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Leveraging international stakeholders' experiences with oral PrEP costs to accelerate implementation of the monthly dapivirine vaginal ring: A qualitative study

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Abstract

Background Costing and financing systematic implementation are recognized barriers to human immunodeficiency virus (HIV) prevention. In the absence of empiric implementation and economic data, perspectives from international stakeholders involved in developing and supporting daily oral pre-exposure prophylaxis (PrEP) policy, and programs can provide critical insights for developing costed plans to support and accelerate the rollout of novel long-acting PrEP (LA-PrEP) methods, such as the monthly dapivirine vaginal ring (PrEP ring).

Methods We interviewed stakeholders from purposively selected international organizations about anticipated PrEP-ring implementation costs, evidence gaps and key process steps for developing a costed rollout plan template (CRPT). We deductively analysed interviews.

Results The 27 stakeholders (11 donors, 10 nongovernmental, 4 academic/research, 2 multilateral) identified 10 cost-related themes: 7 for planning and implementation and 3 for financing, costing and budgeting. Planning and implementation cost considerations included: (1) actionable target setting; (2) multilevel communication strategies for awareness-raising, demand creation, client-level adherence and choice counselling; (3) human resources, encompassing task shifting and integration into non-HIV services; (4) supply chain costs, including commodities, manufacturing diversification, packaging and forecasting; (5) laboratory infrastructure and monitoring; (6) updated health information systems and metrics to monitor and evaluate multiple methods integrated into HIV, non-HIV and de-medicalized delivery settings; and (7) technical assistance and knowledge management. Themes for financing, costing and budgeting comprised: (8) cost and budget analyses, such as cost–effectiveness; (9) economic evidence gaps on service integration; and (10) innovative or co-financing for sustainable and equitable allocation of limited financial resources to support accelerated PrEP-ring delivery. We organized these themes within the CRPT.

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Conclusions The CRPT could expedite planning and enhance the pace and scale of optimized, systematic and sustainable delivery of PrEP methods. Further research is needed to evaluate use cases of the CRPT.

Contributions to the literature

- To address recognized barriers stymieing goals to end the HIV epidemic, we introduced a process and tool to support national-level systematic implementation, costing and financing plans for the monthly dapivirine ring.
- International stakeholders involved in oral PrEP policy and programming highlighted priority areas for costed introduction of the monthly dapivirine ring: (1) target setting, (2) communication and demand creation, (3) human resources, (4) supply chains, (5) laboratories, (6) monitoring and evaluation, (7) technical assistance, (8) cost and effectiveness, (9) service integration and (10) financing partnerships. These priorities are relevant for LA-PrEP as well.
- Participants validated anonymity in reported responses, an important approach in qualitative implementation science, where stakeholder contributions may be sensitive.

Introduction

Globally, ~1.3 million people acquire human immunodeficiency virus (HIV) annually [1]. Most seroconversions occur among cisgender women in low- and middle-income countries (LMICs), the majority in sub-Saharan Africa (SSA) [2, 3]. Cisgender adolescent girls and young women (AGYW) shoulder a disproportionate amount of HIV, accounting for 8% of the global population and 16% of all global seroconversions [2, 3]. The WHO conditionally recommended daily oral PrEP in 2015, and two long-acting HIV pre-exposure prophylaxis (LA-PrEP) interventions: the monthly dapivirine vaginal ring (PrEP ring) in 2021 and long-acting injectable cabotegravir (CAB-PrEP) in 2022 [4–6]. Both LA-PrEP methods are approved or undergoing regulatory review in several LMICs [7].

Epidemic modelling projecting the track to end the HIV epidemic by 2030 assumed 3 million PrEP users by 2020 [8]. Daily oral PrEP delivery did not meet global goals, and efforts are needed to improve the pace and scale as novel LA-PrEP is introduced [7]. The absence of health economic data and financing for the systematic implementation of HIV prevention have stymied the rate of PrEP delivery for population impact, and they must be remedied for successful introduction and scale-up of LA-PrEP choices for women [9]. Economic barriers challenge LA-PrEP implementation in high-income countries and are expected to be a greater challenge in LMICs [10–13]. Recent systematic reviews showed oral PrEP economic studies had relatively low quality: few included primary costing with current cost inputs and assumptions, and many overlooked key implementation inputs and activities included in national PrEP implementation plans [10, 12, 13]. Some advocated for developing costed roll-out plans (CRPs) for HIV prevention – tools to support the development of plans for systematic implementation and the associated costs and budgets. The analogous cost implementation plans (CIPs) has been shown to be instrumental in advancing the financing and systematic implementation of family planning (FP) services to reach FP2020 goals [10, 14]. We observed that four countries with costed plans accounted for 50% of PrEP initiations in SSA. The CRP process can accelerate scale-up by identifying and mobilizing a pathway and resources needed for systematic scale-up, dissemination and advocacy [15, 16].

