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REVIEW

Leveling Up PrEP: Implementation Strategies at System and Structural Levels to Expand PrEP Use in the United States

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Abstract

Purpose of Review Despite highly effective biomedical HIV pre-exposure prophylaxis (PrEP) options, suboptimal PrEP uptake impedes progress towards ending the epidemic in the United States of America (USA). Implementation science bridges what we know works in controlled clinical trial settings to the context and environment in which efficacious tools are intended to be deployed. In this review, we focus on strategies that target PrEP use barriers at the system or structural level, exploring the implications and opportunities in the context of the fragmented USA healthcare system.

Recent Findings *Task shifting* could increase PrEP prescribers, but effectiveness evidence is scarce in the USA, and generally focused in urban settings. *Integration* of PrEP within existing healthcare infrastructure concentrates related resources, but demonstration projects rarely present the resource implications of redirecting staff. *Changing the site of service* via expanded telehealth could improve access to more rural populations, though internet connectivity, technology access, and challenges associated with determining biomedical eligibility remain logistical barriers for some of the highest burden communities in the USA. Finally, a *tailored* care navigation and coordination approach has emerged as a highly effective component of PrEP service provision, attempting to directly modify the system-level determinants of PrEP use experienced by the individual.

Summary We highlight recent advances and evidence surrounding task shifting, integration, service delivery, and tailoring. With the exception of tailored care navigation, evidence is mixed, and the downstream impact and sustainability of task shifting and care integration require further attention. To maximize PrEP outcomes, research will need to continue to examine the interplay between individuals, clinics, and the healthcare system and associated policies within which they operate.

Keywords Fragmented · Implementation science · HIV prevention · Task shifting · Integration

Introduction

Over a decade since biomedical HIV pre-exposure prophylaxis (PrEP) was approved for use in the United States of America (USA), uptake of this highly effective means of HIV prevention remains poor. Despite growing evidence that increases in PrEP coverage are associated with decreases in new HIV diagnoses [1], as of 2021 data, less than 25% of PrEP-eligible persons have received a prescription [2]. Differences in PrEP use reflect racial, regional, and resource inequities across the country [3–7]. For example, PrEP coverage in 2021 was reported by the Centers for Disease Control and Prevention (CDC) as 5.6% among Black or African American individuals assigned male sex at birth with indication for PrEP, as compared to 18.4% among all individuals assigned male sex at birth with this indication [2]. Among the CDC-designated End-the-Epidemic jurisdictions, recent PrEP coverage estimates of those with PrEP indications range from a low of 4.5% in San Bernardino to a high of 42.3% in San Francisco [2]. Gaps in the PrEP "need-to-use" metric are particularly pronounced in the Southern USA, a region that accounts for more than half of new HIV diagnoses but only one-third of PrEP users [8]. PrEP uptake in the South is especially low among young sexual and gender minority men (YSGM) [9, 10], with marked disparities in use among YSGM of color in rural areas [11–17]. As a key pillar of the USA End-the-Epidemic strategy, there is an urgent need to improve PrEP use.

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Drivers of sub-optimal PrEP uptake in the USA are complex—spanning social, clinical, behavioral, and structural factors [18]. Reflecting the widely recognized heterogeneities in determinants of PrEP use, researchers have observed, experimented, and reported extensively on the barriers and facilitators relevant to PrEP uptake [18, 19, 20•, 21]. Heterogeneity of the populations who remain vulnerable to acquiring HIV in the USA, and complex system and policy factors that may interfere with PrEP access and uptake, have complicated how medical and public health systems direct resources for PrEP scale-up. Frequently, interventions focus on the more proximal (to PrEP prescription) behaviors of individuals or clinics—approaches that often do not adequately address the role that healthcare system structures and policies exert on the behaviors of individuals and the broader context in which PrEP is prescribed. A review of the CDC's Evidence-Based and Evidence-Informed intervention compendium (as of February 8, 2024) for PrEP interventions shows that only four out of 16 catalogued interventions have any structural component noted [22]. While past investigations have sought to unpack or demonstrate the effectiveness of innovative solutions to the glaring PrEP need-to-use gaps in a defined population, all studies have one important feature in common: they are set against the backdrop of the USA fragmented and fractured healthcare system within which PrEP care is necessarily delivered.

