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EDITORIAL

Maximizing the impact of HIV prevention technologies in sub-Saharan Africa

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1 | INTRODUCTION

There have been substantial gains in the range and efficacy of technologies available for HIV prevention, with voluntary medical male circumcision (VMMC), treatment as prevention, and pre-exposure prophylaxis (PrEP) being added to the existing toolbox of condoms, lubricant, behaviour change, harm reduction, structural interventions and advocacy programmes. These advances led to the optimism of calls to end the AIDS epidemic by 2030 with a target of fewer than 500,000 new cases a year by 2020 and 200,000 by 2030 [1,2]. However, progress towards these goals is slow with an estimated 1.9 million new infections in 2017 globally, including over a million in sub-Saharan Africa [3]. Although these numbers represent a substantial reduction from the height of the epidemic in the late 1990s, they are well off target despite intensive efforts to promote HIV combination prevention encompassing structural, behavioural and biomedical interventions. The targets were based on modelling which estimated the coverage needed to achieve these reductions, namely meeting 90-90-90 treatment targets, 90% coverage of key populations with combination prevention programmes, 90% reported condom use rates with non-regular partners and 90% male circumcision [2]. However, investment in prevention has been lower than required to achieve this coverage [4], and results from trials of intensive population "test and treat" approaches show a lower impact than hoped for, with up to 30% reduction in incidence, but with lower engagement and coverage of younger people [5,6].

Reducing incident infections is a key to sustainable HIV control, and epidemic models suggest that further primary prevention is necessary in addition to treatment for those already infected if the 2030 targets are to be reached [7]. This all points to the need for increased efforts in order to maximize the impact of technologies, including those currently in development. While there is good evidence for efficacy of the technologies and strategies in some populations [8,9], they have failed to reach their potential in many high incidence populations in sub-Saharan Africa [10]. In particular, the lack of widely available efficacious female-controlled methods has left many young women vulnerable to HIV when their partners are unwilling to use condoms [11]. While newer technologies such as long-acting injectable PrEP have potential for additional impact, they too may disappoint if the lessons of existing programmes are not learned and programmes not scaled sufficiently.

Adolescent girls and young women are at particular risk, accounting for 25% of new HIV infections among adults in sub-Saharan Africa, and with three to five times the prevalence of adolescent boys and young men [7,10]. Reducing the high incidence in these young populations is perhaps the most urgent global challenge, particularly as 60% of the population in sub-Saharan Africa is aged under 25 and absolute numbers of young people will continue to rise over the coming decades [12].

It will be important to identify the mix of prevention technologies and approaches that will meet the needs of these young people, in order to design the interventions that will support their adoption. This requires an interdisciplinary approach, with the appropriate mix of social, behavioural, epidemiological and programme science, with learning from key stakeholders including young people themselves, service providers, policy makers, industry and governments. The community perspectives about health and HIV, and their health seeking behaviour need to be taken into account along with the determinants of decisions about the HIV risk behaviours and the use of HIV prevention technologies. Demographic, geographic and other characteristics should inform how HIV prevention interventions are prioritized and should be designed around the needs and preferences of priority users.

2 | THE TECHNOLOGIES

Condoms provide triple protection against HIV, pregnancy and many other sexually transmitted infections [13]. They are

often easily accessible, inexpensive and when carried provide an option for unplanned sexual activity. Condoms have been promoted over the course of the HIV pandemic with overall use increasing, reducing incidence among key populations (men who have sex with men (MSM) and sex workers) where sexual partnerships can be brief [14,15]. One important lesson from condom programmes in the general population is that marketing and promotion are essential for generating demand. However, funding for condom promotion and marketing has decreased, particularly since 2011, often leading to condom supplies sitting unused due to lack of demand [16]. The lack of demand may reflect problems of access as distribution programmes have been cut and condoms may be less widely available outside of health facilities in some countries. Perhaps the most important lesson from male condoms is that an intervention for women that requires partners to change their behaviour may be an insurmountable barrier to use in many contexts, exacerbated by the perceptions that condoms decrease sexual pleasure and may undermine trust in relationships.

Oral PrEP using tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) is an efficacious HIV prevention product. In developed countries oral PrEP use is reducing HIV incidence among MSM [17]. However, there are important barriers to its uptake and use: it is relatively costly, so it can be difficult to access; it is specific for prevention and treatment of HIV so its uptake and use can be stigmatized; it may have side effects when first taken; it requires daily dosing to be effective for women; and it requires medical monitoring for side effects and breakthrough infections [18]. The introduction of oral PrEP and its scale-up has been slow for many reasons, but we are now in a position where oral PrEP is being introduced for populations of MSM, sex workers, those in HIV sero-discordant couples, and young women in a small number of locations in sub-Saharan Africa. We are just starting to learn from oral PrEP programmes for young women and there will be much to learn from their evaluation. Many future potential interventions (such as cabotegravir injections, broadly neutralizing antibody [bNAb] injections, ARV implants or vaccines) will not have daily use requirements, but will share many of the same barriers to uptake as oral PrEP [19].

VMMC is another efficacious intervention and scale-up across sub-Saharan Africa has been ongoing for several years with mixed effect, but over four million men were circumcised in 2017 alone, and the programme has averted an estimated 230,000 HIV infections. Comprehensive programmes including HIV testing and counselling, safer sex education and condom promotion and distribution [20].

3 | THE HIV PREVENTION CASCADE

HIV prevention programmes are complex to design, deliver and evaluate, and an HIV prevention cascade has been suggested as a tool to support prevention programming [21]. Such cascades identify key steps for interventions to be effective, including identification of populations at risk, perception of risk, intervention uptake and use, and ultimately the efficacy of the intervention. Once the cascade steps are identified and quantified, programme planners can see where the largest gaps lie and take steps to understand and address them. Figure 1 shows how prevention cascades may be used at the programme level, starting from a population at risk and identifying who would benefit from primary prevention packages, that is, those who test HIV negative or who do not know their status. The options illustrated in the figure include VMMC for young men, and condoms or oral PrEP for young men and women, and the cascades show the potential gaps in protection.

For example, defining who is at risk will depend on local HIV prevalence and patterns of risk within the community. There has been relatively little recent work measuring patterns of risk in young women, but in Southern and East Africa the risks include transactional sex (broadly defined), age-disparate partnerships, multiple sex partners, alcohol use, being or having partners uncircumcised, partners who travel, and for young women risk seems to increase with time after sexual debut and be associated with marriage [22-25]. The first step of the cascade is perception of risk, and studies of young women show that perceived risk of HIV acquisition is often lower than actual risk. In various studies in sub-Saharan Africa, between 17% and 50% of women deemed to be at high risk of incident infection perceived themselves to be at risk, while another study showed little association with self-perception of HIV risk and subsequent acquisition of infection [26]. Understanding more about this mismatch between risk and risk perception will be crucial to developing interventions to drive demand and uptake for effective interventions. The next step would be for an individual (and sometimes their partner) to take up and use an intervention. Many factors influence such decisions, and the decisions have to be made and acted upon repeatedly in interventions such as condoms, sexual behaviour change or PrEP use. Consistent use is a particular challenge of HIV prevention: because there is low risk in most partnerships and high risk in a small fraction, HIV prevention interventions have to provide protection across all sex acts within those high-risk partnerships for their benefits to be realized [27].

4 | SOCIAL EPIDEMIOLOGICAL FRAMEWORK

The prevention cascade can be used alongside a social epidemiological framework which highlights the influence of structural factors, such as laws, policies, regulations, relational factors, such as family, relationship status, economic situation and more immediate factors, such as setting and privacy, intimate partner violence, alcohol and drug use [28,29]. These factors will interact with people's preferences and motivations to determine their use of any particular technology. Additional barriers to demand for the uptake and use of interventions include lack of awareness, lack of self-efficacy, difficulty in accessing services, stigma associated with uptake (e.g. by health-care workers), stigma of use (e.g. by partners), difficulty of use and side effects of use.

We can of course learn from examples where programmes have been effective. Reproductive health programmes promoting access to contraception have been extremely successful in many settings, despite requiring many similar behaviours and in similar contexts to HIV prevention. Their successes have been put down to many factors, but key to them are

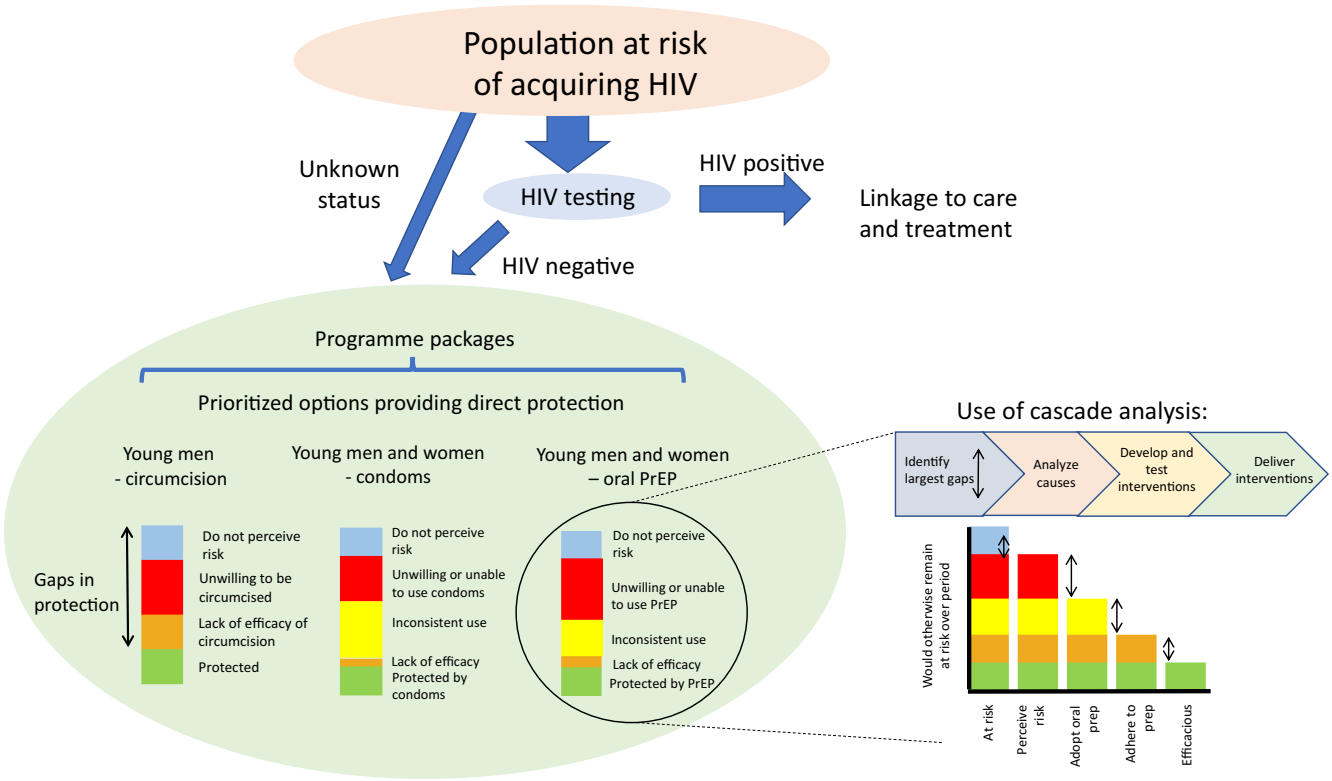

Figure 1. Example of use of HIV Prevention Cascades at Programme Level.
Diagram starts with population at risk of HIV, identifies those who would benefit from a primary prevention intervention package, and for each intervention identifies gaps in protection. For one intervention, oral PrEP, the right side of the diagram suggests how a cascade analysis can identify and address the largest gaps.

leadership and effective management, appropriate communication strategies, evidence-based programming, high quality contraceptive methods, availability, trained staff, client-centred care, choice of methods, access and variety of outlets, affordable, involvement of men and women, and integration with other services [30-32]. Effective HIV prevention programmes for sex workers have also been based on community mobilization, advocacy, access to integrated HIV prevention, STI control, contraception and other services [14].

5 | BANBURY MEETING AND SUPPLEMENT

In 2017, a small meeting took place at the Banbury Center which hosts think-tanks on key questions in molecular biology, genetics neuroscience and science policy, on how to maximize the impact of HIV prevention technologies in sub-Saharan Africa [33]; we brought together international experts from different disciplines to address how to make the development and delivery of HIV prevention technologies more successful. The meeting concluded that many elements will be needed for effective and sustained primary HIV prevention, including local ownership, community engagement and acceptability, good evidence and data to guide planning and implementation and integration of primary HIV prevention into local service provision, including general sexual and reproductive health services (Figure 2). The presentations and discussions at that meeting led to the commissioning of this supplement with contributions addressing some of the gaps in our knowledge, and showing the potential role of disciplines ranging from mathematical modelling and social psychology to marketing and behavioural economics.

In this supplement, we have brought together a number of articles that build on some of the discussions at that meeting, representing a variety of disciplinary perspectives. Mojola and Wamoyi start with a narrative and insightful review into the drivers of HIV risk among young African women [34], and use insights from their own and others' research to show how epidemiological, gender-normative and environmental contexts interact to drive hyperendemics of HIV, and how similar factors undermine preventive interventions. Their deep descriptions of how social drivers result in risky settings and behaviours are then used to suggest how that context can inform intervention planning. In the next article, Skovdal draws on contemporary social theory to illustrate the need for a greater understanding of the links between the different determinants of preventive behaviours [35]. He argues that through exploring social practices we can better understand these phenomena, and proposes a "table of questioning" that can be used by programme planners. The next paper is a viewpoint from Gomez and colleagues who explore the application of market segmentation to prevention programmes [36]. In public health we are used to describing and grouping people by sociodemographic

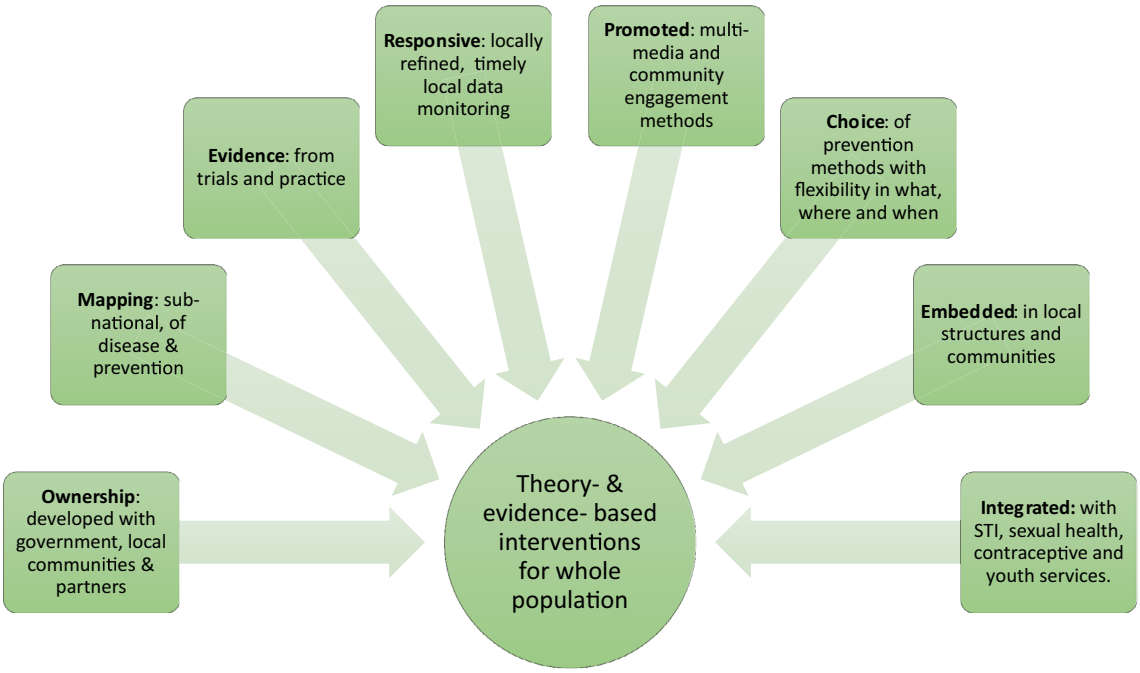

Figure 2. Model for maximizing HIV prevention impact at Programme level.
Model developed through consensus discussion at Banbury Center Meeting, May 2017 [33]. The outer boxes show key characteristics and inputs of a theory- and evidence- based prevention programme which are required to deliver the holistic intervention package.

characteristics that predict risk or define the need for an intervention. In marketing techniques developed in the commercial sector, segmentation is based on a range of other factors, psychographic and behavioural, which are said to better predict consumer behaviours. The authors describe examples of market segmentation in public health, and argue that we would do well to adopt some of these techniques to more closely match our programming to the desires and preferences of the people we want to engage, developing segment-specific campaigns. This resonates with the broad interest in "personalized prevention," but it is clear that evidence is needed as to how and where such approaches are effective.

The next group of papers shift from frameworks to evidence from interventions. Celum and colleagues provide a timely and comprehensive review of the state of knowledge on pre-exposure prophylaxis for adolescent girls and young women in Africa [37]. The paper summarizes lessons from PrEP implementation projects and concludes that these are feasible interventions, but identified significant challenges; like Gomez they identify the need for appropriate and targeted messages for demand creation; the need for youth friendly and integrated services that address wider concerns such as sexually transmitted infections and contraception; the need for novel approaches to supporting adherence. Eakle and colleagues' paper is a scoping review of the evidence on the perspectives and experience of using PrEP among people at risk of HIV in sub-Saharan Africa [38]. From 35 included papers, they were able to identify five themes which affected acceptability and utilization. These resonate with many of the factors highlighted elsewhere in this issue, including empowerment and stigma, complex risk environments and relationships as well as specifics concerning efficacy, side-effects and practical challenges in use. This speaks to the need for more in-depth research into user views and priorities if current and future technologies are to be widely implemented. A further review by Ensor and colleagues draws together quantitative and qualitative evidence from 18 papers on the effectiveness of demand creation interventions for male circumcision programmes [39]. Financial incentives that compensate for loss of income and costs have a large relative impact on uptake, but absolute effect was larger in programmes involving community leaders and education.

Pettifor and colleagues conducted a qualitative study of a cash transfer project in Tanzania, and propose a conceptual framework for the possible mechanisms for reducing HIV risk [40]. Reduced dependence on transactional sex may be one mechanism, but they also identified the importance of business education and mentorship in building young women's efficacy and self-esteem, and argue that these may have a greater impact in the long term. This kind of qualitative research is able to explore how interventions work, an essential part of the transition from efficacy to implementation.

The final group of papers address the programme science of HIV prevention, which should provide evidence of who to target with which interventions, how to evaluate, adjust and continually strengthen programmes in response to feedback [41]. Cowan and colleagues use programme data to inform a mathematical model in order to assess whether scale up of interventions for sex workers could contribute to elimination of HIV in Zimbabwe [42]. They estimate that up to 70% of all new HIV infections could have been averted if sex work interventions had achieved complete coverage in 2010; while they

recognize the limitations of this as a model, the paper raises an important point by showing that appropriate scaling of interventions is essential if they are to have impact at a population level. One obstacle to such scale-up for programmes is cost, and this is addressed in the paper by Roberts and colleagues [43]. Using data from a PrEP implementation project in Kenya, they identified costs of the programme and explored different scenarios to show that incremental costs were sensitive to the delivery approach and the extent to which monitoring, for example routine creatinine testing, were included. The paper provides estimates that can be used to explore the cost-effectiveness and budget impact when providing PrEP that will be an import contribution to policy and practice with this relatively new intervention. The paper has important implications for contemporary discussions of different PrEP delivery models such as pharmacy-based and direct to consumer marketing.

In Kenya, HIV Prevention Cascades have been used as programme management tools, and Bhattacharjee and colleagues describe their use in combination HIV prevention interventions for sex workers [44]. The paper shows that the cascade, while intended as a relatively simple tool, can be quite complex in practice. The first challenge was to agree the target population or denominator, which is challenging for relatively hidden and transient populations, and then measures of uptake have to be defined. Despite these challenges, they show how such data helped identify significant gaps in the programme, and by using the same approach at a delivery level, service providers can reflect on and improve their own performance. The final paper from Moorhouse et al. describes how the HIV Prevention Cascade informed the identification and evaluation of interventions in Zimbabwe [45]. They propose a standard approach to the use of the cascade to develop interventions.

6 | CONCLUSIONS

Technological innovations hold enormous promise for improving health, and in HIV research there have been remarkable advances in the development of efficacious tools for treatment and prevention. Ensuring that these lead to maximum impact is just as much of a challenge as developing the technologies themselves. In populations with the highest HIV incidence, achieving impact will require the close collaboration of a wide range of stakeholders and disciplines, political will, investment and ongoing evaluation and programme iteration. The articles in this supplement have focused on some of the advances and insights from diverse disciplinary backgrounds. The contributions have largely focused on young women, which was an initial priority as we understand that they have often been failed by previous programmes and technologies. Now that we have female-controlled methods the onus is on us to support women in accessing and using them. However, we recognize this focus as a limitation, with men, particularly young men in Southern and East Africa, also being at ongoing risk with limited access to the resources and methods to protect themselves and their partners.

We hope that this journal issue will spark more interest in this evolving field and contribute to the progress required to end AIDS.

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COMPETING INTERESTS

All authors have no competing interest to declare.

AUTHORS' CONTRIBUTIONS

H.W. and G.G. drafted the manuscript, all authors contributed to revisions and approved the final version.

AUTHOR INFORMATION

HW was co-chair of the Banbury meeting held from 16 to 19 May 2017 on the subject of this editorial that led to the idea for this supplement. GG and GD proposed the idea of the Banbury meeting and were participants.

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REFERENCES

1. UNAIDS. Fast-track – ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014.
2. Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD, et al. What is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the fast-track approach. PLoS One. 2016;11(5):e0154893.
3. UNAIDS. Miles to go – closing gaps, breaking barriers, righting injustices. Geneva: UNAIDS; 2018.
4. Izazola-Licea JA, Mattur D. Better targeting of existing investments in prevention is needed to focus on interventions with proven impact: prevention resources need to double by 2020 to reach Fast Track targets. 22nd International AIDS Conference, Amsterdam, July 2018 [cited 2019 Mar 25], Abstract THPED582. Available from: http://programme.aids2018.org/Abstract/Abstract/3752
5. Hayes RJ, Donnell DJ, Floyd S, Mandla N, Bwalya J, Shanaube K, et al. Impact of universal testing and treatment in Zambia and South Africa: HPTN071 (PopART). Presented at CROI 2019 [cited 2019 Mar 25]. Abstract 92 LB. Available from: http://www.croiconference.org/sites/default/files/uploads/92LB.pdf
6. Havlir D, Charlebois E, Balzer L, Clark T, Kwarisiima D, Ayieko J, et al. SEARCH community cluster randomized study of HIV "test and treat" using multi- disease approach and streamlined care in rural Uganda and Kenya. AIDS conference. 2018 [cited 2019 Mar 25]. Available from: http://programme.aids2018.org/Abstract/Abstract/13469
7. UNAIDS. Prevention Gap Report. Geneva: UNAIDS; 2016.
8. Nwokolo N, Hill A, McOwan A, Pozniak A. Rapidly declining HIV infection in MSM in central London. Lancet HIV. 2017;4(11):e482–3.
9. Medland NA, Chow EPF, Read THR, Ong JJ, Chen M, Denham I, et al. Incident HIV infection has fallen rapidly in men who have sex with men in Melbourne, Australia (2013–2017) but not in the newly-arrived Asian-born. BMC Infect Dis. 2018;18:410.
10. Brown K, Williams DB, Kinchen S, Saito S, Radin E, Patel H, et al. Status of epidemic control among adolescent girls and young women aged 15-24 years – seven African countries, 2015-2017. MMWR Morb Mortal Wkly Rep. 2018;67:29–32.
11. Minnis AM, Padian NS. Effectiveness of female controlled barrier methods in preventing sexually transmitted infections and HIV: current evidence and future research directions. Sexually Transmitted Infections. 2005;81:193–200.

12. UN. World population prospects: the 2017 revision. New York, 2017.
13. Stover J, Rosen JE, Carvalho MN, Korenromp EL, Friedman HS, Cogan M, et al. The case for investing in the male condom. PLoS One. 2017;12(5):e0177108.
14. Bekker LG, Johnson L, Cowan F, Overs C, Besada D, Hillier S, et al. Combination HIV Prevention for female sex workers: what is the evidence. Lancet. 2015;385(9962):72–87.
15. Sullivan PS, Carbello-Dieguez A, Coates T, Goodreau SM, McGowan I, Sanders EJ, et al. Successes and challenges of HIV prevention in men who have sex with men. Lancet. 2012;380:388–99.
16. Smith B, Mann C, Jones C, Miller N, Longfield K, Gesuale S. Challenges and recommendation for reacing "Fast-Track" targets for condom use. Mann Global Health. 2018 [cited 2019 Apr 19] Available from https://hivpreventioncoalition.unaids.org/resource/challenges-and- recommendations-for-reaching-fast-track-targets-for-condom-use-2016/
17. Grulich AE, Guy R, Amin J, Jin F, Selvey C, Holden J, et al. Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. Lancet HIV. 2018;5:e629–37.
18. Sidebottom D, Ekstrom AM, Stromdahl S. A systematic review of adherence to oral pre-exposure prophylaxis for HIV – how can we improve uptake and adherence? BMC Infect Dis. 2018;18:581.
19. Johnson J, Jefferys R. Preventive technologies: antiretroviral and vaccine development. HIV, TB, HCV Pipeline Report 2018. Treatment Action Group July 2017 [cited 2019 Mar 25]. Available from: http://www.pipelinereport.org/2017/hivpx
20. WHO. Progress Brief: Voluntary Medical Male Circumcision for HIV Prevention, July 2018. Geneva, 2019 [cited 2019 Mar 25]. Available from: https://www.malecircumcision.org/resource/who-progress-brief-voluntary-medical-male-circumcision-hiv-prevention-July-2018
21. Garnett GP, Hallett TB, Takaruza A, Hargreaves J, Rhead R, Warren M, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. Lancet HIV. 2016;3(7):e297–306.
22. Mojola SA. Love, money and HIV: becoming a modern African woman in the age of AIDS. Oakland: University of California Press; 2014.
23. Price JT, Rosenberg NE, Vansia D, Phanga T, Bhushan NL, Maseko B, et al. Predictors of HIV, HIV Risk Perception, and HIV Worry Among Adolescent Girls and Young Women in Lilongwe, Malawi. J Acquir Immune Defic Syndr. 2018;77(1):53–63.
24. Bórquez A, Cori A, Pufall EL, Kasule J, Slaymaker E, Price A, et al. The Incidence Patterns Model to Estimate the Distribution of New HIV Infections in Sub-Saharan Africa: Development and Validation of a Mathematical Model. PLoS Med. 2016;13(9):e1002121.
25. Stoebenau K, Heise L, Wamoyi J, Bobrova N. Revisiting the understanding of "transactional sex" in sub-Saharan Africa: a review and synthesis of the literature. Soc Sci Med. 2016;168:86–197.
26. Maughan-Brown B, Venkataramani AS. Accuracy and determinants of perceived HIV risk among young women in South Africa. BMC Public Health. 2018;18:42.
27. Garnett GP, White PJ, Ward H. Fewer partners or more condoms? Modelling the effectiveness of STI prevention interventions. Sex Transm Infect. 2008;84:ii4–11.
28. Boerma JT, Weir SS. Integrating demographic and epidemiological approaches to research on HIV/AIDS: the proximate-determinants framework. J Infect Dis. 2005;191:S61–7.
29. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3:e318–22.
30. Hadley A, Chandra-Mouli V, Ingham R. Implementing the United Kingdom government's 10-year teenage pregnancy strategy for England (1999–2010): applicable lessons for other countries. J Adolesc Health. 2016;59:68–74.
31. Sommer M, Mmari K. Addressing structural and environmental factors for adolescent sexual and reproductive health in low- and middle-income countries. Am J Public Health. 2015;105(10):1973–81.
32. UNFPA. Meeting the Need: Strengthening Family Planning Programs. 2006 [cited 2019 Apr 19]. Available from: https://www.unfpa.org/resources/meeting-need-strengthening-family-planning-programs
33. CSHL (Cold Spring Harbor Laboratory). Banbury Center Directors Report. 2017 [cited 2019 Mar 25]. Available from; https://www.cshl.edu/wp-content/uploads/2019/03/Banbury-Annual-Report-2017.pdf
34. Mojola SA, Wamoyi J. Contextual drivers of HIV risk among young African women. J Int AIDS Soc. 2019;22(S4):e25302.
35. Skovdal M. Facilitating engagement with PrEP and other HIV prevention technologies through practice-based combination prevention. J Int AIDS Soc. 2019;22(S4):e25294.
36. Gomez A, Loar R, Kramer AE. Reaching and targeting more effectively: the application of market segmentation to improve HIV prevention programs. J Int AIDS Soc. 2019;22(S4):e25318.
37. Celum CL, Delany-Moretlwe S, Baeten JM, van der Straten A, Hosek S, Bukusi E, et al. HIV pre-exposure prophylaxis for adolescent girls and young women in Africa: from efficacy trials to delivery. J Int AIDS Soc. 2019;22(S4):e25298.
38. Eakle R, Weatherburn P, Bourne A. Understanding user perspectives of and preferences for oral PrEP for HIV prevention in the context of intervention scale-up: a synthesis of evidence from sub-Saharan Africa. J Int AIDS Soc. 2019;22(S4):e25306.
39. Ensor S, Davies B, Rai T, Ward H. The effectiveness of demand creation interventions for voluntary male medical circumcision for HIV prevention in sub-Saharan Africa; a mixed methods systematic review. J Int AIDS Soc. 2019;22(S4):e25299.
40. Pettifor A, Wamoyi J, Balvanz P, Waruguru Gichane M, Maman S. Cash plus: exploring the mechanisms through which a cash transfer plus financial education program in Tanzania reduced HIV risk for Adolescent Girls and Young Women. J Int AIDS Soc. 2019;22(S4):e25316.
41. Becker M, Mishra S, Aral S, Bhattacharjee P, Lorway R, Green K, et al. The contributions and future direction of Program Science in HIV/STI prevention. Emerging themes in epidemiology. 2018;15:7.
42. Cowan FM, Chabata ST, Musemburi S, Fearon E, Davey C, Ndori-Mharadze T, et al. Strengthening the scale up and uptake of effective interventions for sex workers for population impact in Zimbabwe. J Int AIDS Soc. 2019;22(S4):e25320.
43. Roberts A, Barnabas RV, Abuna F, Lagat H, Kinuthia J, Pintye J, et al. The role of costing in the introduction and scale up of HIV pre-exposure prophylaxis: evidence from integrating PrEP into routine maternal and child health and family planning clinics in western Kenya. J Int AIDS Soc. 2019;22(S4):e25296.
44. Bhattacharjee P, Musyoki HK, Becker M, Musimbi J, Kaosa S, Kioko J, et al. HIV Prevention Programme Cascades: insights from HIV Programme Monitoring for Female Sex Workers in Kenya. J Int AIDS Soc. 2019;22(S4):e25311.
45. Moorhouse L, Schaefer R, Thomas R, Nyamukapa C, Skovdal M, Hallett TB, et al. Application of the HIV prevention cascade to identify, develop, and evaluate interventions to improve use of prevention methods: examples from a study in east Zimbabwe. J Int AIDS Soc. 2019;22(S4):e25309.

