Review

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Overcoming structural barriers to diffusion of HIV pre-exposure prophylaxis

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Abstract

HIV prevention with antiretroviral medication in the form of pre-exposure prophylaxis (PrEP) offers a critical tool to halt the HIV pandemic. Barriers to PrEP access across drug types, formulations, and delivery systems share remarkable commonalities and are likely to be generalizable to future novel PrEP strategies. Appreciation of these barriers allows for planning earlier in the drug-development pathway rather than waiting for the demonstration of efficacy. The purpose of this article is to propose a core set of considerations that should be included in the drug-development process for future PrEP interventions. A literature synthesis of key barriers to PrEP uptake in the United States was conducted to elucidate commonalities across PrEP agents and delivery methods. Based on the published literature, we divided challenges into three main categories of structural barriers: (1) provider and clinic characteristics; (2) cost considerations; and (3) disparities and social constructs, with potential solutions provided for each. Pragmatic strategies for examining and overcoming these barriers before future PrEP regulatory approval are recommended. If these strategies are considered well before the time of commercial availability, the potential for PrEP to interrupt the HIV pandemic will be greatly enhanced.

Plain Language Summary

Overcoming Barriers to Diffusion of HIV PrEP

Giving antiretroviral medications to prevent acquiring HIV is called pre-exposure prophylaxis or PrEP. PrEP offers a critical tool to halt the HIV pandemic. Unfortunately, there are many barriers to PrEP access. Whether the PrEP is a pill, an injection, or other drug delivery systems not yet created, they share many common characteristics. Understanding these barriers now can help us plan earlier in the drug-development process rather than waiting for proof that the medication works. We can start overcoming barriers to PrEP access if we think of them before the drugs are developed rather than waiting until they are on the market. The purpose of this article is to propose core considerations to include in the drug-development process for future PrEP methods. The authors conducted a literature synthesis examining key barriers to PrEP uptake in the United States. The published literature was reviewed to identify commonalities across PrEP drugs and delivery methods. Based on the published literature, the authors divided challenges into three main categories: (1) provider and clinic characteristics; (2) cost considerations; and (3) disparities and social constructs. Potential solutions are provided for each. Practical strategies for examining and overcoming these barriers before future PrEP regulatory approval are recommended. If these strategies are considered before the time of commercial availability, the potential for PrEP to stop HIV will be greatly enhanced.

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Background

In the absence of an effective vaccine, HIV prevention with antiretroviral medication offers a critical tool to halt the HIV pandemic. The first antiretroviral therapy studied as pre-exposure prophylaxis (PrEP) for HIV, emtricitabine and tenofovir disoproxil fumarate (F/TDF), has been Food and Drug Administration (FDA) approved in the United States since 2012.[1–4] In 2019, a second oral PrEP agent, emtricitabine and tenofovir alafenamide (F/TAF), was FDA approved for use among cisgender men who have sex with men (MSM) and transgender women. Then, in 2021, the first injectable PrEP agent (long-acting cabotegravir) was FDA approved for at-risk adults and adolescents at risk of HIV via sexual transmission.[5,6] Safe, effective, and well tolerated, these agents offer the potential to substantially decrease HIV incidence and help achieve the ambitious UNAIDS 90-90-90 goals.[5–9] Despite this potential, the global scale-up of PrEP has been slow, and stark racial, ethnic, and gender disparities in PrEP access persist. In the United States, a resource-rich setting with the reasonable expectation of widespread access to PrEP, over 30,000 persons continue to acquire HIV each year,[10] each new infection representing a missed opportunity for HIV prevention. While this article focuses on the United States, it can readily be generalized to global settings.

