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Advancing considerations of context in the evaluation and implementation of evidence-based biomedical HIV prevention interventions: A review of recent research

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Abstract

Purpose of review: A paradigm shift is needed in how we think about biomedical HIV prevention product effectiveness. Often, we expect randomized trial findings to be generalizable across populations and settings where products will be delivered, without consideration of key contextual drivers that could impact effectiveness. Moreover, researchers and policy-makers also generally discount products with varied effect sizes across contexts, rather than explicating the drivers of these differences and using them to inform equitable product choice and delivery. We conducted a review of the recent HIV prevention research to advance considerations of context in choices of when, why, and how to implement biomedical HIV prevention products, with a particular focus on daily oral pre-exposure prophylaxis (PrEP) and the dapivirine vaginal ring (DPV).

Recent findings: Findings across recent studies of PrEP and DPV emphasize that products that do not work well in one context might be highly desirable in another. Key contextual drivers of PrEP and DPV effectiveness, use, and implementation include population, health system, cultural, and historical factors. We recommend conceptualization, measurement, and analysis approaches to fully understand the potential impact of context on prevention product delivery. Execution of these approaches has real-world implications for HIV prevention product choice and could prevent the field from dismissing biomedical HIV prevention products based on trial findings alone.

Summary: Ending the HIV epidemic will require tailored, person-centered, and equitable approaches to design, implement, and evaluate HIV prevention products which necessitates considerations of context in ongoing research and implementation.

Keywords

HIV; context; generalizability; implementation science; prevention

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DECLARATION OF INTERESTS

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INTRODUCTION

Meeting the UNAIDS "95–95-95" HIV reduction targets will require a toolkit of effective HIV prevention modalities,[1] which until now has included one effective biomedical intervention, oral tenofovir (TFV)-based pre-exposure prophylaxis (PrEP). While oral PrEP is sufficient for some, long-acting HIV prevention interventions are also needed to curb the epidemic. Two such methods, the dapivirine vaginal ring (DVR) and cabotegravir long-acting (CAB-LA) injections, were recently found to be efficacious in preventing HIV.[2,3,4**,5**] However, while CAB-LA resulted in a 66–89% reduction in HIV acquisition compared with oral PrEP, HIV reduction estimates for the DVR were more modest (27–35%) in two trials.[2,3,4**,5**] The World Health Organization (WHO) made a conditional recommendation to offer the DVR as an additional option for women at substantial risk of HIV,[6] but the ring has yet to be approved by the United States Food & Drug Administration (FDA). The DVR developer's decision to withdraw the ring from FDA consideration in 2021 caused some to question its safety and efficacy and slowed the scale up of manufacturing, impacting ring availability and pricing.[7,8] Open-label studies have since presented findings on DVR demand, with many women preferring the ring over oral PrEP and using it with adherence after choosing the product.[9**,10**,11**] The field is now grappling with implementation questions about whether, where, and how the DVR should be delivered as an additional HIV prevention intervention.[7]

Answering questions about when and how to offer the DVR and other biomedical interventions in the pipeline will require a paradigm shift in how we think about generalizability of effectiveness estimates. Policy-makers and implementers largely focus on trial effectiveness estimates (with comparisons between this generation of biomedical interventions versus oral PrEP) to inform guidelines about intervention implementation. This focus implies that there is one true intervention effect and that we expect to see it across all settings where the intervention is implemented. This perspective is reinforced by the "Grading of Recommendations, Assessment, Development, and Evaluations" (GRADE) criteria, which penalizes interventions with inconsistent effects across contexts.[12] Often interventions with large differences in effect estimates across settings are given lower quality ratings and implemented less readily.[12]

However, contextual factors (e.g., government policies, social norms, healthcare infrastructure)[13] can influence intervention effectiveness. Rather than treating contextual differences as factors to be adjusted away in analyses or penalized for when considering "consistency" of effects, implementors could use these differences to inform decisons about when, why, and how to tailor intervention delivery. Shifting the focus to contextual differences also opens up the possibility that the true effect of an intervention like the DVR may differ by context. This review sought to advance the consideration of context in the implementation of biomedical HIV prevention interventions by providing: suggestions for specifying and analyzing contextual factors; examples of how context has been considered in oral PrEP implementation; examples of contextual factors to inform decision-making about DVR implementation; and recommendations for consideration of context in long-acting HIV prevention intervention delivery.

