Published in final edited form as:

Curr Opin HIV AIDS. 2015 July ; 10(4): 290–295. doi:10.1097/COH.0000000000000159.

Planning ahead for implementation of long acting HIV prevention: challenges and opportunities

Kathrine Meyers, DrPH, MPP and
Aaron Diamond AIDS Research Center

Sarit A. Golub, PhD, MPH

Professor, Department of Psychology, Hunter HIV/AIDS Research Team (HART), Hunter College of the City University of New York, Chair/Area Head, Basic and Applied Social Psychology PhD Program, CUNY Graduate Center, 695 Park Avenue, New York, NY 10065, 212.396.6304

Sarit A. Golub: sgolub@hunter.cuny.edu

Abstract

Purpose of Review—Broad-based access, uptake, and dissemination of daily oral HIV pre-exposure prophylaxis (PrEP) have been slow, despite strong evidence for efficacy. Effective and efficient implementation of long-acting (LA) HIV prevention products will require both analysis of the dynamics and determinants of daily oral PrEP implementation and identification of the distinct challenges and opportunities inherent in emerging technologies.

Recent Findings—Evidence suggests the importance of addressing implementation issues at three levels: patient, provider, and system. Patient-level factors include targeted education and messaging, tailored supports to enhance acceptability and uptake, and effective strategies for promoting adherence/persistence and retention in care. Provider-level factors include engaging a broad mix of providers, while ensuring adequate training and support for patient assessment, counseling, and follow-up. Systems-level factors include optimal delivery modalities, resource allocation, and ensuring access to populations most in need of new prevention options.

Summary—Formative social/behavioral research must be undertaken proactively in order to prepare for and address future implementation challenges and reduce the gap between proving efficacy in clinical trials and assuring real-world effectiveness. Conceptualizing new HIV prevention technologies as behavioral interventions at the level of the patient, provider, and system will be paramount to effective and efficient implementation.

Keywords

HIV prevention; Pre-exposure prophylaxis; long-acting antiretrovirals; implementation; sociobehavioral research

Correspondence to: Sarit A. Golub, sgolub@hunter.cuny.edu.

Conflicts of interest: There are no conflicts of interest.

Introduction

Implementation of daily oral pre-exposure prophylaxis (PrEP) is a critical case study illustrating the gap between proving efficacy in clinical trials and achieving real-world effectiveness. More than two and a half years after FDA approval of Truvada for daily oral PrEP, broad-based implementation and access remain low, with PrEP available largely in the context of open-label extensions or demonstration projects.(1, 2) As long-acting (LA) HIV prevention products move along the development pipeline, effective implementation will require understanding the dynamics and determinants of past experiences with oral PrEP, while also identifying new challenges inherent to emerging technologies. There is growing acknowledgement of biomedical prevention as inherently behavioral, and of the need to understand social/behavioral variables in efficacy trials.(3–5) However, this understanding of behavioral influences is usually confined to a discussion of *patient-level* factors in acceptability, adoption, adherence, and persistence. This review extends the conceptualization of behavioral factors in biomedical prevention to include provider behavior and the ways with both patient and provider behaviors are shaped by health care systems. Only by identifying barriers and opportunities to behavior at these three levels simultaneously – patient, provider, and system -- will we be able to pave the way for efficient transition between efficacy and implementation of LA prevention products.

Patient-Level Challenges and Opportunities

Perhaps the most exciting factor in the development of new LA HIV prevention products – including both injectable formulations and intravaginal rings – is their ushering in of a new era of user choice. Family planning research has shown that expanding the method mix has been a key factor associated with increasing contraceptive uptake and use over time, (6) as different product profiles appeal to different individuals and individual preferences may change over the reproductive life course. Similarly, we might expect that an increase in the PrEP-method mix would result in greater acceptability and uptake, as users have a range of options and can choose one that best fits their overall and “seasonal” HIV prevention needs. (7)