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COMMENTARY

Contextual drivers of HIV risk among young African women

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Abstract

Introduction: Significant progress has been made in the African HIV pandemic; however, the pace of incidence decline has slowed or stalled in many East and Southern African countries, especially among young women. This stall is worrying because many countries have burgeoning youth populations. There is an important window of opportunity to halt the epidemic as well as the potential for millions more infections if primary prevention efforts are not strengthened.

Discussion: Many hyper-endemic settings have been exposed to numerous interventions; however, HIV incidence among young women has remained high. In this paper, we characterize the intervention context and examine how it can be strategically utilized to maximize HIV prevention interventions among young women. We begin by examining how contextual dynamics drive HIV risk. We illustrate how epidemiological contexts, gendered normative and economic contexts, and environmental contexts work synergistically to make young women especially vulnerable to HIV infection. We then examine how these contexts can undermine HIV prevention interventions. Finally, we discuss the importance of fully mapping out the intervention context to enhance the effectiveness of HIV prevention interventions.

Conclusions: Understanding an intervention context, and how its features work together to amplify young women's risk in hyper-endemic settings can contribute to sustained momentum in reducing HIV incidence among young women and help to limit the reach of the HIV pandemic into new generations of Africans.

Keywords: HIV prevention; adolescent girls; young women; Africa; hyper-endemics; interventions

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1 | INTRODUCTION

Despite significant progress over the last few decades, sub-Saharan Africa continues to bear the brunt of the HIV/AIDS pandemic, with two-thirds of the 1.8 million new HIV infections, and 70% (an estimated 660,000 deaths) of AIDS related mortality [1]. Adolescent girls and young women are disproportionately affected; an estimated 7000 are newly infected each week and 75% of new infections among 15- to 19-year olds are in girls [1]. In South Africa alone, there were an estimated 113,000 new infections among women aged 15 to 24 [2]. Furthermore, many high prevalence countries in East and Southern Africa have between a third to almost half of their populations under the age of 15 [3], and there is a slow down or stall in the pace of decline in new infections [4]. Stalling HIV epidemics combined with burgeoning youth populations present both a challenge and an important window of opportunity where the epidemic can be halted or yield to dramatic increases of those in need of life-long medication [5,6].

Recent years have brought a growing recognition of the spatial concentration of hyper-endemics (settings with persistently high HIV incidence, and/or HIV prevalence exceeding 15% of the adult population [7,8]), and the significance of social context to focus HIV prevention interventions and improve HIV incidence control [9-15]. However, despite numerous interventions [16-20], incidence remains high. How might intervention outcomes be improved? In this paper, we build on previous research by characterizing the intervention context, and examining how it can be strategically utilized to maximize HIV prevention interventions among young women. We begin by describing how contextual dynamics drive HIV hyper-endemics, we then illustrate how they can undermine prevention interventions, and conclude by discussing how fully mapping an intervention context can contribute to more effective HIV prevention interventions among young women. While our conceptual framework is applicable to other settings, we draw on African examples to illustrate our points.

2 | DISCUSSION

2.1 | How social contexts drive HIV hyper-endemics

Many hyper-endemic settings share similar social contexts that interact synergistically to create a dangerous HIV risk environment for girls transitioning to adulthood. Figure 1 illustrates the different contexts which we discuss in turn.

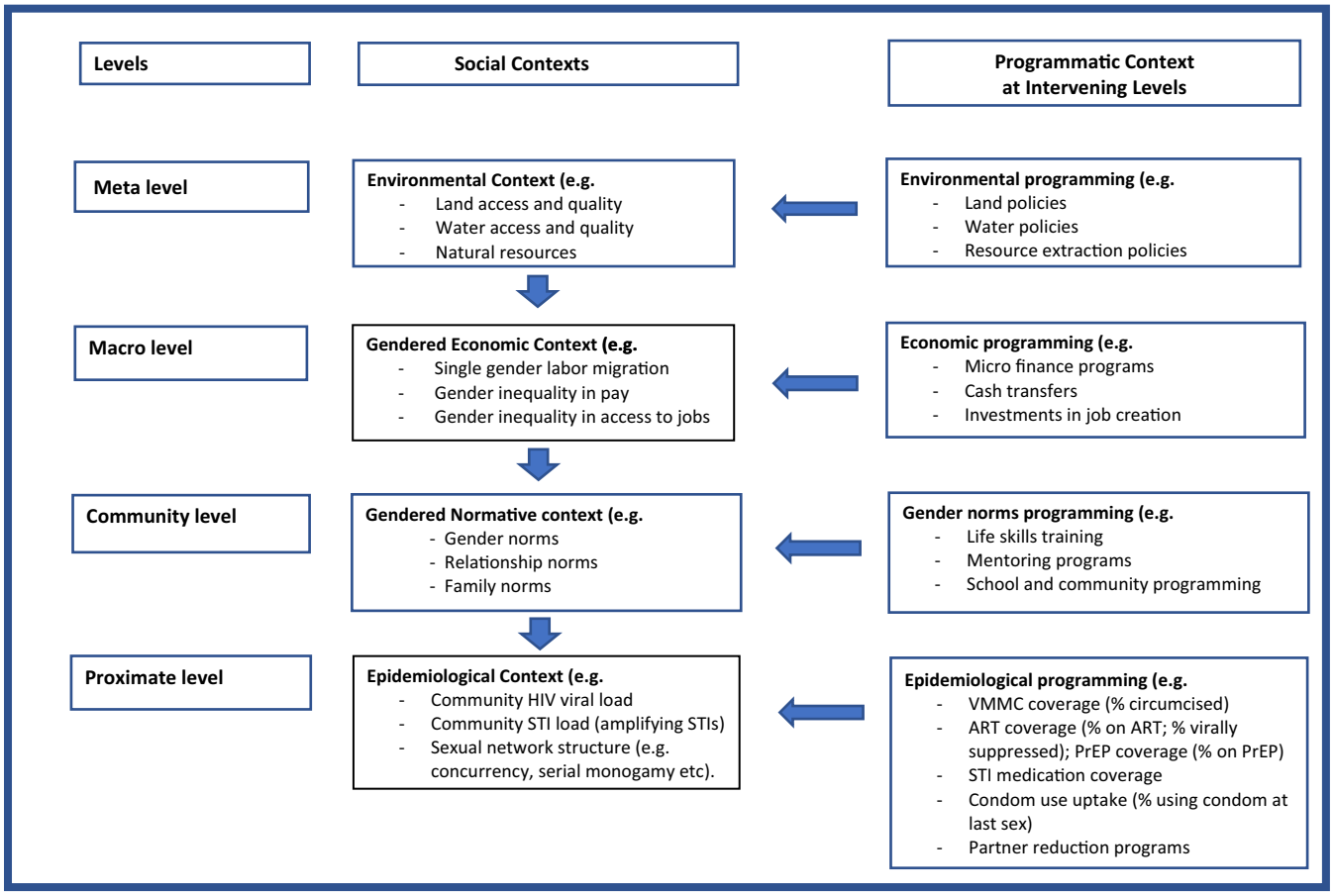

Figure 1. Intervention context

2.1.1 | *The epidemiological context*

Hyper-endemics are often characterized by interacting epidemiological factors that work together to make even a single sexual encounter risky for young women [21]. For example in Kenya, 65% of new infections are concentrated in nine of its 47 counties [22]. Young people (15 to 24) account for half (52%) of new infections in the country's highest incidence and prevalence counties which are Homa Bay (26% prevalence), Siaya (25% prevalence) and Kisumu (20% prevalence) [23], located in Nyanza province. Nyanza also has an amplifying sexually transmitted infection (STI) epidemic; 57% and 38% of women and men respectively have herpes simplex virus type 2 (HSV-2) [24]. STIs such as HSV-2 are associated with a significant increase in HIV acquisition risk [25-27]. Furthermore, the sexual network structure in Nyanza creates vulnerability with high levels of concurrency [28,29]. Despite a risky epidemiological context, uptake of programming targeted at this level (epidemiological programming) is low. In Homa Bay county, 44% of men were uncircumcised, and almost half of those with multiple partners reported not using a condom at last sex. HIV testing among key populations such female sex workers and men who have sex with men was low. While most (63%) adults living with HIV were on antiretroviral therapy (ART), viral suppression was 55% [23]. KwaZulu-Natal (KZN), South Africa has similar combinations of interacting epidemiological factors and the HIV prevalence is 24%. About 51% of 25- to 29-year-old women, and 44% of 30- to 34-year-old men are living with HIV [30,31]. Like Nyanza, KZN also has an amplifying STI epidemic (syphilis, gonorrhoea, chlamydia, *Trichomonas vaginalis*). STI prevalence is 13%, and young women under age 25 are at significantly higher risk [32]. About 77% of men have not been circumcised [33], and while viral suppression among those on medication was high among teenagers (68%) and 20- to 24-year olds (87%), overall, ART use was less than 45% among those aged 15 to 34 [34].

In sum, in hyper-endemic settings like these, young women's sexual lives unfold in epidemiological contexts with high community viral loads of HIV and amplifying STIs. Furthermore, high prevalence means they are likely to encounter a partner with HIV, and their most likely sexual partners – men in their 20s and 30s – generally have low rates of circumcision, report relatively low rates of condom use, and among those living with HIV, have relatively low viral suppression. This combination of interacting epidemiological factors places young women at significant risk for HIV acquisition [21,35].

2.1.2 | *The gendered normative context*

When layered on to a dangerous epidemiological context, the gendered normative context works to further amplify young women's HIV risk. Social norms regulate sexual behaviour by

setting "group level expectations for appropriate behavior that result in negative sanctions for people who violate them." [36, p. 1283, 13]. Gendered community norms set expectations around women's autonomy, ideal or accepted sexual network structures (e.g. concurrency or serial monogamy), gender power and material exchanges within relationships [37-42]. Community members can be sanctioned through stigma and shaming (e.g. of women seen to have too many relationships or men who do not provide for their partners), leaving relationships, and gender-based violence [43-46]. Further, young women are not operating as individuals, but rather, are embedded within families/households and communities through which gendered norms and expectations may be primarily exerted [47,48].

Hyper-endemic HIV risk environments share similar gendered normative contexts characterized by high levels of women's autonomy in entering and exiting relationships, but unequal gender power norms within them that are exacerbated when they are transactional [37-40]. Transactional sexual relationships are common in many hyper-endemic settings [5,37-39,41]. A survey in Kisumu, Nyanza's capital found that 72% of men gave almost 10% of their monthly income to girlfriends in the form of cash, meals, drinks, gifts, transportation and rent support [49] suggesting that men's provision was a normative expectation. Men who can provide are often older, and age-disparate relationships are associated with HIV acquisition among young women due to limited relationship agency resulting in limited leverage to use or insist on prevention technologies such as condoms and HIV testing [5,37,50-52].

It is important to note that gender and relationship norms also amplify men's HIV risk. Masculinity norms in many historically polygamous cultures are supportive of concurrency, and may also lead to men's lower uptake of HIV testing and treatment [5,53-56]. In Uganda, for example, concurrent men found couple HIV testing challenging [55]. Gendered norms are also embedded in community institutions such as health facilities which are often women-focused and sometimes neglect men [57-59].

Overall, the gendered normative context encourages young women to pursue the riskiest partners in their community – men in their 20s and 30s who are able to provide, but who are also more likely to afford and have cultural support in seeking multiple partners, and who are less likely to be reached by epidemiological programming.

2.1.3 | Gendered economic contexts and environmental contexts

Many hyper-endemic settings also have similar economic configurations characterized by widespread inequality and poor employment opportunities [31,60,61]. This contributes to high circular male labour migration to cities, mines, farms, on the road and on water for more lucrative work; women, meanwhile, have relatively limited employment and wage income [5,62-67]. Labour migration has been linked to high rates of concurrency, with patterns of reunion and separation providing regular opportunities for HIV transmission, and serving as bridges between sexual networks in different locations [62,63,65-69]. Female sex work is often symbiotic with labour migration, and places many women at particularly high risk [66,70]. Young women with migrant partners such as fishermen or truck drivers are also especially vulnerable [65-67]. Gendered economies thus amplify the HIV risk environment for young women by creating economic circumstances that can increase their likelihood of being involved in transactional and/or concurrent partnerships with high risk men, as well as commercial sex relationships. This results in a sexual network structure that further exacerbates young women's vulnerability.

Finally, it is important to note that the environmental context is often an underlying driver of gendered economic contexts. For example, unsustainable agricultural livelihoods may contribute to male out-migration; widows displaced from land may turn to sex work; new resource extraction may attract many more men to an area; and an imbalanced lake eco-system may exacerbate fishermen's migratory patterns leading to extended sexual networks and increased vulnerability for women [5,65,70,71].

While many features of these social contexts are not unique to hyper-endemic settings, they are distinguished by how they synergistically work together to significantly amplify young women's HIV vulnerability.

2.2 | How social contexts undermine HIV prevention interventions

There is now a widespread consensus that strategic combinations of multi-level HIV prevention approaches are the way forward, and many hyper endemic settings have been exposed to numerous interventions over the past few decades [13,14,72-79]. The most successful of these have been the widespread roll-out of ART which has led to large-scale reductions in HIV viral load and AIDS mortality, along with voluntary medical male circumcision (VMMC) [31,80-84]. In the following section we discuss how contexts can undermine otherwise efficacious interventions.

2.2.1 | How epidemiological contexts undermine interventions

Epidemiological contexts are often the Achilles heel of HIV prevention interventions. Major pre-exposure prophylaxis (PrEP) trials among young women in high incidence settings have had limited success [18-20]. This might be in part because other interacting factors operating in the epidemiological context were not concurrently engaged through epidemiological programming such as STI test and treat, VMMC, condom use campaigns, and male partner outreach for HIV testing and treatment. Epidemiological programming contributes to reducing the community STI and HIV viral load, thus creating an enabling environment [16] for PrEP to work. Singularly focusing on PrEP places undue weight on the intervention and young women's high adherence to it to protect themselves from HIV. This "single bullet" approach makes intervention success even more challenging when considering the amplifying effect of gendered normative contexts.

2.2.2 | How gendered normative contexts undermine interventions

Many HIV prevention interventions do not adequately work to meaningfully alter the gendered normative context that will ultimately determine prevention uptake and its long-term sustainability [5,20,85,86]. Unequal gender power norms,

reinforced by age-disparate relationships limit young women's leverage and willingness to regularly use and negotiate prevention technologies such as condoms or PrEP [5,37,43,63,85-87]. This is exacerbated in long-term relationships where the potential for repeated exposure to HIV exists alongside love and trust. Indeed this might explain why couple PrEP interventions have been effective [88-90]. Intervention success may be continually undermined when it is not paired with programming to create enabling community norms governing prevention technologies in ways that engage both women and men. Relevant community institutions such as families and schools which may only support abstinence, and health facilities which might limit access for young unmarried women are also important to engage.

2.2.3 | How gendered economic and environmental contexts undermine interventions

Many promising micro-finance or cash transfer interventions have been conducted with limited impact on HIV incidence with few exceptions [91-96]. Economic interventions can be undermined by synergies between the gendered normative and gendered economic context. Intervention design implicitly or explicitly substitutes male partner provision for intervention programme provision. This aligns with young women's limited economic opportunities and their limited ability to purchase desired goods for themselves. While interventions substitute material provision, however, they do not substitute what that provision also expresses – love and commitment [5,63,97-99]. This is likely exacerbated in hyper-endemic settings with large male migrant populations, where migrants express commitment through remittances or material provision. Furthermore, the short-term nature of interventions suggests that when they end, without associated efforts to stabilize young women's income, risk may be heightened with the renewed search for a partner. Finally, environmental interventions to improve land use or water quality, or to increase employment through opening up new resource extraction economies can undermine HIV prevention interventions if they serve to reinforce gendered economies which predominantly employ and differentially compensate men.

2.3 | Mapping and strategically utilizing the Intervention context

As Figure 1 illustrates, new interventions enter into a large ecology of pre-existing social and programmatic contexts that may enable, undermine or have a neutral effect on their ability to achieve their goals. The synergistic nature of contextual drivers of hyper-endemics highlights the importance of analysing and utilizing the intervention context to achieve incidence control.

An important first step is to map out the pre-existing intervention context in a given setting, and then locate the new intervention – and its intended mechanisms to reduce HIV incidence – within it. This will enable intervention designers to clearly see potential barriers and/or catalysts to their proposed intervention. Fully mapping the intervention context also enables designers to assess how much weight is being placed on the new intervention to achieve incidence control, and whether a longer duration or multi-level approach might increase the chances of success [13]. Finally, mapping the intervention context prior to intervention initiation would enable more systematic post-intervention analyses of why similar interventions worked in some settings and not in others [13,15], and ultimately, guide decisions about whether and under what conditions an intervention should be scaled up.

Mapping the intervention context also enables a strategic utilization of pre-existing features of social and programmatic contexts to increase the chances of intervention success. For example, intervening at multiple levels may be beyond the funding scope of an intervention; however, as noted earlier, numerous interventions are often ongoing in hyper-endemic settings [100]. When mapped, programming synergies become visible; they may preclude the need for a combination approach within a given intervention, or enable strategic planning of the most effective combinations given what already exists. Combination prevention interventions such as DREAMS would require different kinds of coordination with pre-existing programming than those aimed at one level (e.g. VMMC or PrEP), but which might need new supportive programming at different levels. An important coordinating role could be played by governments and sub-regional local authorities who typically engage in multi-sectoral planning, as many interventions within an intervention context aimed at HIV prevention might align well with broader community development goals.

3 | CONCLUSIONS

Each year, millions of adolescent African girls begin their sexual debut in hyper-endemic settings where one-fifth to one-third will be HIV positive by the time they are in their late 20s and early 30s. This commentary has examined how contextual drivers might contribute to stalling epidemics, and how they might be deployed to maximize HIV prevention. Understanding how contexts synergistically work together in hyper-endemic settings, and fully mapping and strategically utilizing the intervention context could enable sustained momentum in reducing HIV incidence among young women, and limiting the reach of the HIV pandemic into new generations of Africans.

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COMPETING INTERESTS

The authors report no competing interests.

AUTHORS' CONTRIBUTIONS

S.M. wrote the first draft of the manuscript. J.W. contributed to writing the manuscript. Both authors approved the final draft.

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REFERENCES

1. UNAIDS. 2018: fact sheet July 2018 [cited 2018 Sep 25]. Available at: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf
2. Shisana O, Rehle T, Simbayi LC, Zuma K, Jooste S, Zungu N, et al. South African national HIV prevalence, incidence and behaviour survey, 2012. Cape Town: HSRC Press; 2014.
3. PRB. World population data sheet. Population Reference Bureau. 2018.
4. UNAIDS. All in to end the adolescent AIDS epidemic: a progress report. 2016 [cited 2018 Sep 25]. Available at: http://www.unaids.org/en/resources/documents/2016/ALLIN2016ProgressReport
5. Mojola SA. Love, money, and HIV: becoming a modern African woman in the age of AIDS. Oakland, CA: University of California Press; 2014.
6. Saul J, Bachman G, Allen S, Toiv NF, Cooney C. The DREAMS core package of interventions: a comprehensive approach to preventing HIV among adolescent girls and young women. PLoS ONE. 2018;13(12):e0208167.
7. Principles of epidemiology in public health practice, third edition. An introduction to applied epidemiology and biostatistics. [cited 2019 Mar 18]. Available at: https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section11.html
8. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization. Practical Guidelines for Intensifying HIV Prevention; Towards Universal Access. Geneva, Switzerland: UNAIDS; 2007. ISBN 978 92 9173 557 0 (NLM classification: WC 5032).
9. Cuadros DF, Branscum AJ, Mukandavire Z. Temporal stability of HIV prevalence in high-burden areas regardless of declines in national HIV prevalence in Malawi and Zimbabwe. AIDS. 2018;32(10):1381–3.
10. McGillen JB, Anderson SJ, Dybul MR, Hallett TB. Optimum resource allocation to reduce HIV incidence across sub-Saharan Africa: a mathematical modelling study. Lancet HIV. 2016;3(9):e441–8.
11. Meyer-Rath G, McGillen JB, Cuadros DF, Hallett TB, Bhatt S, Wabiri N, et al. Targeting the right interventions to the right people and places: the role of geospatial analysis in HIV program planning. AIDS. 2018;32(8):957.
12. Wand H, Ramjee G. Targeting the hotspots: investigating spatial and demographic variations in HIV infection in small communities in South Africa. J Int AIDS Soc. 2010;13(1):41.
13. Auerbach JD, Parkhurst JO, Caceres CF. Addressing social drivers of HIV/AIDS for long-term response: conceptual and methodological considerations. Glob Public Health. 2011;6 Suppl 3:S293–309.
14. Blankenship KM, Friedman SR, Dworkin S, Mantell JE. Structural interventions: concepts, challenges and opportunities for research. J Urban Health. 2006;83(1):59–72.
15. Gupta GR, Parkhurst JO, Ogden JA, Aggleton P, Mahal A. Structural approaches to HIV prevention. Lancet. 2008;372(9640):764–75.
16. Hardee K, Gay J, Croce-Galis M, Peltz A. Strengthening the enabling environment for women and girls: what is the evidence in social and structural approaches in the HIV response? J Int AIDS Soc. 2014;17:18619.
17. Jewkes R, Nduna M, Levin J, Jama N, Dunkle K, Puren A, et al. Impact of Stepping Stones on incidence of HIV and HSV-2 and sexual behaviour in rural South Africa: cluster randomised controlled trial. BMJ. 2008;337:a506.
18. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367(5):411–22.
19. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372(6):509–18.
20. Celum CL, Delany-Moretlwe S, McConnell M, Van Rooyen H, Bekker LG, Kurth A, et al. Rethinking HIV prevention to prepare for oral PrEP implementation for young African women. J Int AIDS Soc. 2015;18:20227.
21. Dellar RC, Dlamini S, Karim QA. Adolescent girls and young women: key populations for HIV epidemic control. J Int AIDS Soc. 2015;18:19408.
22. NASCOP, NACC. Kenya HIV prevention revolution road map: countdown to 2030. Nairobi: Government of Kenya; 2014. 13 p.
23. NASCOP. Kenya HIV county profiles. Nairobi, Kenya: National AIDS and STI Control Programme. 2016.
24. Mugo N, Dadabhai SS, Bunnell R, Williamson J, Bennett E, Baya I, et al. Prevalence of Herpes simplex virus type 2 infection, Human immunodeficiency virus/Herpes simplex virus type 2 coinfection, and associated risk factors in a national, population-based survey in Kenya. Sex Transm Dis. 2011;38(11):1059–66.
25. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS. 2006;20(1):73–83.
26. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect. 1999;75(1):3–17.
27. Røttingen JA, Cameron DW, Garnett GP. A systematic review of the epidemiologic interactions between classic sexually transmitted diseases and HIV: how much really is known? Sex Transm Dis. 2001;28(10):579–97.
28. Westercamp N, Mattson CL, Bailey RC. Measuring prevalence and correlates of concurrent sexual partnerships among young sexually active men in Kisumu, Kenya. AIDS Behav. 2013;17(9):3124–32.
29. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS. 1997;11(5):641–648. Morris paper on concurrency.
30. Welz T, Hosegood V, Jaffar S, Bätzing-Feigenbaum J, Herbst K, Newell ML. Continued very high prevalence of HIV infection in rural KwaZulu-Natal, South Africa: a population-based longitudinal study. AIDS. 2007;21(11):1467–72.
31. Tanser F, Bärnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. Science. 2013;339(6122):966–71.
32. Naidoo S, Wand H, Abbai NS, Ramjee G. High prevalence and incidence of sexually transmitted infections among women living in KwaZulu-Natal, South Africa. AIDS Res Ther. 2014;11(1):31.
33. Zungu NP, Simbayi LC, Mabaso M, Evans M, Zuma K, Ncitakalo N, et al. HIV risk perception and behavior among medically and traditionally circumcised males in South Africa. BMC Public Health. 2016;16(1):357.
34. Huerga H, Shiferie F, Grebe E, Giuliani R, Farhat JB, Van-Cutsem G, et al. A comparison of self-report and antiretroviral detection to inform estimates of antiretroviral therapy coverage, viral load suppression and HIV incidence in Kwazulu-Natal, South Africa. BMC Infect Dis. 2017;17(1):653.
35. Karim QA, Baxter C, Birx D. Prevention of HIV in adolescent girls and young women: key to an AIDS-free generation. J Acquir Immune Defic Syndr. 2017;75:S17–26.
36. Mollborn S, Sennott C. Bundles of norms about teen sex and pregnancy. Qual Health Res. 2015;25(9):1283–99.
37. Luke N. Age and economic asymmetries in the sexual relationships of adolescent girls in sub-Saharan Africa. Stud Fam Plann. 2003;34(2):67–86.
38. Wamoyi J, Fenwick A, Urassa M, Zaba B, Stones W. 'Women's Bodies are Shops': beliefs about transactional sex and implications for understanding gender power and HIV prevention in Tanzania. Arch Sex Behav. 2011;40(1):5–15.
39. Stoebenau K, Heise L, Wamoyi J, Bobrova N. Revisiting the understanding of "transactional sex" in sub-Saharan Africa: a review and synthesis of the literature. Soc Sci Med. 2016;168:186–97.
40. Pulerwitz J, Mathur S, Woznica D. How empowered are girls/young women in their sexual relationships? Relationship power, HIV risk, and partner violence in Kenya. PLoS ONE. 2018;13(7):e0199733.
41. Hunter M. The materiality of everyday sex: thinking beyond 'prostitution'. Afr Stud. 2002;61(1):99–120.
42. Bhana D, Pattman R. Girls want money, boys want virgins: the materiality of love amongst South African township youth in the context of HIV and AIDS. Cult Health Sex. 2011;13(8):961–72.
43. Fielding-Miller R, Dunkle K, Jama-Shai N, Windle M, Hadley C, Cooper HLF. The feminine ideal and transactional sex: navigating respectability and risk in Swaziland. Soc Sci Med. 2016;158:24–33.
44. Schatz E. 'Take your Mat and Go!': rural Malawian women's strategies in the HIV/AIDS era. Cult Health Sex. 2005;7(5):479–92.
45. Reniers G. Marital strategies for regulating exposure to HIV. Demography. 2008;45(2):417–38.
46. Zembe YZ, Townsend L, Thorson A, Silberschmidt M, Ekstrom AM. Intimate partner violence, relationship power inequity and the role of sexual and social risk factors in the production of violence among young women who have multiple sexual partners in a peri-urban setting in South Africa. PLoS ONE. 2015;10(11):e0139430.