REVIEW OF THE LITERATURE

"Context" is a broad term which can be defined as the "scope of circumstances and characteristics" that affect implementation.[14*,15] Context is a key focus point of discussions about generalizability. Generalizability is the extent to which an effect size estimated in a study sample can be extrapolated to the broader target population from which it was drawn (Figure 1, Box A) or to a new population altogether (also known as "transportability"; Figure 1, Box B).[16,17] Research findings may range from "generalizable", when they can be broadly applied, to "context-dependent", when those from one context can only be attributed to its unique characteristics or circumstances.[18] In this revew, we grapple with how to weigh potentially "generalizable" knowledge about biomedical HIV prevention intervention effectiveness with "context-dependent" need, effectiveness, and implementation opportunities.

Specifying and analyzing contextual factors

Analysis of contextual factors is important for understanding how generalizable or context-dependent HIV prevention interventions may be. "Transportability theory" provides one framework for specifying contextual factors and explicitly accounting for contextual differences between the sample and target populations when determining the generalizability or context-dependency of effects.[16,19] In order to make claims of generalizability, researchers must clearly define the other context to which they seek to generalize and explore the extent to which their effect sizes are relevant to individuals outside of the study. Transportability theory helps us to: 1) specify the relationship between important contextual characteristics and factors related to the effectiveness and implementation of an intervention; and 2) understand how intervention effectiveness may differ between the sample population and another population to which we wish to generalize.[16,20]

"Selection diagrams" are transportability research tools that aid in specifying contextual characteristics that may influence intervention effectiveness across populations (Figure 2).[16,19,21*] These diagrams depict the relationship between the evidence-based intervention (e.g., PrEP, DVR), its clinical effect (e.g., reduced HIV incidence), and mediators of that effect (e.g., adherence). They also include "selection nodes" (represented by the **"S"** in Figure 2), which indicate where there may be differences between study and target populations. For example, the placement of the selection nodes in Figure 2 implies that the study and target populations have contextual covariates (e.g., demographics, geography) that lead to different levels of effectiveness and adherence. Measuring the covariates represented by the selection nodes allows us to quantify the extent to which our clinical effects are generalizable.

However, the selection diagram shown in Figure 2 is insufficient to make claims about the generalizability of evidence-based HIV prevention interventions effects across real-world delivery settings because it does not account for upstream implementation factors. Implementation strategies (the approaches to deliver interventions) and their mechanisms of action have an important influence on the use and effectiveness of biomedical HIV interventions outside of trial settings (Figure 3).[22,23] Specifying and analyzing these covariates in both study and target populations could bridge the gap between context-

dependent and generalizable knowledge.[22] By quantifying how context-specific factors influence intervention effectiveness, use, and implementation, we can be explicit about generalizability *given* a set of contextual characteristics and guide decision-making about which implementation strategies are likely to maximize intervention effectiveness for certain contexts.

Considerations of context in oral TFV-based PrEP research

The field of oral TFV-based PrEP research, which has moved from randomized trials, to evaluations of adherence support approaches, to community implementation, offers insights into contextual factors that may influence HIV prevention intervention effectiveness (Table 1). Many oral PrEP studies have considered the influence of context (typically population demographics, sexual behavior, or HIV prevalence) on intervention use and subsequent effectiveness.[24,25] A subset of PrEP studies have also explored contextual factors associated with implementation strategies and their mechanisms.[26,27*]

The first trials of daily oral PrEP efficacy were conducted from 2010–2012 among HIV serodiscordant couples, men who have sex with men (MSM), transgender women (TGW), and women and reported a relative reduction in HIV incidence between 44–86% among intervention groups compared to controls.[28–33] Following efficacy trials, demonstration projects conducted from 2012–2015 continued to show success, resulting in the release of the WHO's PrEP guidelines in 2015 and the launch of PrEP delivery initiatives around the world thereafter.[34–40] Since that time, a small proportion of PrEP users have reported breakthrough infections, supporting trial findings of high efficacy when PrEP is taken regularly.[41–43] Despite these positive findings, trials of PrEP conducted among sub-Saharan African women showed lower efficacy than others, which led to a number of secondary analyses to disentangle reasons for contextual differences.[44,45]

Analyses accounting for non-adherence in the trial populations consistently found that higher adherence was associated with higher PrEP efficacy, indicating that women may not have been able to take PrEP with as much regularity as men.[24,25] Other work stratifying PrEP efficacy and HIV incidence by sexual behavior and gender found that PrEP efficacy was similar among high-risk women and men (but lower for low-risk women).[46] Together, these findings suggest that gender, HIV risk perceptions, sexual behavior, and background HIV incidence are all contextual factors that differentially influenced the generalizability of PrEP effectiveness. In addition, qualitative studies have highlighted the importance of trust in medical and research systems and familiarity with PrEP as other contextual factors influencing PrEP use.[47,48]