However, the creation of new options requires complex and nuanced patient education to ensure that these options are truly accessible. In 2015 PrEP knowledge remains low, especially among the populations at greatest risk for infection (8–10) in the US and globally. Developing optimal messaging strategies for LA formulations will be paramount, as oral PrEP uptake appeared to suffer from its association with a medication that was known to treat HIV-infected individuals. (11) Marketing of LA injectable PrEP must be creative, and perhaps veer away from the biomedical term “PrEP” to something more comprehensible to target users. Research into target population lifestyles, values, and motivations should inform messaging and packaging. Educational materials will need to be tailored for low-literacy settings, and contexts in which access to health care is scarce. Messaging for men and women will need to differ, as will messaging tailored to different contexts. Long-acting agents will need to be described in different terms for individuals in serodiscordant relationships as compared to single people. Regardless of population, social-behavioral

research suggests that effective messaging will focus on empowerment, intimacy, and sexual health, rather than risk, mistrust, and fear. (12, 13)

In addition, the availability of new prevention alternatives underscores the importance of attending to modality-specific factors in patient-level acceptability. For example, research on PrEP acceptability and adherence suggest a critical role of subjective risk *perception* in determining uptake and adherence. (14, 15) In many cases, patients' subjective risk perceptions do not match more objective behavioral assessments of their behavior, but still determine PrEP-related attitudes and behavior. Long-acting agents may not be attractive to patients who perceive their own risk for HIV to be low, as they may believe that a product that remains active in the body for months is not necessary for their own level of risk. Similarly, long-acting injectable formulations will not be the right choice for those who have a phobia of needles, (16) who report high perceived-sensitivity to medication, (17) who are particularly concerned about side effects, or who object to a long-acting agent that cannot be extracted or "turned off" in their bodies. Intravaginal ring users must be comfortable with the process of insertion and removal, and must be willing to accept the possibility of the ring being felt by a partner or becoming dislodged during intercourse.(18, 19)

On the other hand, long-acting agents might be a particularly good fit for patients with disclosure concerns, who would benefit from having a shot administered in the privacy of a doctor's office, without needing to store medication on their person or in their home.(16) Similarly, intravaginal rings may be inserted at home without the knowledge of a sexual partner. As such, LA products may be of particular interest to men and women who have little control over how and when sex takes place. (16) They may also be useful for people whose lives are chaotic or unpredictable in ways that could make the use of a daily oral medication more challenging. Although many of these factors appear obvious in the abstract, the challenge of applying them to specific instances of patient-driven decision-making should not be underestimated. In order to truly engage and sustain patients on LA ARV prevention, it will be critical for providers to understand individuals' motivations for choosing to protect themselves with ARV prevention. They will need to elicit enough about the context and structure of patients' lives to best advise them on the most appropriate choice of product, recognize when and why a product is not working, and support discontinuation or product-switching processes.

Bridging the gap between efficacy and effectiveness for LA agents will require significant buy-in from populations who are at highest risk for HIV infection but are often under-represented in randomized controlled trials. Adolescents and emerging adults, transgender individuals, people who inject drugs, and those who engage in sex work may benefit most from LA formulations, but are rarely engaged in formative or efficacy research in significant numbers. Effective LA implementation will require answers to three critical questions: a) are there biological or pharmacokinetic reasons to believe that LA agents might work differently for these populations (e.g., because of developmental factors, use of hormones, drug interactions) and how might we address those differences in product development and testing; b) what are the social or psychological reasons why LA agents might "operate" differently for these populations, and what specific supports might our most vulnerable patients require; and c) how will highly vulnerable individuals and groups perceive LA trial

results if they have not been included, and how will this influence future uptake. At present, PrEP uptake has been delayed among these populations because formative research was not undertaken to ensure they would be effectively engaged. (20, 21)

Finally, patient-level adherence behavior is a key factor in daily oral PrEP efficacy,(22) but is significantly altered in the context of LA formulations. The contraceptive field distinguishes between user-dependent (e.g., pill, condom) and provider-dependent (e.g., injectables, IUDs) methods, indicating a significant reduction in failure rates among provider-dependent methods because they are less susceptible to adherence differences between “perfect use” and “typical” use (23, 24). In the context of LA agents, adherence may be operationalized as “retention in care,” and will not depend on day-to-day behavior, but on navigation of health care systems and related contexts. Factors associated with successful retention in care among diverse target populations in different contexts will need to be identified in order to design appropriate messages and persistence-support strategies.