Barriers to PrEP access, both in general and by diverse populations, share remarkable commonalities and are likely to be generalizable to future novel PrEP strategies. Key barriers continue to include cost, insurance coverage, concern about side effects and long-term health effects, stigma, lack of provider knowledge or comfort with PrEP, ancillary testing costs (e.g. sexually transmitted infection (STI) testing, viral load testing, kidney function), pharmacy access, provider bias, and lack of participant knowledge or adherence support.[10–21] These are cross-cutting barriers to PrEP uptake, impacting the scale-up of both oral and injectable PrEP agents as well as newer delivery systems expected soon.[22–25] Knowledge of these barriers allows for planning earlier in the drug-development pathway rather than waiting for a demonstration of efficacy.

Currently, implementation science and studies of PrEP delivery in healthcare settings are largely conducted only after FDA approval has been granted.[16,17] There is scarce proactive removal of expected (and common) structural barriers to PrEP uptake. For example, in the case of the recently approved injectable cabotegravir, operational issues in medication delivery were not addressed at the time of commercial rollout.[12,14,15,26] At the time of this writing, over 2 years after FDA approval, myriad barriers persist to prescribing and delivering this medication to persons at risk for HIV. Given the similarities in barriers to PrEP uptake, there is an urgent public health need to understand and overcome PrEP delivery challenges so they can be addressed earlier in the drug-development process. The purpose of this article is to propose a core set of considerations that can be included in the drug-development process for future PrEP agents, formulations, and delivery systems. If these are considered well before commercial availability, the potential for PrEP to interrupt the HIV pandemic may be enhanced. With novel PrEP delivery technologies currently in development,[24,25,27] it is critical that these barriers to the scale-up of PrEP are addressed aggressively and proactively.

Methods for elucidating common barriers to PrEP access

Barriers to PrEP uptake are likely to be common across future modes of PrEP delivery, including those currently under investigation (e.g. implants, long-acting subcutaneous injections, vaginal rings, and multipurpose technologies such as those for pregnancy and HIV prevention). We conducted a review of the published literature surrounding barriers and facilitators to PrEP delivery focusing on the US-based regulatory process. We sought papers describing PrEP delivery that are generalizable in nature, rather than clinical trials of a particular PrEP agent. Once papers were identified, two authors independently divided concepts into three main categories of structural barriers: (1) provider and clinic characteristics; (2) cost considerations; and (3) disparities and social constructs. These were then reviewed by study team members in concept and through paper development to ensure agreement. In the next section, we will provide examples of each of these followed by potential solutions along the drug-development pathway. These are summarized in Table 1.

Provider and clinic characteristics

Challenges

Lack of provider awareness, lack of comfort in prescribing, and provider bias represent well-known barriers to PrEP uptake irrespective of modality.[10,13,14,16–21,26,28–40] Particularly when oral PrEP was first deployed, many providers had concerns about PrEP, often causing PrEP to be relegated to infectious disease specialists rather than primary care practitioners. This continues to be a barrier to wider access to PrEP.[20,41] Compared to their specialty counterparts, primary

Table 1. Summary of structural barrier categories and potential solutions.