For considerations of daily oral PrEP among MSM, transportability analyses have been used to extrapolate findings from randomized trials to new populations.[21*] For example, a recent manuscript found that by accounting for differences in gender identity, condomless receptive anal intercourse, and primary sexual role (top, bottom, versatile), we can transport estimates from the iPrEx trial on PrEP effectiveness conducted in six countries in North and South America, Asia, and Africa to population subgroups in San Francisco and Chicago.[21*]

In addition to daily TFV-based PrEP regimens, the WHO now also recommends event-driven PrEP dosing around the time of sex for MSM based on results from IPERGAY and Prevenir trials.[29,49*] However, the HPTN 067 study had mixed findings on the effectiveness of event-driven dosing across Bangkok, Harlem, and Cape Town (Table 1).[37,38] Contextual factors, including employment, financial security, gender norms, and relationship power dynamics, may have driven some observed differences in effectiveness across contexts, with women randomized to the event-driven arm in the Cape Town cohort reporting difficulty predicting when they would have sex and need PrEP.[37,38]

Behavioral PrEP adherence support approaches have also produced varied effects across contexts, including LifeSteps counseling, SMS messaging, and counseling based on drug levels in pharmacologic samples (Table 1). For example, two-way SMS messages resulted in significant PrEP adherence improvements among MSM in the United States but had no effect on adherence among AGYW in South Africa and Kenya.[50–52] Qualitative work since found that factors influencing the generalizability of these SMS interventions include appropriateness of message content and frequency, technological literacy, and consistency of access to a personal phone with airtime.[51*]

Community-based PrEP delivery approaches include multicomponent implementation strategies, such as community-based provision of PrEP as part of an integrated package of sexual health services and telemedicine visits for PrEP initiation and refills. Contextual factors associated with program implementation, PrEP adherence, and HIV outcomes include: community stigma around PrEP; home structures (and privacy and PrEP storage locations); urbanicity; and regulations about who can provide PrEP (Table 1). These factors not only affect generalizability of PrEP effectiveness across community-based settings, they also impact choice of community sensitization or recruitment strategies needed to launch these programs.

Moving from DVR trials to implementation with context in mind

The DVR offers a more recent example of how contextual factors have influenced product effectiveness, use, and implementation (Figure 4). Randomized trials and open-label extension studies have identified population-level demographics—including background HIV incidence, age composition, proportion of the population engaging in anal sex, and housing status—as factors associated with ring adherence and effectiveness across populations.[2,10**,53–56]

More recently, open-label ring studies and qualitative sub-studies have begun to explore the acceptability, feasibility, and effectiveness of a variety of DVR implementation strategies. Implementation strategies include client-centered counseling with supervision and fidelity monitoring; DVR alongside a package of clinic-based HIV and STI servces; and DVR delivery in adolescent-friendly settings with peer support interventions (see Figure 4 for strategies and their mechanisms of action).[10**,53,57–60] Although this work is still nascent, it remind us of the ways in which contextual factors and implementation decisions can impact DVR use and effectiveness.[61]

Product choice is another key driver of DVR adherence and effectiveness and recent research has begun to describe the influence of healthcare system, cultural, and historical factors on product choice (Figure 4). Healthcare system factors include provider training on DVR, availability of other HIV prevention tools, and regulations about who can deliver the ring. Cultural factors include norms around sexual decision-making and stigma around the DVR. Historical factors include trust in the medical system and legacies of colonialism. To restrict DVR access based on trials alone would discount the role these factors play in DVR choice and use.

Recommendations for considering context in biomedical HIV prevention intervention delivery

Based on findings from the oral PrEP and DVR literature, we offer recommendations for considering context in the testing and implementation of biomedical HIV prevention interventions. We organized our recommendations according to the Dynamic Sustainability Framework,[62] which emphasizes that interventions and implementation programs are situated within a broader context and that both the intervention and the context can shift dynamically over time (Figure 5). These recommendations are intended to support initiatives around differentiated oral PrEP delivery, DVR roll-out, and programs to support choice for long-acting HIV prevention options in the research pipeline. They can also guide thinking about contextual factors early in trial design as new HIV prevention products are developed. We have divided recommendations between those related to the biomedical HIV prevention intervention and those related to considerations of the context around the intervention. Underpinning both sets is a call for advocacy for funders, policy makers, researchers, and implementers to adopt new considerations of context in HIV prevention product decision-making.[14*]

Recommendations related to the biomedical HIV intervention: First, it is important for researchers testing new interventions to clearly clearly define the target outcome (e.g., HIV incidence, coverage of sex events), which has implications for potential generalizability. It is also critical that HIV prevention intervention delivery be informed by a health equity lens. Researchers could incorporate equity-focused metrics (e.g., the “PrEP-to-Need” ratio)[63] that center success around considerations of power imbalances and resource distribution across a population. Implementation strategies related to who will deliver the intervention (e.g., nurse, peer), how they will be trained (e.g., collaborative care model), and where it will be delivered (e.g., community-based setting) should also be clearly specified to contexualize effect estimates. Finally, aspects of the intervention and its implementation will likely change from one context to another, which necessitates documentation of all adaptations made at the outset and over time as the population, its needs, and its familiarity with the intervention changes.