Provider-Level Challenges and Opportunities

As discussed above, one of the key benefits to LA formulations are their characterization as “provider-dependent” methods, which are less susceptible to patient-based adherence challenges. At the same time, such methods are particularly dependent on the extent to which they are embraced by prescribing providers and offered to the patients who need them most. In implementation of daily oral PrEP, adoption by providers has been slowed in part by what has been termed the “purview paradox,” in which HIV specialists believe that HIV prevention is the purview of primary care, while primary care providers believe that ARV prescription is the purview of HIV specialists. The main lessons from this paradox are four-fold.

First, the line between HIV prevention and care is continuing to blur, as are the lines between HIV-specific care and primary care that manages HIV as a chronic condition. This blurring of boundaries represents an opportunity to re-structure patient-focused care, re-imagining traditional boundaries in ways that may reduce HIV-specific stigma or exceptionalism. At the same time, such restructuring is bound to face tremendous challenges that must be addressed at the systems-level (see below) before they can be addressed by individual providers or in clinical settings. Lessons from countries in Africa that adopted WHO-recommended task-shifting from physicians to nurses and community-health workers to manage the scale up of ARV treatment could be usefully applied. (25)

Second, it is critical to engage and educate a broad array of providers and specialties in ARV prevention, in order to ensure patient access at a variety of entry points. Some patients may be willing to access ARVs for prevention only through a primary care provider, and might be unwilling to engage in care through an HIV-specific health care setting because of concerns about associated stigma. Other patients may want to seek sexual health care in a setting separate from their primary care, and would be interested in a “prevention-specific” practice to receive ARVs, and HIV/STI testing, or in the case of women, integrated into reproductive health services.

Third, we must acknowledge the extent to which providers continue to struggle with sexual health conversations with their patients. Prescribing ARVs for prevention requires more than knowledge of the medications and their potential side effects; it requires the ability to competently take a sexual history, and identify patients who might benefit from particular biomedical and/or behavioral strategies. Most providers receive little if any training in these types of conversations and assessment, and many report concerns about their ability to effectively discuss such issues with their patients.(26, 27) Even those providers who are comfortable discussing sexual health with their patients face barriers such as limited time with patients with multiple competing needs, or financial pressures that prevent adequate billing for prevention conversations.

And fourth, many providers may struggle with implicit prejudices that impact their willingness to prescribe LA ARVs for prevention. Daily oral PrEP acceptability among providers is directly related to PrEP knowledge, (28) but even among providers who report being willing to prescribe PrEP, few actually have. (29) Providers report being most comfortable prescribing PrEP to serodiscordant couples, (30, 31) which may indicate an underlying bias towards the acceptability of condomless sex in the context of a committed relationship, even though data on treatment as prevention suggests that partners of virally-suppressed individuals are not the highest priority PrEP candidates. (32, 33) In one study, when the race of the patient was experimentally manipulated, providers rated black patients as more likely to engage in risk compensation, and were therefore less likely to prescribe them PrEP. (34) Moving forward toward equity and access of LA agents to populations most vulnerable to infection will require considerations of similar implicit biases and the development of practice guidelines that help public health professionals to overcome them.

Systems-Level Opportunities and Challenges

Many of the provider-level challenges noted above have systems-level counterparts; the organization of the health care system will play a tremendous role in how LA agents are implemented across different settings. As mentioned above, LA formulations could be delivered in a variety of health care settings, and consideration should be given to the potential use of mobile medical units (MMUs). MMUs may be particularly effective for providing LA PrEP in rural areas or communities in which mobile units are already delivering other preventive health care services such as HIV/STI screening or clean needle exchanges. Mobile clinics in Kenya and Malawi have been effective in delivering healthcare services, including HIV treatment, to remote populations and could be leveraged for delivering PrEP (35, 36); however adequate consideration would need to be given to the logistics of collecting and storing blood for lab tests to measure kidney and liver function. One of the most important implementation issues will be the added burden of patient visits on the health care system. Current clinical guidelines for ARV prevention require HIV testing every 3 months and STI and creatinine screening every 6 months; for every 50 patients placed on PrEP, a clinical setting would have to accommodate an additional 200 visits by otherwise healthy individuals each year. Scaling up PrEP modalities of all kinds will require innovative strategies to deal with this visit burden, including the potential for home-based HIV/STI testing. At the same time, popularity of LA agents might increase the number of high-risk individuals who test for HIV and other STIs regularly, and may increase

engagement in primary care among young, healthy individuals who might not otherwise seek out a medical provider.