47. Wamoyi J, Wight D, Remes P. The structural influence of family and parenting on young people's sexual and reproductive health in rural northern Tanzania. Cult Health Sex. 2015;17(6):718–32.
48. Okigbo CC, Kabiru CW, Mumah JN, Mojola SA, Beguy D. Influence of parental factors on adolescents' transition to first sexual intercourse in Nairobi, Kenya: a longitudinal study. Reprod Health. 2015;12(1):73.
49. Luke N. Exchange and condom use in informal sexual relationships in urban Kenya. Econ Dev Cult Change. 2006;54(2):319–48.
50. De Oliveira T, Kharsany AB, Gräf T, Cawood C, Khanyile D, Grobler A, et al. Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: a community-wide phylogenetic study. Lancet HIV. 2017;4(1):e41–50.
51. Schaefer R, Gregson S, Eaton JW, Mugurungi O, Rhead R, Takaruza A, et al. Age-disparate relationships and HIV incidence in adolescent girls and young women: evidence from Zimbabwe. AIDS. 2017;31(10):1461.
52. Gregson S, Mugurungi O, Eaton J, Takaruza A, Rhead R, Maswera R, et al. Documenting and explaining the HIV decline in east Zimbabwe: the Manicaland General Population Cohort. BMJ Open. 2017;7(10):e015898.
53. Tomori C, Francisco LV, Kennedy CE, Kajula-Maonga L, Likindikoki S, Babalola SO, et al. The changing cultural and economic dynamics of polygyny and concurrent sexual partnerships in Iringa, Tanzania. Glob Public Health. 2013;8(7):857–70.
54. Hunter M. Masculinities, multiple-sexual-partners, and AIDS: the making and unmaking of Isoka in KwaZulu-Natal. Transformation. 2004;54(1):123–53.
55. Siu GE, Wight D, Seeley JA. Masculinity, social context and HIV testing: an ethnographic study of men in Busia district, rural eastern Uganda. BMC Public Health. 2014;14(1):33.
56. Skovdal M, Campbell C, Madanhire C, Mupambireyi Z, Nyamukapa C, Gregson S. Masculinity as a barrier to men's use of HIV services in Zimbabwe. Global Health. 2011;7(1):13.
57. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Trop Med Int Health. 2011;16(7):828–9.
58. Shand T, Thomson-de Boor H, van den Berg W, Peacock D, Pascoe L. The HIV blind spot: men and HIV testing, treatment and care in sub-Saharan Africa. IDS Bulletin. 2014;45(1):53–60.
59. Dovel K, Yeatman S, Watkins S, Poulin M. Men's heightened risk of AIDS-related death: the legacy of gendered HIV testing and treatment strategies. AIDS. 2015;29(10):1123.
60. Magadi MA. The disproportionate high risk of HIV infection among the urban poor in sub-Saharan Africa. AIDS Behav. 2013;17(5):1645–54.
61. Fox AM. The HIV-poverty thesis re-examined: poverty, wealth or inequality as a social determinant of HIV infection in sub-Saharan Africa? J Biosoc Sci. 2012;44(4):459–80.
62. Lurie MN, Williams BG, Zuma K, Mkaya-Mwamburi D, Garnett GP, Sweat MD, et al. Who infects whom? HIV-1 concordance and discordance among migrant and non-migrant couples in South Africa. AIDS. 2003;17(15):2245–52.
63. Hunter M. Love in the time of AIDS: inequality, gender, and rights in South Africa. Bloomington, Indiana: Indiana University Press; 2010.
64. Boerma JT, Gregson S, Nyamukapa C, Urassa M. Understanding the uneven spread of HIV within Africa: comparative study of biologic, behavioral, and contextual factors in rural populations in Tanzania and Zimbabwe. Sex Transm Dis. 2003;30(10):779–87.
65. Mojola SA. Fishing in dangerous waters: ecology, gender and economy in HIV risk. Soc Sci Med. 2011;72(2):149–56.
66. Kohli A, Kerrigan D, Brahmbhatt H, Likindikoki S, Beckham J, Mwampashi A, et al. Social and structural factors related to HIV risk among truck drivers passing through the Iringa region of Tanzania. AIDS Care. 2017;29(8):957–60.
67. Kwena ZA, Bukusi E, Omondi E, Ng'Ayo M, Holmes KK. Transactional sex in the fishing communities along Lake Victoria, Kenya: a catalyst for the spread of HIV. Afr J AIDS Res. 2012;11(1):9–15.
68. Morris M, Podhisita C, Wawer MJ, Handcock MS. Bridge populations in the spread of HIV/AIDS in Thailand. AIDS. 1996;10(11):1265–71.
69. Mojola SA, Williams J, Angotti N, Gómez-Olivé FX. HIV after 40 in rural South Africa: a life course approach to HIV vulnerability among middle aged and older adults. Soc Sci Med. 2015;143:204–12.
70. Elmes J, Skovdal M, Nhongo K, Ward H, Campbell C, Hallett TB, et al. A reconfiguration of the sex trade: how social and structural changes in eastern Zimbabwe left women involved in sex work and transactional sex more vulnerable. PLoS ONE. 2017;12(2):e0171916.
71. Dworkin SL, Grabe S, Lu T, Hatcher A, Kwena Z, Bukusi E, et al. Property rights violations as a structural driver of women's HIV risks: a qualitative study in Nyanza and Western Provinces, Kenya. Arch Sex Behav. 2013;42(5):703–13.
72. Padian NS, McCoy SI, Karim SS, Hasen N, Kim J, Bartos M, et al. HIV prevention transformed: the new prevention research agenda. Lancet. 2011;378(9787):269–78.
73. Brown G, Reeders D, Dowsett GW, Ellard J, Carman M, Hendry N, et al. Investigating combination HIV prevention: isolated interventions or complex system. J Int AIDS Soc. 2015;18(1):20499.
74. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
75. Dehne KL, Dallabetta G, Wilson D, Garnett GP, Laga M, Benomar E, et al. HIV prevention 2020: a framework for delivery and a call for action. Lancet HIV. 2016;3(7):e323–32.
76. Coates TJ, Richter L, Caceres C. Behavioural strategies to reduce HIV transmission: how to make them work better. Lancet. 2008;372(9639):669–84.
77. Gibbs A, Willan S, Misselhorn A, Mangoma J. Combined structural interventions for gender equality and livelihood security: a critical review of the evidence from southern and eastern Africa and the implications for young people. J Int AIDS Soc. 2012;15:1–10.
78. Ross DA. Behavioural interventions to reduce HIV risk: what works?. AIDS. 2010;24 Suppl 4:S4–14.
79. Harrison A, Colvin CJ, Kuo C, Swartz A, Lurie M. Sustained high HIV incidence in young women in Southern Africa: social, behavioral, and structural factors and emerging intervention approaches. Curr HIV/AIDS Rep. 2015;12(2):207–15.
80. Gargano JW, Laserson K, Muttai H, Odhiambo F, Orimba V, Adamu-Zeh M, et al. The adult population impact of HIV care and antiretroviral therapy in a resource poor setting, 2003–2008. AIDS. 2012;26(12):1545–54.
81. Grabowski MK, Serwadda DM, Gray RH, Nakigozi G, Kigozi G, Kagaayi J, et al. HIV prevention efforts and incidence of HIV in Uganda. N Engl J Med. 2017;377(22):2154–66.
82. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369(9562):657–66.
83. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005;2(11):e298.
84. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369(9562):643–56.
85. Mugo NR, Ngure K, Kiragu M, Irungu E, Kilonzo N. PrEP for Africa: what we have learnt and what is needed to move to program implementation. Curr Opin HIV AIDS. 2016;11(1):80.
86. Atujuna M, Newman PA, Wallace M, Eluhu M, Rubincam C, Brown B, et al. Contexts of vulnerability and the acceptability of new biomedical HIV prevention technologies among key populations in South Africa: a qualitative study. PLoS ONE. 2018;13(2):e0191251.
87. Jama Shai N, Jewkes R, Levin J, Dunkle K, Nduna M. Factors associated with consistent condom use among rural young women in South Africa. AIDS Care. 2010;22(11):1379–85.
88. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365(6):493–505.
89. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367(5):399–410.
90. Ware NC, Wyatt MA, Haberer JE, Baeten JM, Kintu A, Psaros C. What's love got to do with it? Explaining adherence to oral antiretroviral pre-exposure prophylaxis (PrEP) for HIV serodiscordant couples. J Acquir Immune Defic Syndr. 2012;59(5):463–8.
91. Pronyk PM, Hargreaves JR, Kim JC, Morison LA, Phetla G, Watts C, et al. Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomised trial. Lancet. 2006;368(9551):1973–83.
92. Dworkin SL, Blankenship K. Microfinance and HIV/AIDS prevention: assessing its promise and limitations. AIDS Behav. 2009;13(3):462–9.
93. Baird SJ, Garfein RS, McIntosh CT, Özler B. Effect of a cash transfer programme for schooling on prevalence of HIV and Herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet. 2012;379(9823):1320–9.
94. Handa S, Halpern CT, Pettifor A, Thirumurthy H. The government of Kenya's cash transfer program reduces the risk of sexual debut among young people age 15-25. PLoS ONE. 2014;9(1):e85473.
95. Pettifor A, MacPhail C, Hughes JP, Selin A, Wang J, Gómez-Olivé FX, et al. The effect of a conditional cash transfer on HIV incidence in young women in rural South Africa (HPTN 068): a phase 3, randomised controlled trial. Lancet Global Health. 2016;4(12):e978–88.

96. Cui RR, Lee R, Thirumurthy H, Muessig KE, Tucker JD. Microenterprise development interventions for sexual risk reduction: a systematic review. AIDS Behav. 2013;17(9):2864–77.
97. Poulin M. Sex, money, and premarital partnerships in southern Malawi. Soc Sci Med. 2007;65(11):2383–93.
98. Mojola SA. Multiple transitions and HIV risk among orphaned Kenyan schoolgirls. Stud Fam Plann. 2011;42(1):29–40.
99. Mojola SA. Material girls and material love: consuming femininity and the contradictions of post-girl power among Kenyan schoolgirls. Continuum. 2015;29(2):218–29.
100. Wamoyi J, Mshana G, Mongi A, Neke N, Kapiga S, Changalucha J. A review of interventions addressing structural drivers of adolescents' sexual and reproductive health vulnerability in sub-Saharan Africa: implications for sexual health programming. Reprod Health. 2014;11(1):88.

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COMMENTARY

Facilitating engagement with PrEP and other HIV prevention technologies through practice-based combination prevention

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Abstract

Introduction: Recent years have witnessed a rapid expansion of efficacious biomedical HIV prevention technologies. Promising as they may be, they are largely delivered through standard, clinic-based models, often in isolation from structural and behavioural interventions. This contributes to varied, and often poor, uptake and adherence. There is a critical need to develop analytical tools that can advance our understandings and responses to the combination of interventions that affect engagement with HIV prevention technologies. This commentary makes a call for practice-based combination HIV prevention analysis and action, and presents a tool to facilitate this challenging but crucial endeavour.

Discussion: Models and frameworks for combination HIV prevention already exist, but the process of identifying precisely what multi-level factors that need to be considered as part of a combination of HIV interventions for particular populations and settings is unclear. Drawing on contemporary social practice theory, this paper develops a "table of questioning" to help interrogate the chain and combination of multi-level factors that shape engagement with HIV prevention technologies. The tool also supports an examination of other shared social practices, which at different levels, and in different ways, affect engagement with HIV prevention technologies. It facilitates an analysis of the range of factors and social practices that need to be synchronized in order to establish engagement with HIV prevention technologies as a possible and desirable thing to do. Such analysis can help uncover local hitherto un-identified issues and provide a platform for novel synergistic approaches for action that are not otherwise obvious. The tool is discussed in relation to PrEP among adolescent girls and young women in sub-Saharan Africa.

Conclusions: By treating engagement with HIV prevention technologies as a social practice and site of analysis and public health action, HIV prevention service planners and evaluators can identify and respond to the combination of factors and social practices that interact to form the context that supports or prohibits engagement with HIV prevention technologies for particular populations.

Keywords: HIV prevention; combination prevention; innovations; HIV prevention technologies; PrEP; social practice theory

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1 | INTRODUCTION

Despite some successes in HIV prevention, 1.8 million people were infected with HIV in 2017, and rates of infection grew in more than 50 countries [1]. In sub-Saharan Africa, the region worst affected by the HIV epidemic, more than a third of new infections in 2017 occurred among young people (15 to 24 years) [1]. Although adolescent girls and young women (15 to 24) only make up 10% of the population in sub-Saharan Africa, they account for a quarter of all new HIV infections [2]. This, coupled with a so-called "youth bulge" in sub-Saharan Africa [3], has contributed to a sense of urgency to harness recent biomedical and health service successes in HIV treatment and rapidly expand the availability of biomedical HIV prevention technologies.

Promising as these innovations may be, biomedical HIV prevention technologies are largely implemented in isolation from structural and behavioural interventions, with little recognition of their synergies [4]. The difficulty of identifying the combination of biomedical, structural and behavioural interventions required for strategic advantage and synergy is widely recognized [4-6]. This challenge is compounded by the absence of an analytical framework to help HIV prevention service planners and evaluators identify the combination of interventions that work, under what circumstances, for whom, and with which HIV prevention practices in focus. This commentary has two aims. One, to argue that the biomedical turn in HIV prevention presents both a need and an opportunity to conceptualize practice-based combination prevention as an approach for disentangling and responding to the range of behavioural, biomedical and structural elements that interact with non-linear and multiplying effects to shape HIV prevention practices, including engagement with HIV prevention technologies. Two, to develop and demonstrate a tool for interrogating and

responding to the chain, sequence or combination of factors that affect engagement (or otherwise) with HIV prevention technologies, as well as the role of other shared social practices.

2 | DISCUSSION

2.1 | The biomedical turn in HIV prevention

Remarkable progress has been made in expanding the portfolio of biomedical HIV prevention technologies available to young people. We now know that people living with HIV (PLHIV) and on antiretroviral therapy can reach undetectable levels of viral load, which prevents them from transmitting HIV to their sexual partners [7]. This is referred to as treatment as prevention (TasP). Antiretroviral drugs can also be taken orally by HIV negative people as a pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP), significantly reducing the risk of becoming infected [8,9]. Alternative ways of delivering antiretroviral drugs, such as through vaginal rings [10], microbicide gels [11] or films [12], are being tested in demonstration projects. Voluntary medical male circumcision (VMMC) has proved efficacious, lowering men's risk of HIV infection by up to 60% [13]. These technologies, with the exception of VMMC, are considered "highly user-dependent" and adherence is repeatedly stated as the strongest determinant of their effectiveness [14,15].

Unfortunately, examples from across the globe highlight varied uptake and adherence to these HIV prevention technologies, particularly among young people [2,16]. While uptake and adherence to PrEP is generally high among certain groups of men who have sex with men in high-income settings [17], disappointing levels of uptake and adherence to PrEP among adolescent girls and young women (AGYW) is widespread in sub-Saharan Africa [18,19]. Systematic reviews have found PEP adherence to be generally poor, but particularly so among adolescents [20]. Uptake of VMMC continues to be slow in a number of sub-Saharan African countries [21], although some countries, like South Africa [22], have witnessed rapid increases of uptake in recent years. Successes in VMMC scale-up, however, are often attributed to school-based programmes targeting males 10 to 14, with young men falling behind [23]. While treatment as prevention has demonstrated its effectiveness, emerging evidence from South Africa suggest that poor levels of antiretroviral drug adherence among sexually active adolescents living with HIV may undermine treatment as a form of secondary prevention [24]. These varied outcomes suggest that populations and settings appropriate and respond to HIV prevention technologies in different ways. To optimize engagement with HIV prevention technologies, we need to meet young people where they are [25], and uncover local hitherto un-identified issues that obstruct their uptake and engagement with these technologies, and identify novel approaches for action that are not otherwise obvious.

Current emphasis on biomedical HIV prevention technologies confronts HIV prevention service planners and evaluators with two challenges. One, to refrain from falling into the trap of assuming that individuals are capable of making informed, rational and unfettered choices for themselves, renewing emphasis on the behaviour of individuals to make use of, and consistently adhere to, HIV prevention technologies. Two, to consider how a broader set of political, social, cultural and ethical issues interact to shape the ability and decision of young people to engage or disengage with HIV prevention technologies. Herein lies the opportunity for a more focused and practice-oriented approach to combination HIV prevention. Rather than utilizing standard, clinic-based models to promote uptake and adherence – assuming young people to be observers of specific behaviours following recommendations from a healthcare provider – there is a need to recognize the broader set of factors and other shared social practices (structural elements) that need to be synchronized to shape engagement (behavioural elements) with HIV prevention technologies (biomedical elements). Practice-based combination prevention, in an era of biomedical HIV prevention, is therefore about identifying and responding to the combination of multi-level factors and other shared social practices whose synergies create the context for particular populations that supports or prohibits the practice of engaging with HIV prevention technologies.

2.2 | Existing combination HIV prevention models and frameworks

A few existing frameworks and models for combination HIV prevention do exist, and include among others the Multiple Domain Model [26], the Dynamic Social Systems Model [27], the Network-Individual-Resource Model [28], the HIV prevention cascade [29-31] and Complex Systems theory [4,32]. Each of these models and frameworks usefully highlight how a range of factors influence each other in complex ways, with implications for how individuals effectively deploy HIV prevention technologies or behaviours. Useful as they are, the process of identifying precisely what multi-level factors that need to be considered as part of a combination HIV prevention intervention for particular HIV prevention practices, populations, settings and stages of the epidemic is unclear. Interventions are often selected based on available evidence, but key factors may be missed if HIV prevention service planners and evaluators primarily draw on published evidence from other contexts. Furthermore, pinpointing exactly how structure and the social intersect with individual behaviour, affecting HIV prevention, is difficult and complex, hampering both empirical research and combination prevention interventions. This challenge has been noted by Susan Kippax [33] who warns against HIV research and public health models that identify structural factors without interrogating the mediating links between individual, community and societal phenomena. Kippax [34] posits that it is through social practices we can understand and shape the relationship between multiple levels of influence. For these reasons, I look to contemporary theories of practice and draw on the vocabulary they have developed to propose a tool for analysing and understanding how structure, individual behaviour and biomedical technologies interact and come together to affect engagement with HIV prevention technologies. The tool supplements existing models and frameworks for combination HIV prevention by sparking conversations and local research to uncover new issues and connections between defining factors, which may lead to specific actions.

2.3 | A "table of questioning" tool for practice-based combination HIV prevention

Reckwitz [35: p. 249] defines a practice as "[a] routinized type of behaviour which consists of several elements, interconnected to one other: forms of bodily activities, forms of mental activities, 'things' and their use, a background knowledge in the form of understanding, know-how, states of emotion and motivational knowledge." According to this definition, agency and the routine practice of engaging with HIV prevention technologies is enabled by numerous overlapping factors of influence coming together. These different factors form part of the fabric of our everyday lives, across scales from the individual to the macro as well as space and time. The factors consist of, or give rise to, a broad domain of human activities, which both reproduce or transform the factors themselves and social practices that overlap to coordinate and synchronize the practice of engaging (or otherwise) with HIV prevention technologies. According to Blue et al. [36], looking at public health practices is critical if health service planners and evaluators are to disentangle the configuration of factors, or hybrid of social practices, which establish healthy practices as (im)possible or (un)desirable.

Drawing on the work of contemporary social practice theorists, including Kemmis et al. [37] and Shove et al. [38], the proposed "table of questioning" offers a strategy for facilitating analysis and action for practice-based combination HIV prevention. The tool presents 10 questions, which in a two-step process seek to facilitate reflection and analysis of the range of factors that shape (dis)engagement with a particular HIV prevention technology. The tool is by no means all encompassing. It merely provides a flavour of how placing emphasis on the practice of (dis)engaging with HIV prevention technologies can offer new insight and direction for practice-based combination HIV prevention. Practices vary in scope and size, and the boundaries (type of technology, setting, population group, timing), while permeable, should be established by the objectives of the analysts [36].

The tool presents a matrix with five different types of factors across four socio-ecological levels (see Figure 1). The four ecological levels, namely "macro," "meso," "micro" and individual levels, akin to Bronfenbrenner's socio-ecological framework [39], have been plotted into the tool in response to a call for greater clarity of how practices, enacted by people at a micro-level, are positioned in macro structures [40]. The tool encourages HIV prevention service planners and evaluators to first explore the constellation of factors that affect engagement with HIV prevention technologies for a particular population in a particular setting (step 1). Insights from this step can then be used to interrogate links and connections between the factors, and examine how these synergies, often in interaction with other shared social practices, shape the ability or desire for specific population groups to engage, or disengage, with HIV prevention technologies (step 2). To facilitate the exploration, both steps lists a series of questions. The questions have been formulated to spark conversation about how a practice, such as engagement with HIV prevention technologies, either emerges, persists or disappears. Reflecting the work of Blue et al. [36] and Shove et al. [38], the questions allow analysts to explore how best to make or break links between defining factors; understand the competition and collaboration that exists between the factors and associated practices; and develop insight into how practitioners get recruited, maintained or defected from the social practice under scrutiny. By asking these questions, HIV prevention service planners and evaluators will be able to explore, explain and respond to differences in practice between people and settings. Practically, the tool can be used figuratively to tabulate the range of factors and social practices associated with engagement with a particular HIV prevention technology, or one can draw on the questions in a variety of formats and fora to instigate reflection and analysis, with the matrix visually reminding the analysts to consider different dimensions and levels of analysis.

2.4 | Practice-based combination HIV prevention for PrEP among AGYW in sub-Saharan Africa

As exemplified by the DREAMS programme [43], PrEP increasingly forms part of the expanding portfolio of interventions being made available to AGYW in sub-Saharan Africa to prevent HIV acquisition [41,42]. The DREAMS programme represents a breakthrough in HIV prevention in sub-Saharan Africa, by laudably availing layers of quality and evidence-informed interventions, covering biomedical, structural and behavioural initiatives. Saul et al. [43: p. 12], in describing the potential of DREAMS, argue that "meeting the needs and demands of AGYW requires unpacking the data to identify challenges and risks for an individual girl or young woman. Once identified, then and only then, can a response be tailored to mitigate risks in a holistic way." Rather than implementing structural, behavioural and biomedical interventions in isolation, the DREAMS programme allow service providers to target AGYW with a number of interventions. Promising as this may be, it is unclear what constitutes "data," and what frameworks are used to ascertain which interventions to offer particular AGYW, and with what combination-synergies. Furthermore, the DREAMS programme focuses on creating an enabling environment for HIV prevention, but pays less attention to the motivation of AGYW to engage with HIV prevention practices routinely. While comprehensive, the DREAMS programme is not exhaustive, and it is likely that local material, symbolic, competence, relational and motivational factors, and associated social practices that affect AGYW motivation and capacity to engage with PrEP have not been considered. This may either be because "data" are not available, or because the core package interventions focus on "what works" (evidence-informed programming), as opposed to how the interventions work in a given context, for whom, and with what interactions to achieve strategic advantage and synergy [4].

The proposed "table of questioning" can help HIV prevention programme planners and evaluators hone in on local determining factors and social practices. This can help them uncover, monitor and respond to the constellation of factors, and related social practices that affect engagement with PrEP. In the case of PrEP, this is important for a number of reasons. While PrEP can reduce risk of HIV by over 90% when taken consistently [8], PrEP trials with African women have found adherence levels so low, particularly among young women, that efficacy could not be ascertained [18,19]. Commentators highlight numerous demand-side, supply-side and adherence

Step 1: Identify and explore factors affecting engagement with HIV prevention technologies					**Step 2: Explore and respond to interactions between factors and other social practices affecting engagement with HIV prevention technologies**
Factors affecting the practice of engaging with HIV prevention technologies	**Ecology of spatially and temporally specific factors**				
	Macro-level	*Meso-level*	*Micro-level*	*Individual-level*	
1. What **material** factors condition the *'doings'* that affect engagement with HIV prevention technologies?	E.g., government funding; access to technologies, health infrastructures; guidelines	E.g., availability of HIV prevention technologies at a clinic-level; HIV service provisions; guidelines	E.g., household income;	E.g., disposable income; access to technologies; the body; private spaces	6. How does the absence, presence or interactions between specific factors affect engagement with HIV prevention technologies?
2. What **symbolic** factors condition the *'sayings'* that affect engagement with HIV prevention technologies?	E.g., public discourses; media representations; complacencies;	E.g., social representations and acceptability; social and cultural norms; stigmatising attitudes	E.g., social network precepts; peer and partner acceptability of the practice	E.g., acceptability; principles about the practice; fear of stigma	7. How can differences between populations and settings be explained by changes happening over time and place, and how might these be targeted by policy?
3. What **competence** factors condition the *'knowings'* that affect engagement with HIV prevention technologies?	E.g., availability of science; national campaigns; Media coverage	E.g., healthcare provider know-how and skills; surveillance systems; community HIV competence	E.g., peer and partner knowledge and perception of the practice;	E.g., risk perception; bodily experience; know-how and skill	8. What can be done to create, maintain or break synergies between different factors that affect engagement with HIV prevention technologies?
4. What **relational** factors condition the *'relatings'* that affect engagement with HIV prevention technologies?	E.g., punitive and protective laws; institutionalised marginalisation	E.g., Community- and faith based groups; community activism; health system discrimination; provider-user relations	E.g., partner and power relations; disclosure of engagement with prevention methods; peers and partners engaging with the practice	E.g., individual dispositions such as gender, sexual orientation, ethnicity and socio-economic status;	9. How do shared social practices interfere with, or support, the practice of engaging with HIV prevention technologies?
5. What **motivational** factors condition the *'aimings'* that affect engagement with HIV prevention technologies?	E.g., international targets; national action plans; political commitments	E.g. community participation, community visions	E.g., peer, partner, and couple desires and visions	E.g., individual desires and visions	10. What factors and practices are relevant to a particular individual's situation, and might be targeted by a doctor, nurse, community worker, parent, peers etc.?

Figure 1. A "table of questioning" for practice-based combination HIV prevention.

barriers [25,41,44], warranting urgent attention to constellations of factors and social practices that recruit and maintain AGYW as "engagers" with PrEP. In other words, PrEP should not merely be seen as a biomedical intervention to be included in a combination of HIV preventions, but recognized as a practice that is contingent on the configuration of multi-level factors that establish engagement with PrEP as (im)possible and (un)desirable. Haberer et al. [25] argue that we must consider the broad range of local factors that make PrEP both relevant, appealing and available to AGYW. The proposed "table of questioning" can help HIV prevention service planners and evaluators identify what those factors and social practices may be. Specifically, the "table of questioning" can help disentangle how the presence or absence of material, symbolic, competence, relational, and motivational factors, either enable or constrain the array of activities, or "doings," "sayings," "knowings," "relatings" and "aimings" that affect AGYWs engagement with PrEP. What may some of these factors be?

If the public or AGYW brand PrEP as a "promiscuity pill" [45], or consider PrEP ineffective and inappropriate for dissemination [46], this may limit demand for PrEP. Knowledge and awareness of HIV risk is a defining element of willingness to engage with PrEP, yet, a Zimbabwean study has found that many young people at increased infection risk did not perceive to be at high risk [47]. Relatedly, the FEM-PrEP study found women to underestimate their risk of infection and that perceived risk was associated with greater engagement with PrEP [48]. Social relations and partner relations also matter. If male partners, in contexts of male dominance, are not supportive of their partners using PrEP, this may prevent some AGYW from engaging with PrEP [49]. Similarly, HIV prevention service providers may not be supportive of AGYW seeking PrEP because of attitudes towards adolescent sexuality, and concerns about behavioural disinhibition due to PrEP [50]. In terms of motivational factors, a study in South Africa found that a personal desire for HIV protection, and a wish to keep engagement with a HIV prevention technology a secret, positively affected demand for PrEP [51]. Among HIV-uninfected Kenyan women in serodiscordant relationships, the desire to remain HIV uninfected and have a HIV-free infant have also been found to motivate uptake and continued use of PrEP during pregnancy [52].

Haberer et al. [25] note that adolescents and young people live social and connected lives, which are characterized by their quest for novelty and sensation. The everyday practices of young people inevitably intersect with engagement with PrEP. Scorgie et al. [53], for instance, have found both the timing and location of young South African women's sexual intimacy to be unpredictable, making engagement with on-demand oral PrEP a challenge. These factors not only differ significantly from setting to setting, explaining varied engagement with PrEP, but also interact in complex ways. If a setting experiences drug stock-outs (perhaps due to cuts in funding), this may not only remove a defining material factor, but also negatively impact PrEP users trust in health services, and acceptability of the prevention method. Comparing and contrasting scenarios where AGYW or other population groups at risk are either able or unable to engage with PrEP can reveal differences in the composition of factors and social practices that establish engagement with PrEP as (im)possible and (un)desirable. Such analysis can highlight the missing links, and the actions required to avail the factors and practices that support engagement with PrEP. For instance, if differences in the uptake of PrEP within a country can partly be explained by

differences in healthcare provider PrEP awareness, familiarity, comfort and prescribing experiences [54], this could constitute a missing link and avenue for action.

3 | CONCLUSIONS

Practice-based combination prevention treats HIV prevention practices as sites of analysis and public health action. Taking a practice-oriented approach to combination prevention enables HIV prevention service planners and evaluators to recognize and consider the range of factors, social practices and interventions that need to be synchronized in order to establish engagement with HIV prevention technologies as a desirable thing to do for particular groups of people, in specific settings. It is a particular pertinent approach in an era of biomedical disease prevention, where the concept of "adherence" has locked us into a narrow understanding of medicine taking and disease self-management. Rather, practice-based combination prevention calls for recognition and greater understanding of the range and combination of factors that establish (dis)engagement with HIV prevention technologies as (un)desirable and (im)possible. It also draws attention to the role of other social practices that are associated with engagement with HIV prevention technologies. Given the low rates of PrEP uptake and adherence among AGYW in sub-Saharan Africa, the proposed "table of questioning" provides a much needed framework and vocabulary to support HIV prevention service planners and evaluators identify system-synergies [4] for PrEP engagement, which may not otherwise be obvious.

The proposed "table of questioning" cautions against once-size-fits-all responses, recognizing the complex realities of people and differences in the cultural, political and socioeconomic fabric of different settings. However, some factors or interventions may well be applicable and generalizable to different population groups. Differentiating between global (general) and local (specific) factors on the ecology continuum, may reveal macro-level factors that apply to a large number of population groups, while meso-, micro- and individual-level factors may require more localized responses. The tool highlights the roles of different stakeholders in making or breaking links to establish engagement with HIV prevention technologies as desirable and possible. Practice-based combination prevention thus allow us to go beyond the biomedical differentiated care agenda, and work towards differentiated combination preventions. However, first, operational research and evaluations applying and validating this tool to different contexts is urgently needed.