Recommendations related to the population, practice, and ecological setting: Researchers and prospective implementers must identify the broad array of contextual factors that could influence the intervention and its implementation, use, and effectiveness. While the HIV prevention literature and prior data offer useful starting points, participatory approaches are needed to ground contextual considerations in the

perspectives of local stakeholders.[14] Prior HIV prevention studies have measured population demographic and healthcare variables as contextual factors, but few have explicitly assessed social and structural determinants that drive inequities in HIV outcomes, such as structural racism, systems of oppression and colonialism, and historical mistrust in research and medical systems.[13] Selection diagrams may be useful tools for formalizing how contextual factors influence HIV intervention implementation, use, and effectiveness.

We found that many PrEP and DVR studies made broad statements about generalizability with little underlying evidence, and few defined how and when they measured contextual factors. Future studies could address this gap with clear descriptions of contextual factors, how and when they were measured, and how data were analyzed to advance understandings of generalizability. Contextual factors are complex and change dynamically over time.[14*] We recommend that researchers and implementers revisit these recommendations throughout a study or program to modify measurement and analysis approaches as needed.

CONCLUSION

HIV researchers, policy-makers, funders, and implementers are at risk of shelving biomedical HIV prevention interventions based on efficacy estimates from trials that compare new products to daily oral PrEP. However, considerations of context can provide a more nuanced view about how intervention need and choice vary across settings and may reveal that an intervention that did not work well in one context is highly desired and effective in another when delivered differently. The DVR provides one instructive example of this, with early trials having lower efficacy estimates than open-label studies using implementation strategies focused on client choice and empowerment.

Recent oral PrEP projects provide a larger body of evidence on how contextual factors can influence PrEP delivery, use, and effectiveness and how they can be measured across study populations. Considerations of context are also important when making decisions about packaging biomedical HIV prevention interventions together. For example, one recent mathematical modeling study found that the optimal, cost-effective intervention package differs based on contextual factors like geography, population characteristics, and HIV transmission dynamics.[64*] By explicitly and thoughtfully incorporating contextual factors into our work, we can begin to strategically leverage inconsistencies across settings to improve our understanding of whether and where to implement biomedical HIV prevention interventions.

Ultimately, how we deal with differences in intervention effects across contexts has real-world implications for biomedical HIV prevention intervention choices and health equity. Before implementing any intervention, we must first ask, “For whom, in what settings, and under what delivery conditions is this intervention effective?” By focusing on understanding and parsing out, rather than adjusting away, drivers of effect heterogeneity, we can also offer equity-based approaches to biomedical HIV prevention intervention delivery and scale-up. Ending the HIV epidemic will require tailored approaches that explicitly acknowledge how contextual factors play a role in the effective delivery of evidence-based HIV prevention interventions.

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SUMMARY

- We conducted a review of the recent HIV prevention research to advance considerations of context in the implementation of biomedical HIV prevention products.
- We found that HIV prevention products (e.g., daily oral pre-exposure prophlyaxis and the dapivirine vaginal ring) that do not work well in one context might be highly desirable in another.
- This emphasizes the need to conceptualize, measure, and analyze the potential impact of context (e.g., population, health system, cultural factors) on product delivery to prevent dismissal of new HIV prevention products on trial findings alone.
- Considerations of context in ongoing HIV research and implementation will help us design and implement person-centered and equitable prevention products that can move us closer to ending the HIV epidemic.