In the absence of economic data on LA-PrEP, stakeholders with experience in planning, financing and implementing daily oral PrEP can provide critical and unique experiential insights on planning and costing systematic delivery of LA-PrEP. To inform the development of a costed roll-out plan template (CRPT) for LA-PrEP, we conducted in-depth interviews with international stakeholders engaged in oral PrEP policy, program planning and implementation across multiple sectors. We report their perspectives on a CRPT process, cost considerations and knowledge gaps.

Methods

Orientation and reflexivity

We approached this study using interpretive phenomenology, a theoretical approach incorporating researchers' backgrounds, experiences and worldviews throughout the process via careful self-acknowledgement and reflexivity [17]. We structured this article using the consolidated criteria for reporting qualitative studies (COREQ) reporting standards (Supplemental Material 1) [18]. Accordingly, we used COREQ's guidelines to present our team's composition – which can influence methods, results and interpretations – in Supplemental Material 2.

Study context

We originally conducted these semi-structured interviews to develop a CRPT for the Preparing for Ring Opportunities through Market Introduction Support and Knowledge Exchange (PROMISE) consortium, a project financially supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) and US Agency for International Development (USAID). We employed an interview schedule starting with stakeholders working at the global level to inform the questions and content for interviews with national and local stakeholders. Due to funding changes, we were only able to engage global-level stakeholders.

Participants

We reviewed publicly available participant rosters from global PrEP meetings that generated a list of 138 potential representatives from 47 organizations. From 27 January through 22 April 2021, we purposively sampled international representatives from public/governmental and private donor agencies, multilateral organizations, research and academic institutions and international nongovernmental organizations (INGOs) involved in policy, program planning and implementation, health economics or health service research. We asked participants to recommend other stakeholders with whom we should engage. We invited all participants via an email summarizing the interview's purpose, context and application. We initially interviewed 34 stakeholders from 16 organizations. We re-approached all stakeholders for their written informed consent to use their responses for research and report on those providing written informed consent.

Data collection

The interview team (D.C., C.J.H., J.D., K.K. and K.M.) comprised a facilitator, notetaker and audiovisual manager. Stakeholders within the same organization were interviewed in one session ranging from one to five participants. No stakeholder was interviewed more than once. We conducted interviews for approximately 1 h via Zoom. Two interviews were not audio recorded due to technical errors. External professionals transcribed the audio files, and the data collection team corrected any mistakes and/or mis-transcriptions. We did not provide participants the transcripts.

Participants answered open-ended questions (Supplemental Material 3) about oral PrEP implementation activities considered critical for scaling-up and adequacy of their costing. Participants were then asked to consider these activities' perceived relevance and anticipated costs for PrEP-ring implementation. Lastly, we asked stakeholders' perspectives on key steps in the processes of developing costed plans that achieved inclusive, comprehensive, transparent engagement.

We used Delphi methodology to adapt questions according to organizational focus and participant responsibilities to capture insights specific to their role and vantage point in PrEP policy, research and implementation. We modified questions to elicit more nuanced topical insights whenever they reached saturation, interpreted as the same responses repeated by multiple stakeholders. We conducted rapid, iterative analyses to identify response patterns and formulate modified questions that retained the essence of the original question while probing deeper into the recurring topic [19].

Analysis

Deductive approach

We analysed the transcripts using a deductive approach. The lead interviewer (D.C.) identified the initial costing and financing themes from team debriefs, interview notes, transcript reviews, facilitation insights and professional experiences. The initial themes underwent minimal changes when presented to the data collection team (C.J.H. and J.D.) for refinement.

Coding

Two analysts (C.J.H. and K.Y.) independently coded the transcripts by attributing quotes to the deductive themes. Following, the analysts and lead interviewer convened to identify themes that were candidates for collapsing, segmenting (that is, sub-themes), and exclusion due to lack of data. The coronavirus disease 2019 (COVID-19)-related theme "COVID-19 mitigation plans" was the only theme excluded. We used Microsoft Word for data management and analysis.

CRPT development

We created a CRPT from thematic insights, a review of FP CIP templates and oral PrEP costed plans [14, 20–24]. We reviewed and identified implementation and costing commonalities within and across publicly available costed PrEP plans. The review's methods and findings from national plans are described elsewhere [10]. We created the CRPT's initial structure using FP CIPs and supplemented the content of CRPT elements from the thematic findings.