Structural barrier	Potential solutions along drug-development pathway
Provider and clinic characteristics	
Lack of provider awareness about PrEP Lack of provider comfort providing PrEP and discussing sexual health and prevention with patients PrEP relegated to specialty clinics versus primary care Provider bias	Integration of provider training and dissemination of information to providers and clinics concurrent with Phase 3 studies Extension of PrEP training to primary care, community-based, and family-planning settings Integration of a range of investigators and providers in protocol, beyond infectious disease specialists Focused training to overcome provider bias based on race, ethnicity, gender, sexual orientation, or type of HIV risk Provider training on methods of discussing sexual health and HIV prevention
Lack of time and personnel for clinics to manage complicated PrEP prescriptions and insurance approvals Lack of patient resources to support PrEP uptake, adherence, and persistence	Funding for ancillary staff and capacity-building integrated into early drug scale-up Planning for approval and prescribing operations streamlined and established during the drug-development process
Lack of research to identify optimal methods for PrEP implementation success	Require study designs to investigate implementation questions within the Phase 3 studies to provide evidence of optimal implementation methods alongside efficacy endpoints
Cost	
Pricing puts PrEP out of reach for un- and under-insured Logistics of pricing and access identified too late	Require transparent pricing negotiations at the point of drug approval request and link approval to cost accessibility Development of PrEP delivery systems within pharmacies and standalone clinics to reduce costs Require cost transparency to be disclosed as a part of the IRB review of studies, and disclosed to participants
Copay programs for people on private assistance may not cover ancillary testing, just medication State- or federal-insurance programs may cut funding for HIV prevention based on political climate	Expand copay programs to cover all costs of being on PrEP, not only medication Strengthen public health programs and laws to ensure that public insurance channels provide optimal access to all HIV prevention methods
Lack of reinvestment of profits into greater medication access	Address patent issues to insure profits are reinvested into public health and greater medication access Require clarity regarding ownership and profits into the future to ensure ongoing support of greater patient access
Concerns that older medications are more harmful than newer, more expensive medications	Patient education should be provided by the companies to reduce misinformation and confusion regarding older regimens
Disparities and social constructs	
Non-inclusive study designs Lack of racial, ethnic, gender, sexual orientation, geographic, and type of HIV risk diversity in study participants	Require registrational study designs to include methods to increase diversity and inclusion Require study designs to have enrollment targets proportionate to affected populations
Biases including racism, sexism, and heteronormative views and structures Lack of community support or community-based participatory guiding principles	Integration of provider training and dissemination of information to providers and clinics concurrent with PrEP development Include research to measure participant perception of biases Develop and test novel approaches to bias reduction within each protocol Eventual packaging and promotion of PrEP agents should be developed in consultation with communities and using community-based participatory guiding principles

PrEP: pre-exposure prophylaxis; IRB: institutional review board.

care providers are less likely to offer PrEP and may lack the training to discuss sexual and drug-use risks of HIV infection or harm reduction.[33,39] In addition, provider bias is known to impact willingness to prescribe PrEP to those in greatest need, even in situations where HIV risk has been identified.[13,28–32,42–46] These challenges can result in a mismatched allocation of resources, with costly specialty practices being overburdened with PrEP prescribing that could be better

addressed in primary care clinics.[20,39] (That is, having infectious disease specialists, because they are already comfortable with prescribing antiretrovirals, take on the bulk of prevention care may not be the best use of resources, in the same way that having obstetricians/gynecologists responsible for the bulk of contraception care may be less impactful than having contraceptives offered in primary care.)[39]

In many healthcare settings, there may be a lack of time focused on patients and ancillary services to support patients to adopt or adhere to PrEP. Challenges in provider availability, adequate ancillary staff, and lack of support such as adherence counseling or patient education[7,16,20,40–43,47–51] may limit the provider's ability to ensure that patients stay on PrEP to achieve its greatest impact. Most healthcare settings lack sufficient staff to manage the multidisciplinary needs of the PrEP patient, which may include testing for other STIs, psychosocial support, or education. Further, clinic settings may lack sufficient ancillary personnel to manage the complicated insurance requirements which often require prior authorizations, differentiation between medical and pharmacy benefits, eligibility verification, appealing rejections, purchasing and storage of medications, and so forth.[16,18,26,27,52,53] These are likely to demand more intense resources from clinic personnel closer to the time of FDA approval before systems for insurance approval, purchasing, or administration are established. In the case of injectable cabotegravir, these barriers have resulted in the slow implementation of a new, highly effective medication that offers HIV prevention in a completely original way. Unfortunately, these burdens on healthcare providers may mean fewer individuals can benefit from new prevention technologies.