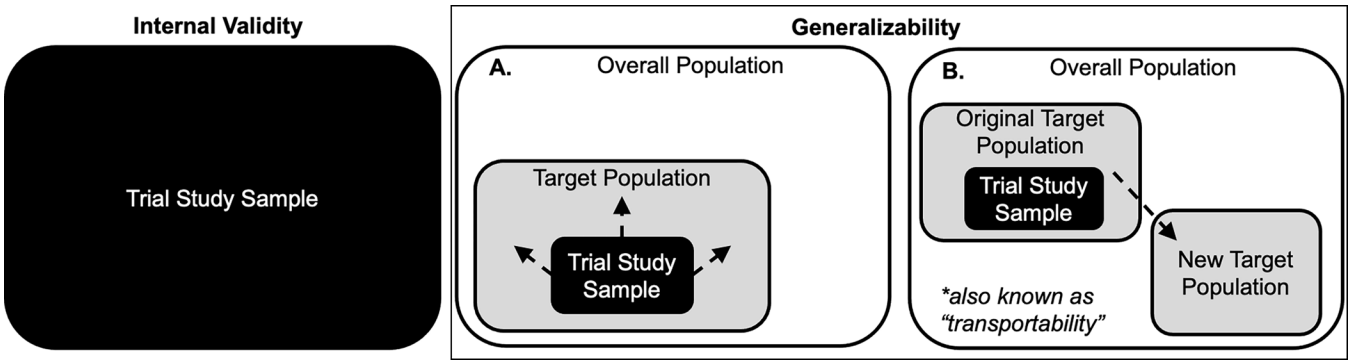

Figure 1.
Generalizability of intervention effects

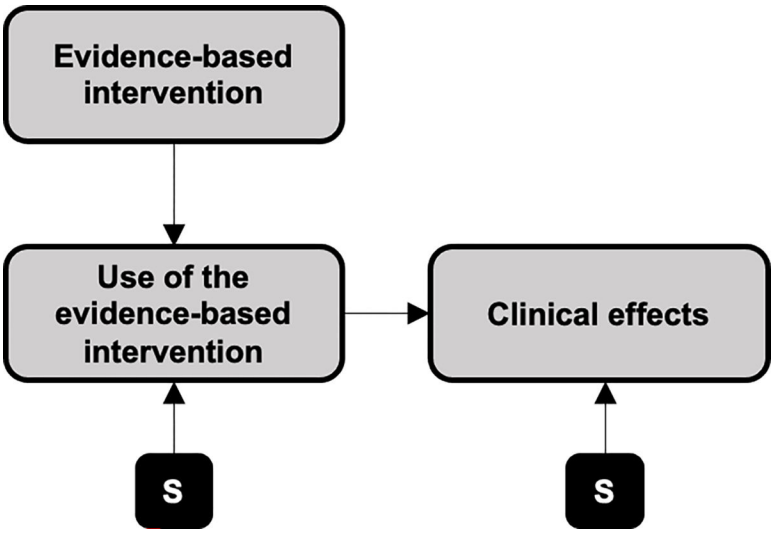

Figure 2.

Selection diagram depicting the role of context in intervention use and effect estimates "S" represents "selection node". In this example, the selection nodes on the mediator and outcome imply that these two factors differ between the study population and the target population.

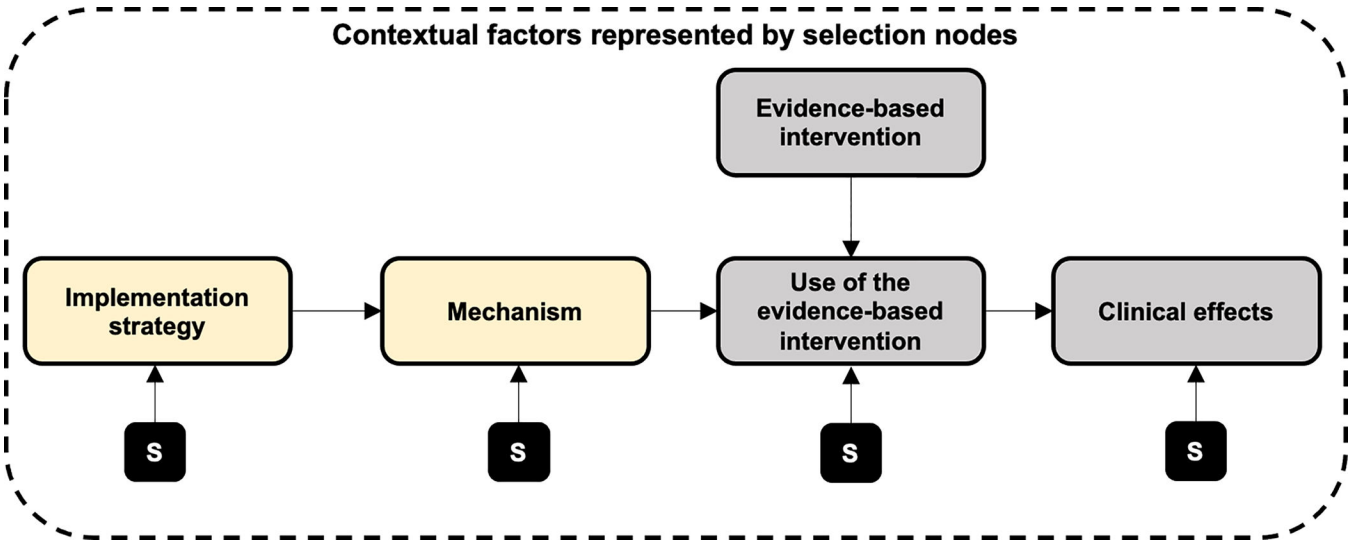

Figure 3.