Similar to systems-level issues related to implementation of daily oral PrEP, LA formulations for prevention will be subject to concerns about the “zero-sum” nature of health care delivery and resources. As has happened with daily oral PrEP, advocacy for LA ARVs for prevention may be pitted against advocacy for increased availability of treatment, especially in resource-poor settings. It is critical that LA product availability not lead us to recapitulate historical tensions between treatment and prevention, but rather allow us to highlight the connections between these two goals and the extent to which the populations reached by both services represent individuals at different stages of the care continuum.

Difficult decisions will need to be made regarding the prioritization of LA PrEP for key populations and how the constellation of PrEP products will be allocated and funded. It will be important to funnel resources toward populations at highest risk without being paternalistic in pushing LA agents or biomedical modalities more broadly. When combination ARV treatment first became available, certain populations were deemed “unsuitable” for treatment because of adherence concerns. Similar beliefs may cause these same populations to be targeted for LA formulations, with or without their full consideration or input. In the contraceptive field, a skewed method mix can simply be an indicator of social / cultural preferences, or signify a lack of choice, or provider bias. (37) Once several efficacious biomedical prevention modalities are approved, method mix in the HIV prevention field will need to be measured and a skew in the mix must be evaluated in order to ensure that it is not a reflection of compromised user choice or a paternalistic system imposing specific modalities on specific populations. In the US, young men of color who have sex with men may feel that ARV medication is being foisted upon them as a biomedical palliative to underlying dynamics of racism and classism that fuel disproportionate incidence rates in their communities.

Conclusions

Considerations of implementation challenges often raise more questions than they answer, as the complexities of real-world engagement, delivery, and retention shed light on inherent inequities and limitations of existing practice models. The review above suggests several key recommendations for proactive implementation work as LA formulations move forward in development. First, efficacy trials of LA agents should integrate psychosocial and behavioral variables likely to influence later adoption and implementation. Budgets for biomedical prevention trials should include appropriate funding for social and behavioral components so that this work is considered central to the research endeavor. Second, social science research critical to understanding the political, economic, and social contexts, as well as the health care systems in which ARV prevention interventions may be provided, should be conducted in parallel to efficacy trials in order to inform implementation planning. Third, preparatory research and education should be conducted with providers who are likely to prescribe LA agents. Consideration should be given to the importance of engaging providers from a variety of practice settings – primary care, sexual and reproductive health, harm reduction/substance use, adolescent medicine, etc. Finally, education and marketing of

emerging LA agents should not be conceived based on a public health sensibility, but should be conducted to maximize interest and acceptability among populations most vulnerable to new infections. Conceptualizing new HIV prevention technologies as behavioral interventions at the level of the patient, provider, and system will be paramount to effective and efficient implementation with the potential for the greatest impact on the epidemic.

Acknowledgments

The authors gratefully acknowledge Amy Hilley, Dr Asa Radix, Dr Julie Myers, and Dr David Greenberg for conversations that informed this article.