Innovative ancillary wraparound services for those on PrEP are also seldom supported or paid for by insurers. This is the case even for currently available oral PrEP. For example, client-centered care coordination (C4)[42,43,47–49] was explored as a vanguard intervention to support Black MSM in the uptake and adherence of F/TDF and demonstrated positive signals of effectiveness.[42,43,47,48] However, this intervention has not been fully examined in a randomized trial despite the ongoing urgency of developing new methods to support PrEP use among Black MSM. Similarly, adherence counselors who would be useful in helping to increase PrEP adherence and persistence[18] are seldom paid for in current insurance paradigms. Although community-based settings may have more opportunities to provide this type of psychosocial support, for many patients and at-risk individuals receiving standard care, such services may be out of reach.

Methods of overcoming these challenges

These provider and clinic challenges are similar across all types of current PrEP; these also would be likely to exist for future delivery systems including future multiprevention technologies that may integrate PrEP with STI-prevention and/or contraception.[22,23,25] One way to overcome these challenges would be to ensure that implementation issues are included in the drug research in the first place. For example, rather than studying only the HIV and safety endpoints in a Phase 3 study, protocols could examine service delivery structures to support the specific novel intervention under study. Integrated healthcare delivery models and ways to leverage community models of care could be examined during the study phase rather than only after the medications are approved. Factorial designs[54] could be leveraged to see which clinic supports are best positioned to enhance medication adherence, for example. Even open-label extension phases of protocols—which frequently are tacked onto Phase 3 studies after a medication is found to be effective—could be modified to have ancillary care services examined rigorously within the protocols for specified measurable outcomes. This would provide evidence not only about the best strategies for the deployment of the medication but also could provide clear indications for insurance coverage of the ancillary services as well as the medication. Most clinical trials of new PrEP methods collect data on acceptability and feasibility;[55–57] although this is important and useful, they do not examine directly the best method for intervention delivery and implementation in a real-world setting, nor do they provide the necessary leverage to demand insurance companies cover this additional cost. Similarly, while pharmaceutical companies frequently conduct implementation science explorations, these generally occur after the drug is approved and while it is being scaled up for expanded release; for many people and healthcare settings, this may be too late. Patients may decide they cannot or will not work to get the new PrEP method, or clinic settings may decide the burden on staff is too great. For recently approved long-acting injectable cabotegravir for PrEP, this is a clear challenge. By way of example, the nearly decade-long delay in the development of adequate evidence-based support strategies for F/TDF could have been overcome by requiring that methods for scale-up and implementation, such as C4,[42,43,47–49] were included in the drug-development process. This would require pharmaceutical company investment and not primarily the efforts of federal and grassroots organizations to solve these implementation issues. Finally, ensuring that providers are trained on how to address sexual health and HIV prevention in culturally appropriate ways, proactively giving providers tools to talk about HIV risk and support patients to engage in HIV prevention behavior and effectively use the biomedical tools available to them.

Cost

Challenges

The cost of new PrEP formulations can be expected to be a barrier to their uptake, irrespective of the drug's delivery method (e.g. oral vs injectable vs implant). Drug pricing is impacted by a host of considerations far beyond the scope of this article.[58–61] However, it is critical to note that one of the primary barriers to PrEP is cost,[13] and this limits its accessibility and contributes substantively to continued disparities in PrEP access, prolonging the HIV epidemic. For the FDA-approved PrEP regimens to date, initial pricing often puts them out of the reach of populations with the greatest need, resulting in considerable and durable health disparities. Furthermore, even with eventual reductions in price, due to either availability of generic formulations or revised pricing due to competition, the reduced costs may come too late. Perceived initial cost barriers may limit the audience for novel formulations of PrEP at the outset such that potential PrEP users do not view themselves as likely candidates for the medication. While at this point, many insurance companies have elected to cover daily, oral PrEP, this was not the case just after the ground-breaking FDA approval of F/TDF as effective HIV prevention. Cost remains a prohibitive barrier to those in need of effective biomedical HIV prevention, including those with and without insurance. Although oral PrEP costs have been reduced, there are still clear disparities in access by income and race that may not be addressed through insurance coverage. Furthermore, changing political tides may impact the availability of PrEP provided by state- or federal-insurance programs.[62] Regardless, by the time the costs decrease, the window of excitement in the regimens may have passed. This lesson can be readily applied to the roll-out of long-acting injectable cabotegravir, where uptake and implementation have been costly and therefore slow and arduous. Potential patient communities may believe the older, generic versions are not as good as the newer regimens, creating concern about inferior or more harmful regimens being offered to a stigmatized or underserved population. This was observed when F/TAF came on the market, yielding considerable challenges in the ongoing delivery of F/TDF, a proven safe drug, once it became generic.[63] These challenges cannot be overcome by the copay assistance provided by some pharmaceutical companies alone. Although older formulations will remain accessible once they become generic, novel and more effective technologies will be out of reach for many.

