by Marx and her co-authors [28], STD clinics haven't been designed for primary care delivery, thus hindering the ongoing medical monitoring required of persons who are on a PrEP regimen. And while there are various resources to make PrEP more accessible to uninsured and underinsured clients through "expanded insurance coverage, discount programs and statewide initiatives" [28], STD clinics frequently lack the personnel and billing systems necessary to take advantage of these opportunities on behalf of their clients. Another way to visualize the infrastructure challenges faced by many public STD clinics is to consider the widespread cuts in operating budgets and subsequent reductions in clinical services experienced by many of these entities [30]—at the same time that the United States is facing sharp increases in STD rates [31]. Certainly not an optimal situation for implementing a new program service, no matter how pressing and relevant its need.

That's not to say that these infrastructural impediments couldn't be mediated, and that public STD clinics couldn't be re-tooled to provide comprehensive PrEP services to high-risk clients. However, system-wide change of this magnitude would require a shift in perspective, enabling local, state and federal leaders to visualize STD clinics as sites of sexual health promotion and not solely destinations for disease diagnosis and treatment. Such a re-tooling would require an investment into infrastructure beyond "bricks and mortar," investments that would ensure a capable, qualified workforce, up-to-date data and information systems (including billing systems), and the capacity to assess and respond to emerging public health needs in a timely manner [32]. Positive findings from a demonstration project offering PrEP in two STD clinics in San Francisco and Miami and a community health center in Washington, DC suggest that PrEP implementation could be feasible in similar settings [33]. However, the offer of free medication and follow-up monitoring that was provided to participants as part of the demonstration project doesn't match the reality of settings where high-risk individuals may be without insurance and/or unable to manage the co-pays and laboratory costs associated with an ongoing PrEP regimen. To that point, in 2015, New York state implemented the PrEP Assistance Program (PrEP-AP) in response to some clients needing coverage for clinic visits and lab testing [34]; PrEP-AP reimburses health care providers for the costs associated with providing health care and laboratory services associated with PrEP to uninsured or underinsured patients [35].

As per the example above, insurance coverage has been shown to influence both uptake as well as adherence to PrEP, reinforcing our premise that efforts to promote health often require regulatory and other structural supports, in addition to the availability of high-quality preventive services, if they are to be successful. In a study of 201 persons attending PrEP clinics in three different U.S. cities (Jackson, MS, St. Louis, MO and Providence, RI) Patel and colleagues found that even after adjusting for socio-demographic differences, insured patients were four times more likely to report PrEP use at a 3-month follow-up visit compared to those who were

uninsured [36]. A longitudinal cohort study of young MSM in the Chicago area found that 33% of 197 men who had used PrEP in the last 6 months had discontinued its use—and 20% of those cited issues related to insurance coverage or loss thereof as the primary reason why [37]. And one is hard-pressed to ignore the results of a cost effectiveness analysis that concluded that "PrEP drug costs need to be reduced in order to be cost effective across a range of background HIV prevalence," adding that "at its current cost, PrEP is not a cost-effective prevention intervention for all MSM in the U.S." [38].

Citing the many factors that can influence the successful implementation and uptake of PrEP services should not be construed as an exercise in pessimism or a passive resignation to sub-optimal health outcomes. For each of the impediments describe above, stigma, inadequate organizational capacity, financial disincentives, including insufficient insurance coverage—and the others that have not been elucidated in this brief commentary—there are actionable remedies that are feasible if we support public health responses to HIV prevention that extend beyond traditional disease prevention approaches and embrace the promotion of overall sexual health. Such thinking is clearly in line with the actions outlined by the United Nations in their resolution to end the AIDS epidemic by 2030, which includes a call to commit to "building people-centered systems for health" with equitable and universal access to sexual and other necessary health care services [39]. Rather than limiting our focus to risk and vulnerability as reasons to promote PrEP as a means of preventing HIV infection, let's begin to focus on PrEP use as part of an overall strategy that empowers individuals to thrive, even in the face of significant challenges to their health. Investing in such a strategy would yield intersectional benefits across a variety of medical and public health problems and could be counted as a decisive action toward achieving the laudable goal of health for all.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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