Financial support and sponsorship: Dr Golub receives funding for PrEP implementation research from the National Institute on Alcohol Abuse and Alcoholism (R01AA022067; Golub, PI). Both Drs Golub and Meyers receive funding for LAI PrEP implementation research through the National Institute of Mental Health (R01MH105269; Golub, PI). The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Krakower DS, Jain S, Mayer KH. Antiretrovirals for Primary HIV Prevention: the Current Status of Pre- and Post-exposure Prophylaxis. *Current HIV/AIDS reports*. 2015
- 2*. Burns DN, Grossman C, Turpin J, Elharrar V, Veronese F. Role of oral pre-exposure prophylaxis (PrEP) in current and future HIV prevention strategies. *Current HIV/AIDS reports*. 2014; 11(4): 393–403. The paper reports on the slow uptake of oral PrEP, identifies important barriers to uptake and provides concrete suggestions on how to overcome such barriers. [PubMed: 25283184]
3. Kippax S, Stephenson N. Beyond the distinction between biomedical and social dimensions of HIV prevention through the lens of a social public health. *American journal of public health*. 2012; 102(5):789–99. [PubMed: 22493997]
4. Koblin BA, Andrasik M, Austin J. Preparing for the unexpected: the pivotal role of social and behavioral sciences in trials of biomedical HIV prevention interventions. *J Acquir Immune Defic Syndr*. 2013; 63(Suppl 2):S183–6. [PubMed: 23764634]
5. van der Straten A, Van Damme L, Haberer JE, Bangsberg DR. Unraveling the divergent results of pre-exposure prophylaxis trials for HIV prevention. *AIDS (London, England)*. 2012; 26(7):F13–9.
6. Ross J, Stover J. Use of modern contraception increases when more methods become available: analysis of evidence from 1982–2009. *Global health, science and practice*. 2013; 1(2):203–12.
7. Baeten JM, Haberer JE, Liu AY, Sista N. Preexposure prophylaxis for HIV prevention: where have we been and where are we going? *J Acquir Immune Defic Syndr*. 2013; 63(Suppl 2):S122–9. [PubMed: 23764623]
- 8*. Auerbach JD, Kinsky S, Brown G, Charles V. Knowledge, Attitudes, and Likelihood of Pre-Exposure Prophylaxis (PrEP) Use Among US Women at Risk of Acquiring HIV. *AIDS patient care and STDs*. 2014 This study reports on data collected by focus groups among high-risk women in the US. The women reported low levels of knowledge about PrEP, but high degree of interest if cost and side effects are minimal.
9. Ayala G, Makofane K, Santos G-M, Beck J, Do TD, Hebert P, et al. Access to Basic HIV-Related Services and PrEP Acceptability among Men Who Have sex with Men Worldwide: Barriers, Facilitators, and Implications for Combination Prevention. *Journal of Sexually Transmitted Diseases*. 2013; 2013:11.
10. Kubicek K, Arauz-Cuadra C, Kipke MD. Attitudes and Perceptions of Biomedical HIV Prevention Methods: Voices from Young Men Who Have Sex with Men. *Archives of sexual behavior*. 2015; 44(2):487–97. The paper reports on attitudes of young MSM of color towards oral PrEP and rectal microbicides. The young MSM of color in this study had positive reactions to both oral PrEP and rectal microbicides, however express concern about challenges with adherence, cost, and side effects. [PubMed: 25633499]