A historic model for this issue is seen in birth control methods such as oral contraceptives, rings, long-acting reversible contraceptives (LARC) such as intrauterine devices (IUD), and implants.[64] As the "menu" of options increases, general access to novel therapies will increase as well. However, this is expected to take time: multiple generic and brand name versions of contraceptives benefit the consumer by making access available to patients desiring the products at all price points and with multiple avenues for coverage. With only three PrEP agents currently available, that point has not yet arrived. Numerous novel PrEP approaches are currently under study,[24,25,35,55,65,66] and it is critical to work diligently to ensure widespread access to all of them. Poor access to PrEP is a driver of HIV acquisition. We must identify ways to require accessible pricing for all until there is a critical mass of PrEP agents available to the public to generate competition, clear insurance coverage, and fair pricing structures.

Ancillary testing and services present another challenge. All PrEP regimens will require regular HIV and STI testing; some may also require safety monitoring, such as serum creatinine, cholesterol, or triglycerides.[67] When delivered in insurance-covered settings, clinician visits and labs are required to be covered due to the US Preventive Services Task Force Grade A recommendation;[68,69] however, for those persons who are self-pay or covered with pharmaceutical company-provided copay assistance, this may not be the case. This can introduce thousands of dollars of extra costs beyond that of the drug alone, furthering cost barriers to wider distribution of all PrEP modalities.

Methods of overcoming these challenges

It can be expected that, barring significant changes to the drug-development process, future new generation PrEP methods—either delivery systems or novel agents—will cost more than their predecessors. Given this, cost considerations should be examined during the protocol and regulatory approval pathways and not only upon drug approval. Currently, in the United States, pricing is generally not a publicly required discussion until after FDA approval.[70,71] Revising this process so that pricing is transparently communicated up front would help reduce cost barriers to PrEP delivery. Cooperative relationships between federal agencies, pharmaceutical companies, insurers, and researchers could facilitate lowering cost barriers; by reducing silos and fostering collaboration between these partners, profits could be reinvested into the patient population to ensure access. This would obviate patent challenges that are currently underway, putting patient access before profit.[72,73] If transparent pricing requirements cannot be introduced into the regulatory pathway, then institutional review boards (IRB) at institutions and commercial single IRBs could potentially opt to make cost transparency a requirement of the protocol. For example, local policies may indicate that institutions will not review or approve studies that do not articulate fair pricing policies in the protocols and convey them to participants in studies.

Another strategy includes increased development of standalone PrEP clinics or pharmacy partnerships. These could similarly be studies earlier in the drug-development process and their cost-effectiveness researched simultaneously. For

example, partnerships with pharmacies have been effective in distributing vaccines for COVID-19, influenza, shingles, and other preventable diseases. Future studies of novel PrEP regimens could collaborate with pharmacies[74,75] during clinical trials to set up best practices in dissemination early on. Upon regulatory approval, these regimens could be rolled out without delay to those without clinical providers, insurance, or other access to PrEP. Researchers cannot alone address these barriers, but attention to them by regulatory and community partners prior to study implementation may successfully mitigate these challenges.