Participant checking

We invited the respondents to review the results to confirm quotes were sufficiently de-identified.

Results

Of the initial 34 stakeholders, 27 consented to using their research data. Consenting participants represented five INGOs ($n=10$ participants), four research/university institutions ($n=4$), four donors ($n=11$) and two multilaterals ($n=2$). Of the INGO participants, 80% were from implementing organizations. Stakeholders were based in the USA, western Europe, southeast Asia and eastern and southern Africa, with seven residing in the eastern and southern Africa region. In all, 16 participants reviewed study results, and 1 requested minor edits.

The seven excluded individuals never responded to communication and invitations to consent, and all but one belonged to an organization already included in our sample; the one excluded organization was a research/university institution. Responses from non-consenting individuals were highly concordant with participating stakeholders, with one exception: two non-consenters offered unique insights on supply chain considerations that could not be used.

CRPT synthesis

Figure 1 illustrates the CRPT outline, which comprises the 10 thematic areas: 7 for implementation planning, and 3 for financing, costing and budgeting. A detailed description of the themes is in Supplemental Material 4.

Planning and implementation themes

Theme 1: Setting achievement targets

Several stakeholders underscored the multipurpose importance of setting achievement targets. Targets should inform funding, scale and pace of program implementation and costing activities. A multilateral stakeholder advocated for realistic, practical, scalable targets to guide program planning and delivery:

> *Start with the need and then advocate for funding but set realistic, sensible targets. Do not go to a country and say our initial target is 100 patients.*

Target setting requires careful consideration of feasibility, desired pace, reach, commodities, financial and human resources, priority population(s) and potential impact. Importantly, achieving a program target does

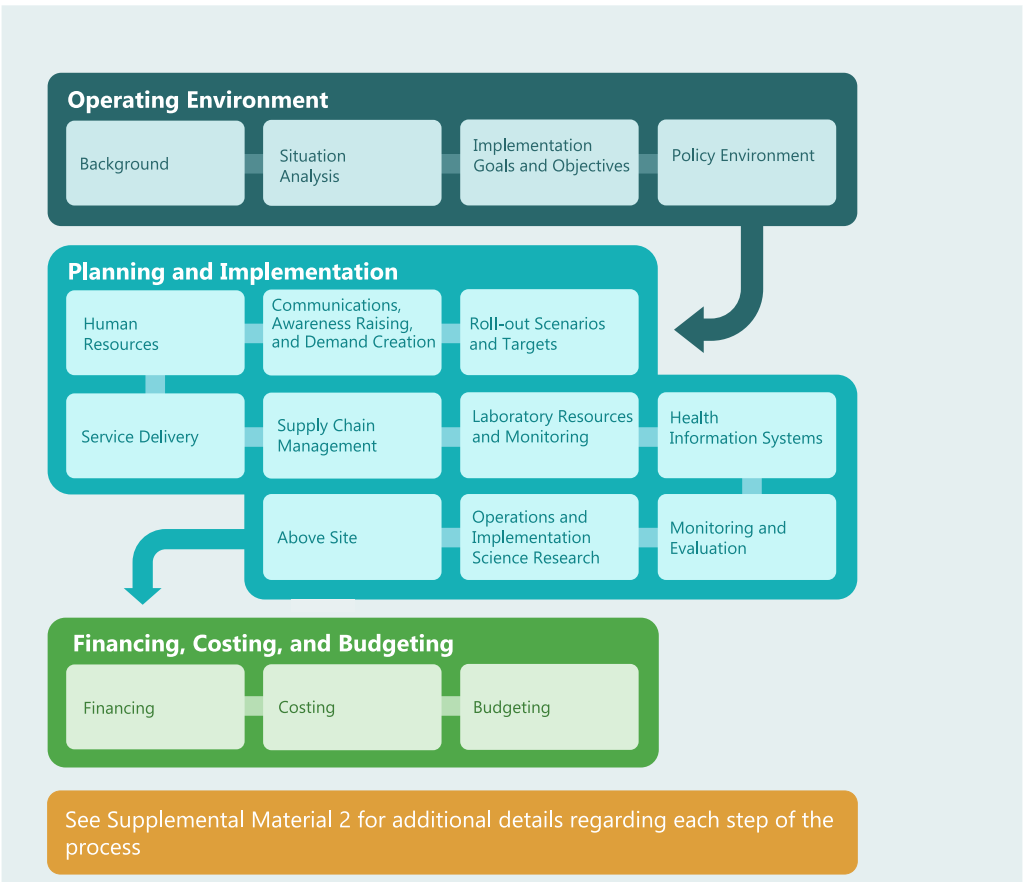

Fig. 1 Coasted rollout plan template

not guarantee success. Targets should be developed to increase access for priority populations and advance population-level outcomes towards epidemic control. One implementer discussed how narrow PrEP targeting can inversely affect program reach and cost:

> *[W]e made [oral PrEP rollout] too hard and the target populations too narrow...we [only] targeted [AGYW] and sex workers who, for varying reasons, were never going to have huge uptake…that made the cost of the program very high because these very complicated programs don't reach lots of people.*

One donor stated that target setting would help rationalize funding, research and development on future ring technologies:

> *We [should] think of this as the first launching of a specific type and model of PrEP that will provide a lot of data and understanding of how to think about this type of delivery mechanism, and not thinking just large scale…but how to target populations and use the feedback loops to then inform new product development. (Donor).*

The same donor also linked targeting with user preferences:

> *Targeting is important in understanding…user preferences and which populations are more likely to want which products and have greater uptake over others.*

One researcher described that a narrow target setting could underestimate cost–effectiveness:

> *The cost-effectiveness of prevention hinges on [successfully] targeting higher-risk folks. With oral PrEP, we didn't manage to get the most at-risk people in first.*

Theme 2: Costs for communication and demand creation

Stakeholders described investments in communication and demand generation as insufficient and "often get left to the bottom of the pile" (Donor). HIV prevention services have been historically underutilized by populations in need. Innovative communication and demand-generation activities will be necessary to entice potential end users. Figure 2 presents stakeholders' feedback on salient communication strategies to be considered and costed. One donor underscored the cost-saving importance of streamlining and synergizing communication campaigns across programs in the same geographic area (Fig. 2, Donor). One implementer emphasized that HIV prevention branding needs to be more aspirational and that the PrEP-ring could benefit from broader availability and framing (Fig. 2, Implementer #1). Another implementer highlighted that the dynamic nature of the human element in shaping thoughts, perceptions and agency is hard to cost and often overlooked in communication activities (Fig. 2, Implementer #2). Similarly, one researcher underscored the difficulty of costing and forecasting demand for HIV-prevention products (Fig. 2, Researcher/University #1A). Implementing creative, effective communication and demand campaigns requires prioritized investments in formative activities such as human-centred design studies, designing and printing/recording new media and securing dissemination channels. Costs and budgets are influenced by the level of effort and resources needed to develop new and/or update clinical aids. One researcher raised that, with the introduction of LA-PrEP, demand will soon be relative, differential and preferential. Thus, funding of social science and behavioural economic studies is imperative to understand demand, particularly how and why certain products are more popular (Fig. 2, Researcher/University #1B). Researchers also commented on prior HIV prevention failures caused by underestimating communication activities for providers (Fig. 2, Researcher/University #2A) and the unintended consequences of incentivizing mobilizers to link users, skewing initial experience with PrEP care (Fig. 2, Researcher/University #2B).

Theme 3: Human resource costs

Figure 3 shows the human resource cost considerations cited by stakeholders. All stakeholders cited adequate staffing as the most prominent factor in human resource costs for daily oral PrEP care. Programs may need to hire additional staff to manage tasks associated with the PrEP ring, such as counselling or possible increases in client volume. Stakeholders indicated that PrEP-ring counselling might take up additional time as a new method, at least during the initial visit and introductory phase of implementation (Fig. 3, Researcher/University #1). Although counselling for PrEP-ring initiation might require more time than oral PrEP because providers will need to assist with the initial insertion, PrEP-ring counselling might be cheaper overall. Clinics might also need to hire more same-gendered providers for PrEP-ring counselling (Fig. 3, Donor).

Client volume could grow if the PrEP-ring meaningfully increases initiations or re-initiations. One donor posited that, if additional staff are not hired, providers would need additional compensation because of their increased workload and capacitation. On the basis of experiences with HIV self-testing, one researcher predicted that, as product familiarity increased, workflow burden would decrease (Fig. 3, Researcher/University #2A). One INGO proposed shifting tasks to lower healthcare cadres as a

Fig. 2 Thematic insights on communication and demand creation

Fig.3 Theme on human resource costs

potential time- and cost-saving approach (Fig. 3, INGO #1). PrEP-ring continuation visits, requiring HIV testing and no other lab monitoring, could be relatively brief, infrequent and task-shifted to lay workers or other de-medicalized/de-centralized delivery.