11. Smith DK, Toledo L, Smith DJ, Adams MA, Rothenberg R. Attitudes and program preferences of African-American urban young adults about pre-exposure prophylaxis (PrEP). *AIDS education and prevention : official publication of the International Society for AIDS Education*. 2012; 24(5): 408–21. [PubMed: 23016502]
12. Gallagher KM, Updegraff JA. Health message framing effects on attitudes, intentions, and behavior: a meta-analytic review. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine*. 2012; 43(1):101–16. [PubMed: 21993844]
- 13*. Golub SA. Tensions between the epidemiology and psychology of HIV risk: implications for pre-exposure prophylaxis. *AIDS and behavior*. 2014; 18(9):1686–93. The paper calls attention to the psychological differences that motivate patterns of unprotected intercourse and urges the field to take these differences into account when designing and tailoring HIV prevention and PrEP messaging to target users. [PubMed: 24719201]
14. Khawcharoenporn T, Kendrick S, Smith K. HIV risk perception and preexposure prophylaxis interest among a heterosexual population visiting a sexually transmitted infection clinic. *AIDS patient care and STDs*. 2012; 26(4):222–33. [PubMed: 22404427]
- 15*. Young I, McDaid L. How acceptable are antiretrovirals for the prevention of sexually transmitted HIV?: A review of research on the acceptability of oral pre-exposure prophylaxis and treatment as prevention. *AIDS and behavior*. 2014; 18(2):195–216. This review of the TasP and PrEP acceptability literature revealed very few articles on TasP, and a PrEP acceptability literature highly skewed towards MSM in the US context. The authors further noted that “acceptability” was inconsistently defined across studies and urged for elaborations of acceptability that also considered the influences of social and structural factors. [PubMed: 23897125]
16. Mack N, Evens EM, Tolley EE, Brelsford K, Mackenzie C, Milford C, et al. The importance of choice in the rollout of ARV-based prevention to user groups in Kenya and South Africa: a qualitative study. *Journal of the International AIDS Society*. 2014; 17(3 Suppl 2):19157. [PubMed: 25224616]
17. Horne R, Faasse K, Cooper V, Diefenbach MA, Leventhal H, Leventhal E, et al. The perceived sensitivity to medicines (PSM) scale: an evaluation of validity and reliability. *British journal of health psychology*. 2013; 18(1):18–30. [PubMed: 22524270]
18. Montgomery ET, van der Straten A, Cheng H, Wegner L, Masenga G, von Mollendorf C, et al. Vaginal ring adherence in sub-Saharan Africa: expulsion, removal, and perfect use. *AIDS and behavior*. 2012; 16(7):1787–98. [PubMed: 22790902]
- 19*. MacQueen KM, Tolley EE, Owen DH, Amico KR, Morrow KM, Moench T, et al. An interdisciplinary framework for measuring and supporting adherence in HIV prevention trials of ARV-based vaginal rings. *Journal of the International AIDS Society*. 2014; 17(3 Suppl 2):19158. This paper posits adherence as a behavior emerging from the social context of the user and proposes a three-pronged approach for measuring and supporting adherence in the context of vaginal ring trials. These include: 1) development and evaluation of ongoing adherence support methods; 2) creation of self-reported psychometric measures, and 3) identification of more objective measurement of adherence. [PubMed: 25224617]
- 20*. Escudero DJ, Kerr T, Operario D, Socias ME, Sued O, Marshall BD. Inclusion of trans women in pre-exposure prophylaxis trials: a review. *AIDS care*. 2014:1–5. This study reviewed data from seven PrEP trials to reveal that transwomen comprised only 0.2% of participants overall, despite the disproportionately high risk of HIV faced by transwomen. The authors advocate for more research to assess feasibility of PrEP in this population and identify barriers unique to this population.
- 21*. Syvertsen, JL.; Bazzi, AMR.; Scheibe, A.; Adebajo, S.; Strathdee, SA.; Wechsberg, WM. African Journal of Reproductive Health: Special Edition on HIV/AIDS. 3. 2014. The promise and peril of Pre-Exposure Prophylaxis (PrEP): using social science to inform PrEP interventions among female sex workers: review article; p. 74-83. The authors articulate the important role that social science research has to play in biomedical HIV prevention, by elucidating the socio-cultural and political environments in which individuals experience HIV prevention efforts in their lives and communities
- 22**. Amico KR, Mansoor LE, Corneli A, Torjesen K, van der Straten A. Adherence support approaches in biomedical HIV prevention trials: experiences, insights and future directions from