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COMPETING INTEREST

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REFERENCES

1. UNAIDS, UNAIDS Data 2018. Geneva: UNAIDS; 2018.
2. UNAIDS. Global AIDS update 2018: miles to go. Geneva: UNAIDS; 2018.
3. UNAIDS. The youth bulge and HIV. 2018. [cited 2018 Dec 18]. Available at: http://www.unaids.org/sites/default/files/media_asset/the-youth-bulge-and-hiv_en.pdf
4. Brown G, Reeders D, Dowsett GW, Ellard J, Carman M, Hendry N, et al. Investigating combination HIV prevention: isolated interventions or complex system. J Int AIDS Soc. 2015;18(1):20499.
5. Gupta GR, Parkhurst JO, Ogden JA, Aggleton P, Mahal A. Structural approaches to HIV prevention. Lancet. 2008;372(9640):764–75.
6. Kaufman MR, Cornish F, Zimmerman RS, Johnson BT. Health behavior change models for HIV prevention and AIDS care: practical recommendations for a multi-level approach. J Acquir Immune Defic Syndr. 2014;66:S250–8.
7. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med. 2016;375(9):830–9.
8. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2016;387(10013):53–60.
9. Krakower DS, Jain S, Mayer KH. Antiretrovirals for primary HIV prevention: the current status of pre-and post-exposure prophylaxis. Curr HIV/AIDS Rep. 2015;12(1):127–38.
10. Nel A, van Niekerk N, Kapiga S, Bekker LG, Gama C, Gill K, et al. Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. N Engl J Med. 2016;375(22):2133–43.
11. Karim QA, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010;329(5996):1168–74.
12. Bunge KE, et al. FAME-04: a Phase 1 trial to assess the safety, acceptability, pharmacokinetics and pharmacodynamics of film and gel formulations of tenofovir. J Int AIDS Soc. 2018;21(8):e25156.
13. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005;2(11):e298.
14. Desai M, Field N, Grant R, McCormack S, et al. State of the art review: recent advances in PrEP for HIV. BMJ. 2017;359:j5011.
15. Amico KR, Dezzutti CS, Hendrix CW, Marzinke MA, Spiegel HML, Moncla BJ, et al. Adherence support approaches in biomedical HIV prevention trials: experiences, insights and future directions from four multisite prevention trials. AIDS Behav. 2013;17(6):2143–55.
16. UNAIDS. Prevention Gap report. Geneva: The Joint United Nations Programme on HIV/AIDS (UNAIDS); 2016.
17. Zablotska IB, Vaccher SJ, Bloch M, Carr A, Foster R, Grulich AE, et al. High adherence to HIV pre-exposure prophylaxis and no HIV seroconversions despite high levels of risk behaviour and STIs: the Australian demonstration study PrELUDE. AIDS Behav, 2018;1–10, https://doi.org/10.1007/s10461-018-2290-3
18. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372(6):509–18.
19. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367(5):411–22.
20. Ford N, Irvine C, Shubber Z, Baggaley R, Beanland R, Vitoria M, et al. Adherence to HIV postexposure prophylaxis: a systematic review and meta-analysis. AIDS. 2014;28(18):2721–7.
21. Carrasco MA, Nguyen TQ, Kaufman MR. Low uptake of voluntary medical male circumcision among high risk men in Malawi. AIDS Behav. 2018;22(2):447–53.
22. Baisley K, Chimbindi N, Mthiyane N, Floyd S, McGrath N, Pillay D, et al. High HIV incidence and low uptake of HIV prevention services: the context of risk for young male adults prior to DREAMS in rural KwaZulu-Natal, South Africa. PLoS One. 2018;13(12):e0208689.
23. Grund JM, Grund JM, Davis SM, Ridzon R, Mattingly M, Wilkinson J, et al. Systematic review of the effect of economic compensation and incentives on uptake of voluntary medical male circumcision among men in sub-Saharan Africa. AIDS Care. 2018;30(9):1071–82.
24. Toska E, Cluver L. Barriers to U=U for adolescents living with HIV: predictors of high HIV-transmission risk from a longitudinal cohort study in 2nd International Workshop on HIV Adolescence-Challenges & Solutions. 2018: Cape Town, South Africa.

25. Haberer JE, Mugo N, Baeten JM, Pyra M, Bukusi E, Bekker LG. PrEP as a Lifestyle and Investment for Adolescent Girls and Young Women in Sub-Saharan Africa. J Int Assoc Provid AIDS Care. 2019;18:1–5.
26. Zimmerman RS, Noar SM, Feist-Price S, Dekthar O, Cupp PK, Anderman E, et al. Longitudinal test of a multiple domain model of adolescent condom use. J Sex Res. 2007;44(4):380–94.
27. Latkin C, Weeks MR, Glasman L, Galletly C, Albarracin D. A dynamic social systems model for considering structural factors in HIV prevention and detection. AIDS Behav. 2010;14(2):222–38.
28. Johnson BT, Redding CA, DiClemente RJ, Mustanski BS, Dodge B, Sheeran P, et al. A network-individual-resource model for HIV prevention. AIDS Behav. 2010;14(2):204–21.
29. Garnett GP, Hallett TB, Takaruza A, Hargreaves J, Rhead R, Warren M, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. Lancet HIV. 2016;3(7):e297–306.
30. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
31. Moorhouse L, et al. Application of the HIV prevention cascade to identify, develop, and evaluate interventions to improve use of prevention methods: examples from a study in east Zimbabwe. J Int AIDS Soc. 2019;22(S3):e25309.
32. Brown G, Reeders D, Cogle A, Madden A, Kim J, O'Donnell D. A systems thinking approach to understanding and demonstrating the role of peer-led programs and leadership in the response to HIV and hepatitis C: findings from the W3 project. Front Public Health. 2018;6:231.
33. Kippax S. Effective HIV prevention: the indispensable role of social science. J Int AIDS Soc. 2012;15(2):17357.
34. Kippax S, Stephenson N, Parker RG, Aggleton P. Between individual agency and structure in HIV prevention: understanding the middle ground of social practice. Am J Public Health. 2013;103(8):1367–75.
35. Reckwitz A. Toward a theory of social practices a development in culturalist theorizing. Eur J Soc Theory. 2002;5(2):243–63.
36. Blue S, Shove E, Carmona C, Kelly MP. Theories of practice and public health: understanding (un) healthy practices. Crit Public Health. 2016;26(1):36–50.
37. Kemmis S, Wilkinson J, Edwards-Groves C, Hardy I, Grootenboer P, Bristol L. Changing practices, changing education. London: Springer Science & Business Media; 2013.
38. Shove E, Pantzar M, Watson M. The dynamics of social practice: everyday life and how it changes. London: Sage Publications; 2012.
39. Brofenbrenner U. *The ecology of human development : experiments by nature and design*. Cambridge, MA: Harvard University Press; 1979. xv, 330 p.
40. Nicolini D. Is small the only beautiful? Making sense of 'large phenomena' from a practice-based perspective, in The Nexus of Practices. New York: Routledge; 2016. 110-125.
41. Baxter C, Abdool Karim S. Combination HIV prevention options for young women in Africa. Afr J AIDS Res. 2016;15(2):109–21.
42. Hosek S, Pettifor A. HIV prevention interventions for adolescents. Curr HIV/AIDS Rep. 2019;16(1):120–128.
43. Saul J, Bachman G, Allen S, Toiv NF, Cooney C. The DREAMS core package of interventions: a comprehensive approach to preventing HIV among adolescent girls and young women. PLoS One. 2018;13(12):e0208167.
44. Cowan FM, Delany-Moretlwe S, Sanders EJ, Mugo NR, Guedou FA, Alary M, et al. PrEP implementation research in Africa: what is new? J Int AIDS Soc. 2016;19(7S6):21101.
45. Mugo NR, Ngure K, Kiragu M, Irungu E, Kilonzo N. PrEP for Africa: what we have learnt and what is needed to move to program implementation. Curr Opin HIV AIDS. 2016;11(1):80.
46. Rubincam C, Newman PA, Atujuna M, Bekker LG. 'Why would you promote something that is less percent safer than a condom?': perspectives on partially effective HIV prevention technologies among key populations in South Africa. SAHARA J. 2018;15(1):179–86.
47. Schaefer R, Thomas R, Nyamukapa C, Maswera R, Kadzura N, Gregson S. Accuracy of HIV risk perception in East Zimbabwe 2003–2013. AIDS Behav. 2018;1–11; https://doi.org/10.1007/s10461-018-2374-0
48. Corneli A, Perry B, Agot K, Ahmed K, Malamatsho F, Van Damme L. Facilitators of adherence to the study pill in the FEM-PrEP clinical trial. PLoS One. 2015;10(4):e0125458.
49. Govender E, Abdool Karim Q. Understanding women and men's acceptability of current and new HIV prevention technologies in KwaZulu-Natal, South Africa. AIDS Care. 2018;30(10):1311–4.
50. Pilgrim N, Jani N, Mathur S, Kahabuka C, Saria V, Makyao N, et al. Provider perspectives on PrEP for adolescent girls and young women in Tanzania: the role of provider biases and quality of care. PLoS One. 2018;13(4):e0196280.
51. Govender E, Mansoor L, MacQueen K, Abdool Karim Q. Secrecy, empowerment and protection: positioning PrEP in KwaZulu-Natal, South Africa. Cul Health Sex. 2017;19(11):1268–85.
52. Pintye J, Beima-Sofie KM, Kimemia G, Ngure K, Trinidad SB, Heffron RA, et al. "I Did Not Want to Give Birth to a Child Who has HIV": experiences using prep during pregnancy among HIV-uninfected Kenyan women in HIV-serodiscordant couples. J Acquir Immune Defic Syndr. 2017;76(3):259–65.
53. Scorgie F, Stadler J, Baron D, Ju S, Ikaneng T, Mabude Z, et al. "It Was Not My Aim to Sleep There": the impact of timing and location of sex on adherence to coitally-dependent HIV pre-exposure prophylaxis. AIDS Behav. 2018;22(11):3692–704.
54. Petroll AE, Walsh JL, Owczarzak JL, McAuliffe TL, Bogart LM, Kelly JA. PrEP awareness, familiarity, comfort, and prescribing experience among US primary care providers and HIV specialists. AIDS Behav. 2017;21(5):1256–67.

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VIEWPOINT

Reaching and targeting more effectively: the application of market segmentation to improve HIV prevention programmes

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Marketing techniques from the commercial sector, applied to the promotion of primary HIV prevention offer an opportunity to improve programme impact and deserve further exploration. One such technique, market segmentation, divides populations into groups and designs programmes that respond to groups' distinct needs [1]. Efficient and effective HIV prevention requires well targeted and well-designed programmes responding to client characteristics and needs. Following best practices in commercial marketing would allow for more refined knowledge of those at risk and enable more tailored prevention interventions; specifically, the use of market segmentation that measures psychographic (psychological attributes such as values, attitudes and beliefs) and behavioural factors that might relate to product use and then describes segments of the population by their distinct needs, characteristics, or behaviours, facilitates the differentiation of products and/or marketing approaches by segment [2,3]. Market segmentation has recently been used in voluntary medical male circumcision (VMMC) programmes, providing a template worthy of consideration by other HIV prevention interventions [4,5]. This viewpoint argues that, well done, market segmentation should be an important component in developing and delivering HIV prevention interventions.

Successful market segmentation is a multi-stage process, including: (1) qualitative work exploring the beliefs, attitudes, influences, habits and feelings of a population sample; (2) quantitatively surveying a representative sample of the population with questions derived from the qualitative analysis; (3) statistical analysis of survey data to generate non-overlapping segments and narrative descriptions to distinguish how people in a given segment relate to potential products; (4) tailored programmes that appeal to each segment so they are persuaded to use the product; and (5) monitoring, rapid evaluation and correction when needed [2,3,6]. In public health, market segmentation also considers who can benefit from a product or intervention, and the objective is not increased sales and profit, but the public good and a healthier population [1].

Segmentation is useful when it groups people according to characteristics that can be associated with marketing approaches, which in turn drive quantifiable outcomes [6]. Segments should be identifiable, substantial, accessible and sustainable. In the context of HIV prevention, segments would need to be identifiable, discrete groups of those at risk of HIV, with attributes related to their beliefs, attitudes, influences, and habits related to HIV risk and HIV prevention. They should be substantial enough to make investments in products for HIV prevention and their promotion worthwhile. It should be easy, financially and emotionally, for those in the segment to access HIV prevention products and services. Finally, the risks of HIV and segment characteristics should be stable enough to allow for investments that would sustainably provide segment-specific HIV prevention.

In our work on market segmentation, we have reviewed applications to public health and whilst some broad elements of segmentation, such as age and geography, have been employed, psychographics and behaviour have been less commonly used. This may be because psychographics, which measure client attitudes and interests, are harder, or more expensive to identify, and are seen as more subjective, less replicable and more prone to reporting bias than objective, demographic criteria. However, well-applied psychographics provide a deeper understanding of the desires, needs and decision-making considerations of a potential user of a product or service [3]. Transferring methods and tools from the commercial to the public sector is likely also hampered by requirements for evidence by decision makers. In the commercial context, sales and profits provide rapid evidence; in public health, impact is typically observed in the medium- to long-term.

Successful HIV prevention strategies to date share several features: political leadership, community engagement, attention to social norms and open communication [7]. These

Table 1. Examples of segments from HIV prevention studies

Perception of HIV risk and self-efficacy (Malawi) [5]		Condom attitude segments (Zimbabwe) [12]		Attitude to VMMC among uncircumcised men (Zambia) [13]		Attitude to VMMC amongst uncircumcised men (Zimbabwe) [13]	
Responsive	35%	Playful	21%	Enthusiasts	21%	Socially supported believer	11%
Avoidance	8%	Caring	12%	Champions	6%	Self-reliant believer	9%
Proactive	47%	Easy going	10%	Neophytes	19%	Knowledgeable hesitant	10%
Indifference	10%	Daring	17%	Scared rejectors	17%	Friends-driven hesitant	19%
		Status[a]	19%	Embarrassed rejectors	16%	Scared rejector	17%
		Composed	21%	Highly resistant	21%	Indifferent resistant	27%
						Traditional believer	6%

[a]People concerned with their status in the community.

successes have mainly been in key populations who have been engaged communities, highly motivated by HIV risk, or in more general populations responding to widespread HIV-associated mortality [8]. The current situation in southern and eastern Africa, where HIV is not the primary concern of young people may require additional approaches. Here, male and female condoms, VMMC and oral pre-exposure prophylaxis (PrEP) are efficacious, but there are major barriers to uptake [9,10]. Designing social marketing strategies for these interventions, tailored for groups based on their values, attitudes and decision-making creates the greatest likelihood that people will adopt them [5]. The messages for behaviour change reducing numbers of risky sexual partnerships could also be tailored to specific segments, where the barriers to accessing and adopting prevention technologies are less, but the social contexts and norms may be challenging. There is experience of market segmentation in social marketing of condoms [11], but, to our knowledge, little has been documented and published in the peer-reviewed literature. Table 1 describes the labels used to describe segments that have been used to categorize populations and the proportion of the population they represent in the few published studies from Malawi, Zimbabwe and Zambia [5,12,13]. The segments provide information on the potential for success that interventions targeting particular segments might have, along with the scale of the benefits to be derived from successful campaigns. In addition, understanding the motivation of those within a category allows tailored messaging. For example, "scared rejectors" of circumcision would require interventions that address their fears, "friends-driven hesitant" might respond to peer driven interventions. The studies of men's attitudes towards VMMC in Zambia and Zimbabwe revealed that the men responded best to information communicated individually rather than collectively, needed to overcome fear of pain, and needed to be prompted to attend the clinic [4,13]. These insights allowed Population Services International to develop specific VMMC campaigns through human-centred design prototyping and testing [13]. The approaches are now being applied across VMMC programmes and used in a cluster-randomized trial to test the effectiveness of promotional materials informed by attitudes expressed by men engaged in the research. Defining the segments is a first step in the process of developing messages and interventions that need to be designed, trialled and delivered. Such intervention design should engage local communities to ensure acceptability and ownership.

Building on work in VMMC, qualitative and quantitative surveys are underway amongst adolescent girls and young women (AGYW) in South Africa to explore attitudes to HIV prevention, generally and in terms of oral PrEP, and among young men and their attitudes around HIV testing [1]. Experience shows that HIV prevention products are not automatically adopted by those at risk of HIV, but we believe that marketing best practices can increase the likelihood of success. Defining and describing segments is partly objective analysis and partly a creative narrative, the success of which can be judged by its utility in designing segment-specific campaigns, in measuring the cost of those programmes, and ultimately in the uptake of prevention.

There is a need to study and document the identification of segments, the design of interventions to reach those segments, and the uptake of HIV prevention interventions within those segments.

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COMPETING INTERESTS

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AUTHORS' CONTRIBUTIONS

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DISCLAIMER

The content of this article is solely the responsibility of the authors and does not necessarily represent the views of the Gates Foundation, PEPFAR, USAID, or the United States Government.

REFERENCES

1. USAID market development approaches working group. Market segmentation primer. 2009 [cited 2018 Oct 28]. Available from: https://www.rhsupplies.org/uploads/tx_rhscpublications/MDAWG_Market_Segmentation_Primer_FINAL_doc.pdf
2. Sgaier SK, Engl E, Kretschmer S. Time to scale psycho-behavioral segmentation in global development. Stanford Social Innovation Review, Fall. 2018 [cited 2018 Sep 12], 48-55. Available from: https://ssir.org/pdf/Fall_2018_Time_to_Scale_Psycho-behavioral_Segmentation_in_Global_Development.pdf
3. Samuel A. Psychographics are just as important for marketers as demographics. Harvard business review, 11 March 2016 [cited 2018 Nov 14]. Available from: https://hbr.org/2016/03/psychographics-are-just-as-important-for-marketers-as-demographics
4. Sgaier SK, Baer J, Rutz DC, Njeuhmeli E, Seifert-Ahanda K, Basinga P, et al. Toward a systematic approach to generating demand for VMMC: insights and results from field studies. Glob Health Sci Pract. 2015;3(2):209–29.
5. Rimal RN, Brown J, Mkandawire G, Folda L, Böse K, Creel AH. Audience segmentation as a social-marketing tool in health promotion: use of the risk perception attitude framework in HIV prevention in Malawi. Am J Public Health. 2009;99(12):2224–9.
6. Bannon DP. Marketing segmentation and political marketing. Political Studies Association Annual Conference, University of Lincoln, United Kingdom, 4 April 2004 [cited 2018 Nov 14], pp. 5-8. Available from: https://www.researchgate.net/profile/Declan_Bannon/publication/228539764_Marketing_segmentation_and_political_marketing/links/5b44925e458515b4f65f63a2/Marketing-segmentation-and-political-marketing
7. Bertozzi S, Padian NS, Wegbreit J, DeMaria LM, Feldman B, Gayle H, et al. HIV prevention and treatment. Chapter 18. In: Jameson DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, Jha P, Mills A, Musgrove P, editors. Disease control priorities in developing countries. 2nd ed. New York: Oxford University Press; 2006. p. 331–69.
8. Halperin DT, Magurungi O, Hallett TB, Muchini B, Campbell D, Magure T, et al. A surprising prevention success: why did the HIV epidemic decline in Zimbabwe? PLoS Med. 2011;8(2):e1000414.
9. Terris-Prestholt F, Windmeijer F. How to sell a condom? The impact of demand creation tools on male and female condom sales in resource limited settings. J Health Econ. 2016;48:107–20.
10. Eakle R, Venter R, Rees H. Pre-exposure prophylaxis (PrEP) in an era of stalled HIV prevention: can it change the game? Retrovirology. 2018;15:29.
11. Lampty PR, Price JE. Social marketing sexually transmitted disease and HV prevention: a consumer centred approach to achieving behaviour change. AIDS. 1998;12 Suppl. 2:S1–9.
12. Longfield K, Taruberekera N, Leuschner S, Chatora K, Skorochod B, Munjoma M, et al. The impact of social marketing on improving condom supply and demand in Zimbabwe. 2018.
13. Sgaier SK, Eletskaya M, Engl E, Mugurungi O, Tambatamba B, Ncube G, et al. A case study for a psychographic-behavioral segmentation approach for targeted demand generation in voluntary medical male circumcision. eLife. 2017;6:e25923.

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COMMENTARY

HIV pre-exposure prophylaxis for adolescent girls and young women in Africa: from efficacy trials to delivery

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Abstract

Introduction: Adolescent girls and young women (AGYW) in Africa have high HIV incidence despite scale-up of HIV testing and HIV treatment. Placebo-controlled trials of tenofovir-based pre-exposure prophylaxi (PrEP) in diverse populations demonstrated that PrEP works with close to 100% effectiveness if taken with high, but not perfect, adherence. Divergent efficacy estimates among African AGYW led to demonstration and implementation projects to better understand motivations for HIV prevention, uptake, adherence and persistence to PrEP. To inform PrEP programmes, the design and initial findings from PrEP demonstration projects for AGYW are reviewed.

Discussion: Early lessons from PrEP implementation projects among young African women include: (1) awareness and demand creation with positive messaging about the benefits of PrEP are critical to motivate AGYW to consider this novel prevention technology and to foster awareness among peers, partners, parents and guardians to support AGYW's effective PrEP use; (2) PrEP initiation is high in projects that are integrating PrEP into youth-friendly clinics, family planning clinics and mobile clinics; (3) young African women at risk are initiating PrEP, based on behavioural characteristics, history of intimate partner violence, depression and 30% prevalence of chlamydia and/or gonorrhoea; (4) provision of youth-friendly PrEP delivery programmes that integrate reproductive health services, including contraception and the diagnosis and treatment of sexually transmitted infections, increase health impact; (5) messages that emphasize the necessity for high adherence while at potential risk of HIV exposure and support strategies that addresses AGYW's adherence challenges are essential; and, (6) a substantial proportion of AGYW do not persist with PrEP, and strategies are needed to help AGYW assess their ongoing need, motivation and challenges with persisting with PrEP.

Conclusions: PrEP is feasible to implement in integrated reproductive health service delivery models to reach African AGYW. While PrEP demonstration projects indicate that women with behavioural risks and high rates of sexually transmitted diseases are initiating PrEP; effective strategies to support AGYW's adherence and persistence with PrEP are needed. Lessons learned from oral PrEP delivery, a novel first generation HIV prevention product, are relevant to longer-acting and less adherence-dependent strategies which are currently in clinical trials.

Keywords: HIV prevention; pre-exposure prophylaxis; adolescents; young women; Africa

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1 | INTRODUCTION

Adolescent girls and young women (AGYW) in Africa account for approximately 25% of new HIV infections globally, and have large unmet needs for HIV prevention [1]. African AGYW experienced high HIV incidence despite monthly counselling and prevention services in recent biomedical HIV prevention trials [2]. Excitement about pre-exposure prophylaxis (PrEP), a novel approach to HIV prevention, coalesced when trials demonstrated estimates of HIV protection of >90% in women and men [3]. However, in PrEP efficacy trials, protection ranged from 0 to 75% in different populations [4-9] with the variation largely explained by differences in participants' level of adherence, based on retrospective testing of drug levels. Indeed, PrEP is a user-controlled method, highlighting the strong behavioural component to PrEP uptake, adherence and persistence, which was most apparent among African AGYW. This commentary synthesizes evidence and expert opinion about PrEP efficacy and implementation for African AGYW, spanning from efficacy trials to emerging data from multiple demonstration projects.

2 | DISCUSSION

2.1 | Challenges with oral PrEP among young African women

Protection was 72% among young, high-risk women in subgroup analyses of female partners in HIV serodiscordant

couples in the Partners PrEP study where adherence was 80% [10]. In contrast, in the VOICE and FEM-PrEP trials, young women were not protected, most of whom had a partner of unknown HIV status, and among whom only 25% had detectable tenofovir levels [4,5]. In VOICE, young women (<25 years) were at greatest risk for HIV infection and less likely to adhere. Nevertheless, a subsequent meta-analysis of all PrEP trials including women estimated 61% PrEP efficacy among women with > 75% adherence based on drug levels [11].

The results of the VOICE and FEM-PrEP trials led to concerns that young African women did not recognize their risk, would lack motivation or be unable to adhere to daily pill-taking for HIV prevention. Notably, the quantitative measure of risk perception in these trials was based on a single question, which may be insufficient for understanding how women viewed their risk. In contrast, in-depth interviews indicated that women often recognized their risk [12]. Socio-behavioural research during and following the VOICE and FEM-PrEP trials found that participants had altruistic motivations for joining the studies but were balancing this against the practical realities of their daily lives. In the African context where access to quality care and resources is limited, participants desired access to non-judgemental, confidential clinical services, counselling support, and contraception, HIV and sexually transmitted infection (STI) testing and treatment which were provided by the trial sites [13,14]. Small study reimbursements (<$15) helped participants meet transport costs and other needs [14-16].

Women faced many challenges in these studies, including their concerns about receiving a placebo or an investigational drug of unknown efficacy and potential side effects [17-20]. "Present bias" is the tendency to disproportionately focus on rewards in the present to the detriment of achieving desired long-term outcomes [21-23], and is a strong motivator in AGYW, which could have discouraged committed product usage. Qualitative research suggests that rumours and peers' comments about not using their study products influenced participants in terms of their adherence and willingness to disclose actual product use [24]. Women often experienced low social support for joining the trials or for using a female-controlled method of HIV prevention, and had to balance their motivation for HIV prevention with fear of their partner's reactions and possible violence. Indeed, women's desire to preserve their relationship and trust their partner may weigh more in their lives than their risk of acquiring HIV and prevention considerations [19,25]. Intimate partner violence (IPV) has since been shown to have been associated with non-adherence [26-28]. HIV and stigma associated with antiretrovirals were also barriers to product use. AGYW reported having limited private storage space, fears of inadvertent disclosure to family and partners, and subsequent misperceptions about HIV serostatus, contributing to poor adherence among those who tried to conceal product use [29]. Adherence to a daily product was particularly challenging for young women where executive functions and organizational skills are still developing [30-32]. Executive function has been shown to play a role in adolescent medication adherence for chronic illnesses as well as preventive care [33-37].

Acceptability research conducted since VOICE and FEM-PrEP indicate that women desire low burden prevention strategies that are compatible with their lifestyles and provide peace of mind [38,39]. Indeed, a daily pill regimen can be both logistically and emotionally burdensome (as it may remind women about HIV or IPV) [16]. When offered HIV prevention alternatives through discrete choice experiments which assess hypothetical preferences and trade-offs between them, women prefer longer-acting and more adherence "forgiving" products, supporting the development of a range of PrEP delivery modalities – ring, injectable, implantable – from which young women can choose [38,40,41]. In parallel with development of formulations with less frequent dosing, it is important to learn about delivery and use of oral PrEP, a vanguard product.

2.2 | Lessons about PrEP effectiveness from other populations

Open-label PrEP studies have demonstrated that risk perception and HIV prevention motivation might be less of a challenge than initially anticipated. Significantly higher effectiveness than efficacy was observed in open-label studies, including the PROUD study (immediate vs delayed open-label PrEP among men who have sex with men (MSM) attending sexual health clinics in the UK) [42] and HIV serodiscordant couples in the Partners Demo Project [43,44], which provided time-limited PrEP for HIV-uninfected partners until the HIV-positive partner was virally suppressed on antiretroviral therapy (ART). Similarly, effectiveness of the first longer acting PrEP product – the dapivirine ring – was higher in an open-label extension study than in the placebo-controlled efficacy trials [45].

Studies specific to adolescents and youth have provided useful and encouraging data. In the HPTN 067/ADAPT trial of daily, fixed intermittent or event-driven dosing among young women in Cape Town, adherence to daily PrEP was 75% and daily dosing provided the highest coverage of sex acts [46]. A US-based study of oral PrEP among MSM ages 15 to 17 (Adolescent Trials Network [ATN] 113) demonstrated that the majority had intracellular tenofovir-diphosphate (TFV-DP) levels commensurate with HIV protection (>700 fmol TFV-DP/punch) over the first three months [47], which decreased over the second six months when visits became quarterly. Similarly, the PlusPills study conducted in South Africa among adolescent boys and girls ages 15 to 19, found that PrEP was safe, acceptable and well-tolerated in this age group, but that adherence dropped in the second half of the study when visits were spaced quarterly instead of monthly [47]. In summary, open label PrEP studies have demonstrated that risk perception, HIV prevention motivation, and time-bounded use of PrEP might be less of a challenge than initially anticipated, although strategies are needed to support PrEP adherence and persistence.

2.3 | PrEP implementation for African young women: early lessons

In 2016, WHO recommended that PrEP be targeted to persons at "substantial" risk for HIV, defined as an annual HIV incidence of 3% or higher without PrEP [48], which includes AGYW in high burden geographies in Africa. Initial PrEP demonstration projects for African young women focused on supporting and studying adherence. Notably, the goal for oral PrEP use should not be perfect adherence but "prevention

effective adherence" with high adherence during periods of risk [49].

A number of PrEP implementation projects for African young women are studying PrEP uptake, adherence and persistence, and some projects will evaluate impact using a counterfactual estimate of HIV incidence without PrEP (Table 1). These projects have highlighted the challenges of implementing a novel prevention intervention prior to national guidelines in African countries, and thus in advance of provider training, with limited PrEP awareness and availability.

2.4 | Demand creation for PrEP

The need for awareness and demand creation became clear early after launching PrEP demonstration projects for young African women, a population that typically accesses health services primarily for contraception. In the case of PrEP, demand creation involves clear, concise and compelling descriptions about PrEP and why women should be interested in it, especially in the context where there is very limited precedent for taking a pill purely for prevention, as most African AGYW use injectable rather than oral contraception. Importantly, antiretroviral use continues to have substantial stigma and AGYW consistently report concerns that others will think that they are HIV positive. Effective demand creation for PrEP creates awareness and motivates persons at risk of HIV to formulate their sexual health goals and motivations for HIV prevention.

Qualitative and ethnographic research was conducted to develop a demand creation strategy for PrEP among young women for the 3P (Partners, Perceptions and Pills) project in Cape Town, and found that pills are perceived as being for treatment rather than prevention and that emphasizing the positive benefits of PrEP in increasing confidence and empowerment would motivate AGYW to consider PrEP [25]. Feedback from young women in focus group discussions during development of a video and print materials recommended that demand creation materials show strong, aspirational and stylish women, message the positive benefits of PrEP in terms of young women's empowerment, and include images of men [50]. Demand creation and communication materials about PrEP need to avoid perceptions that PrEP is only for women, and implications that women are responsible for HIV prevention. While 72% of women who viewed the brief motivational video expressed strong interested in PrEP, a minority enrolled soon after viewing the video and those who enrolled and initiated PrEP in the 3P study often needed to hear about PrEP from community outreach workers, community events, peers, and parents [50]. AGYW reported that it was difficult to be both a PrEP user and advocate if community, neighbours and significant others were unaware of it [51].