Respondents also emphasized funding for training and capacity-strengthening efforts to improve provider

self-efficacy to counsel or prescribe PrEP through knowledge, and/or support (Fig. 3, INGO #2). Increased investments in supportive supervision may also improve provider buy-in and counselling practices (Fig. 3, Multilateral). Stakeholders suggested studying FP services with a history of offering multiple products and the female condom in HIV prevention to gauge time and cost when providers are unfamiliar and then are familiarized (Fig. 3, Researcher/University #2B).

Theme 4: Supply chain management

Stakeholders focused on manufacturing and forecasting activities for sustaining choice as critical supply chain cost considerations, drawing lessons from FP. One donor representative mentioned that manufacturing diversification, including generic and private label suppliers, could increase scale and reduce costs. Diversified manufacturers will require augmented logistics and systems to monitor manufacturing, procurement, shipping and storage. HIV prevention has been relatively difficult to forecast due to demand variability. This can lead to under-/overstocking, storage concerns and misaligned budgets. Product introduction activities can also be delayed if product orders exceed manufacturing output. An implementer noted, "We've had [oral PrEP] stock-outs…[leaving] folks concerned about continuation"; regular and consistent stocking is imperative for PrEP use. The PrEP ring's longer shelf life was perceived positively for forecasting with stable costs, but factors such as relatively larger packaging may have space constraints and affect stocking.

Theme 5: Laboratory resource, commodity and monitoring costs

Stakeholders mentioned the lower threshold of laboratory assessments with PrEP-ring use. Other than HIV testing, few other laboratory costs were anticipated. Consequently, few stakeholders discussed laboratory monitoring and assessments. Stakeholders mentioned outlining and costing the inclusion of new PrEP methods in national pharmacovigilance monitoring systems. One INGO stakeholder was unsure "if it costs countries anything [extra] or [if] they include it in their current ministerial activities" but thought "there may be costs for activities in the risk management plan". In contrast, stakeholders discussing CAB-PrEP anticipated numerous requisite labs (for example, viral load testing, resistance testing, commodities and equipment) and higher costs.

Theme 6: Estimating costs for monitoring and evaluation and health management information systems

Stakeholders discussed the general cost implications of updating monitoring and evaluation (M&E) tools – such as forms, prescription pads and health management information systems (HMIS) – to ensure accurate tracking and quantification of clients and dispensing of all PrEP products. One donor wondered about the logistical challenges of defining metrics and using M&E for all PrEP methods and delivery modalities, particularly oral PrEP and the PrEP ring, are integrated into services:

> *[H]ow sites track use and what kind of metrics would be monitored, and [with FP] integration, how that data feed back into HIV program management and knowing already some challenges with measuring oral PrEP use, thinking about how the ring is similar and different and the challenges that would come with measuring and monitoring use.*
> *If [the PrEP-ring is] self-guided after initial insertion, will programs track continued use and, if so, how do you support that while also supporting women [not coming back] every month? Is it more about measuring commodity flow as a proxy for use? [This is] important information for where to roll it out, how much it's going to cost, and the monitoring aspects.*

Establishing new M&E metrics necessitates contracting and convening industry experts to create clear, distinct operationalization, which will likely require further refinement based on setting, population and context. Moreover, updating systems for de-centralized product delivery requires social and financial capital. Proportional cost-sharing between HIV programs and the integrated and/or de-medicalized service providers requires careful negotiation, as cost-sharing agreements will likely involve HIV services covering the largest share, given differentials in funding envelopes.

Theme 7: Technical assistance

Stakeholders representing funders described technical assistance costs, especially at the planning and early implementation stage; few other stakeholders mentioned these costs. One donor advised using smaller programs to guide scale-up, "not starting out [with] large-scale programs, but more defined programs that help support understanding around product use and scale up". Another donor recommended "collecting the best evidence so that policy decisions are informed by broader evidence on whether to add this to a formulary".