Selection diagram depicting the role of context in intervention implementation, use, and effect estimates

"S" represents "selection node". In this example, the selection nodes on the implementation strategy, mechanism, use of evidence-based intervention, and clinical effects imply that these four factors differ between the study population and the target population. It is insufficient to consider covariates that differ for the use of the evidence-based intervention and the clinical effects alone, as this does not account for more upstream contextual differences between populations.

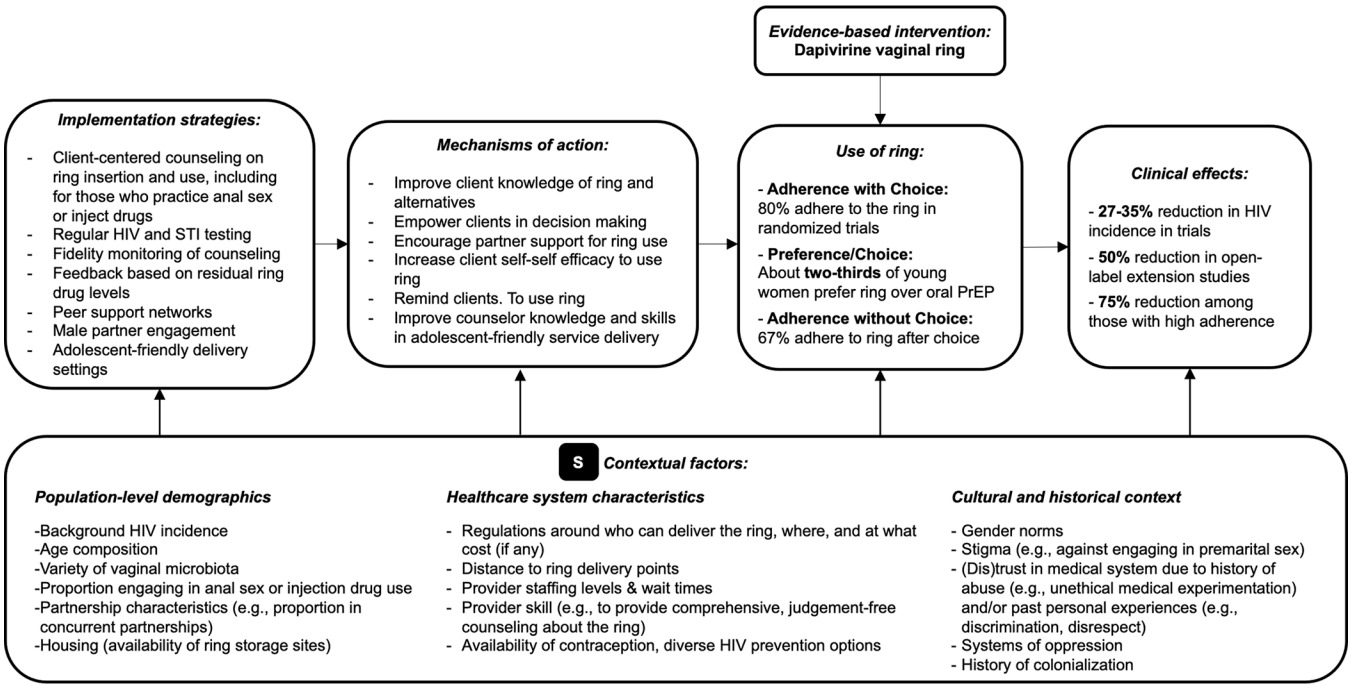

Figure 4.

Potential contextual factors influencing dapivirine vaginal ring delivery, use, and effect estimates