The effectiveness of PrEP—both oral and injectable—is no longer in question, rather we are faced with an implementation problem. Implementation science, specifically the development, evaluation, and application of strategies to improve the uptake of evidence-based practices, offers a tantalizing approach to addressing the persistent and pervasive gaps in PrEP uptake and use in the USA. Traditional clinical trials are designed to intentionally control elements that would interfere with the ability to evaluate the efficacy of a therapy or intervention approach (for example, providing study drug so that cost is not a barrier to PrEP uptake or sustained use in the context of a study). As a result, the trials that generate evidence typically do not reflect real-world provider or patient experiences. There is a critical role for implementation science approaches in scaling up PrEP to overcome this limitation.

Perhaps one of the most compelling aspects of implementation science as applied to this and other healthcare service delivery problems is the explicit acknowledgement of and attention to the broader context in which an intervention is being deployed [23•]. Certainly when it comes to PrEP use, there is no one-size-fits-all, as diversity in patients, providers, and policies coalesce into a broader context with discrete challenges and opportunities. Through the use of frameworks and models which explicitly recognize the importance of the system and policies in which individuals engage in healthcare decision-making, implementation science offers an opportunity to examine the complexities that shape individual attitudes and behaviors and influence an individual's ability to maintain a behavior over time.

Building on earlier reviews [18, 20•, 21, 24], in this paper, we examine recent implementation strategies that explicitly target PrEP use barriers at the system or structural level, and which may be particularly relevant in the context of the conditions that perpetuate fragmentation in healthcare delivery in the USA [25]. Organized by the ERIC taxonomy for implementation strategies [26], we focus on four key areas: revising professional roles through task shifting to pharmacists, changing service sites through integration within existing health infrastructures, changing service sites through expanding telehealth services, and tailoring service strategies with navigation and care coordination.

Operating in a Fragmented System

The term "healthcare fragmentation" is used to describe an increasingly siloed approach to healthcare provision with inadequate coordination in the USA [27]. Fragmentation is described at the provider level (i.e., increasing sub-specialization, siloed workforce), but its drivers reflect the unique history of health services in the USA—namely a quasi-public–private system in which incentives and policies fail to align in a manner that maximizes provision of efficient, high-quality healthcare [28]. In the absence of a unified system for incentives, information, or policies, access to health services—particularly preventive health services—suffers.

When it comes to PrEP use in the USA, this fragmentation may be associated with inadequate access to PrEP due to provider deserts (e.g., peri-urban or rural regions with fewer providers familiar with or licensed to prescribe PrEP), a private insurance system that undervalues preventive healthcare, and lack of commitment to a single-payer system through which pressure to decrease drug costs could be achieved. Even as science advances, and policymakers recognize the potential of multiple modalities of PrEP to change the face of the epidemic [29, 30], outstanding litigation could interfere with widespread coverage for insured persons, and out-of-pocket expenses for both insured and uninsured persons continue to impede uptake [31].

Perhaps the most striking example of this system failing to align incentives and exert pressure to make modern therapeutics affordable is long-acting injectable PrEP. Despite its proven superior effectiveness [32••, 33], it is sparsely available in the USA, with cost and coverage complexities impeding uptake [34]. While recent analyses by the Clinton Health Access Initiative estimate a potential per person per year (PPPY) cost of manufacturing CAB-LA at under $40 USD

[35], the current sole manufacturer (Viiv) estimated price of the drug is $22,200 PPPY [36], a cost that places CAB-LA far beyond the global production estimates for daily oral ($48 USD PPPY) or event-driven ($12 USD PPPY) PrEP [37]. Further, the *production* cost of these therapeutics does not align with the cost to the health system to *deliver* the medications, and the "bottom line" cost to a patient varies widely depending on health insurance coverage (privately insured pay more), gender (men pay more), age (individuals over 65 pay more), and geographic region (South and Midwest pay more) [38•, 39••]. Cost is not only a barrier for the newest agents—even older oral PrEP agents that are now off patent can pose an out-of-pocket patient cost upwards of $1284 for a year of medication coverage (not including provider co-pays or lab tests) [38•]. Even modest out-of-pocket costs associated with prescription co-pays, provider visits, and required laboratory monitoring to safely initiate and maintain PrEP will exacerbate existing disparities in PrEP coverage.