Financing, costing and budgeting themes

Theme 8: Understanding product cost and cost–effectiveness

Stakeholders commonly discussed thresholds for acceptable PrEP-ring pricing linked to perceived ring effectiveness. One stakeholder posited lower prices for products with lower effectiveness and higher prices for

more effective products, the PrEP-ring "would have to be a lot cheaper than [CAB-PrEP] to be [more] cost-effective". Countering this point, a donor suggested that the PrEP-ring could be incrementally more cost–effective despite its higher product cost if more infections were averted through better effective use of the PrEP-ring than oral PrEP (Donor). An INGO representative stated that the cost–effectiveness of LA-PrEP methods could "make a case for reallocation of funding [or] expansion of the envelope". A researcher commented:

> *If you show that you reduce incidence, now you've got all those HIV costs, direct and indirect, to measure against the cost of the program and an expensive program may be cheaper than it looks.*

One implementer cautioned that the intersection of cost and effectiveness can influence availability and accessibility, stating:

> *[if] the unit cost [is] expensive, we're going to gatekeep it more, so you need to…get that price under [US]$1.00.*

This idealized price conflicts with the projected costs of US$13 for PrEP-ring at the time of data collection [25]. Products that are truly low effectiveness and high cost would not meet a profile for implementation. Therefore, communication strategies to mitigate perceived versus real costs and effectiveness may be needed to produce more streamlined and transparent budgeting planning for all PrEP methods (that is, PrEP ring and LA-PrEP).

Theme 9: Costing integration

Subtheme 9A: Costing knowledge gaps regarding integrated service delivery Figure 4 illustrates the synthesis of stakeholder insights on integration costs. All stakeholders noted the need for cost data on integrating the PrEP-ring into non-HIV services that women access, such as FP. This data gap in daily oral PrEP must be redressed for the PrEP ring. Although normative costs can be estimated pre-implementation, one donor representative framed this gap as a "chicken and egg problem", for "you can't cost a program that's not been implemented yet" (Fig. 4, Donor #1A). Stakeholders mentioned space to privately counsel and demonstrate use as cost drivers of PrEP ring. Unless the PrEP-ring or CAB-PrEP is fully integrated into a service such as FP (that is, PrEP administered at the same time as the chosen FP method), clinics must create private rooms complete with an exam table, models and other apparatuses to counsel end users and administer products.

Stakeholders expressed the importance of generating empirical, real-world cost and expenditure evidence to inform data gaps on integrated delivery. One researcher stated the importance of conducting additional economic analyses that measure additive, redundant or degressive elements of integration models (Fig. 4, Researcher/University). An implementer and a multilateral stakeholder independently emphasized the need for empirical cost data of pragmatic PrEP offerings within different services (Fig. 4, Implementer, Multilateral). Another respondent (INGO) noted that dynamic willingness-to-pay studies would illuminate end-user preferences for non-HIV service access points and out-of-pocket costs. Stakeholders' desire for real-world integration costs highlights the importance of implementation science studies with implementation, impact and economic outcomes.

Subtheme 9B: Blended financing approaches Donors, the primary respondents describing funding approaches, discussed leveraging funding sources informed by incremental cost estimations of ring provision, particularly for FP (Fig. 4, Donor #1B and Donor #2). Successful service integration requires augmentation to existing costed plans, where updates may be hampered by bureaucratic and coordination challenges between offices and ministries (Fig. 4, Donor #1C). Optimal and equitable co-financing requires coordination and transparency within and between national and external government agencies and other donors.

Theme 10: Innovative financing partnerships

Figure 5 presents stakeholder viewpoints regarding financing partnerships. One multilateral questioned whether LA-PrEP would siphon funds away from oral PrEP, hoping cost reductions would enable countries to eventually assume PrEP costs typically funded by donors (Fig. 5, Multilateral #1). Another multilateral representative commented on the dismal state of HIV prevention funding and its hindrance to the pace of oral PrEP scale-up (Fig. 5, Multilateral #2). One donor also noted that HIV prevention has been primarily project-based because of a lack of significant commitments from donors and governments and, thus, they had difficulty envisioning sustainable systems for biomedical prevention. Stakeholders viewed government and multilaterals as critical providers of financing and resources needed to develop and operationalize costed implementation plans for the PrEP ring. Stakeholders expressed that co-financing innovations are necessary to mitigate the long-term impact of static prevention funding and meet the expected costs of new HIV prevention products. Funding advocacy should be global and local, with women's groups encouraging governments to fund LA-PrEP (Fig. 5, Donor #1A). Additional insight into the role of private entities in contributing funds, products or global health efforts would help better guide costing activities.