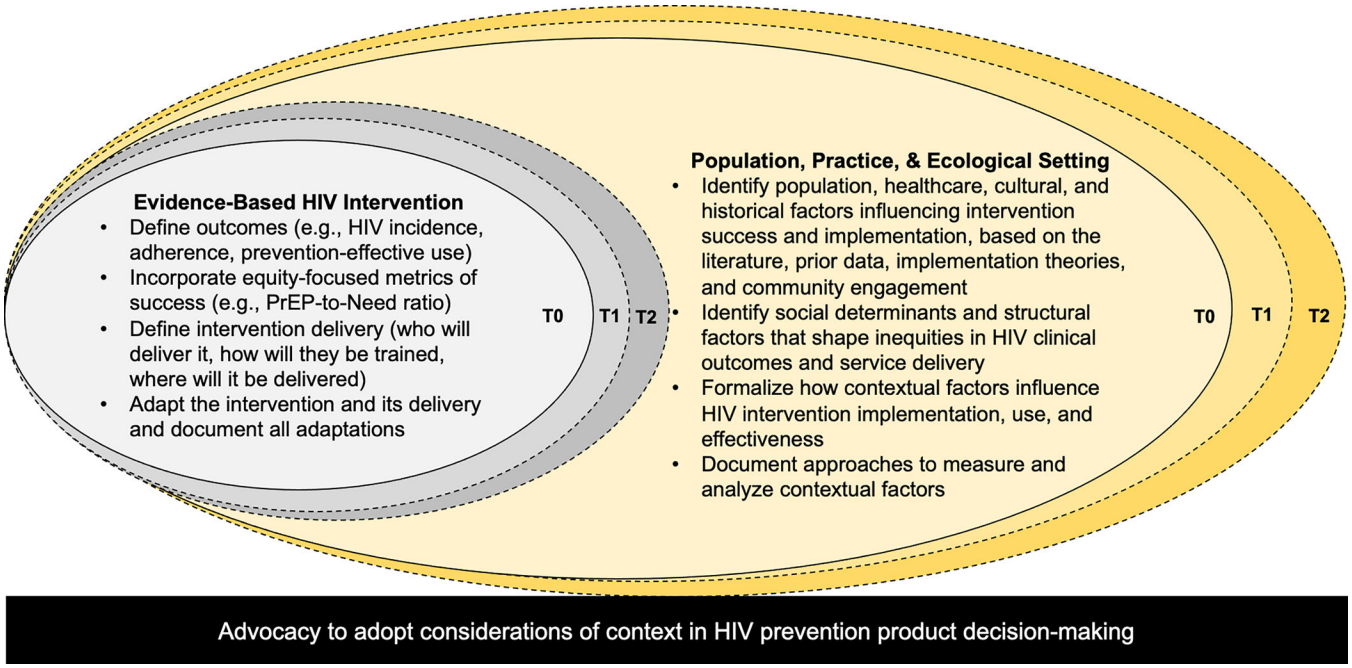

Figure 5.

Recommendations for considering context in HIV prevention intervention product delivery, based on the Dynamic Sustainability Framework

T0=time point 0; T1=time point 1; T2=time point 2; PrEP=pre-exposure prophylaxis

Table 1.

Examples of PrEP interventions and contextual factors influencing their generalizability across studies

Level	Intervention	Successful findings in one context	Alternative findings in another context	Contextual factors influencing generalizability
Biological	TDF/FTC PrEP, prescribed as a daily oral pill	**iPrEx OLE:** TDF/FTC resulted in a 44% reduction in HIV incidence compared to a placebo group among MSM and TGW in the U.S., Peru, Ecuador, South Africa, and Thailand.[65] **PROUD:** Among MSM in England, those randomized to receive TDF/FTC immediately had a 86% relative reduction in HIV incidence compared to those randomized to receive TDF/FTC after a 1-year deferral period.[28] **Partners PrEP:** Among serodiscordant couples in Kenya, TDF/FTC reduced HIV infection rate by 84% among men and 66% among women compared to their counterparts in a placebo group.[30]	**FEM-PrEP:** Among heterosexual women in Kenya, South Africa, and Tanzania, TDF/FTC did not significantly reduce HIV incidence compared to a placebo group. Less than 40% of participants in TDF/FTC group had evidence of recent pill use[24,45,66]	• Population demographics (e.g., gender, age, education level) • Sexual behavior and perceived HIV vulnerability • Familiarity with the intervention and community stigma around HIV prevention • Trust in the intervention, providers, medical system and research • Social capital and social networks • Quality of counseling delivered • Use of adherence reminder tools (e.g., setting reminder alarm)
	TDF/FTC PrEP, prescribed for event-driven dosing	**IPERGAY:** Among MSM in France and Canada, event-driven PrEP reduced risk of HIV infection by 86%.[29] **PREVENIR:** Among MSM in France, HIV incidence did not significantly differ between those using daily PrEP and those using event-driven PrEP.[49]	**HPTN 067/ADAPT:** Event-driven PrEP resulted in lower coverage of sex events and adherence among heterosexual women in South Africa, MSM in the U.S., and MSM and TGW in Thailand compared to oral PrEP, with the latter two cohorts also having lower protective drug concentrations with event-driven PrEP compared to daily oral PrEP.[37,38,48]	• Population demographics including gender, age, education level • Sexual behavior (vaginal versus anal sex) • Financial resources and employment • Predictability of sex act timing, and related factors, including relationship power dynamics and empowerment around sexual decision-making • Trust in intervention effectiveness
Behavioral	LifeSteps cognitive-behavioral PrEP adherence counseling	**Pilot RCT:** Among MSM in the U.S., Life-Steps had mixed results. Compared to standard counseling, the intervention did not lead to significantly better adherence at 3 or 6 months according to Wisepill or at 3 months according to tenofovir plasma levels but did result in significantly better adherence according to tenofovir plasma levels at 6 months.[67]	**Open-label demonstration project:** Among cisgender women in the U.S., those experiencing PrEP adherence challenges received LifeSteps for PrEP (in addition to 2-way SMS and Integrated Next Step Counseling); however, adequate PrEP adherence for protective drug concentrations was not achieved.[26]	• Quality of counseling delivered • Fit and cultural appropriateness of LifeSteps adaptations • Who is delivering the counseling (e.g., healthcare provider, peer) • Intevention delivery setting (e.g., clinic vs. community).
	SMS messages for PrEP adherence support	**EPIC:** Among young MSM in the U.S., two-way SMS for PrEP adherence resulted in significantly higher tenofovir plasma levels compared to standard of care (adherence counseling plus access to a clinician via pager).[50]	**PrEP SMART:** Among AGYW in South Africa, weekly SMS messages for PrEP adherence did not significantly change adherence compared to WhatsApp support groups at 2 and 9 months of follow-up.[51] **MPYA:** Among AGYW in Kenya, daily SMS reminders did not significantly improve adherence.[52]	• Appropriateness of message content and frequency • Technology literacy • Consistency of access to personal phone with airtime