Despite the need for greater community awareness about PrEP, these projects have demonstrated that there is demand for PrEP when AGYW are educated about it, as indicated by >90% uptake in HPTN 082 (Table 2) [52]. Young women who are initiating PrEP in these demonstration projects are at risk, as measured by the very high rates of depression symptoms (almost 50%), history of IPV (20% to 50%), and 30% prevalence of gonorrhoea and chlamydia, most of which was asymptomatic [53]. These high rates of curable STIs in AGYW initiating PrEP highlight that syndromic case management is inadequate and needs to be replaced with etiologic STI testing, the cost of which has been a barrier to implementation. STI testing can be part of PrEP demand creation for AGYW, inform their risk perception and need for PrEP, and STI treatment can avoid adverse impacts on their fertility.

2.5 | PrEP adherence and persistence

PrEP demonstration projects among African AGYW indicate the early drop off rates in the first few months after PrEP start are approximately 50%, with about 20% of AGYW restarting PrEP within six months in the POWER study [54]. Qualitative

Table 1. Pre-exposure prophylaxis (PrEP) implementation research projects in African young women

Study name and clintrials.gov number	Population	N	Primary objectives
PlusPills NCT03142256	150 men and women 15 to 19 years, Soweto and Cape Town, South Africa	150	PrEP uptake (i.e. acceptance and initiation) and persistence (i.e. continuation)
EMPOWER South African National Clinical Trials 4353	Young women 16 to 24 years; Johannesburg South Africa and Mwanza, Tanzania	431	Effect of empowerment clubs on PrEP uptake and persistence
HPTN 082 NCT02732730	427 women 16 to 21 years in Cape Town and Johannesburg, South Africa, and Harare, Zimbabwe	427	PrEP uptake, effect of drug level feedback on PrEP adherence, and modelled impact compared to a counterfactual HIV incidence estimate
3P (Partners, Perception, Pills) NCT03142256	200 women 16 to 21 years in Cape Town, South Africa	200	Effect of incentives conditioned on adherence (i.e. objectively measured with drug levels) on subsequent PrEP adherence and persistence
POWER NCT03490058	1504 women 16 to 21 years in:Cape Town and Johannesburg, South Africa, and Kisumu, Kenya	1504	PrEP delivery models (mobile van, youth friendly clinic, family planning clinics) and cost-effectiveness
Community PrEP NCT03977181	Young women 16 to 25 years in Buffalo City, Eastern Cape Province, South Africa	640	PrEP uptake, persistence and community models of delivery to promote persistence and adherence

research is exploring whether this early stopping is related to AGYW experimenting with a novel idea, concerns about PrEP side effects, not liking or being able to take a pill a day, or reassessment of their sexual health goals. Encouragingly, several demonstration projects have shown higher adherence than in VOICE and FEM-PrEP based on drug levels; at the three month visit in HPTN 082 intracellular TFV-DP was detected in 84% of AGYW and 25% had high TFV-DP levels [52,55] and in the 3P study, 99% of participants had detectable tenofovir and 50% had high TFV-DP levels at three months [56].

Young persons are likely to need more PrEP adherence support and more frequent contact with health providers for effective PrEP use and persistence. It is important to build in flexibility into PrEP programs for refill timing, as AGYW may not use PrEP daily and may not come for refills until they are out of pills. One strategy to foster PrEP persistence is to integrate PrEP delivery and refills with other reproductive health services (e.g. every three month injectable contraception and STI testing), making clinic visits more salient and efficient.

Peer support is also important and can be fostered through PrEP clubs, which were well-attended and valued by two-thirds of participants in HPTN 082 [52]. Peer support has been shown to improve adherence in outpatients starting ART [57], and adolescents [58]. Group-based interventions for youth offer an effective way to implement intervention content while providing social support from peers, given the importance of peer opinion during adolescence and evidence that peer norms [59–61] are important in shaping adolescent behavior [62]. Adherence support clubs were pioneered in the FACTS 001 trial [63,64], were found to be feasible and acceptable to participants and staff, and were identified spontaneously by participants during in-depth interviews as an important source of adherence support [65]. In HPTN 082, adherence clubs were incorporated into the standard adherence package that all participants received, were reported to be highly acceptable and rewarding, and club attendance was associated with higher adherence at three months (>700 fmol/punch TFV-DP per punch) [52]. In contrast, in the EMPOWER study which randomized participants to clubs that included a four-session empowerment curriculum or standard adherence support, clubs did not translate into additional benefits for PrEP persistence, although they were viewed as a valuable source of peer support [66]. The Community PrEP Study in the Eastern Cape (Table 1) is testing adherence clubs in a rural setting compared to clinic-based drug pick ups. Alternate strategies to promote peer support through virtual clubs (e.g. WhatsApp groups) have the potential to overcome the logistical barriers of in-person meetings, and warrant further investigation.

PrEP requires attention to detail, organizational skills, and quarterly clinic visits by a young, healthy person. This may be particularly difficult for adolescents with many other salient challenges, including poverty which may impose a cognitive cost that crowds out the attention needed to focus on daily prevention activities which have diffuse and long-term rewards [67]. Small incentives have been shown to improve adherence [68], and $15 cash incentives conditioned on TFV-DP levels

Table 2. Findings from pre-exposure prophylaxis (PrEP) implementation projects in African young women

Observations from PrEP demonstration and delivery projects	Supporting data from PrEP projects
Demand creation is needed, both prior to and after national guidelines and wider PrEP availability and knowledge about PrEP exist	High interest in PrEP after 90 second motivational video in Cape Town, supplemented with other educational and recruitment strategies [76]
AGYW at risk of HIV are initiating PrEP with high uptake	90% to 95% PrEP uptake in EMPOWER, POWER [55,77] and HPTN 082 [50,55] among women, as indicated by high rates of IPV and STIs
STI prevalence are high among AGYW initiating PrEP	30% prevalence of chlamydia and/or gonorrhoea in EMPOWER, POWER [78] and HPTN 082 [53]
Importance of PrEP education among influencers of young women (e.g. parents, partners) as they act often as detractors or supporters of PrEP use	*We would meet with other participants and encourage each other during the adherence clubs that we did, we would encourage each other to take PrEP.* HPTN 082 participant *I like the adherence clubs, because we will be learning from each other, everyone will be talking about their experiences in taking PrEP. So if you have some things that you hear in the neighbourhood that used to hurt you, and you hear it from other people, you will feel relieved.* HPTN 082 participant *He [my partner] can even send me a WhatsApp message and ask whether I haven't forgotten to take my pills. Then I would say that I haven't forgotten I will take them. And maybe we are messaging each other and its ten past eight, and then I quickly get up and take them. So he also reminds me sometimes.* HPTN 082 participant
Need to make PrEP access convenient and evaluate the feasibility of community-based delivery (i.e. existing points of contact with young women such as hairdressers, support groups, adherence clubs)	*I would prefer to access PrEP at a nearby place – than having to travel a distance. Because sometimes you don't have taxi fare, so you end up delaying collection for another day. Or leave it completely. . .* POWER participant

AGYW, Adolescent girls and young women; IPV, intimate partner violence; STI, sexually transmitted infection.

are being evaluated in the 3P project to determine whether incentives are effective to focus adolescents' attention on immediate rewards, support pill-taking habit formation, and help overcome potential cognitive biases that make prevention behaviours particularly challenging [69,70].

3 | CONCLUSIONS

PrEP works, works for women, works when taken during periods of HIV exposure, and offers powerful protection for women who take PrEP. It is useful to consider the lessons from PrEP demonstration projects for African AGYW. Demand creation efforts have underscored the need for positive framing about PrEP that include empowerment messages to create interest, as well as the need for broader community awareness and support to overcome the unfamiliarity with PrEP and to reduce stigma associated with using antiretrovirals for prevention. From a clinical perspective, PrEP can be delivered in simple ways, even through peers as has been demonstrated in Thailand [71]. One of the greatest lessons from PrEP projects to date is how little is necessary to deliver it, and that only a subset of users may need more adherence support or frequent contact. Risk assessment and PrEP decision tools need to be evaluated as ways to operationalize prevention effective adherence, reduce provider burden and to augment provider counselling. Simpler models of PrEP delivery are being evaluated, including community-based refills and use of self-testing for HIV to expedite visits. Adherence clubs are being evaluated as a strategy to support PrEP persistence, similar to the model of community ART clubs have been demonstrated to be very acceptable and improve ART persistence and adherence among those living with HIV [72].

An important tension with simple, parsimonious PrEP delivery for African AGYW is that they have high rates of depression, IPV, and STIs, and ideally PrEP programmes should include wrap-around services for mental health and STIs. If PrEP programs are not able to address them directly, they must be prepared for them and have adequate referral sources in place. Given the remarkably high rates of asymptomatic curable bacterial STIs in young African women initiating PrEP, syndromic STI case management is inadequate and needs to be replaced with sensitive and affordable STI testing.

Health economic modelling is needed to define the minimal level of PrEP use at the individual level (based on their "seasons of risk") and at a population level to have a public health impact. Given constrained resources, cost analyses and time-motion studies are needed of different facility-based, mobile and community-based PrEP delivery models. To estimate the health benefit of PrEP, prevention effective adherence will need to be balanced against the risk of HIV acquisition and the impact of PrEP delivery on health resources, which are the opportunity costs of delivering PrEP. Within a streamlined PrEP delivery model in a high HIV burden setting, PrEP use among persons at risk could reduce HIV incidence [73]. For moderate burden settings, mathematical models can project the incremental benefits and costs of PrEP in addition to, and, in comparison to other HIV prevention interventions. Data on real world uptake and use are needed here to guide program delivery. Integration of PrEP into platforms that provide health care, such as family planning services and STI testing, can share administrative costs thus decreasing the cost of PrEP delivery. Routine programme evaluation, including costing, can be used to estimate the cost of streamlined PrEP delivery within and outside facilities [74,75].

In summary, oral PrEP is a novel HIV prevention strategy which has high efficacy when used consistently around the time of HIV exposure and about which we are learning about successful delivery. The early lessons from oral PrEP demonstration projects among African AGYW are relevant to longer-acting and less adherence-dependent HIV prevention formulations which are in development, including the dapivirine vaginal ring, injectable cabotegravir, and antiretroviral implants. Longer-acting PrEP formulations will be simpler for women to use but will also require demand creation, goal setting, risk assessment, adherence support, and simple delivery models in order to achieve the coverage needed to have a public health impact. As with the contraception field, it is important to provide women with a choice of products that meet their reproductive and HIV prevention needs and learn how to support their choice and facilitate their uptake and persistence during periods of high risk.

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CC designed and wrote the paper. SD-M, JB, AV-S, SH, EB, MM, RB and LGB contributed data, drafted sections of the manuscript and reviewed the final manuscript.

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REFERENCES

1. UNAIDS. Global AIDS update. Miles to go: closing gaps, breaking barriers, righting injustices. Geneva: UNAIDS; 2018.

2. Baeten JM, Palanee-Phillips T, Brown ER, Schwartz K, Soto-Torres LE, Govender V, et al. Use of a vaginal ring containing dapivirine for HIV-1 prevention in women. N Engl J Med. 2016;375:2121–32.
3. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. AIDS. 2016;30(12):1973–83.
4. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372(6):509–18.
5. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367(5):411–22.
6. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363(27):2587–99.
7. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367(5):399–410.
8. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2013;381(9883):2083–90.
9. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med. 2012;367(5):423–34.
10. Murnane PM, Celum C, Mugo N, Campbell JD, Donnell D, Bukusi E, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. AIDS. 2013;27(13):2155–60.
11. Hanscom B, Janes HE, Guarino PD, Huang Y, Brown ER, Chen YQ, et al. Preventing HIV-1 infection in women using oral pre-exposure prophylaxis: a meta-analysis of current evidence. J Acquir Immune Defic Syndr. 2016;73(5):606.
12. Argo N, Krishnamurti T, Fischhof B. Should I take PrEP? A mental models assessment of young African women's motivations for and barriers to PrEP initiation and adherence. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.
13. Corneli A, Perry B, Agot K, Ahmed K, Malamatsho F, Van Damme L. Facilitators of adherence to the study pill in the FEM-PrEP clinical trial. PLoS ONE. 2015;10(4):e0125458.
14. Katz A, Mensch B, Woeber K, Musara P, Etima J, van der Straten A. Understanding women's motivations to participate in MTN-003/VOICE, an HIV prevention trial with low adherence. HIV Research for Prevention Conference (HIVR4P); October 17-20; Chicago, IL; 2016.
15. Macphail C, Delany-Moretlwe S, Mayaud P. "It's not about money, it's about my health": determinants of participation and adherence among women in an HIV-HSV2 prevention trial in Johannesburg, South Africa. Patient Prefer Adherence. 2012;6:579–88.
16. Magazi B, Stadler J, Delany-Moretlwe S, Montgomery E, Mathebula F, Hartmann M, et al. Influences on visit retention in clinical trials: insights from qualitative research during the VOICE trial in Johannesburg, South Africa. BMC Womens Health. 2014;14:88.
17. Corneli AL, McKenna K, Perry B, Ahmed K, Agot K, Malamatsho F, et al. The science of being a study participant: FEM-PrEP participants' explanations for overreporting adherence to the study pills and for the whereabouts of unused pills. J Acquir Immune Defic Syndr. 2015;68(5):578–84.
18. van der Straten A, Stadler J, Luecke E, Laborde N, Hartmann M, Montgomery ET. Perspectives on use of oral and vaginal antiretrovirals for HIV prevention: the VOICE-C qualitative study in Johannesburg, South Africa. J Int AIDS Soc. 2014;17(3 Suppl 2):19146.
19. van der Straten A, Stadler J, Montgomery E, Hartmann M, Magazi B, Mathebula F, et al. Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa. PLoS ONE. 2014;9(2):e89118.
20. van der Straten A, Musara P, Etima J, Woeber K, Montgomery ET, Hartmann M, et al. Disclosure of pharmacokinetic (PK) drug results promotes open discourse on non-adherence among women in VOICE. AIDS Res Hum Retrov. 2014;30:A42–3.
21. Laibson D. Golden eggs and hyperbolic discounting. Q J Econ. 1997;112(2):443–77.
22. O'Donoghue T, Rabin M. Doing it now or later. Am Econ Rev. 1999;89(1):103–24.
23. Linnemayr S. HIV prevention through the lens of behavioral economics. J Acquir Immune Defic Syndr. 2015;68(4):e61–3.
24. Montgomery ET, Mensch B, Musara P, Hartmann M, Woeber K, Etima J, et al. Misreporting of product adherence in the MTN-003/VOICE trial for HIV prevention in Africa: participants' explanations for dishonesty. AIDS Behav. 2017;21(2):481–91.
25. Hartmann M, McConnell M, Bekker LG, Celum C, Bennie T, Zuma J, et al. Motivated reasoning and HIV risk? Views on relationships, trust, and risk from young women in Cape Town, South Africa, and implications for oral PrEP. AIDS Behav. 2018;22(11):3468–79.
26. Palanee-Phillips T, Roberts ST, Reddy K, Vaneshree G, Naidoo L, Siva S, et al. Impact of partner-related social harms on women's adherence to the dapivirine vaginal ring during a phase III trial. J Acquir Immune Defic Syndr. 2018;79:580.
27. Roberts ST, Haberer J, Celum C, Mugo N, Ware NC, Cohen CR, et al. Intimate partner violence and adherence to HIV pre-exposure prophylaxis (PrEP) in African women in HIV serodiscordant relationships: a prospective cohort study. J Acquir Immune Defic Syndr. 2016;73(3):313–22.
28. Cabral A, Ngure K, Velloza J, Odoyo J, Celum C, Muwonge T, et al. Intimate partner violence and self-reported pre-exposure prophylaxis interruptions among HIV-negative partners in HIV serodiscordant couples in Kenya and Uganda. J Acquir Immune Defic Syndr. 2018;77(2):154–9.
29. Montgomery ET, van der Straten A, Stadler J, Hartmann M, Magazi B, Mathebula F, et al. Male partner influence on women's HIV prevention trial participation and use of pre-exposure prophylaxis: the importance of "understanding." AIDS Behav. 2015;19(5):784–93.
30. Geier CF. Adolescent cognitive control and reward processing: implications for risk taking and substance use. Horm Behav. 2013;64(2):333–42.
31. Smith AR, Chein J, Steinberg L. Impact of socio-emotional context, brain development, and pubertal maturation on adolescent risk-taking. Horm Behav. 2013;64(2):323–32.
32. Romer D. Adolescent risk taking, impulsivity, and brain development: implications for prevention. Dev Psychobiol. 2010;52(3):263–76.
33. Perez KM, Patel NJ, Lord JH, Savin KL, Monzon AD, Whittemore R, et al. Executive function in adolescents with type 1 diabetes: relationship to adherence, glycemic control, and psychosocial outcomes. J Pediatr Psychol. 2017;42(6):636–46.
34. O'Hara LK, Holmbeck GN. Executive functions and parenting behaviors in association with medical adherence and autonomy among youth with spina bifida. J Pediatr Psychol. 2013;38(6):675–87.
35. Bagner DM, Williams LB, Geffken GR, Silverstein JH, Storch EA. Type 1 diabetes in youth: the relationship between adherence and executive functioning. Children's Health Care. 2007;36(2):169–79.
36. Reed-Knight B, Blount RL, Gilleland J. The transition of health care responsibility from parents to youth diagnosed with chronic illness: a developmental systems perspective. Fam Syst Health. 2014;32(2):219–34.
37. Gutierrez-Colina AM, Eaton CK, Lee JL, Reed-Knight B, Loiselle K, Mee LL, et al. Executive functioning, barriers to adherence, and nonadherence in adolescent and young adult transplant recipients. J Pediatr Psychol. 2016;41(7):759–67.
38. Luecke EH, Cheng H, Woeber K, Nakyanzi T, Mudekunye-Mahaka IC, van der Straten A. Stated product formulation preferences for HIV pre-exposure prophylaxis among women in the VOICE-D (MTN-003D) study. J Int AIDS Soc. 2016;19(1):20875.
39. van der Straten A, Shapley-Quinn MK, Reddy K, Cheng H, Etima J, Woeber K, et al. Favoring "peace of mind": a qualitative study of african women's HIV prevention product formulation preferences from the MTN-020/ASPIRE trial. AIDS Patient Care STDs. 2017;31(7):305–14.
40. Minnis AM, Roberts ST, Agot K, Weinrib R, Ahmed K, Manenzhe K, et al. Young women's ratings of three placebo multipurpose prevention technologies for HIV and pregnancy prevention in a randomized, cross-over study in Kenya and South Africa. AIDS Behav. 2018;22(8):2662–73.
41. van der Straten A, Agot K, Ahmed K, Weinrib R, Browne EN, Manenzhe K, et al. The tablets, ring, injections as options (TRIO) study: what young African women chose and used for future HIV and pregnancy prevention. J Int AIDS Soc. 2018;21(3):e25094.
42. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet. 2016;387(10013):53–60.
43. Heffron R, Ngure K, Odoyo J, Bulya N, Tindimwebwa E, Hong T, et al. Pre-exposure prophylaxis for HIV-negative persons with partners living with HIV: uptake, use, and effectiveness in an open-label demonstration project in East Africa. Gates Open Res. 2017;1:3.
44. Baeten J, Heffron R, Kidoguchi L, Mugo N, Katabira E, Bukusi E, et al. Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-

1–serodiscordant couples: a prospective implementation study in Kenya and Uganda. PLoS Med. 2016;13(8):e1002099.
45. Baeten J, Palanee-Philips T, Mgodi N, Mayo A, Nel A, Rosenberg Z, et al. High uptake and reduced HIV-1 incidence in an open-label, trial of the dapivirine ring. Conference on Retroviruses and Opportunistic Infections (CROI); March 4-7; Boston, MA; 2018.
46. Bekker LG, Roux S, Sebastien E, Yola N, Amico KR, Hughes JP, et al. Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial. Lancet HIV. 2018;5 (2):e68–78.
47. Hosek SG, Landovitz RJ, Kapogiannis B, Siberry GK, Rudy B, Rutledge B, et al. Safety and feasibility of antiretroviral preexposure prophylaxis for adolescent men who have sex with men aged 15 to 17 years in the United States. JAMA Pediatr. 2017;171(11):1063–71.
48. World Health Organization. WHO implementation guidance for pre-exposure prophylaxis of HIV infection. Geneva, Switzerland: World Health Organization; 2016.
49. Haberer JE, Kidoguchi L, Heffron R, Mugo N, Bukusi E, Katabira E, et al. Alignment of adherence and risk for HIV acquisition in a demonstration project of pre-exposure prophylaxis among HIV serodiscordant couples in Kenya and Uganda: a prospective analysis of prevention-effective adherence. J Int AIDS Soc. 2017;20(1):21842.
50. Meyers L, Bekker L-G, Aunger R, van der Straten A, Morton J, McConnell M, et al. A behaviour-centered design approach to creating demand for oral PrEP among young women in Masiphumelele, South Africa. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.
51. Wagner LD, Roberts S, O'Rourke S, Celum C, Baeten J, Bukusi E, et al. Challenges with oral pre-exposure prophylaxis (PrEP) disclosure among adolescent girls and young women (AGYW) in Kenya and South Africa. The HIV Research For Prevention Conference (HIVR4P); October 21-25; Madrid, Spain; 2018.
52. Celum C, Mgodi N, Bekker L-G, Hosek S, Donnell D, Anderon P, et al. Adherence 3 months after PrEP initiation among young African women in HPTN 082. Conference on Retroviruses and Opportunistic Infections (CROI); March 4-7; Seattle, WA; 2019.
53. Delany-MoretlweS, Mgodi N, Bekker L-G, Baeten J, Pathak S, Donnell D, et al. High curable STI prevalence and incidence in HPTN 082. Conference on Retroviruses and Opportunistic Infections (CROI); March 4-7; Seattle, WA; 2019.
54. Rousseau-Jemwa E, Bekker L-G, Bukusi E, Delany-Moretlwe S, Omollo V, Traveill D, et al. Early persistence of HIV pre-exposure prophylaxis (PrEP) in African adolescent girls and young women (AGYW) from Kenya and South Africa. HIV Research for Prevention Meeting (HIVR4P); October 21-25; Madrid, Spain; 2018.
55. Celum C, Delany-Moretlwe S, Hosek S, Dye B, Bekker L, Mgodi N, et al. Risk behavior, perception, and reasons for PrEP among young African women in HPTN 082. Conference on Retroviruses and Opportunistic Infections (CROI); March 4-7; Boston, MA; 2018.
56. Celum C, Gill K, Morton J, Stein G, van der Straten A, Baeten J, et al. High adherence among young women in Cape Town in the first 3 months after PrEP START. Conference on Retroviruses and Opportunistic Infections (CROI); March 4-7; Seattle, WA; 2019.
57. Simoni JM, Huh D, Frick PA, Pearson CR, Andrasik MP, Dunbar PJ, et al. Peer support and pager messaging to promote antiretroviral modifying therapy in Seattle: a randomized controlled trial. J Acquir Immune Defic Syndr. 2009;52 (4):465–73.
58. Spiegel HM, Futterman DC. Adolescents and HIV: prevention and clinical care. Curr HIV/AIDS Rep. 2009;6(2):100–7.
59. Denison JA, Banda H, Dennis AC, Packer C, Nyambe N, Stalter RM, et al. "The sky is the limit": adhering to antiretroviral therapy and HIV self-management from the perspectives of adolescents living with HIV and their adult caregivers. J Int AIDS Soc. 2015;18(1):19358.
60. Massy M, Bauermeister JA, Victor M, Judith B, Kiweewa F, Snow RC, et al. Psychosocial challenges and strategies for coping with HIV among adolescents in Uganda: a qualitative study. AIDS Patient Care STDS. 2015;29 (2):86–94.
61. Sung-Hee K, Susan M, Samuel K, Caroline F, Sarah F. Importance of self-motivation and social support in medication adherence in HIV-infected adolescents in the United Kingdom and Ireland: a multicentre HYPNet study. AIDS Patient Care STDS. 2015;29(6):354–64.
62. Fisher EB, Boothroyd RI, Coufal MM, Baumann LC, Mbanya JC, Rotheram-Borus MJ, et al. Peer support for self-management of diabetes improved outcomes in international settings. Health Aff. 2012;31(1):130–9.
63. Scorgie F, Stadler J, Baron D, Ju S, Ikaneng T, Mabude Z, et al. "It was not my aim to sleep there": the impact of timing and location of sex on adherence to coitally-dependent hiv pre-exposure prophylaxis. AIDS Behav. 2018;22 (11):3692–704.
64. Delany-Moretlwe S, Lombard C, Baron D, Bekker L-G, Nkala B, Ahmed K, et al. Tenofovir 1% vaginal gel for prevention of HIV-1 infection in women in South Africa (FACTS-001): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Infect Dis. 2018;18(11):1241–50.
65. Mudhune S, Delany-Moretlwe S, Baron D, Pato S, Stadler J, Ngcobo N, et al. Motivating, measuring and monitoring adherence in the FACTS 001 tenofovir gel microbicide study. HIV Research For Prevention Conference (HIVR4P); October 27-31; Cape Town, South Africa; 2014.
66. Ramskin L, Baron D, Makgamathe K, Schutzman J, Stangl A, Sievwright K, et al. EMPOWER clubs for young women using oral PrEP as part of an HIV prevention package: what we've learned so far. Adherence to HIV prevention and treatment. Adherence to HIV Prevention and Treatment; April 26-27; Harare, Zimbabwe; 2018.
67. Mani A, Mullainathan S, Shafir E, Zhao J. Poverty impedes cognitive function. Science. 2013;341(6149):976–80.
68. Linnemayr S, Stecher C, Mukasa B. Behavioral economic incentives to improve adherence to antiretroviral medication. AIDS. 2017;31(5):719–26.
69. Dupas P. Health behavior in developing countries. Annu Rev Econom. 2011;3(1):425–49.
70. Loewenstein G, Price J, Volpp K. Habit formation in children: evidence from incentives for healthy eating. J Health Econ. 2016;45:47–54.
71. VannakitR, Kim M, Charoenying S, Mills S, Avery M, Phanuphak PN, et al. Key population-led health services (KP-LHS) critical to PrEP introduction among MSM and TG in Thailand. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.
72. Tsondai PR, Wilkinson LS, Grimsrud A, Mdlalo PT, Ullauri A, Boulle A. High rates of retention and viral suppression in the scale-up of antiretroviral therapy adherence clubs in Cape Town, South Africa. J Int AIDS Soc. 2017;20 Suppl 4:21649.
73. McGillen JB, Anderson SJ, Hallett TB. PrEP as a feature in the optimal landscape of combination HIV prevention in sub-Saharan Africa. J Int AIDS Soc. 2016;19(7 Suppl 6):21104.
74. Peebles K, Mugwanya K, Irungu E, Odoyo J, Wamoni E, Morton J, et al. Low costs and opportunities for efficiency in the first year of programmatic PrEP delivery in Kenya's Public Sector. HIV Research for Prevention Conference (HIVR4P); October 21-25; Madrid, Spain; 2018.
75. Roberts A. The role of costing in the introduction and scale up of pre-exposure prophylaxis: evidence from integrating PrEP into routine maternal and child health and family planning clinics in western Kenya. J Int AIDS Soc. Submitted.
76. Gill K. Evaluation of PrEP demand creation and uptake among young women in a Cape Town township: the 3P study. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.
77. Rousseau-Jemwa E, Celum C, Baeten J, Bekker L-G. A comparative study of risk among adolescent girls and young women who accept or decline PrEP uptake from a community-based mobile clinic. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.
78. Morton J, Bukusi E, Delaney-Moretlwe S, Bekker L-G, Omollo V, Travill D, et al. High prevalence of curable STIs among young women initiating PrEP in Kenya and South Africa. International AIDS Conference; July 23-27; Amsterdam, The Netherlands; 2018.

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REVIEW

Understanding user perspectives of and preferences for oral PrEP for HIV prevention in the context of intervention scale-up: a synthesis of evidence from sub-Saharan Africa

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Abstract

Introduction: Oral pre-exposure prophylaxis (PrEP) for HIV prevention has been proven to significantly reduce new HIV infections yet scale-up has been slow. As contexts continue to adjust to make space for PrEP, it is crucial to understand the perspectives and experiences of potential end-users. In order to inform PrEP and demand creation interventions, this paper examines personal perspectives on adopting and using PrEP among HIV at-risk populations in sub-Saharan Africa.

Methods: Using the principles of a scoping review in July 2018, we explored the extent, range, and nature of published literature regarding PrEP uptake and use among; men who have sex with men, HIV serodiscordant couples, adolescent girls and young women, pregnant and breastfeeding women, women partners of migrant workers; and people who use drugs. Steps included: identification of the research question; identification of relevant studies; study selection; charting the data; and collation – summarizing and reporting results. PubMed and PsycInfo were searched for papers relating to PrEP uptake and use in sub-Saharan Africa. Resulting papers were reviewed with data extracted and compiled in Excel for analysis. A broad content analysis was conducted and organized into high-level themes.

Results and discussion: Thirty-five papers were included in this review. There was little opposition in general to oral PrEP; however, there were significant nuances in its broader acceptability, applicability, and usability. We identified five themes within which these are discussed. These relate to balancing complexities of personal empowerment and stigma; navigating complex risk environments; influences of relationships and partners; efficacy and side effects; and practicalities of use. This body of research suggests that while product attributes and the logistics of PrEP delivery and use are important topics, it is vital to consider stigma, the interactions of PrEP use with relationships, and the need for broader understanding of ARVs for prevention versus treatment.

Conclusions: Planning for, programming and promoting the adoption of oral PrEP necessitates a deeper understanding of end-user priorities in order to ensure successful interventions. This review illustrates the nuances facilitating or deterring PrEP use that may affect the larger effort of PrEP scale-up.

Keywords: HIV prevention; pre-exposure prophylaxis; acceptability; end-user; public health; key and vulnerable populations

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1 | INTRODUCTION

Oral pre-exposure prophylaxis (PrEP) for HIV prevention has been proven to significantly reduce new HIV infections in efficacy trials [1], yet introduction has been slow. PrEP is being implemented in nearly 50 countries to varying degrees [2], though predominantly in phased implementation approaches limiting service delivery sites and access [3,4]. This has particularly been the case in sub-Saharan Africa owing largely to strained national health budgets.