Fig. 4 Costing integration subthemes

Fig. 5 Thematic insights on financing

Numerous stakeholders noted the influence of the US President's Emergency Plan for AIDS Relief (PEPFAR) on the global rollout of daily oral PrEP. Fewer mentioned the Global Fund to Fight AIDS, Tuberculosis and Malaria. In addition to noting PEPFAR's support of oral PrEP, the same donor representative highlighted countries' initial hesitance to procure oral PrEP amidst budget constraints resulting in inadequate treatment funding and compounded by insufficient cost data and/or other funding for LA-PrEP products (Fig. 5, Donor #1B). Regarding the concern for high costs amid static budgets, one researcher noted that, if the high costs associated with product introduction (for example, infrastructure) are included in scale-up projections, rather than costing at other points, long-term costs might be overestimated, "If you only cost the first year and use that to scale up, you're going to get far higher costs than you probably need over time". Continual assessment and communication of costs at scale will keep budgets and cost projections rooted in pragmatism and potentially assuage financing concerns.

Stakeholders mentioned potential co-financing schemes with HIV funding complementing funds from other services, such as FP and sexual and reproductive health. One INGO representative noted non-HIV services might have a hard time rationalizing the increased cost of multipurpose technologies over traditional methods (for example, contraceptives alone), suggesting HIV programs will likely need to cover any additional costs (Fig. 5, INGO). Current funding mechanisms do not facilitate co-financing; FP is not a funding priority for the Global Fund despite being highly complementary with HIV services (Fig. 5, Researcher/University). Co-financing discussions are bound to increase as service integration plans progress. While HIV-FP integration was frequently mentioned, one donor discussed the difficulty of rolling out products in FP and said it would be better to focus on PrEP programs, where the funding stream is known (Fig. 5, Donor #2). HIV-FP integration might also be precluded by sector-dependent funding mechanisms, requiring more formative cross-sector efforts to enable integration.

Discussion

This qualitative analysis of international stakeholder consultations identified 10 themes within three areas for a CRPT: operational context; planning and implementation; and financing, costing and budgeting. The themes emphasized were target setting, communication and demand creation, human resources, de-medicalization and integration. Other important themes with lesser emphasis were laboratory, supply chain, M&E, HMIS and technical assistance. Although the study focused on PrEP-ring, relevant discussions of CAB-PrEP were also included. Laboratory monitoring was primarily discussed when stakeholders mentioned CAB-PrEP. Stakeholders expressed concern regarding the reported costs and uncertainty of PrEP-ring alone and CAB-PrEP costs relative to oral PrEP. Stakeholders discussed the role of clinical trial effectiveness in establishing product price, planning and financing scale-up for population-level effectiveness and impact. However, perspectives varied within and across sectors. Global stakeholders also described the importance of costing the PrEP-ring at different stages of implementation to ensure the use of valid assumptions, data collection and cost functions. Stakeholders discussed implementation and associated cost-data gaps, most pervasively in relation to innovative financing to integrate PrEP-ring into FP services. Stakeholders described advocating for innovative financing at global and local levels but shared little insight on financial resources or innovations to blend financing. Stakeholders highlighted data gaps in co-financing models, structural and bureaucratic impediments to co-financing and provided no historical examples of co-financing successes or best practices.

These thematic findings align with a recent scoping review identifying 15 relevant oral PrEP implementation inputs and activities needed for LA-PrEP implementation [10]. A recent qualitative study on provider perspectives of CAB-PrEP highlighted similar considerations when costing PrEP products and the need for national implementation guidance [26]. Despite CIPs' demonstrated utility in accelerating FP program planning and implementation, they remain rarely developed and used in HIV programming, a gap that should be remedied to increase the pace of PrEP-ring introduction and scale-up [10, 14]. To our knowledge, the CRPT (Fig. 1) is the first published resource combining implementation and costing to accelerate robust and systematic PrEP-ring or LA-PrEP planning and delivery throughout all implementation stages.

Previous evidence from South Africa corroborated stakeholders' view that social and behavioural change communication activities need further cost analyses [27]. Recent studies suggest some groups preferred PrEP-ring and others injectables or daily oral PrEP, highlighting a range in values and preferences and the need for all methods to be available [28–30]. Delaney et al. noted that knowledge gaps about values and preferences will impact

real-world uptake of LA-PrEP [31]. The mix of PrEP methods, and factors such as values and preferences may also have implications for future PrEP cost. The need for behavioural economics and cost–effectiveness research, critical for understanding how to address end-users' preferences with programs, increases with the expanding prevention landscape [11]. Evidence is needed to align assumptions and actual costs.

Stakeholder feedback on costing at various implementation stages has been touted by numerous reports [10–13, 27]. Stakeholders' perception of PrEP-ring and CAB-PrEP laboratory costs based on each product's safety profile and potential to expand service delivery to FP/SRH, pharmacies, community delivery or non-health platforms has also been corroborated [32, 33]. Over time, lower laboratory costs could compound benefits, but expanding access points to meet demand could have greater cost implications for aligning M&E and supply chain management systems [33, 34]. Technical assistance, knowledge management and results utilization have been identified as important for implementation, and can be catalytic, but few stakeholders discussed the cost implications and these have not been costed by many studies [10].