- four multisite prevention trials. *AIDS and behavior*. 2013; 17(6):2143–55. This paper synthesizes the adherence support experiences from four pivotal PrEP trials to draw key lessons for optimizing adherence in future research and PrEP implementation. Lessons include: using patient-centered approaches, separating adherence measurement from adherence counseling, fostering motivation, developing practical strategies beyond education, and taking into account the specific individual contexts in which PrEP is used. [PubMed: 23435697]
23. Blumenthal PD, Voedisch A, Gemzell-Danielsson K. Strategies to prevent unintended pregnancy: increasing use of long-acting reversible contraception. *Human Reproduction Update*. 2011; 17(1): 121–37. [PubMed: 20634208]
 24. Trussell J, Wynn LL. Reducing unintended pregnancy in the United States. *Contraception*. 2008; 77(1):1–5. [PubMed: 18082659]
 - 25*. Iwu EN, Holzemer WL. Task shifting of HIV management from doctors to nurses in Africa: clinical outcomes and evidence on nurse self-efficacy and job satisfaction. *AIDS care*. 2014; 26(1):42–52. The authors reviewed recent articles about physician to nurse task-shifting for AIDS care in Africa and surmised that patient outcomes were comparable in all but one study; several studies reported higher retention in care and lower loss to follow up in nurse-managed groups. [PubMed: 23701374]
 26. Althof SE, Rosen RC, Perelman MA, Rubio-Aurioles E. Standard operating procedures for taking a sexual history. *The journal of sexual medicine*. 2013; 10(1):26–35. [PubMed: 22970717]
 27. Lanier Y, Castellanos T, Barrow RY, Jordan WC, Caine V, Sutton MY. Brief sexual histories and routine HIV/STD testing by medical providers. *AIDS patient care and STDs*. 2014; 28(3):113–20. [PubMed: 24564387]
 28. Tripathi A, Ogbuanu C, Monger M, Gibson JJ, Duffus WA. Preexposure prophylaxis for HIV infection: healthcare providers' knowledge, perception, and willingness to adopt future implementation in the southern US. *Southern medical journal*. 2012; 105(4):199–206. [PubMed: 22475669]
 - 29*. Karris MY, Beekmann SE, Mehta SR, Anderson CM, Polgreen PM. Are we prepped for preexposure prophylaxis (PrEP)? Provider opinions on the real-world use of PrEP in the United States and Canada. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2014; 58(5):704–12. This paper reports on a large survey of infectious disease doctors across the US to measure attitudes towards PrEP and PrEP prescription practices and reveals that great variability exists in the real-world practice of PrEP. [PubMed: 24319083]
 30. Tellalian D, Maznavi K, Bredeek UF, Hardy WD. Pre-exposure prophylaxis (PrEP) for HIV infection: results of a survey of HIV healthcare providers evaluating their knowledge, attitudes, and prescribing practices. *AIDS patient care and STDs*. 2013; 27(10):553–9. [PubMed: 24053478]
 - 31*. Spector AY, Remien RH, Tross S. PrEP in substance abuse treatment: a qualitative study of treatment provider perspectives. *Substance abuse treatment, prevention, and policy*. 2015; 10(1): 1. This is the first study to examine substance abuse providers' attitudes towards PrEP. It identified important barriers and opportunities from the standpoint of providers who will be responsible for PrEP uptake in substance abuse treatment settings.
 32. Lasry A, Sansom SL, Wolitski RJ, Green TA, Borkowf CB, Patel P, et al. HIV sexual transmission risk among serodiscordant couples: assessing the effects of combining prevention strategies. *AIDS (London, England)*. 2014; 28(10):1521–9.
 33. Lucas, A. The cost-effectiveness of targeting HIV pre-exposure prophylaxis based on partner treatment status in men who have sex with men in the US. Abstract presented at: the 36th Annual Meeting of the Society for Medical Decision Making; 2014 October 18–22; Miami, FL.
 - 34*. Calabrese SK, Earnshaw VA, Underhill K, Hansen NB, Dovidio JF. The impact of patient race on clinical decisions related to prescribing HIV pre-exposure prophylaxis (PrEP): assumptions about sexual risk compensation and implications for access. *AIDS and behavior*. 2014; 18(2):226–40. This first study to examine the potential role of provider bias on access to PrEP suggested that provider bias could result in inequitable access to PrEP across racial groups. [PubMed: 24366572]
 35. Gorman SE, Martinez JM, Olson J. An assessment of HIV treatment outcomes among utilizers of semi-mobile clinics in rural Kenya. *AIDS care*. 2014:1–4.

36. Lindgren TG, Deutsch K, Schell E, Bvumbwe A, Hart KB, Laviwa J, et al. Using mobile clinics to deliver HIV testing and other basic health services in rural Malawi. *Rural and remote health*. 2011; 11(2):1682. [PubMed: 21787108]
37. Bertrand JT, Sullivan TM, Knowles EA, Zeeshan MF, Shelton JD. Contraceptive method skew and shifts in method mix in low- and middle-income countries. *International perspectives on sexual and reproductive health*. 2014; 40(3):144–53. [PubMed: 25271650]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Key points

- The experience of daily oral PrEP implementation offers important lessons for long-acting HIV prevention products currently in clinical development.
- In order to minimize the gap between proving efficacy in trials and achieving real-world effectiveness, clinical trials of long-acting HIV prevention agents should measure psychosocial and behavioral variables likely to influence later adoption and implementation.
- Social science research critical to understanding the political, economic, and social contexts, as well as the health care systems in which ARV prevention interventions may be provided, should be funded and conducted in parallel to efficacy trials in order to inform implementation planning.
- Providers who are likely to prescribe long-acting HIV prevention agents, including not only infectious disease doctors, but those in adolescent medicine, primary care, reproductive health, and harm reduction/substance abuse, should receive training and education on these novel products as soon as efficacy is shown.
- Education and marketing of emerging LA prevention agents should be conducted to maximize interest and acceptability among populations most vulnerable to new infections.