Inadequate access to PrEP providers, legislation regarding PrEP coverage, and cost-prohibitive pricing highlight relevant system and policy levers and use determinants. The system has indeed been perfectly designed to get the suboptimal results we are seeing. And so to change those results means changing the system. Implementation science explores the interaction between individuals and systems. Critically, the role of the individual cannot be ignored or diminished when considering drivers of suboptimal PrEP uptake in the USA—low PrEP awareness among prescribers and potential users and underestimation of HIV acquisition risk also impede use [18]. But addressing these individual-level barriers to PrEP requires commitment to widespread education, placing value on preventive health, and providing access to unbiased medical care, which fundamentally requires system-level changes. Importantly, awareness is only a first step. Ultimately, structural and policy-level changes create space for the expansion of innovative and new implementation strategies, by altering the constraints for individual actors—be they policymakers, providers, or potential PrEP users.

In the next sections, we explore some of the most recent advances and evidence surrounding implementation strategies to improve PrEP uptake in the USA, focusing on strategies that emphasize the role and influence of health systems [26].

Revising Professional Roles: Task Shifting to Pharmacists

In response to the call for expanded service delivery approaches to increase access to PrEP, there is increasing interest in the pharmacy-based distribution of PrEP [40–42]. Regarding structural and individual-level barriers to PrEP use, pharmacies may offer several advantages over traditional clinic spaces including longer hours of operation, shorter travel distance, and greater privacy and confidentiality [43]. Pharmacies may also be perceived as more welcoming among individuals who have experienced or anticipated stigma and discrimination within the healthcare system [43, 44•].

Despite support for this strategy among many pharmacists and patients [44•], a recent systematic review identified 16 relevant studies on PrEP initiation and continuation in pharmacies, none of which had results confirming that offering PrEP through a pharmacy was any more effective than traditional PrEP prescribing practices for initiating or continuing PrEP [45]. For example, one analysis of on-site referral to pharmacists for same-day prescriptions suggested high rates of PrEP prescriptions filled [46], but subsequent follow-up confirmed that most individuals provided with same-day prescriptions never started PrEP [47], highlighting the challenge associated with relying on prescriptions to capture PrEP use. Although other highlighted case studies—all conducted in urban areas in the USA—suggest a range of PrEP initiation and retention, none compared the effectiveness of pharmacy-access versus more traditional provider-access models.

While the question of whether task shifting to pharmacists effectively improves PrEP use remains unanswered, this strategy and the trials therein expose an important and often ignored (or at least unmeasured) ripple effect of expanding practice scope through task shifting. For example, while some support this role as an "untapped" opportunity to fill a gap in care provision [41], other interest groups perceive this expanded scope of practice as compromising the quality of healthcare delivery and potentially exacerbating existing inequities in health outcomes [48, 49]. Although the evaluation of pharmacy-based PrEP studies focuses on PrEP use outcomes, the total health impact is more nuanced once considering implications beyond the relatively controlled contexts of clinical trial settings. For example, task shifting provision of preventive prescriptions could expand access to other indicated medications [50], but could also decrease engagement in physician-based preventive screening and evaluation [51]. More attention to these potential downstream impacts of task shifting policies is needed to comprehensively evaluate the intended and experienced effect.

Change Service Sites: Integrating Within Existing Healthcare Infrastructure

Another widely studied strategy to improve PrEP uptake in the USA is leveraging clinics that already provide health services as an onramp to PrEP distribution and management.

Evaluation of health-department HIV prevention programs funded through the Centers for Disease Control and Prevention Enhanced Comprehensive HIV Prevention Planning project suggested that shifting resources to focus on prevention services in these settings helped to scale up HIV testing, though this study was conducted prior to widespread use of PrEP (2010–2013) [52]. Other compelling opportunities to integrate PrEP with related services include family planning clinics, methadone clinics, and sexually transmitted infection (STI) clinics [53–55], all of which are logical entrées to HIV prevention.

Despite the convenience and potential efficiencies of collocating related services, there are important limitations to this integration strategy. First, many of these clinics are designed to provide episodic care and may lack the resources or systems to manage longitudinal care such as that required by PrEP, particularly given the complexity surrounding financial assistance and navigation of financial needs [55]. Even in settings equipped to expand to quarterly visits, heterogeneity in clinic structure and staffing models complicate this one-size fits-all approach. Furthermore, without additional dedicated funding to support PrEP-specific activities as integrated into an existing care environment, these efforts are likely pulling staff and clinical personnel away from other activities. This opportunity cost of integration may be difficult to monitor, but could have an unanticipated negative impact on the service delivery already in place [56].