Budgeting and financing considerations most frequently highlighted service integration, a cross-cutting thematic area. Expanding to other delivery platforms, particularly private entities, introduces new considerations into incurred costs, reimbursement mechanisms, public funding allotment and other cost-related factors, necessitating additional research into these service delivery models, as advocated by stakeholders. Introducing multi-purpose technologies may catalyse HIV-FP integration but raises several questions regarding co-financing of products and service delivery. These novel technologies may also expand HIV donors' commitments to complementary health sectors. Costing evidence can inform integrated service delivery's appropriateness, utility and cost-saving potential. However, few economic or budget impact studies of PrEP integration have been conducted [32, 35, 36], engendering knowledge gaps regarding the empirical effect of integration on lowering costs.

Our analysis has some strengths and limitations. Purposefully selecting global stakeholders was both a strength and a limitation. As previously noted, participants were selected because of their and/or agency's historical involvement in global oral PrEP implementation. These stakeholders provide a unique cost perspective given their global and multi-country role in HIV prevention. Conversely, the selection criteria, snowball sampling and stepwise recruitment approach may have produced respondents with greater homophily, and responses may underrepresent the breadth of priority areas to consider for costing and nuances within the areas identified. Additionally, due to our inability to interview ministry of health representatives, insights regarding costing facilitators and barriers at national and local levels are likely limited. Since they are often key partners in PrEP implementation trials, future studies must include governmental stakeholders, for their practical understanding of contextual economic and programmatic factors can help tailor efforts to consolidate, strengthen and streamline health systems within their country/location. Given the uniqueness of the sample, having stakeholders verify the anonymity of responses was a methodological strength, although only half assessed the results. Most stakeholders were based in the USA and UK, yielding few insights from national-level stakeholders. Additionally, stakeholders had varied levels of experience with planning implementation, generating and using health economic data, so data might be skewed by organization or sector. We interviewed stakeholders shortly following WHO's recommendation of the PrEP-ring (January 2021) and the unblinding of HPTN 084 (November 2020) [4, 37]. Since then, evidence has increased supporting PrEP-ring preference among some samples of women in sub-Saharan Africa [29, 31]. Furthermore, real-world challenges with implementing CAB-PrEP in high-income settings may have dampened enthusiasm for CAB-PrEP's impact globally [38]. Finally, we may have underrepresented potentially salient quotes and/or topics because we summarized two stakeholders' perspectives using written notes due to lack of recordings.

Conclusion

Countries, particularly LMICs with higher HIV burden, will be assessing funding envelopes to make decisions about procuring and deploying HIV prevention methods, including oral and LA-PrEP, potentially affecting the speed and scale of LA-PrEP availability and accessibility. PrEP funding and budgeting decisions will continue to mis-estimate implementation costs until costing knowledge gaps are filled with empirical, contemporaneous data. For planning and implementation cost considerations, global stakeholders underscored target setting, communication strategies, human resources, supply chain logistics, laboratory monitoring and technical assistance and knowledge management. They also highlighted cost–effectiveness, minimal service integration cost data and innovative and co-financing as important financing, costing and budgeting factors for planning, introducing, scaling up and delivering current and future PrEP methods. By collating knowledge on needs, preferences, costs and financing, costed implementation plans can be instrumental in identifying data gaps, aligning

resources and needs and streamlining product introduction and scale-up.

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

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Author contributions
D.C. and C.J.H. conceptualized this study. C.J.H., D.C., J.D., K.K. and K.M. participated in the interviews, providing support ranging from facilitation, note-taking, question generation and audio/visual support. C.M. and M.L. provided technical support and assistance. D.C. created the initial set of themes. C.J.H. and K.Y. analysed the transcripts. K.K., A.D., S.T.R., F.B., C.O., K.M., D.Q., S.W., S.F. and M.E.S. synthesized and interpreted the qualitative data. C.J.H. and D.C. drafted the initial version of this manuscript. DC secured funding. The corresponding author confirms that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors read and approved the final manuscript.

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Availability of data and materials
Due to the sensitive nature of these qualitative data and the possibility of de-anonymization, even after removal of potentially identifiable data, such as names, initials, titles and organizational details, the transcripts are not publicly available.

Declarations

Ethics approval and consent to participate
Columbia University's ethics committee reviewed and approved the protocol (#AAAU1602).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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