Epidemiological modelling suggests that PrEP will be most cost effective if offered to those at highest risk [5–9], and where PrEP has gained momentum both in community support and scale-up among World Health Organization (WHO) recommended higher risk populations [10], such as Australia and the United Kingdom, significant falls in HIV incidence have been observed [11,12]. Conversely, many of the phased approaches have come with limited demand generation and communications strategies [3]. These barriers perpetuate challenges for uptake and effective use of PrEP among current and potential end-users. Rendering the UNAIDS goal of reaching three million people at high risk with PrEP by 2020 unlikely [13].

As programmes shift to integrate PrEP, it is crucial that we understand the perspectives of those taking up and using PrEP in order to demonstrate demand, facilitate use, and

mitigate multi-level barriers. At the centre of successful proven theories and practices concerning intervention scale-up are time, communication and user-acceptability [14]. Acceptability can be defined in a myriad of ways, but the key elements, also reflected in this paper, include: (1) the applicability of the innovation (oral PrEP), or the relevance and responsiveness of the innovation to the lives of those who need it; as well as, (2) the acceptability which speaks to a more internal, emotional, user-centred [15]) perspective. Fundamentally, it can be argued that the uptake and continued use of PrEP will occur at scale only if populations/end-users are at the centre and PrEP is: a known product, meets needs, can be integrated into everyday lives. Our previous research relating to female initiated HIV prevention technologies demonstrated how, historically, interventions have focused on the easiest goals, such as ensuring clinical access and examining product attributes [16]. However, it was often personal and relationship concerns, such as comfort, trust, and sexual pleasure, in addition to practicalities, that actually played a central role in uptake and use [16]. As the rollout of PrEP continues, it is essential that researchers and implementers continue to examine how it is influencing and changing the lives of end-users.

In this review, we synthesize published literature concerning both the actual experience of using PrEP and the perspectives of potential end-users (which we refer to as "theoretical use"). This work builds on previous mixed method and qualitative reviews [16,17]. Our aim is to elucidate the broad perception or experience of PrEP, including motivations for use, barriers to uptake or continued use, and the manner in which it impacts (or could impact) everyday life. We seek to highlight current gaps in the literature to facilitate the scale-up of PrEP.

2 | METHODS

This research utilizes scoping review methods to establish the extent, range, and nature of published literature assessing the experience of PrEP uptake and use, or the theoretical perspective of use, in terms of applicability and acceptability [18]. Often, but not always, a forerunner to full systematic reviews, scoping reviews provide a means of rapidly appraising emerging subject matter and can provide a mechanism by which complex findings are summarized for policy makers and practitioners. Arksey and O'Malley outline five necessary phases: identification of the research question; identification of relevant studies; study selection; charting the data; and collation, which summarizes and reports results [18].

Our review of the literature was informed by the question, "What are the lived experiences or personal perspectives of those HIV at-risk populations in sub-Saharan Africa adopting and using PrEP?" Acknowledging the growing interest and motivation to expand review methods to allow for less rigid, and more inclusive, synthesis of data [19], we sought to combine data from mixed methods research (i.e. both quantitative and qualitative) as well as lessons learned from pre-cursor studies which addressed theoretical rather than actual acceptability and use of PrEP. We also sought to look across HIV at-risk populations to explore where there may be commonalities or differences in perspectives on PrEP.

The search was conducted in August 2018 in PubMed and PsycInfo using the keywords: Africa (and all countries classified in the UN region), pre-exposure prophylaxis (PrEP), Acceptability, Willingness, Barriers, Facilitators, Use and Preferences. Papers were included if they: focused on theoretical or actual use of PrEP and took place in Africa. After deduplication, the search returned 68 papers, which were divided among all three authors for review. Thirty-three were excluded for the following reasons: they had no bearing on the topic; did not include primary, empirical data (e.g. was a review or a study protocol); contained only research relating to providers, policy maker or other perspectives on PrEP; or research took place outside of Africa. There were no date or language exclusions. Note that studies only emerged from sub-Saharan Africa.

All three authors extracted and compiled relevant data in a spreadsheet. Bibliographic data, study populations and study locations, as well as whether the study involved actual use or theoretical perspectives of PrEP (e.g. "If PrEP were to be available in your area, would you wish to use it?" and associated data) were recorded in addition to themes covered in the papers. Once all data were compiled, we conducted a broad content analysis [20]. Codes, concepts, and ideas were documented, before being organized into relevant meta-themes. Authors then reviewed the consolidated dataset of all data and author findings. A limited subset of the final list of included papers was reviewed by two of the authors to ensure agreement of findings. This analysis also built upon a previous adapted meta-ethnography (led by two of the authors of this paper), which developed a framework for understanding user-perspectives of female initiated biomedical HIV prevention products [16]. Note that where a mixed-methods paper was included, the quantitative data were incorporated to support the qualitative themes (e.g. such as perspectives on risk compensation and statistical analyses showing none was found). Additionally, there is no quality assessment of data since this review is focused on exploring data to elucidate current understanding of PrEP and identify areas for further research. Finally, since the results and discussion are combined in this paper, additional supporting reviews and data papers are included in the sections that follow.

3 | RESULTS AND DISCUSSION

This review generated 35 papers primarily from studies of potential but not actual PrEP users, from qualitative components of product efficacy studies, or from participants in demonstration projects undertaken in sub-Saharan Africa, where HIV infection remains both common and very highly stigmatized. These studies include a range of populations including male and female sex workers; men who have sex with men (MSM); HIV serodiscordant couples; adolescent girls and young women (AGYW); pregnant and breastfeeding women; women partners of migrant workers; and people who use drugs (PWUD). Included papers are listed in Table 1.

Very few studies reported clear opposition to PrEP as an HIV prevention tool, although some generated evidence of community distrust of study/trial designs or of the concept of PrEP itself [21]. Theoretical studies among potential end-users typically found high acceptability of PrEP [22–31]. By including the theoretical research, a range of regimens are included in

Table 1. Review papers included

Authors	Title	Pub year	Type of PrEP use (theoretical/actual)	Population(s)	Location
Agot *et al.*	Accuracy of self-report and pill count measures of adherence in the FEM-PrEP clinical trial: implication for future HIV-prevention trials	2015	Actual	High-risk adult women	Kenya, South Africa, Tanzania
Amico *et al.*	Experiences with HPTN 067/ADAPT study-provided open-label PrEP among women in Cape Town: facilitators and barriers within a mutuality framework	2017	Actual	High-risk adult women	South Africa
Bazzi *et al.*	Perspectives on biomedical HIV prevention options among women who inject drugs in Kenya	2018	Theoretical	Women who inject drugs	Kenya
Busisiwe *et al.*	Influences on visit retention in clinical trials: insights from qualitative research during the VOICE trial in Johannesburg, South Africa	2014	Actual	High-risk adult women	South Africa
Carroll *et al.*	Gendered differences in the perceived risks and benefits of oral PrEP among HIV serodiscordant couples in Kenya	2016	Actual	Serodiscordant couples	Kenya, Uganda
Corneli *et al.*	Motivations for reducing other HIV risk-reduction practices if taking pre-exposure prophylaxis: findings from a qualitative study among women in Kenya and South Africa	2015	Theoretical	High-risk adult women	Kenya, South Africa
Corneli *et al.*	Facilitators of adherence to the study pill in the FEM-PrEP clinical trial	2015	Theoretical	High-risk adult women	Kenya, South Africa
Corneli *et al.*	Participants' explanation for nonadherence in the FEM-PrEP trial	2016	Actual	High-risk adult women	Kenya, South Africa
Corneli *et al.*	A descriptive analysis of perceptions of HIV risk and worry about acquiring HIV among FEM-PrEP participants who seroconverted in Bondo, Kenya and Pretoria, South Africa	2014	Actual	High-risk adult women	Kenya, South Africa
Corneli *et al.*	The science of being a study participant: FEM-PrEP participants' explanations for overreporting adherence to the study pills and for the whereabouts of unused pills	2015	Actual	High-risk adult women	Kenya, South Africa
Eakle *et al.*	Exploring acceptability of oral PrEP prior to implementation among female sex workers in South Africa	2018	Theoretical	FSW	South Africa
Luecke *et al.*	Stated product formulation preferences for HIV pre-exposure prophylaxis among women in the VOICE-D (MTN-003D) study	2016	Actual and theoretical	High-risk adult women	South Africa
Fowler *et al.*	Attitudes of serodiscordant couples towards antiretroviral-based HIV prevention strategies in Kenya: a qualitative study	2014	Theoretical	Serodiscordant couples	Kenya
Kibengo *et al.*	Safety, adherence and acceptability of intermittent tenofovir/emtricitabine as HIV pre-exposure prophylaxis (PrEP) among HIV-uninfected Ugandan volunteers living in HIV-serodiscordant relationships: a randomized, clinical trial	2013	Actual	Serodiscordant couples	Uganda
Mutua *et al.*	Safety and adherence to intermittent pre-exposure prophylaxis (PrEP) for HIV-1 in African men who have sex with men and female sex workers	2012	Actual	MSM, FSW	Kenya

Table 1. (*Continued*)

Authors	Title	Pub year	Type of PrEP use (theoretical/actual)	Population(s)	Location
Guest *et al.*	Acceptability of PrEP for HIV Prevention Among Women at High Risk for HIV	2010	Actual	High risk adult women	Ghana
Falcao *et al.*	Willingness to use short-term oral pre-exposure prophylaxis (PrEP) by migrant miners and female partners of migrant miners in Mozambique	2017	Actual	Male migrant miners and female partners	Mozambique
Hartmann *et al.*	Motivated Reasoning and HIV Risk? Views on Relationships, Trust, and Risk from Young Women in Cape Town, South Africa, and Implications for Oral PrEP	2018	Theoretical	Young women	South Africa
Namey *et al.*	When and why women might suspend PrEP use according to perceived seasons of risk: implications for PrEP-specific risk-reduction counselling.	2016	Theoretical	Sexually active women at higher risk of HIV	Kenya, South Africa
Mack *et al.*	The importance of choice in the rollout of ARV-based prevention to user groups in Kenya and South Africa: a qualitative study	2014	Theoretical	FSW, Serodiscordant couples, AGYW,	Kenya, South Africa
Ngure *et al.*	I Knew I Would Be Safer. Experiences of Kenyan HIV Serodiscordant Couples Soon After Pre-Exposure Prophylaxis (PrEP) Initiation	2016	Actual	Serodiscordant couples	Kenya
Mugo *et al.*	Understanding Adherence to Daily and Intermittent Regimens of Oral HIV Pre-exposure Prophylaxis Among Men Who Have Sex with Men in Kenya	2015	Actual	MSM	Kenya
Pintye *et al.*	HIV-Uninfected Kenyan Adolescent and Young Women Share Perspectives on Using Preexposure Prophylaxis During Pregnancy	2018	Theoretical	Young pregnant or post-partum women	Kenya
Pintye *et al.*	"I Did Not Want to Give Birth to a Child Who has HIV": Experiences Using PrEP During Pregnancy Among HIV-Uninfected Kenyan Women in HIV-Serodiscordant Couples	2017	Actual	Serodiscordant couples	Kenya
Restar *et al.*	Perspectives on HIV Pre- and Post-Exposure Prophylaxes (PrEP and PEP) Among Female and Male Sex Workers in Mombasa, Kenya: Implications for Integrating Biomedical Prevention into Sexual Health Services	2017	Theoretical	Young male and female sex workers	Kenya
Roberts *et al.*	Intimate Partner Violence and Adherence to HIV Pre-exposure Prophylaxis (PrEP) in African Women in HIV Serodiscordant Relationships: A Prospective Cohort Study	2016	Actual	Negative women in serodiscordant relationships	Kenya, Uganda
Robinson *et al.*	"How I Wish This Thing Was Initiated 100 Years Ago!" Willingness to Take Daily Oral Pre-Exposure Prophylaxis among Men Who Have Sex with Men in Kenya	2016	Theoretical	MSM	Kenya
Shaver *et al.*	Comparing Provider and Client Preferences for HIV Prevention Services in South Africa among Men Who Have Sex with Men	2017	Theoretical and actual	MSM	South Africa
Sithole *et al.*	HIV prevention needs for men who have sex with men in Swaziland	2017	Theoretical	MSM	Swaziland

Table 1. (*Continued*)

Authors	Title	Pub year	Type of PrEP use (theoretical/actual)	Population(s)	Location
Van der Elst *et al.*	High acceptability of HIV pre-exposure prophylaxis but challenges in adherence and use: qualitative insights from a phase I trial of intermittent and daily PrEP in at-risk populations in Kenya	2012	Actual	MSM, FSW	Kenya
van der Straten *et al.*	Perspectives on use of oral and vaginal antiretrovirals for HIV prevention: the VOICE-C qualitative study in Johannesburg, South Africa	2014	Actual	High-risk adult women	South Africa, Uganda, Zimbabwe
van der Straten *et al.*	Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa	2014	Actual	High-risk adult women	South africa, Uganda, Zimbabwe
Ware *et al.*	Lay Social Resources for Support of Adherence to Antiretroviral Prophylaxis for HIV Prevention Among Serodiscordant Couples in sub-Saharan Africa: A Qualitative Study	2015	Actual	Serodiscordant couples	Uganda
Ware *et al.*	Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-1 serodiscordant couples in East Africa: a qualitative evaluation study in Uganda	2018	Actual	Serodiscordant couples	Uganda
Ware *et al.*	What's love got to do with it? Explaining adherence to oral antiretroviral pre-exposure prophylaxis for HIV-serodiscordant couples	2012	Actual	Serodiscordant couples	Uganda

the review including: oral daily and intermittent (the definition of which is particular to the given study), as well as emerging injectable and vaginal ring products.

One theoretical study suggested a limited motivation to take PrEP in light of HIV treatment needs and few pre-existing social norms relating to prophylactic medication [24]. However, no clinical trial or demonstration project reported significant challenges with recruitment, potentially due to financially incentivized participation and/or provision of higher calibre health care as compared to the norm [32]. Some studies reported altruism [32] or "Ubuntu," [21] the concept of contributing something positive to your community, as research motivators to advance HIV prevention. Actual use research also found PrEP acceptability to be high but also described a range of benefits and problems that can arise, which we address under five key themes below.

3.1 | Balancing the complexities of personal empowerment and potential stigma

The potential to use anti-retroviral therapy (ART) to prevent HIV infection seemed counter-intuitive to some potential users where prior experience was focused on treating sick people with ART. When PrEP was described to a naïve potential user, concern was common that taking the same medications used to treat diagnosed HIV will mean "people will just assume I have HIV" [23]. Such findings suggest that HIV related stigma is still so pervasive that it may pose a challenge to PrEP provision whether or not it is linked to services also providing ART to HIV positive people [33].

Several studies suggest that PrEP is conflated with ART not just in personal understandings of PrEP but in expectations of how others will respond, generating fear of HIV-related stigma and discrimination. This potential stigma has been highlighted among MSM in Kenya [23]; women who inject drugs in Kenya [30]; female sex workers in Kenya and South Africa [34,35]; female partners of migrant workers returning to Mozambique for short periods [36]; and women at high risk of HIV infection in South Africa [37–39]. Participants in all these studies broadly welcomed the opportunity to avoid HIV infection but were apprehensive about being seen to take ART. All feared being identified as HIV infected which would lead to social isolation and other harms. Some went to great lengths to disguise their involvement in research and were secretive about using PrEP with regular partners and immediate family, even when this made adherence very difficult. These fears could ultimately affect the impact of PrEP where related use becomes limited.

Conversely, PrEP use in some studies raised hope and offered potentially transformative opportunities. Participants cited increased control over one's sexual health [40] and hope in avoiding infection as values of taking PrEP, especially among women with limited trust in the monogamy of their partner and limited power to ensure condom use. This is also true for men and women involved in selling sex or in known serodiscordant relationships. By offering negative partners of people

with diagnosed HIV a semblance of control, it provided a means to sustain a desired relationship and/or to have children [41]. Similarly, male and female sex workers in Kenya saw PrEP as a potential "expression of self-love and self-care" tantamount to "making a choice to live" [27].

3.2 | Navigating the risk environment: perceptions, realities and compensation

PrEP has the potential to slow HIV transmission in geographic areas, or in sub-populations, where there remains high HIV prevalence with low sustained viral suppression, and otherwise few viable options for prevention. Compared to condoms it is especially useful for those populations with limited control over their risk of sexual exposure (as is sometimes the case for sex workers), or others where there is a sustained risk of infection is sustained, such as people in serodiscordant relationships.

For women and girls in patriarchal societies, PrEP may be the first viable HIV prevention option that they can use on their own terms. In situations where they struggled to control exposure to HIV from male partners, and where sex outside the relationship was a concern, access to PrEP was welcomed [29], both as a means to manage risk perception and to avoid actual infection. Even within marriage and during pregnancy, women worried partners might "bring HIV into the home" [36,41]. Many women only acknowledged risk of HIV infection within their primary relationship [31] but fear of rape and other violence was also cited as a motivator for PrEP use [25].

In two earlier theoretical studies, concerns about PrEP "replacing" or decreasing condom use in general were common among sex workers [22,34]. However, male and female sex workers overall were supportive of the idea of PrEP providing "added protection" even in the context of aspirations to always use condoms [27]. Additionally, three other papers noted that risk behaviour did not change over time among participants actually using PrEP including migrant workers and female partners, MSM, FSW and serodiscordant couples [36,42,43]. It should also be noted that two systematic reviews also have shown no significant changes in behaviour among PrEP users [1,17].

3.3 | Relationship influences and expectations

Oral PrEP related research has documented how partners of potential or actual users have significant influence over use, as has been the case with other products. Condom use, or lack thereof, is often determined by male partners [44–47], which was similarly found in microbicide gel studies[37,38]. Indeed, in a theoretical study about motivations to use PrEP [32] female participants believed that the tablet would help to alleviate challenges they faced in partner condom negotiation. They described how condoms were a source of conflict in relationships where men insisted against use and women held genuine concerns about the risk of acquiring HIV or other STIs where a partner's status was unknown or the partner was suspected of external relationships.

While some have sought to promote antiretroviral (ARV) based prevention as a female controlled or initiated HIV prevention technology [48,49], several studies have shown that male partners still often exert considerable influence, either positive or negative. Carroll *et al*. examined gender dynamics within relationships and how these influence decision making relating to PrEP, identifying a wide variety of experiences [50]. HIV-negative women in their study overwhelmingly reported that the decision for either partner to initiate ART or PrEP, as appropriate, belonged entirely to their husbands. HIV-positive men also reported that they possess the ultimate authority to make medical decisions for themselves and their spouses. Similarly, HIV-negative men expressed frustration with the PrEP regimen and indicated that the burden of taking medication had been thrust upon them by their HIV-positive wives [50].

In Roberts *et al*., 16% of women in their serodiscordant couple study reported intimate partner violence (IPV) at some point during the trial [51]. They also had increased risk of low adherence as assessed by pill count and by plasma tenofovir. Verbal, economic and physical IPV were all associated with low adherence. In-depth interviews identified several ways in which IPV affected adherence, including stress and forgetting, leaving home without pills, and partners throwing pills away. Conversely, in a theoretical study, female sex workers articulated fear of violence as a motivator for taking PrEP [34].

Despite these issues, women commonly cited the option of disclosure as a benefit of PrEP use [16,22,34,52,53], thus empowering to prevent HIV infection in scenarios where their partners insist on condomless sex. Indeed, in the Partners Demonstration Project, PrEP provided additional protection as a "back-up" mechanism when their partners refused to use condoms and in cases of condom breakage [54]. However, other papers identified a wide range of disclosure decisions and experiences. In their study of PrEP adherence influencing factors as part of FEM-PrEP, Corneli *et al*. reported some male partners of female participants were very supportive and would remind them to take the pills [31]. Some had partners who merely acquiesced to their pill use, while a few opted not to tell their partners at all for fears of negative reaction and insistence of cessation.

Ware *et al*. report that while the presence of HIV serodiscordance can destabilize a couple, given that the HIV-negative partner often reacts with anger or fear to the HIV infection (and the potential infidelity it represents), PrEP can be seen as a solution [55]. Ultimately it can provide a means of safeguarding health without ending the relationship. Simultaneous use of ARVs by the HIV-positive partner turned management of HIV into a shared experience, and serodiscordant couple-focused services (including attending appointments and counselling as a couple) brought partners together, increasing mutual support through having a space to become educated and comfortable with PrEP [41,56]. This might suggest a potential positive impact of PrEP in developing relationship intimacy, a key aspect of health and well-being that is often overlooked in public health and social care interventions [57].

Several papers briefly highlighted the complexities of PrEP monitoring and adherence for people in romantic or regular relationships. They describe how adherence to PrEP may at times diminish as a consequence of changing sex patterns within the relationship, such as reduced libido as a result of partner absence from the home [29,58]. Some study participants reported they may wish to cease PrEP use if in a committed relationship, within which their concern about HIV transmission would diminish [55]. This should of course be an

empowered choice for all wishing to start, or stop, PrEP, but poses challenges for those seeking to utilize stringent measures of PrEP adherence that do not reflect the reality of relationships.

3.4 | Efficacy and side effects managing PrEP use

Defining and understanding the concept of ARVs for preventing HIV is complicated and multi-dimensional, including the management of potential stigma and understanding efficacy. For instance, some studies identified that developing an initial understanding of taking ARVs to prevent HIV remained confusing to study participants even after they had completed a rigorous informed consent process and had been participating in the study [21,37]. This emerged as a central issue the trials showing no efficacy, suggesting that misunderstanding of PrEP as an efficacious prevention modality may be a significant barrier in scale-up.

Perceived efficacy (i.e. the extent to which PrEP prevents HIV acquisition) was found to be a significant component of acceptability among most populations [22,35]. Beliefs about PrEP efficacy were directly related to whether people could be sufficiently adherent to the medication, and were influenced by lack of communication or open support from places of authority (clinics, providers and Ministries of Health) [21]. In efficacy research, the possibility of being on placebo and the unknown efficacy of the active PrEP pill were directly linked to lack of use in some studies, pointing to the importance of highlighting the high efficacy of PrEP in actual service delivery [37,58,59]. It will be important to capitalize; however, on the curiosity about PrEP, its novelty and its protective value if taken consistently, to encourage use among those at highest risk [23,54].

Side effects, or fear of potential side effects, were common in both efficacy and implementation studies. Initial side effects among female partners of migrant mine workers in Mozambique dissipated over time but were tolerated because they took the side effects to mean that PrEP was working [36]. Concerns about side effects during discussions of theoretical acceptability were common among women in one study, including partners in serodiscordant couples, adolescent girls and young women (AGYW), and sex workers [22]. Sex workers in Kenya suggested they would prefer intermittent use to reduce potential side effects over time since they anticipated a longer period of potential exposure to HIV as a result of their work [27]. This should also be noted as a potential motivator for intermittent PrEP use.

PrEP could play an important role in safer conception, but side effects need to be clearly discussed with clients. In one study, women said they would stop PrEP if trying to conceive due to worry of how it might affect the foetus [29]. However, women in the Partners study in Kenya who experienced minor side effects still affirmed that having an HIV-negative baby was worth the risk [41].

Finally, it should be noted that a recent meta-analysis suggested that very few major, and limited minor, side effects will occur when using PrEP [1]. This has been confirmed by multiple demonstration projects where minor side effects were limited to the first few days/weeks of use [60]. This suggests a significant disjuncture between the perception of potential side effects, the attribution of illness to the use of PrEP, and side effects actually triggered by the medication. Communicating this to interested, but concerned, end-users should be a priority for intervention scale-up.

3.5 | Practical considerations for PrEP use

User preferences for specific product attributes and the practicalities of PrEP use have been widely investigated [16]. These practical considerations remain important in planning for PrEP scale-up both for service delivery and day-to-day end-user experiences. Among actual end-users, basic practicalities such as clinic access, pill storage and managing adherence in the context of everyday obligations were significant considerations, as was negotiating with family, schools or employers to make time for appointments [23,33].

The service delivery environment also played a key role in successful PrEP implementation. This was a particularly pressing issue for key populations who already commonly face stigma attending health clinics [61]. Fear of rebuke from providers for not adhering to the medication, or being dropped from a study as a result, was cited as reason for lying about adherence [62,63], and points to the need to ensure constructive, open engagement between providers and clients. Open exchanges and high quality counselling were noted as being of particular value [32]. Negative clinic experiences directly deterred PrEP use [21,33], whereas good quality care was highly valued and increased clinic attendance [33,58]. In the FEM-PrEP study, repeated HIV-negative tests (even if on placebo) reinforced the notion that PrEP worked [32,33], although in another study it was noted that having to test often for HIV could be a barrier to continued PrEP use [36].

In Kenya and Uganda, women felt that providers play a key role in supporting PrEP use, especially outside of the trial environment for women who may not fully understand their own risk and the benefits of PrEP for conceiving babies free of HIV [41]. Women in Uganda also worried that the shortage of doctors/clinical staff could stand in the way of PrEP rollout due to already limited capacity to deliver existing services [59]. Importantly, community awareness of PrEP to promote support for use, access, and coverage has been noted as a critical component for successful implementation [26,34,41].

Consistent adherence while taking PrEP is the cornerstone of effective use and yet it was challenging in several of the efficacy studies to maintain adequate levels of use [1]. Women in several studies acknowledged forgetting, ambivalence, personal barriers (travel, family issues), missing clinic visits and refills, and worry about side effects as reasons for inconsistent use [37,43,58,62]. Similarly, the active management of actual side effects is an important factor to consider in scale-up, directly linking with the need for supportive counselling to encourage consistent use over time. Conflicts with partners and having to hide pill taking was also reported to cause people to forget to take their pills [58].

The use of alcohol and drugs was another concern related to efficacy and consistent use. This was particularly highlighted among sex workers, MSM, and young women, where participants were concerned that PrEP may not protect them from HIV when using other substances [22,23,34]. These participants also acknowledged potentially forgetting to take their pills if they were inebriated. Some potential PrEP users reported their own prior inability to finish pills (such as

antibiotics) as a signal they might not be able to successfully take oral PrEP [23].

Overall, the importance of developing pill taking behaviours and strategies is paramount to successful use and most have found manageable solutions [21,36]. Behaviours can be supported by early, and continued engagement with counsellors which has been shown to generate consistent use [54]. Interestingly, one older study found that those experiencing more difficulties in pill taking were more likely to stay in the study and were also able to develop strategies over time [64]. Related to the supportive environment and intimate relationships, studies that involved serodiscordant couples found the relationship provided an easier context in which to use PrEP, as it became a "shared commitment to HIV management and the relationship" [54] where adherence/use was considered a "family affair" [59].

Diverse perspectives were shared in relation to alternative, non-daily PrEP options. For some populations, such as female partners of migrant miners [36], shorter term use was preferable and intermittent dosing, for when partners were at home, was appealing.

Some of the papers in this review included theoretical perspectives on future products where women expressed preferences for long-acting PrEP [34,52]. One paper reported how some women anticipated their preferences would change over time [39], and some participants expressed wanting to have systemic protection while others prefer to have drug only in one area of their bodies [39]. Highlighting the importance of choice in this VOICE-D ancillary study South Africa, young women preferred pills which seemed less dangerous and more trustworthy, while female partners in serodiscordant couples and sex workers preferred long-acting products which require less maintenance [22]. These perspectives will be important to consider within the context of all that has been learned through oral PrEP implementation to ensure access to a range of appropriate and relevant interventions and products as they emerge.

4 | CONCLUSIONS

This review demonstrates the ways in which PrEP can, and already is, having a significant impact on the personal, relational, and social lives of HIV affected populations in sub-Saharan Africa. Those considering investment in and implementation of PrEP should take note of the robust and nuanced evidence suggesting great potential for PrEP to reduce HIV related anxiety, empower people (especially women) to take control of their sexual health, and to positively influence relationships (particularly those that are serodiscordant). These are significant benefits playing a role in reducing new infections.

However, this review also makes clear that the incorporation of PrEP into everyday lives is not without its challenges. There are pervasive concerns about side effects, and, to some extent, that the current required clinical engagement is overly burdensome. These issues exist in combination with health services that can be stigmatizing or insufficiently welcoming of key populations [65]. Uncertainty as to the effectiveness of PrEP remains especially where ingrained messages featuring 100% condom use has been the focus of HIV prevention campaigns over several decades. Belief and trust in PrEP will take time to develop and achieving this will also require the maintenance of efforts to reduce HIV-related stigma. Several studies identified how conflation of PrEP as ART and therefore being HIV positive could be perceived negatively by partners, family or friends. Through PrEP education and addressing HIV related stigma we can reduce this concern and potential barrier.

Notions of risk compensation were not common among the actual use studies in this review, and reported sexual behaviour did not change over time in any of the efficacy trials or demonstration projects [1,66,67]. However, this has continued to be a concern expressed from higher level stakeholders. Rhetoric perpetuating the assumption that PrEP will automatically encourage increased risk-taking behaviours should be carefully monitored to avoid.

Much of the research to date has emerged within the confines of clinical trials or demonstration projects. As such, some of the findings reported may be specific to that environment and may not have (as much) relevance in real-world settings. Examples include positive feelings towards PrEP in the context of high quality wrap around study services; uncertainties about efficacy of drugs given where randomization to placebo was possible; and practical concerns of being seen attending a trial site often synonymous with HIV treatment. Such issues may be unavoidable in the shorter-term given the requirement for rigorous HIV testing but it will be important to mitigate these issues in longer-term implementation.

Thus far research has been perhaps overly focused on practical dimensions of adherence (i.e. where pills are kept, how they are stored etc.). Less often have papers examined how significant others shape and inform continued PrEP use, especially the ways in which couples could be supported to effectively negotiate use within their relationship. It is interesting to note that despite much global level discourse framing PrEP as emancipatory for women – they finally have an efficacious female initiated technology to protect themselves from HIV - it seems there is good evidence that many men still wield significant authority over if and how it is used. Given socially and culturally pervasive gender imbalances, this should not be surprising, and is a reminder to be cognisant of how the notion of empowerment is communicated.