Effective health service integration therefore requires specific definitions of what is meant by integration and how the potential benefits of said integration should be evaluated. Health service integration would be expected to impact all levels of patient care—from human resources to supplies and technologies [57]. Particularly pertinent for strategies regarding integrated PrEP services, integration could also include improving referral networks and strategies, a particularly appealing approach where human and laboratory resources are limited or where volume is expected to be (relatively) limited. However, referrals to external PrEP providers rarely result in PrEP initiation, with notably poor uptake among youth and non-Hispanic Black populations [58–60].

Several studies have demonstrated the potential to expand PrEP services within existing, sexual-health adjacent service lines, and often with encouraging initial results [53–55, 61•]. However, these projects often explore the potential impact of integration by controlling for other factors (e.g., out-of-pocket costs) that impede use. For example, one promising study demonstrated high PrEP uptake and persistent use when services were integrated into STI and community health clinics and PrEP was provided free of charge, thereby eliminating the extensive resources often required to link prospective patients to necessary financial assistance programs [62]. Future areas for study on integrated service delivery approaches include understanding the downstream consequences of task shifting, evaluating sustainability, and accurately measuring outcomes in real-world contexts (e.g., when not controlling for out-of-pocket costs).

Change Service Sites: Expanding Telehealth with Centralized Specialization

Telehealth for PrEP reduces engagement barriers, including those related to access and stigma, and may be particularly useful for reaching both rural and urban underserved populations [63, 64]. In many ways, the need for this role evolved as a direct result of the complex care system we expect patients to navigate—the hours spent linking potential PrEP recipients to financial assistance programs are a stark example of our fractured healthcare system.

Telehealth delivery of HIV prevention and treatment services has been shown to be highly acceptable [65, 66] with positive outcomes for ART [67, 68•] and comparable PrEP use outcomes comparing pharmacist-led telehealth versus in-person clinical evaluation [69]. Historically, the main hurdle of telehealth-based PrEP was reimbursement. However, the COVID-19 pandemic spurred increased telehealth capacity and more robust service reimbursement mechanisms [70]. Patients, providers, and payors are more adept and accustomed to telehealth as a viable alternative to face-to-face visits, paving the way to extend successful telehealth for PrEP services [71•].

Challenges remain, however. A recent review of telehealth strengths and drawbacks highlighted inequities in access, satisfaction, and health outcomes for older adults; racial and ethnic minority populations; and those with lower comfort/familiarity using telehealth [72]. Internet connectivity, variation across technology access and ownership, and concerns about privacy also pose barriers to the optimal utilization and expansion of telehealth for HIV prevention and care [72, 73]. There are also still areas for growth and innovation in addressing the telehealth "laboratory service gap" [74••] to ensure that the biomedical eligibility and ongoing monitoring tests needed for safe and effective use of PrEP medications can be administered in a way that aligns with the ease of a telehealth visit.

Despite these challenges, telehealth will almost certainly continue to represent an expanding portion of all PrEP service delivery in the USA. In selecting different models of telehealth, programs can assess the best fit for their capacity and patient populations—whether fully remote or hybrid (e.g., intake visit in-person with follow-up telehealth; provider visits via telehealth with labs in-person) and whether managed "in-house" or referred out to commercial services (e.g., Nurx, PlusCare, CallonDoc). As individual clinics, providers, health systems, and research endeavors consider whether and how

to include telehealth options, implementation science methods offer valuable guidance helping to examine barriers to adoption or reach, optimize the effectiveness and efficiency of telehealth approaches (e.g., differentiated service delivery [75]), and provide tools for evaluating fidelity and sustainability [76].

Tailor Strategies: Navigation and Care Coordination

Patient navigation and care coordination services have evolved to be an essential component in many PrEP service provision programs—for many of the reasons identified above in terms of the complexity of accessing care within fragmented systems and task shifting within a resource-strained health system. Primary navigator responsibilities include things like helping patients: understand various PrEP care options, engage with PrEP care services, complete necessary paperwork for insurance and drug assistance programs, and connect to other related health and social services that could facilitate engagement in PrEP care (e.g., transportation programs, mental health services). Navigation services may be particularly important to pair with changes in PrEP service sites in order to minimize the documented drop-off associated with external referrals [59, 60, 77]. Even robust urban programs that successfully link STI clinic patients to PrEP lack the capacity to longitudinally manage financial needs of PrEP patients without additional individualized navigation [55]. The diverse needs of potential PrEP recipients likely exceed what can be reasonably provided by staff in standalone clinics.