Level	Intervention	Successful findings in one context	Alternative findings in another context	Contextual factors influencing generalizability
	Drug-level feedback counseling	**PrEP-PP:** HIV self-testing distribution and biofeedback counseling following urine tenofovir testing at PrEP clinic visits increased adherence at one month among postpartum South African women who initiated PrEP in pregnancy.[68]	**HPTN 082:** Drug-level feedback from intracellular tenofovir diphosphate levels in dried blood spots at the 2-month and 3-month PrEP visits did not increase PrEP adherence at 6 months among South African AGYW.[69]	• Availability of combination HIV prevention packages (e.g., drug-level feedback with self-testing) • Choice of pharmacologic medium (e.g., urine, dried blood spots) for drug-level feedback,considering availability of laboratory infrastructure, technicians, and result turn-around time
Community	Safe spaces for integrated PrEP delivery	**DREAMS South Africa**: Among AGYW, HIV incidence was lower during the 3 years of DREAMS implementation (2.8 per 100 person-years) than the previous 5 years (4.5 per 100 person-years)[70]	**DREAMS Namibia**: After 10 months of participation in HIV prevention programming, only 12.4% of AGYW refilled PrEP one month after initiation[71]	• Community stigma around PrEP • Social capital and social networks • Delivery setting (e.g., home, community safe spaces) • Individual delivering services (e.g., nurse, peer), including regulations around who can provide PrEP • Geography/rurality • Home structures (and amount of privacy at home) • Access to technology, WiFi, and internet connectivity for telehealth visits, remote supervision • Technology literacy
	Community-based PrEP delivery	**SEARCH:** Compared to clinic-based PrEP delivery, community-based delivery was associated with significantly higher PrEP continuation at 36 weeks among adult PrEP users in Kenya and Uganda and, in a counterfactual simulation model, demonstrated 74% lower HIV incidence.[72,73]	**POWER:** Facility-based PrEP delivery and delivery via mobile vans providing reproductive health services to AGYW in South Africa found that PrEP uptake was high but continuation was low (10% to 25% at month 3 or 6).[27] **Love O2O:** Among MSM and TGW in Thailand, PrEP initiation was not significantly higher in community drop-in centers compared to clinics.[74]	
	Telehealth for PrEP delivery	**Brazil National PrEP Program:** From April 2020 to October 2020, a telehealth model (virtual visits for initial PrEP screening and follow-up and 120-day PrEP refills) resulted in a 288% increase in PrEP initiations and a 53% increase in PrEP refills to existing clients.[75,76]	**Nurx:** Among individuals (primarily MSM under 30) accessing PrEP via a U.S.-based telehealth model, some expressed concerns about the cybersecurity of the platform and were hesitant to answer sensitive questions.[77]	

PrEP=pre-exposure prophylaxis; TDF=tenofovir disoproxil fumarate; FTC=emtricitabine; MSM=men who have sex with men; TGW=transgender women; SMS=short message service