Notable in their (near complete) absence from this review are people who use drugs and transgender people. Only one paper specifically examined the theoretical perspectives of people who use drugs, and in brief, reports only on a concern for side effects. Marginally more attention has been paid to MSM but not the extent that is required given high HIV incidence across the continent [65]. Further research with MSM, PWUD and transgender people is required to understand issues such as relational support for PrEP use, stigma that may be associated with use and how to address it, as well as the effects of criminalization on access to PrEP and continued PrEP use. Criminalization of key populations and practices such as sex work was not specifically addressed in the papers identified in this review and should be carefully considered as a significant barrier to PrEP use. Papers outside this review have also underscored this point [68,69].

This paper describes a scoping review of available research relating to the experience of using PrEP, or perspectives about potentially doing so. It presents the extent of evidence and

summarizes key issues that may influence uptake and continued use by key populations. It is not, however, a systematic review or meta-analysis of all available data. Our review was limited to peer reviewed academic articles and does not include grey literature. This is a rapidly emerging field of research and many studies of real-world PrEP use are still being analysed and disseminated. The paper does, however, provide a comprehensive overview of significant issues that have relevance to demand creation, health promotion, and clinical interventions that aim to increase uptake and effective use of PrEP.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHORS' CONTRIBUTIONS

R.E. conceived the paper. A.B. and R.E. conducted the initial literature search, and all authors extracted and reviewed data, compared findings, and developed thematic categories. R.E., A.B. and P.W. co-wrote the paper and approved the final version.

REFERENCES

1. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. AIDS Lond Engl. 2016;30(12):1973–83.
2. AVAC. Country Updates[Internet]. PrEPWatch. [cited 2017 Apr 26]. Available from: http://www.prepwatch.org/scaling-up/country-updates/
3. Pillay Y. Challenges of South Africa's sex worker PrEP programme: Lessons learned, moving towards other key populations. In: PrEP in the real world – Early lessons for scale up among key populations [Internet]. Amsterdam, the Netherlands; 2018. Available from: http://programme.aids2018.org/Programme/Session/206
4. Matse S. The Kingdom of eSwatini's leading the design and scale up of PrEP for all populations. In: PrEP in the real world – Early lessons for scale up among key populations [Internet]. Amsterdam, the Netherlands; 2018. Available from: http://programme.aids2018.org/Programme/Session/206
5. Cambiano V, Miners A, Dunn D, McCormack S, Ong KJ, Gill ON, et al. Cost-effectiveness of pre-exposure prophylaxis for HIV prevention in men who have sex with men in the UK: a modelling study and health economic evaluation. Lancet Infect Dis. 2018;18(1):85–94.
6. Cremin I, Alsallaq R, Dybul M, Piot P, Garnett G, Hallett TB. The new role of antiretrovirals in combination HIV prevention: a mathematical modelling analysis. AIDS. 2013;27(3):447–58.
7. Cremin I, McKinnon L, Kimani J, Cherutich P, Gakii G, Muriuki F, et al. PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study. Lancet HIV. 2017;4(5):e214–22.
8. Gomez GB, Borquez A, Case KK, Wheelock A, Vassall A, Hankins C. The cost and impact of scaling up pre-exposure prophylaxis for HIV prevention: a systematic review of cost-effectiveness modelling studies. PLoS Med. 2013;10(3):e1001401.
9. Hallett TB. Priorities across the continuum of care: modelling the impact of interventions on mortality and HIV transmission. Vancouver Canada: 2015.
10. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - Second edition [Internet]. 2016[cited 2016 Jun 28]. Available from: http://www.who.int/hiv/pub/arv/arv-2016/en/
11. Brady M. Pre-exposure prophylaxis as HIV prevention in the UK. Ther Adv Chronic Dis. 2016;7(3):150–2.
12. Grulich A, Guy RJ, Amin J, Schmidt H-M, Selvey C, Holden J, et al. Rapid reduction in HIV diagnoses after targeted PrEP implementation in NSW, Australia. In: Of mice, monkeys, and men: prep from preclinical to population level impact [Internet]. Boston, Massachusetts; 2018[cited 2018 Oct 10]. Available from: http://www.croiconference.org/sessions/rapid-reduction-hiv-diagnoses-after-targeted-prep-implementation-nsw-australia
13. UNAIDS. Prevention Gap Report [Internet]. 2016 [cited 2018 Sep 29]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf
14. Rogers EM. Diffusion of Innovations, 4th ed. New York, NY: Simon and Schuster; 2010. 550 p.
15. Montgomery CM, Gafos M, Lees S, Morar NS, Mweemba O, Ssali A, et al. Re-framing microbicide acceptability: findings from the MDP301 trial. Cult Health Sex. 2010;12(6):649–62.
16. Eakle R, Bourne A, Jarrett C, Stadler J, Larson H. Motivations and barriers to uptake and use of female-initiated, biomedical HIV prevention products in sub-Saharan Africa: an adapted meta-ethnography. BMC Public Health. 2017;17:968.
17. Koechlin FM, Fonner VA, Dalglish SL, O'Reilly KR, Baggaley R, Grant RM, et al. Values and preferences on the use of oral pre-exposure prophylaxis (PrEP) for HIV prevention among multiple populations: a systematic review of the literature. AIDS Behav. 2017;21(5):1325–35.
18. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005;8(1):19–32.
19. Gough D. Qualitative and mixed methods in systematic reviews. Syst Rev [Internet]. 2015;4. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4681176/
20. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77–101.
21. Amico KR, Wallace M, Bekker L-G, Roux S, Atujuna M, Sebastian E, et al. Experiences with HPTN 067/ADAPT study-provided open-label PrEP among women in Cape Town: facilitators and barriers within a mutuality framework. AIDS Behav. 2017;21(5):1361–75.
22. 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. J Int AIDS Soc. 2014;17 3 Suppl 2:19157.
23. Karuga RN, Njenga SN, Mulwa R, Kilonzo N, Bahati P, O'Reilley K, et al. "How I Wish This Thing Was Initiated 100 Years Ago!" willingness to take daily oral pre-exposure prophylaxis among men who have sex with men in Kenya. PLoS One. 2016;11(4):e0151716.
24. Fowler N, Arkell P, Abouyannis M, James C, Roberts L. Attitudes of serodiscordant couples towards antiretroviral-based HIV prevention strategies in Kenya: a qualitative study. J Int AIDS Soc. 2014;17 4 Suppl 3:19563.
25. Hartmann M, McConnell M, Bekker LG, Celum C, Bennie T, Zuma J, et al. Motivated Reasoning and HIV Risk? views on relationships, trust, and risk from young women in cape town, South Africa, and implications for oral PrEP. AIDS Behav. 2018;22(11):3468–79.
26. Sithole B. HIV prevention needs for men who have sex with men in Swaziland. Afr J AIDS Res. 2017;16(4):315–20.
27. Restar AJ, Tocco JU, Mantell JE, Lafort Y, Gichangi P, Masvawure TB, et al. Perspectives on HIV pre- and post-exposure prophylaxes (PrEP and PEP) Among female and male sex workers in Mombasa, Kenya: implications for integrating biomedical prevention into sexual health services. AIDS Educ Prev. 2017;29(2):141–53.
28. Pintye J, Beima-Sofie KM, Makabong OP, Njoroge A, Trinidad SB, Heffron RA, et al. HIV-uninfected Kenyan adolescent and young women share perspectives on using preexposure prophylaxis during pregnancy. AIDS Patient Care STDS. 2018;32(12).
29. Namey E, Agot K, Ahmed K, Odhiambo J, Skhosana J, Guest G, et al. When and why women might suspend PrEP use according to perceived seasons of risk: implications for PrEP-specific risk-reduction counselling. Cult Health Sex. 2016;18(9):1081–91.
30. Bazzi AR, Yotebieng KA, Agot K, Rota G, Syvertsen JL. Perspectives on biomedical HIV prevention options among women who inject drugs in Kenya. AIDS Care. 2018;30(3):343–6.
31. Corneli A, Namey E, Ahmed K, Agot K, Skhosana J, Odhiambo J, et al. Motivations for reducing other HIV risk-reduction practices if taking pre-exposure prophylaxis: findings from a qualitative study among women in Kenya and South Africa. AIDS Patient Care STDS. 2015;29(9):503–9.
32. Corneli A, Perry B, Agot K, Ahmed K, Malamatsho F, Van Damme L. Facilitators of adherence to the study pill in the FEM-PrEP clinical trial. PLoS One. 2015;10(4):e0125458.
33. Magazi B, Stadler J, Delany-Moretlwe S, Montgomery E, Mathebula F, Hartmann M, et al. Influences on visit retention in clinical trials: insights from qualitative research during the VOICE trial in Johannesburg, South Africa. BMC Womens Health. 2014;14:88.

34. Eakle R, Bourne A, Mbogua J, Mutanha N, Rees H. Exploring acceptability of oral PrEP prior to implementation among female sex workers in South Africa. J Int AIDS Soc. 2018;21(2).
35. Van der Elst E, Mbogua J, Operario D, Mutua G, Kuo C, Mugo P, et al. High acceptability of HIV pre-exposure prophylaxis but challenges in adherence and use: qualitative insights from a phase I trial of intermittent and daily PrEP in at-risk populations in Kenya. AIDS Behav. 2013;17:2162–72.
36. Falcao J, Ahoua L, Zerbe A, di Mattei P, Baggaley R, Chivurre V, et al. Willingness to use short-term oral pre-exposure prophylaxis (PrEP) by migrant miners and female partners of migrant miners in Mozambique. Cult Health Sex. 2017;19(12):1389–403.
37. van der Straten A, Stadler J, Montgomery E, Hartmann M, Magazi B, Mathebula F, et al. Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa. PLoS One. 2014;9(2):e89118.
38. Stadler J, Delany-Moretlwe S, Palanee T, Rees H. Hidden harms: women's narratives of intimate partner violence in a microbicide trial, South Africa. Soc Sci Med. 2014;110:49–55.
39. Luecke EH, Cheng H, Woeber K, Nakyanzi T, Mudekunye-Mahaka IC, van der Straten A, et al. Stated product formulation preferences for HIV pre-exposure prophylaxis among women in the VOICE-D (MTN-003D) study. J Int AIDS Soc. 2016;19(1):20875.
40. Bazzi AR, Leech AA, Biancarelli DL, Sullivan M, Drainoni ML. Experiences using pre-exposure prophylaxis for safer conception among HIV serodiscordant heterosexual couples in the United States. AIDS Patient Care STDS. 2017;31(8):348–55.
41. Pintye J, Beima-Sofie KM, Kimemia G, Ngure K, Trinidad SB, Heffron RA, et al. "I Did Not Want to Give Birth to a Child Who has HIV": experiences using PrEP during pregnancy among HIV-uninfected Kenyan women in HIV-serodiscordant couples. J Acquir Immune Defic Syndr. 2017;76(3):259–65.
42. Mutua G, Sanders E, Mugo P, Anzala O, Haberer JE, Bangsberg D, et al. Safety and adherence to intermittent pre-exposure prophylaxis (PrEP) for HIV-1 in African men who have sex with men and female sex workers. PLoS One. 2012;7:e33103.
43. Kibengo FM, Ruzagira E, Katende D, Bwanika AN, Bahemuka U, Haberer JE, et al. Safety, adherence and acceptability of intermittent tenofovir/emtricitabine as HIV pre-exposure prophylaxis (PrEP) among HIV-uninfected Ugandan volunteers living in HIV-serodiscordant relationships: a randomized, clinical trial. PLoS One. 2013;8(9):e74314.
44. Guest GP, Shattuck DMS, Johnson LMA, Akumatey BM, Kekawo Clarke EEMD, Chen P-LP, et al. Changes in sexual risk behavior among participants in a PrEP HIV prevention trial. Sex Transm Dis. 2008;35:1002–8.
45. Kacanek D, Dennis A, Sahin-Hodoglugil NN, Montgomery ET, Morar N, Mtetwa S, et al. A qualitative study of obstacles to diaphragm and condom use in an HIV prevention trial in sub-Saharan Africa. AIDS Educ Prev Off Publ Int Soc AIDS Educ. 2012;24(1):54–67.
46. Sahin-Hodoglugil NN, Montgomery E, Kacanek D, Morar N, Mtetwa S, Nkala B, et al. User experiences and acceptability attributes of the diaphragm and lubricant gel in an HIV prevention trial in southern Africa. AIDS Care. 2011;23(8):1026–34.
47. Montgomery ET, Chidanyika A, Chipato T, van der Straten A. Sharing the trousers: gender roles and relationships in an HIV-prevention trial in Zimbabwe. Cult Health Sex. 2012;14(7):795–810.
48. Sahin-Hodoglugil NN, van der Straten A, Cheng H, Montgomery ET, Kacanek D, Mtetwa S, et al. Degrees of disclosure: a study of women's covert use of the diaphragm in an HIV prevention trial in sub-Saharan Africa. Soc Sci Med. 1982. 2009.;69(10):1547–55.
49. MacPhail C, Terris-Prestholt F, Kumaranayake L, Ngoako P, Watts C, Rees H. Managing men: women's dilemmas about overt and covert use of barrier methods for HIV prevention. Cult Health Sex. 2009;11(5):485–97.
50. Carroll JJ, Ngure K, Heffron R, Curran K, Mugo NR, Baeten JM. Gendered differences in the perceived risks and benefits of oral PrEP among HIV-serodiscordant couples in Kenya. AIDS Care. 2016;28(8):1000–6.
51. Roberts ST, Haberer J, Celum C, Mugo N, Ware NC, Cohen CR, et al. Intimate Partner Violence and Adherence to HIV Pre-exposure Prophylaxis (PrEP) in African Women in HIV Serodiscordant Relationships: a Prospective Cohort Study. J Acquir Immune Defic Syndr. 2016;73(3):313–22.
52. Quaife M, Eakle R, Cabrera M, Vickerman P, Tsepe M, Cianci F, et al. Preferences for ARV-based HIV prevention methods among men and women, adolescent girls and female sex workers in Gauteng Province, South Africa: a protocol for a discrete choice experiment. BMJ Open. 2016;6(6):e010682.
53. Braksmajer A, Senn TE, McMahon J. The potential of pre-exposure prophylaxis for women in violent relationships. AIDS Patient Care STDs. 2016;30(6):274–81.
54. Ngure K, Heffron R, Curran K, Vusha S, Ngutu M, Mugo N, et al. I knew I would be safer. Experiences of kenyan HIV serodiscordant couples soon after pre-exposure prophylaxis (PrEP) initiation. AIDS Patient Care STDS. 2016;30(2):78–83.
55. Ware NCP, Wyatt MA, Haberer JEMDMS, Baeten JMMDP, Kintu AMD, Psaros CP, et al. What's Love Got to Do With It? Explaining adherence to oral antiretroviral pre-exposure prophylaxis for HIV-serodiscordant couples. J Acquir Immune Defic Syndr. 2012;59:463–8.
56. Ware NC, Pisarski EE, Nakku-Joloba E, Wyatt MA, Muwonge TR, Turyameeba B, et al. Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-1 serodiscordant couples in East Africa: a qualitative evaluation study in Uganda. J Int AIDS Soc. 2018;21(5):e25113.
57. Mendelsohn JB, Calzavara L, Daftary A, Mitra S, Pidutti J, Allman D, et al. A scoping review and thematic analysis of social and behavioural research among HIV-serodiscordant couples in high-income settings. BMC Public Health. 2015;15(1):241.
58. Corneli A, Perry B, McKenna K, Agot K, Ahmed K, Taylor J, et al. Participants' explanations for nonadherence in the FEM-PrEP clinical trial. J Acquir Immune Defic Syndr. 2016;71(4):452–61.
59. Ware NC, Pisarski EE, Haberer JE, Wyatt MA, Tumwesigye E, Baeten JM, et al. Lay social resources for support of adherence to antiretroviral prophylaxis for HIV prevention among serodiscordant couples in sub-Saharan Africa: a qualitative study. AIDS Behav. 2015;19(5):811–20.
60. McGrory Elizabeth, Murungu Joseph, Aguolu Rose, Alagi Matthew, Alary Michel, Baeten Jared, et al. Delivering PrEP: lessons from early demonstration projects. Amsterdam, the Netherlands: AIDS Conference 2018; 2018.
61. Shaver J, Sullivan P, Siegler A, de Voux A, Phaswana-Mafuya N, Bekker LG, et al. Comparing provider and client preferences for hiv prevention services in South Africa among men who have sex with men. J Int Assoc Provid AIDS Care. 2017;16(6):562–71.
62. Agot K, Taylor D, Corneli AL, Wang M, Ambia J, Kashuba AD, et al. Accuracy of self-report and pill-count measures of adherence in the fem-PrEP clinical trial: implications for future HIV-prevention trials. AIDS Behav. 2015;19(5):743–51.
63. Corneli AL, McKenna K, Perry B, Ahmed K, Agot K, Malamatsho F, et al. The science of being a study participant: FEM-PrEP participants' explanations for overreporting adherence to the study pills and for the whereabouts of unused pills. J Acquir Immune Defic Syndr. 2015;68(5):578–84.
64. Guest G, Shattuck D, Johnson L, Akumatey B, Clarke EEK, Chen P-L, et al. Acceptability of PrEP for HIV prevention among women at high risk for HIV. J Womens Health. 2010;19(4):791–8.
65. Stahlman S, Sanchez TH, Sullivan PS, Ketende S, Lyons C, Charurat ME, et al. The prevalence of sexual behavior stigma affecting gay men and other men who have sex with men across sub-Saharan Africa and in the United States. JMIR Public Health Surveill [Internet]. 2016 [cited 2019 Mar 29];2(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4978863/
66. Eakle R, Gomez GB, Naicker N, Bothma R, Mbogua J, Escobar MAC, et al. HIV pre-exposure prophylaxis and early antiretroviral treatment among female sex workers in South Africa: results from a prospective observational demonstration project. PLoS Med. 2017;14(11):e1002444.
67. Baeten JM, Heffron R, Kidoguchi L, Mugo NR, Katabira E, Bukusi EA, et al. Integrated delivery of antiretroviral treatment and pre-exposure prophylaxis to HIV-1-serodiscordant couples: a prospective implementation study in Kenya and Uganda. PLoS Med. 2016;13(8):e1002099.
68. Guise A, Albers ER, Strathdee SA. 'PrEP is not ready for our community, and our community is not ready for PrEP': pre-exposure prophylaxis for HIV for people who inject drugs and limits to the HIV prevention response. Addiction. 2017;112(4):572–8.
69. Pettifor A, Nguyen NL, Celum C, Cowan FM, Go V, Hightow-Weidman L. Tailored combination prevention packages and PrEP for young key populations. J Int AIDS Soc [Internet]. 2015 [cited 2018 Sep 29]. 18 2 Suppl 1. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344537/

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REVIEW

The effectiveness of demand creation interventions for voluntary male medical circumcision for HIV prevention in sub-Saharan Africa: a mixed methods systematic review

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Abstract

Introduction: UNAIDS has recommended that in 14 countries across sub-Saharan Africa (SSA), 90% of men aged 10 to 29 years should be circumcised by 2021 to help reduce transmission of HIV. To achieve this target demand creation programmes have been widely implemented to increase demand for Voluntary Medical Male Circumcision (VMMC). This review explores the effectiveness of demand creation interventions and factors affecting programme implementation.

Methods: We completed a mixed methods systematic review searching Medline, Embase, Global health, psycINFO and CINAHL databases in August 2018 with no time restrictions. Demand creation interventions conducted in SSA were categorized and quantitative data about VMMC uptake was used to compare relative and absolute effectiveness of interventions. Qualitative data were summarized into themes relevant to the delivery and impact of programmes.

Results and discussion: Eighteen of the 904 titles were included in the review. Effective interventions were identified in each demand creation category: financial incentives, counselling or education, involvement of influencers and novel information delivery. Of the 11 randomized controlled trials (RCTs), the greatest absolute impact on VMMC prevalence was seen with a complex intervention including VMMC promotion training for religious leaders (compared to control: 23% (95% CI 22.8 to 23.8) absolute increase; odds ratio (OR) 3.2 (1.4 to 7.3)). Financial incentives generally produced the largest relative effects with men up to seven-times more likely to undergo VMMC in the intervention arm compared to control (adjusted OR 7.1 (95% CI 2.4 to 20.8), 7.1% (3.7 to 10.5) absolute increase). Qualitative findings suggest that interventions are more impactful when they are judged appropriate and acceptable by the target population; delivered by people with relevant personal experience; and addressing broader social and cultural influences through partnership with and education of community leaders.

Conclusions: A range of demand creation interventions can increase VMMC uptake. The most acceptable and effective interventions are financial incentives framed as fair compensation (relative effect) and programmes of education or counselling delivered by people who are influential in the community (absolute effect). Future research should include larger studies with longer follow-up and a consistent definition of VMMC uptake.

Keywords: HIV infections; Circumcision; Male; Systematic review; Programme evaluation; Africa South of the Sahara; Health Services Needs and Demand

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | INTRODUCTION

Despite global Human Immunodeficiency Virus (HIV) incidence peaking in 1997, prevalence continues to rise [1]. There are an estimated 36.9 million people currently infected, with 53% residing in sub-Saharan Africa (SSA) [1].

Voluntary medical male circumcision (VMMC) is 50% to 60% effective at preventing the acquisition of HIV infection in men [2-4]. UNAIDS had an original target to reach 80% population coverage in men aged 15 to 49 years, in order to avert an estimated 6 million infections and 3 million deaths by 2025 in priority countries [5]. This target has now been increased to 90% coverage in men aged 10 to 29 years [6]. By 2017, over 90% of the 20.8 million target number of VMMCs had been performed, averting an estimated 230,000 HIV infections [6]. Advances in technology and increased VMMC availability have contributed to recent increases in the uptake of the procedure, but uptake remains limited by poor demand in some target countries [7].

The HIV Prevention Cascade has been suggested as a framework that maps the steps required to prevent transmission [8-10]. It is broadly based around three domains: demand, supply and adherence, or more recently refined as motivation, access and use [11]. It is intended to help identify issues surrounding poor adoption of HIV prevention in different populations and for specific technologies. When applied to VMMC, the key elements of the cascade are demand, or motivation and access. Once VMMC is carried out there is no ongoing issue with adherence, although some cascades include a final step of efficacy [10].

Demand creation programmes have been implemented in many settings to encourage VMMC uptake [7,12]; however until recently the evidence for the effectiveness of these interventions has been limited. In 2016, an eleven-paper series assessed the effectiveness of seven different VMMC demand creation programmes in SSA. Sgaier *et al.* reviewed the impact evaluations from five randomized controlled trials (RCTs) and two quasi-experimental studies [13-22]. Three interventions, two offering financial incentives [19,20] and one novel football-based education sessions [16], reported significant impact, while qualitative components from others gave good insight into their implementational shortcomings [7]. Two further systematic reviews report the beneficial impact of financial incentives on VMMC uptake [23,24]. The meta-analysis of six financial interventions reported that men in the intervention arm were almost five times more likely to undergo the procedure compared to the control arm (combined odds ratio (OR) 4.78 (95% CI 4.17 to 5.48)) [23]. Another recent systematic review has summarized the overarching barriers and facilitators to VMMC uptake by men in SSA [25]. The authors identified important differences in the key factors acting at the community, service provider and individual/interpersonal level across priority settings.

To date, systematic reviews have focused on the quantitative impact of financial incentives. This review aims to assess the effectiveness of all VMMC demand creation interventions at increasing VMMC uptake and to synthesize the factors facilitating and impeding effective implementation from the perspective of the demand creation component of the HIV Prevention Cascade.

2 | METHODS

2.1 | Selection criteria

A mixed methods systematic review was conducted. The full inclusion criteria are presented in Appendix S1. Briefly, study populations must include males older than 10 years, matching the age used in a previous systematic review [12], and studies must have taken place in SSA. Study designs eligible for inclusion were RCTs, quasi-experimental, case-control, cohort, comparative and observational. Conference abstracts, letters or editorials were excluded, and no time or language restrictions were imposed.

2.2 | Search strategy

Searches were conducted in Medline, Embase, Global Health, psycINFO and CINAHL using common search strategies consisting of keywords and MeSH during March and April 2017 and updated in August 2018. The search strategy was developed with the assistance of a Medical Librarian (Appendix S2). Search terms were based upon those used in Cochrane reviews and were structured around five concepts; VMMC (e.g. "Circumcision," "VMMC"), HIV (e.g. "hiv," "human immunodeficiency virus"), Outcome (e.g. "uptake," "demand*"), Location (SSA) and study design (e.g. "randomi*," "comparative*") [26,27]. Database searching was supplemented with reference list searching, including of the previously published reviews, and monitoring of published literature (e.g. with Google Scholar).

2.3 | Data analysis

Full titles and abstracts of the search results were compiled in reference management software. Duplicates were removed, and the remaining results had pre-defined inclusion and exclusion criteria (Appendix S3) applied to them by two reviewers (BD & SE). Discrepancies in the articles deemed fit for inclusion were settled by consensus.

Studies that met the inclusion criteria were assessed for quality by one reviewer (SE), using the Mixed-Methods Appraisal Tool (MMAT), with queries being settled by consensus within the review team. An *a priori* cut off > 25% was chosen for studies to be eligible for inclusion. All included studies were reviewed.

One reviewer (SE) extracted and a second (BD – quantitative; HW – qualitative) checked data from the included articles using a template: setting, study design and methodology, sample (intervention population and sample sizes), blinding and randomization methods, intervention, control, duration, quantitative and qualitative outcomes (primary and secondary), limitations and funding. Demand creation interventions were reviewed and categorized into broad approaches. For the quantitative analysis, descriptive data including study setting, population and intervention duration were compared, individual intervention effect sizes (ORs) were analysed and any change in VMMC uptake was compared. We calculated the absolute impact of intervention on the outcome, *post* hoc, where the available data was included in the study. Qualitative studies were reviewed and three authors (SE, TR, HW) extracted details of aims, methods, outcome measures, key findings and conclusions. These were then summarized into themes relevant to the delivery and impact of demand creation intervention programmes.

3 | RESULTS

3.1 | Search results

A total of 1655 articles were returned (Figure 1). Reference list searching identified two further articles. Duplicates (n = 754) were removed and 903 papers underwent title and abstract screening. Full text was obtained for 29 titles; 18 were included in the final review.

3.2 | Study characteristics

The 18 papers included were published between 2014 and 2018 and presented data associated with 16 studies; five

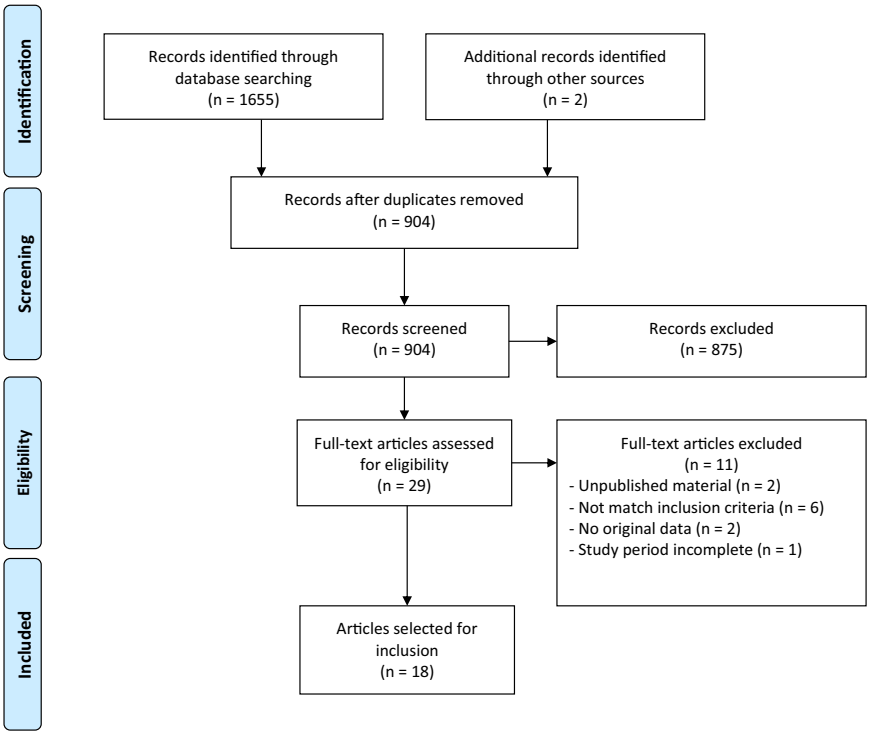

Figure 1. PRISMA flowchart.

cluster randomised control trials (CRCTs) [13,14,16,28-30], six RCTs [17,19,20,31-33], two prospective interventional cohorts [34,35], two quasi-experimental [18,36] and one "non-experimental" study (amended from an RCT due to delays with VMMC service implementation) [21] (Table 1). Studies took place across seven countries in SSA. Most of the studies (n = 14) had single country settings; South Africa (n = 3), Zambia (n = 3), Tanzania (n = 2), Kenya (n = 2), Uganda (n = 2), Zimbabwe (n = 1) and Malawi (n = 1), while 1 study took place in both South Africa and Uganda. The majority (n = 12) of the included papers presented only quantitative data (Table 2), three were only qualitative, obtained through in-depth interviews (IDIs) and focus group discussions (FGDs), and three presented both quantitative and qualitative results. The size of the study populations varied greatly across studies: quantitative study populations ranged from 522 to 145,028 participants and qualitative study populations ranged from 10 to 289.

3.3 | Quality assessment

No major limitations or conflicts of interest were found during data extraction. All eligible studies received at least 25% on MMAT and were included in the analysis (Appendix S4).

3.4 | Quantitative results

Interventions were categorized into four major types: (i) financial incentives, (ii) counselling or education for prospective candidates, (iii) education and involvement of influencers, and (iv) novel information delivery, although some included more than one of these approaches. Most (n = 13) studies [13,16-21,28,29,31-34] presented data on the number of circumcisions completed at the end of the study period, while the remaining two studies [30,35] reported the prevalence of circumcision in the cohort. Table 2 shows the key findings from each study with both relative and absolute effects (where reported in the paper or calculated from raw data).