The evidence base for navigation services varies widely but shows high acceptability, feasibility, and promise of impact. Navigators have successfully increased PrEP prescription and uptake in diverse clinical settings [78, 79] and are essential roles in other STI clinic-based PrEP services [55]. The THRIVE national CDC demonstration project (n = 9538 PrEP-eligible men who have sex with men [MSM]) found a range across study sites of 10.7% to 95.9% (mean 53.8%) of eligible screened participants linked to PrEP services (defined as attending an initial PrEP appointment), with substantially fewer being prescribed PrEP (37.2%). At sites where PrEP navigation was provided, 48.5% of MSM who used navigation were linked to PrEP as compared to 2.8% being linked among those who did not use navigation [80••]. Among an urban sample of 2106 PrEP-priority eligible MSM attending sexual health clinics in New York City who were offered PrEP navigation services, 288 (13.6%) linked to a PrEP provider and 235 (11.2%) received a PrEP prescription [79].

Conclusion

PrEP uptake in the USA is dismal, impeding stated priorities of ending the HIV epidemic [81]. The diversity of determinants of PrEP use among PrEP-eligible persons highlights the challenge of focusing strategies at the individual level. For example, although improving PrEP awareness and appropriate dispensing practices could contribute to additional PrEP prescriptions, these approaches do not fully address the pressures and (dis) incentives imposed by existing systems and policies. Social and behavioral interventions that focus on the individual as the unit of change are unlikely to be sufficient in the absence of strategies that simultaneously address structural, environmental, and economic vulnerabilities [82]. The structural impediment to PrEP use is especially pertinent in the USA, where a fragmented health system with a powerful private insurance network undervalues prevention services and complicates efforts to incentivize or simplify provision of PrEP services. Failure to launch long-acting injectable PrEP is but one of many examples in which a highly efficacious biomedical intervention is stalled by logistics and inability to negotiate lower drug rates. While not intended as a systematic review, our findings, and those from other recent reviews examining determinants of PrEP uptake in the USA [18, 20•, 21, 24], expose an important discrepancy between the small number of studies focusing on systems and organizational-level interventions as compared to those examining individual behaviors, such as adherence and stigma.

Implementation strategies that focus on modifying determinants of PrEP access or use at a system level are critical. In this review, we highlighted recent evidence surrounding these more system-directed strategies in the form of task shifting, integration, adjustment in site of PrEP delivery (i.e., telehealth), and care navigation. Many of these intervention approaches have only been tested in more populous urban settings, highlighting the persistent research gap in less dense, under-resourced rural areas of the USA. Task shifting, integration, and expanding PrEP site delivery models have been extensively studied in low- and middle-income countries (LMIC), where these strategies are well known and proven effective and efficient components of HIV care delivery [43, 83–87]. Interestingly, these strategies are frequently incorporated as part of a differentiated service delivery model—widely embraced to target scarce resources based on the gaps and needs of a population [75, 88–90]. Researchers interested in leveling up PrEP use in the USA using these implementation strategies may explore adaptation from the lessons learned in LMIC. A critical step in this adaptation would include mapping contextual differences that may

complicate adoption such as payment systems and provider credentialing that could impact the feasibility of PrEP care task shifting or service delivery models [91].

Indeed, a common thread across many of these systems-level implementation strategies is the need for innovation *with expanded investment* to mitigate unintended consequences. For example, if the expansion of telehealth services threatens to exacerbate health inequities across sociodemographic lines, these programs should be paired with investment in technology infrastructure and technology literacy support. Just as supplemental transportation services have long been critical for getting patients to medical facilities, new forms of supplemental support will be needed for telehealth and hybrid models. Similarly, assessments of the downstream effects of task shifting and collocating of PrEP services are needed alongside creative solutions so that these promising approaches can be deployed successfully to promote PrEP without overburdening already-strained systems or disrupting the established benefits of primary care.

It should be noted that the highlighted implementation strategies are not mutually exclusive—task shifting PrEP delivery to pharmacists also changes the delivery location of PrEP, navigation services can be delivered via telehealth, and integrating PrEP services within related clinical service lines may expand the scope of work and require revisions to roles and responsibilities of existing staff. Furthermore, strategies that target a structural or system-level determinant of PrEP use do not exist in isolation of the individual: the behaviors, perspectives, and perceptions of individuals are all part of the implementation context and climate. Implementation strategies that embrace and address the inherent complexities and interconnectedness of individuals, systems, and policies are crucial to identify and eventually overcome persistent barriers to PrEP use in the USA, and implementation science methods are ideally situated to measure these needs and monitor progress.

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Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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