Disparities and social constructs

Challenges

In addition to provider characteristics and cost, there are more pervasive barriers to PrEP access. Widespread structural barriers also play a role in limiting PrEP uptake and adherence. These include biases such as racism, sexism, and heteronormative practices that exclude large swaths of the population from accessing PrEP. This may occur in several ways. There can be actual exclusion from the study design, as was seen with the DISCOVER trial,[2] which excluded cisgender women from the trial and has resulted in cisgender women only having access to two current PrEP agents.[24,66] Cisgender women in the United States continue to have the least access to PrEP despite over a decade of availability.[8,66,76] Transgender women and transgender men are also frequently excluded and lack access.[51,77–80] Often there is disproportionate inclusion of participants not reflective of populations at highest risk. For example, Black individuals made up only 8.6% of the iPrEx study[1] sample, despite the excess HIV risk seen among Black MSM. Similarly, Black individuals, including Black MSM,[8,44,81,82] continue to access available PrEP regimens at strikingly lower rates relative to their White counterparts.[8,44,81,82]

Lack of gender and racial diversity in the trial can also generate mistrust of the data and eventually approved drugs,[83–86] as populations not tested in the original clinical trials may not fully trust newly approved agents. General medical, as well as PrEP-specific mistrust, can result in community-based alarm. Other widespread structural barriers include stigma, a general lack of preventive care, fractured healthcare systems overall, and myriad others. These diffuse structural factors negatively impact access to care.[7,11,13–16,18,19,26–29,31,34,40,41,45,79,80,87]

Ways to overcome these challenges

These disparities and social constructs limit the diffusion of medical advancement in many ways; overcoming them will require resources and political will beyond the conversation of increasing PrEP access. Focusing on future novel PrEP access and structural changes to the process of PrEP development may ultimately extend to overcoming some of these other challenges as well. Specific to PrEP, there still are methods for overcoming these pervasive structural barriers that could be very effective. Requiring efficacy protocols to enroll diverse populations can be one first step in improving equity in access to future interventions; the registrational trials for long-acting cabotegravir as PrEP that required gender, age, and racial diversity in pre-specified enrollment targets are a strong example.[3,4] This resulted in confidence that the drug is safe for all populations at risk of HIV and FDA approval that embraced all populations. Current long-acting regimen studies are starting to incorporate this approach as well.[65] Working with communities early in the drug-development process to examine concerns and fears about PrEP is urgently needed for future regimens. Companies may not wish to invest resources in collaborating with communities until the drugs are approved, but this viewpoint is short-sighted. Especially with new methods for PrEP delivery, connecting early on with those who will ultimately use the medication on the population level is needed. Adopting robust community-based participatory research principles[88] throughout PrEP clinical trials and not only late in the implementation continuum may increase trust in the medication and the providers.

Summary of recommendations

These solutions to overcome challenges in PrEP dissemination will require a critical review of drug-development research. If a specific medication was unique in its challenges to PrEP access, a case could be made to wait until it was approved to initiate implementation science and operationalize scale-up. However, as discussed above, challenges to PrEP are likely to be the same no matter the specifics of the regimen. A reorganization of our conceptualization about where implementation science methods belong in the drug-development process is needed if we want to increase access to those at greatest risk of HIV. Taking the US FDA as an example, a new PrEP agent might be approved after approximately 9–14 years of drug-development research,[70] followed by additional time for regulatory review and manufacturing scale-up. During this time, there is typically very little in the way of implementation science, logistical planning, or community input into understanding how the drug will ultimately be delivered until the medications are approved. This may seem reasonable given that drug developers are reluctant to invest resources into such explorations in the event the medication is not effective or successfully approved. However, given the commonalities of barriers to PrEP access outlined above, it would be appropriate to require integrated scale-up considerations concurrent with the drug-development process rather than only upon completion. All of the above solutions could be integrated into the

drug-development process because, quite frankly, the challenges to PrEP dissemination are knowable upfront.

Conclusion

This review has several limitations and strengths. This was conducted as a literature synthesis to understand key structural barriers to uptake of PrEP; it was not intended to be a systematic review or comprehensive of the many valuable papers examining this issue. There are many important contributions to this area of thought and we recognize that we may have inadvertently omitted some. The focus of this article was to elucidate common structural barriers to PrEP uptake in the United States and this necessarily omits a wealth of global literature and unpublished literature. Similar reviews of structural barriers to PrEP that focus on other regions would be valuable. With drug development crossing geographical boundaries through increased harmonization, efforts to include regulatory strategies that are applicable everywhere will be critical. Global models of PrEP should be considered and leveraged to improve information sharing across regions and develop novel strategies that can be studied and used in many locations. We are aware that this review does not encompass all barriers, nor is it possible to easily remove all challenges, either by regulatory requirements, study design, or even emerging political will. Still, while granular barriers to scale-up may vary slightly by location, sub-population, or regimen (e.g. viral load testing for injectable products, or different safety testing by drug type), overarching challenges are unlikely to vary substantially, making it possible to be proactive. Finally, this review is informed by the experience of the authors in an urban academic health care setting, which may be very different from other locations even in the United States. This review also has several strengths. Evaluation of structural barriers may ultimately allow development of new strategies for increasing PrEP access. We are encouraging consideration of challenges in delivering PrEP to those at greatest risk of HIV earlier in the drug-development process. We are hopeful that these approaches contribute to improvements in the way we study biomedical HIV prevention interventions. Perhaps eventually study endpoints will not only be whether we prevent HIV acquisition but whether we can get the drugs to those in need in both a reasonable period of time and at a reasonable cost.

Given that each delay in PrEP diffusion potentially results in the tragic consequence of unnecessary HIV infection, there is an urgent need to develop methods that decrease the time from drug discovery to scale-up and implementation in those communities at greatest risk of HIV. The solutions outlined in this article provide potential steps to enhance drug access with greater speed, harnessing the power of the common strategies. By devoting attention to these expected challenges as a requirement of the drug-development process, and integrating operationalization of drug delivery and implementation science concerns into clinical trials, we may be able to increase the wide access at the time the drug is approved—and not a decade later. This is especially critical for populations at the greatest risk of not accessing medication. Simultaneous attention to operational issues in PrEP scale-up should be considered throughout the drug-development phase rather than after it. This includes ensuring diversity and generalizability of participants during the trial, policies, and payment structures that support patient access, patient knowledge and engagement, overcoming provider barriers to prescribing PrEP, and attention to structural barriers expected to interfere with equitable PrEP distribution. The hazards of sequential attention to scale-up are evident when considering the disparities in PrEP distribution when that approach is used. Institutionalizing consideration of logistical needs to organize and finance implementation strategies with community input is an ethical imperative. Extending respect to persons is morally necessary and will ultimately improve outcomes, facilitate a sense of trust, and ensure justice is woven through all aspects of scientific exploration and eventual provision of care.

Declarations

Ethical approval and consent to participate

There was no participant contact or data analysis; this is a literature review of published peer-reviewed papers only. As such, this is considered non-human subjects research by the George Washington University Institutional Review Board (IRB) policies, and no IRB review or approval is required. There was no contact with participants in any way that would necessitate informed consent.

Consent for publication

Not applicable.

Author contributions

Manya Magnus: Conceptualization; Data curation; Investigation; Methodology; Project administration; Supervision; Writing – original draft; Writing – review & editing.
Hannah Yellin: Conceptualization; Data curation; Methodology; Writing – original draft; Writing – review & editing.
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Jeanne Jordan: Conceptualization; Investigation; Writing – original draft; Writing – review & editing.
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Irene Kuo: Data curation; Investigation; Methodology; Writing – review & editing.
Marc Siegel: Conceptualization; Investigation; Methodology; Project administration; Supervision; Writing – original draft; Writing – review & editing.

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Availability of data and materials

This literature review is not derived from any one study, data set, or from any funded activity. There was no participant contact and this is considered non-human subjects research by the George Washington University Institutional Review Board (IRB) policies.

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