3.4.1 | *Financial incentives*

Six of the studies in this review describe interventions with a financial incentive component not offered to the control or comparator groups [13,19,20,31,32,34]. Overall, financial incentives worth at least two-days wages – food vouchers (over $8.75) (n = 2) or conditional cash transfers (>$10) (n = 1) – were found to have a large significant effect on the likelihood of having a VMMC procedure (AOR 4.3 to 7.1) but a small absolute change in VMMC uptake compared to the control group (<7.5%) [19,20,31]. A $17 conditional-cash-transfer combined with motivational interviews was associated with a 25% increase in VMMC uptake in an observational cohort [34]. Lottery-based incentives (n = 2) did not demonstrate an impact on the number of VMMCs performed in the intervention compared to control groups [13,19].

Thirumurthy *et al.* conducted two RCTs to explore the effect of giving different valued food vouchers on VMMC uptake (Table 2) [19,31]. Vouchers were equivalent to transport costs plus one to three days wages. Vouchers worth US $15 (adjusted OR (AOR) 6.2 (2.6 to 15.0)) [31], $12.50 (7.1 (2.4 to 20.8)) [19] and $8.75 (4.3 (1.7 to 10.7)) significantly increased VMMC uptake [31]. The $15 compensation was not significantly more effective than $8.75 ($p = 0.21$) [31]. The authors also found that the interventions were effective at

Table 1. Summary of studies included in analysis.

Author (date)	Setting (VMMC prevalence)	Population	Study date (F/U months)	Sample size		Study design
				Quant	Qual	
Barnabus (2016)	Rural South Africa & Uganda	Uncircumcised HIV-negative men aged 16 to 49, with private text-messaging	Jun 2013 to Mar 2015 (9)	750	-	RCT
Bazant (2016)	Rural Tanzania (49% to 60%)	Uncircumcised men aged >20	Nov 2014 to Feb 2015 (3)	1186	72	Cluster randomized evaluation + FGD
Cook (2016)[a]	Urban Zambia	Sub-group: uncircumcised, HIV negative men aged >18 with female partner	Not presented	668	-	CRCT
DeCelles (2016)[b]	Urban Zimbabwe	Men aged 18 to 30 playing in football clubs and trial coaches	2012 to 2013	-	46	IDIs + FGD
Downs (2017)	Rural Tanzania (<20%)	Total male population	Jun 2014 to Dec 2015 (7)	145,028	-	CRCT + FDG
Evens (2016)[c]	Rural & Urban Kenya	Thirumurthy (2014) trial participants	Not presented	-	64	IDI
Kaufman (2016)[b]	Urban Zimbabwe (>20%)	Male students aged 14 to 20	Mar to Oct 2014 (4)	1148	-	CRCT
Leiby (2016)	Urban & peri-urban Zambia	Uncircumcised male subscribers to national SMS platform aged 15 to 30	May to Oct 2014 (6)	1652	-	RCT
Marshall (2017)	Peri-urban South Africa (57%)	Uncircumcised men	Aug to Nov 2015 (2)	226	-	Prospective cohort
Montague (2014)	Rural South Africa	HIV-negative male students aged 11 to 20 at 42 selected high schools	Mar 2011 to Feb 2013 (24)	11,088	-	Prospective cohort
Miiro (2017)	Peri-urban Uganda	Uncircumcised male students in Forms 2 and 3 (median age 16 to 17)	Oct to Nov 2015	-	10	IDI
Semeere (2016)	Urban Uganda (28%)	Pregnant women with an uncircumcised spouse	May 2014 to Jan 2015 (3)	601	117	Retrospective pre/post study +IDI
Thirumurthy (2014)[c]	Urban & Rural Kenya	Uncircumcised men aged 25 to 49	Jun 2013 to Feb 2014 (2)	1502	-	RCT
Thirumurthy (2016)	Urban & Rural Kenya (< 80%)	Uncircumcised men aged 21 to 39	Apr to Sept 2014 (3)	911	-	RCT
Thornton (2016)	Urban Malawi (~2%)	Uncircumcised men aged 18 to 30	2010 (3)	1649	-	RCT
Weiss (2015)[a]	Urban Zambia (12%)	Uncircumcised, HIV-negative men aged >18 with female partners (optional)	Feb 2012 to Oct 2014 (12)	800	-	CRCT
Wilson (2016)	Peri-urban South Africa (25.2%)	Men aged >18	Jun to Aug 2014 (2)	4000	-	RCT + FDG
Zanolini (2016)	Rural Zambia	Men aged ≥18	Jun 2014 to Feb 2015 (5)	N/A	-	Time series (amended RCT)

ART, anti-retroviral therapy; CRCT, Cluster randomized control trial; F/U, follow-up; FGD, focus group discussion; IDI, individual in-depth interviews; MTC, "Make the cut;" Quant, quantitative; Qual, qualitative; RCT, randomized control trial; VMMC, voluntary medical male circumcision.
[a]Contain data from same study; [b]both contain data from MTC+ study. DeCelles (2016) also contains data from separate MTC study; [c]contain data from same study.

increasing the likelihood of VMMC uptake in traditionally harder to reach groups, including married men (AOR 4.5 (2.3 to 9.1)) and men over 33 years (AOR 7.9 (2.7 to 22.7)) [31]. Wilson *et al.* conducted a RCT comparing a $10 conditional-cash-transfer advertised via postcards containing information about the benefit of VMMC [20]. The intervention group had a large relative increase in VMMC uptake compared to the control group (OR 5.30 (2.20 to 12.76)) but the absolute effect was not presented. The study was markedly underpowered (74 out of 4000 postcards returned compared to an estimated sample size of 2484).

Bazant *et al.* randomized pairs of facilities into providing VMMC alone or VMMC plus entrance into a lottery for a smart-phone [13]. There was a non-significant increase in the absolute number of VMMCs performed in both the intervention and control facilities compared to the number performed in the same facilities during the previous 12 months (47% (p = 0.150) and 8% (p = 0.850) respectively) [13]. The RCT by

Table 2. Quantitative study design and results.

Author	Intervention	Control/comparator	Outcome measure	Descriptive data	Absolute change in VMMC uptake (intervention minus control)	Relative change/ Effect size
Barnabus	Standard of care + randomized to mobile phone SMS reminders or home visits to promote service linkage	Counselling about VMMC, referral card to local circumcision facilities	VMMC uptake (three months)	Control: 62/224 (27%) SMS: 137/284 (48%) Counsellor: 106/226 (47%)	**20.6% (12.3 to 28.8)** **19.2% (10.5 to 28.0)**	**RR 1.7 (1.4 to 2.2)** **RR 1.7 (1.3 to 2.1)**
Bazant	Control + invite to weekly lottery (for smartphone worth $85.60) after VMMC	Mass media messages and peer-promotor conversations	Change in number of VMMCs compared to previous year	Control 8% ↑ (pre n = 257, post n = 278) Intervention 47% ↑ (pre n = 264, post n = 388)	39% ↑ (NS)	Not presented
Cook	Spear and shield: for men see Weiss (2015). Female partners received four separate weekly group education sessions + $6/visit	For men see Weiss (2015). Female partners: four video-based health education group sessions + $6/visit	Likelihood of VMMC uptake	Control: 69/328 (20.9%) Intervention:141/340 (41.4%)	**20.4% (13.6 to 27.3)**	**OR[a] 2.7 (1.9 to 3.7)**
Downs	Day of training for church leaders + follow up group or individual discussions every two weeks	Standard outreach	% of population attending for VMMC	Control: 25,484/86,492 (29.5%) Intervention: 30,889/58,536 (52.8%)	**23.3% (22.8 to 23.8)**	**OR 3.2 (1.4 to 7.3)**
Kaufman	"MTC+": football-based group education session (one hour) by trained facilitator + contact for further group meetings + transport to VMMC + non-monetary incentive worth $5	Usual care	% VMMC uptake in uncircumcised at baseline	Control: 17/371 (4.6%) Intervention: 37/304 (12.2%)	**7.6% (3.4 to 12.1)**	**OR 2.7 (1.2 to 5.9)**
Leiby	Conventional or tailored set of 21 SMS test messages about VMMC	Routine access to SMS service to engage counsellors on any topic	Self-reported VMMC uptake	Control: 57/771 (7.4%) Conventional: 66/770 (8.6%) Tailored: 67/771 (8.7%)	1.2% (−1.5 to 3.9) 1.3% (−1.4 to 4.0)	AOR[b] 1.2 (0.8 to 1.7) AOR[b] 1.2 (0.8 to 1.8)
Marshall	Three individual motivational interviews and $17 post-VMMC	Baseline circumcision prevalence	Circumcision prevalence	Baseline: 296/522 (56.7%, (52.4% to 60.9%)) Final:425/522 (81.4%. [77.9% to 84.6%)])	**24.7% (19.3 to 30.1) $p < 0.001$**	

Ensor S et al. *Journal of the International AIDS Society* 2019, **22**(S4):e25299
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25299/full | https://doi.org/10.1002/jia2.25299

Table 2. (*Continued*)

Author	Intervention	Control/comparator	Outcome measure	Descriptive data	Absolute change in VMMC uptake (intervention minus control)	Relative change/ Effect size
Montague	Community engagement + in-school VMMC awareness sessions + peer recruitment + travel to clinic	70% prevalence target	# of VMMCs performed	5165/11,088 (47% prevalence)	No baseline data presented	
Semeere	Education on VMMC + communication skills training for women + transport voucher ($8.50) redeemed after VMMC	Standard care + $8.50 transport voucher for men undergoing VMMC	% of women whose spouse had VMMC by one month	Control: 4/296 (1.4%) Intervention: 7/305 (2.3%)	0.9% (−1.2 to 3.1)	OR 1.5 (0.4 to 5.2)
Thirumurthy (2014)	Food vouchers for $2.50, $8.75 or $15 after VMMC	Information about nine clinics providing free VMMC	% VMMC uptake	Control: 6/370 (1.6%) $2.50: 7/376 (1.9%) $8.75: 25/381 (6.6%) $15: 34/377 (9.0%)	0.3% (−1.6 to 2.1) **4.9% (2.1 to 7.7)** **7.4% (4.2 to 10.6)**	AOR[c] 1.1 (0.4 to 3.3) **AOR[c] 4.3 (1.7 to 10.7)** **AOR[c] 6.2 (2.6 to 15.0)**
Thirumurthy (2016)	Food voucher for $12.50 or entry into lottery (expected values $12.50) after VMMC	Information about free VMMC clinics + $0.6 voucher after VMMC	% VMMC uptake	Control: 4/299 (1.3%) Voucher: 26/308 (8.4%) Lottery: 10/302 (3.3%)	**7.1% (3.7 to 10.5)** 2.0% (−0.4 to 4.4)	**AOR[c] 7.1 (2.4 to 20.8)** AOR[c] 2.5 (0.8 to 8.1)
Thornton	Voucher subsidized VMMC (cost $0-$6)	Free VMMC	% VMMC uptake	>$0: 30/1257 (2.39%) $0: 12/392 (3.0%)	0.7% (−1.2 to 2.6)	OR[a] 1.3 (0.7 to 2.6)
Weiss	"Spear and shield":4 weekly 90- minute group education sessions + $6 per assessment	4 weekly 90-minute video-based group education sessions on endemic diseases + $6	Likelihood of VMMC uptake	Control: 96/400 (24%) Intervention: 161/400 (40%)	**16.3% (9.9 to 22.6)**	**AOR[d] 2.5 (1.2 to 4.9)**
Wilson	Control postcards + offer of $10 to attend for counselling, challenge message or novel VMMC information	Postcards with routine VMMC information + clinic details	# of VMMCs	Overall 74/4000 men returned postcards $10:?/1000 Challenge:?/1000 Information:?/1000		**OR 5.3 (2.2 to 12.8)** **OR 2.7 (1.1 to 6.9)** OR 1.7 (0.6 to 4.6)
Zanolini (2016)	Clients undergoing VMMC asked to refer ≤5 uncircumcised men, paid $2/referral	Comparison with 2012 health data rends trends from non-intervention facilities	Mean monthly difference in # of VMMCs	Control: not presented Active Intervention: 848 VMMCs, 2402 (699 men given vouchers; 348 used vouchers)	Mean monthly difference 7.6 VMMCs (−20.4 to 40.8)	Adjusted mean monthly difference 10.2 (−18.3 to 33.9)

Statistically significant effect sizes are shown in bold.AOR, Adjusted odds ratio; CRCT, cluster randomized control trial; M, men; MTC, "Make the Cut;" F/U, follow-up; NS, Non-significant; OR, Odds ratio; RCT, randomized control trial; RR, Relative risk; VMMC, Voluntary medical male circumcision; W, women.
[a]OR and CIs calculated by SE/BD; [b]adjusted for intention level, adulthood, district, circumcised family members, high-uptake tribe, number of surveys to which individual responded, and verifiability. effect size calculated after loss to follow up; [c]adjusted for age, educational attainment, marital status and wealth; [d]adjusted for age, education level and baseline stage of readiness for voluntary medical male circumcision.

Thirumurthy *et al*. also included a lottery incentive with an expected value of $12.50 (equivalent to the food voucher). Participants in the lottery arm were not significantly more likely to have a VMMC compared to the control group (AOR 2.5 (0.8 to 8.1)) [19]. Thornton *et al*. studied the effect of offering subsidized circumcision (at different rates) on VMMC uptake [32]. Discounting the cost to $0 did not lead to a significant increase in VMMC uptake compared to the men paying between $0.55 and $6.75 for the procedure (OR 1.3 (0.7 to 2.6)). There was no absolute difference in uptake between the $0 group and the others (3.06% (n = 12/392) compared to 2.39% (n = 30/1257), $p = 0.4597$). This study looked at a secondary outcome of VMMC uptake by voucher value and *ex ante* sexual risk which suggests that men with the highest sexual risk behaviours only underwent VMMC when it was offered for free.

The study by Marshall *et al*. describes the change in VMMC prevalence in the study population offered a nine-week programme of individual motivational interviews plus $17 post-VMMC [34]. The prospective cohort did not have a control arm and both the counselling and cash transfer were given to all men who underwent VMMC. 522 men were invited to participate in the cohort, of whom 226 were uncircumcised and 148 (69.8% (63.4 to 75.7)) presented for VMMC within nine weeks. Nine procedures were delayed for medical reasons and the authors estimate that during follow-up circumcision prevalence rose significantly from 56.7% (52.4 to 60.9, 296/522) to 81.4% (77.9 to 84.6, 425/522) ($p < 0.001$), a 24.7% absolute increase [34].

3.4.2 | *Counselling or education*

Four included studies considered the impact of group-education or awareness raising interventions on VMMC uptake [16,28,29,35]. A further two studied the effect of individual counselling on participation [33,34]. Overall, group education sessions increased the likelihood of VMMC around 2.5-fold with a 8% to 20% absolute increase in uptake compared to control groups [16,28,29]. It is estimated that 13 uncircumcised men need to participate with group education for one to undergo VMMC [16]. Individual-level counselling was shown to increase the uptake of VMMC by men who attended a circumcision facility by almost 70% compared to the control group (absolute increase 19%) [33].

The study by Marshall described in the preceding section is not considered further here as it is not possible to disentangle the effect of the motivational interviewing from the conditional cash transfer [34]. Barnabus *et al*. undertook an RCT comparing the effectiveness of two interventions: SMS reminders and lay-counsellor follow-up, on VMMC uptake in men who participated with HIV testing and attended a circumcision facility [33]. The men who received lay-counsellor follow-up after their visit to the circumcision facility were almost 70% more likely to undergo VMMC than the men randomized to receive promotion materials (RR 1.67 (1.29 to 2.14), absolute increase 19%) [33].

Weiss *et al*. undertook a CRCT of the "Spear and Shield" intervention, which compared the uptake of VMMC in men participating in specific HIV-focused group education sessions to men participating with control education sessions about endemic diseases [28]. Participants in both arms were given $6 reimbursement per assessment. When compared to the control group, men in the intervention arm were 2.5 times more likely to undergo VMMC (AOR 2.45 (1.24 to 4.90)), an absolute increase of 16.3% (9.9 to 22.6) [28]. Men were encouraged to enrol in the study with their female partners. For those who did, Cook *et al*. conducted a sub-group analysis (n = 668/800) which identified a similar absolute increase in uptake of VMMC in the intervention compared to control group (20.4% (13.6 to 27.3)) [29]. The authors estimated that an additional 5.9% of men received VMMC due to positive changes in their partner's attitudes.

Kaufman *et al*. undertook a CRCT of the "MTC+ (Make-The-Cut-Plus)" football-based group education intervention, for male students aged 14 to 20 years [16]. The intervention was delivered by trained "coaches" who followed-up and supported participants interested in becoming circumcised. Of adolescents who were uncircumcised at baseline, those in the intervention schools were significantly more likely to undergo VMMC compared to those in the control schools (OR 2.65 (1.19 to 5.86)) [16]. Montague *et al*. describes a further school-based intervention that used a phased approach including community engagement, VMMC awareness sessions and peer-recruitment [35]. Peer-recruiters were early adopters of VMMC and were given vouchers worth $3 for cell-phones plus other small prizes (t-shirts, watches etc.). The intervention included a competition element with prizes for recruiters and schools. Of the 11,088 male students at the 47 selected schools, 47% (n = 5165) underwent a circumcision during the two-year intervention. No data is presented on baseline circumcision rates and there is no comparator group.

3.4.3 | *Influencers: education and involvement*

Four studies trained "influencers" (religious leaders (n = 1), female partners (n = 1), circumcised peers (n = 2)) to promote VMMC within their partnerships, community or social circle [18,21,30,35]. Training Church leaders was associated with a 23% increase in the proportion of the population attending for VMMC compared to control settings and was one of the few studies to show impact at scale [30]. In contrast, training female partners and peers has not been shown to increase VMMC uptake.

The study by Montague *et al*. has been considered in the earlier section as the peer-recruiter role formed part of a complex intervention with an educational component [35]. Downs *et al*. conducted a CRCT which trained church leaders to educate and promote VMMC to their congregations (one-day course) [30]. Eight pairs of villages were randomized with an estimated population of 145,028 exposed to Church leaders' teachings. In the eight intervention villages 1194 leaders received training. The proportion of the male population who had presented for VMMC by the end of the study was 23.3% (22.8 to 23.8) higher in intervention villages compared to the paired control villages (52.8% compared to 29.5%; OR 3.2 (1.4-7.3)) The authors estimated that this led to an additional 13,000 circumcisions being performed in the intervention villages [30].

Peer-recruiters were the sole intervention in the study by Zanolini *et al*. The authors offered men who had recently undergone circumcision small monetary incentives ($2 per referee) to promote it to their peers [21]. The majority of eligible men

(82%) enrolled in the intervention but the mean number of circumcisions performed per month did not significantly increase compared to the comparator non-intervention facilities (change in mean monthly VMMCs 7.6 (−20.37 to 40.83)) [21].

Semeere *et al*. undertook a pre/post comparison of VMMC rates in the partners of pregnant women to evaluate the impact of educating pregnant women about VMMC [18]. Absolute VMMC uptake was very low in both periods (intervention 7/305 and control 4/296) compared to *a priori* estimates and no effect on VMMC uptake in the month following the intervention was seen (OR 1.5 (0.4 to 5.2)).

3.4.4 | *Novel information delivery*

Three studies included in this review compared the impact of SMS text message packages (n = 2) or innovative postcard messages (n = 1) on the uptake of VMMC [17,20,33]. Delivering messages that were challenging or encouraging were shown to significantly increase VMMC uptake over the control groups.

The RCT by Barnabus *et al*. described above also included an SMS "encouragement" arm where men who attended a circumcision facility were sent a message ("this could be the best decision you make – act now!") three weeks after their HIV test and a phone-call at four weeks [33]. The men in the SMS arm were 70% more likely to undergo VMMC than those randomized to receive promotion materials (RR 1.72 (1.36 to 2.17), absolute increase 20%) [33].

Leiby *et al*. undertook an RCT comparing the impact of packages of informative and motivational text messages, either tailored or untailored to the individual's self-reported stage of behavioural change [17]. Text message packages were found to increase the proportion contacting a VMMC counsellor for more information compared to the control (53%, n = 817/1541 compared to 19%, n = 143/771) however neither conventional (AOR 1.17 (0.80 to 1.72)) nor tailored (AOR 1.24 (0.84 to 1.81)) packages demonstrated a significant effect on self-reported VMMC uptake [17].

Wilson *et al*. compared the impact of postcards with a message "challenging" men to become circumcised ("Are you tough enough?") or a novel VMMC health benefit to control postcards containing basic VMMC and clinic information [20]. The "challenge" postcards were associated with a significant increase in VMMC uptake at two months (OR 2.69 (1.05 to 6.91)) compared to control, but those displaying information only did not demonstrate a significant difference from the control group (OR 1.67 (0.61 to 4.62)) [20].

3.5 | Qualitative results

The qualitative studies explored a range of outcomes including preferences, acceptability, attitudes and perceptions of programme components and delivery. Participants in interviews and focus groups included men who were and were not circumcised, their female partners, and key informants involved in implementation. The details of each study including key findings are summarized in Table 3 [13-15,18,30,36].

Bazant *et al*. and Evens *et al*. used focus group discussions and interviews to explore preferences for and perceptions of incentives [13,15]. While the lottery approach was reported to have promoted interest, "a buzz," in the area, it was regarded by some as inappropriate (a smart phone), impractical (for people with no electricity) and the high value generated some suspicion [13]. The other study suggested that the compensation removed a key barrier to uptake for some men but was of insufficient value for others [15].

Two studies used interviews and focus groups to explore perceptions of MTC and MTC+, football-based interventions, one in relation to a trial and the other as part of a feasibility study in a new setting [14,36]. Younger participants were particularly appreciative of the coaches' personal stories which helped allay fears, and their personal support was valued in both settings. In the feasibility study in Uganda it was felt that more attention should be paid to families and peers as well as coaches [36].

The role of influencers was further explored in two studies, one using pregnant women to target partners, the other aimed at religious leaders [18,30]. Both aimed to address social and family norms which can be barriers to uptake of VMMC. The pregnant women reported discomfort in delivering the message to partners, although together with the provision of travel vouchers it did seem to prompt some men who were already thinking about circumcision. In contrast the religious leaders seemed comfortable talking to their communities and recognized that their strong influence could be valuable.

Across the studies we identified the following emerging themes relevant to the success of demand creation interventions. First, interventions are better where they are judged appropriate and acceptable by the target population. Some responses to the smartphone lottery and of older men to MTC showed how a misjudged intervention may be counterproductive and raise suspicions and even undermine trust [13]. Second, more personal interventions delivered by people with relevant experience can resonate well, as with the football interventions [14,36]. Third, addressing broader social and cultural influences through partnership with and education of community leaders can have a wide impact [30].

4 | DISCUSSION

4.1 | Main findings

4.1.1 | *Quantitative*

The uptake or prevalence of VMMC increased with interventions from all four demand creation categories: financial, counselling, influencers and novel information delivery. The greatest population-level impact (23% absolute increase in VMMC prevalence; 13,000 excess procedures; threefold relative increase in prevalence) was seen with a CRCT of a complex intervention that included a one-day VMMC promotion training session for Church leaders [30]. The largest relative increases in VMMC uptake (>4-fold, absolute effect <8% increase) were seen with fixed financial incentives [19,20,31].

4.1.2 | *Qualitative*

We identified insights into how demand creation interventions based on addressing barriers can be more or less effective, for example financial incentives appeared more acceptable framed as fair compensation than as a lottery, but clearly have an important role particularly in "nudging" men who were

Table 3. Qualitative study designs and results.

Author	Study design	Intervention	Main aim and outcomes for qualitative study	Key findings from qualitative study	Authors' conclusion	Strengths and limitations
Bazant (2016)	Focus groups with sub-set of clients who had undergone circumcision and peer educators as part of randomized evaluation of lottery	Entry into weekly lottery for smartphone worth $85.60 conditional on becoming circumcised	Preferences for VMMC incentives	1. The lottery created interest in VMMC – "a buzz" 2. Suspicion about the phone incentive which was too high in value 3. Preference for an incentive for all (rather than lottery) 4. Mixed views, but preference for money as reimbursement (rather than phone)	The lottery might work at some stages of a programme, e.g. late adopters, but not when need wide uptake	Little detail on method to assess quality, e.g. what was asked in focus groups. No data from those who did not seek VMMC
Evens (2016)	In depth interviews with circumcised and uncircumcised men and female partners as part of RCT of financial compensation. Inductive thematic analysis	Food vouchers of varying amounts conditional on becoming circumcised	Perceptions of how compensation provision influenced decisions about circumcision	1. Loss of income is a significant barrier to circumcision and the financial compensation programme helped motivate men in three ways: (a) removed the financial barrier, without the money they would not have been circumcised; (b) the money prompted it in men who had already decided to be circumcise, i.e. it was a "nudge;" (c) it was the information that prompted them, the money was a bonus only 2. Those who did not get circumcised cited (a) the compensation was insufficient; (b) a primary reason other than finance (e.g. not discussed it with female partner, fear of pain); (c) they felt the decision should not be linked to compensation 3. Female partners were supportive of decisions, but thought the compensation was insufficient 4. There was no evidence that economic compensation was perceived as being coercive	Financial compensation can be an important tool in increasing circumcision uptake, but the amount needs to be carefully judged, and other barriers, notably fear of pain, also need to be addressed	Relatively small sample size but included both circumcised and uncircumcised men and their female partners. Methods are clearly described
DeCelles (2016)	A process evaluation with in depth	Soccer-themed educational	Perceptions of programme	1. Coaches' individual stories were helpful in sharing knowledge about	The programme was acceptable, the	

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Table 3. (*Continued*)

Author	Study design	Intervention	Main aim and outcomes for qualitative study	Key findings from qualitative study	Authors' conclusion	Strengths and limitations
	interviews and focus groups with soccer coaches, circumcised and uncircumcised men linked to RCT	session and follow-up to promote circumcision	impact, intervention components and delivery; understanding of intervention content; factors related to uptake	circumcision and in motivating boys and men, with the coach-participant relationship being particularly valued and trusted 2. Older men were less likely to be convinced that it was relevant to them 3. Follow-up texts and coaches accompanying participants to the clinic were highly valued by some	quality of the coach-participant relationship was highly valued, particularly discussion of personal experience	Small sample size particularly in MTC
Miiro (2017)	Mixed methods: cross sectional survey and in-depth interviews with male school students associated with feasibility study in Uganda	Soccer-themed educational session and follow-up to promote circumcision	Acceptability, feasibility and perceptions of implementation of a soccer-based intervention among schoolboys	1. General favourable towards circumcision and good acceptability in principle 2. Feasibility study showed need for further engagement with parents and school to improve uptake 3. Interviews showed importance of family and peer support in preparing participants for circumcision 4. Sessions with the coaches were found to prompt decision in those who were already receptive, helped by their personal experience of the procedure and individual follow-up after 5. The main reasons for getting circumcised were hygiene and reduced HIV risk, while main reasons against were fear of pain, loss of contact with the coach or family opposition	The intervention can be adapted and effective but needs to attend to the key role of family and peer support, and to address practical issues of timing and delivery through schools	A small feasibility study, but able to identify some key factors that could help improve implementation of MTC in a new setting
Semeere (2016)	Nested interview study as part of quasi-experimental behaviour change intervention study. Interviews with	Education for pregnant women to encourage them to refer their male partners for circumcision	Evaluation of the causal chain of the intervention including women's perceptions of benefits of circumcisions, and how the	1. After the intervention, women had a high level of discomfort about talking to their partners about circumcision but they mostly still delivered the messages 2. Men who did get circumcised after the intervention reported already contemplating it, and the conversation	Interventions using female partners are feasible but further work is needed to develop this	A pilot study with short follow-up (three months), but was able to seek views of women, men and key informants

Table 3. (*Continued*)

Author	Study design	Intervention	Main aim and outcomes for qualitative study	Key findings from qualitative study	Authors' conclusion	Strengths and limitations
	women, men and key informants.		information may have affected men's decisions	with their partner plus the transport voucher acted as a catalyst 3. For the men who did not get circumcised, they and their partners cited well established barriers including lost wages, pain and religious/cultural reasons		
Downs (2017)	Focus groups with church leaders, nested in a community cluster randomized trial	Education of religious leaders who were then left to decide how to address circumcision in their community	Attitudes of religious leaders to male circumcision	1. There was considerable misinformation about and suspicion of circumcision among church leaders, and they would welcome more education (control villages) 2. The intervention empowered church leaders and they reported high levels of acceptance among their communities (intervention villages) 3. Church leaders recognized their strong influence felt they could be effective in promoting circumcision (all villages)	Working through religious leaders is an innovative model to promote healthy behaviour, addressing structural and cultural factors in a locally acceptable way	The large trial demonstrated impact. Focus groups with leaders but no qualitative data from participants

already motivated or sensitized. Provision of information and support to overcome barriers related to knowledge of risks and benefits appeared acceptable when delivered by someone with direct personal experience or who was trusted and influential to the individual or group.

Taking both quantitative and qualitative evidence together, we consider that this study adds further insight into what works, how it works and why programmes need to be appropriate and acceptable in the particular setting and phase of the programme. This resonates with the growing interest in human-based design approaches which adapt effective interventions to both the social context and individual preference.

4.2 | Strengths and limitations

The main strength of this review is the comprehensive search strategy and broad inclusion criteria for qualitative and quantitative studies. This review extends the work of Tamuzi *et al.* as demand creation interventions of all types were assessed allowing comparisons between and within intervention types [23]. The mixed methods approach builds on the work by Carrasco *et al.* and enhances understanding of contextual factors important to the interventions which should prove useful for policy makers [24].

The main limitation is that the reviewed studies were markedly heterogeneous. Data from seven of the fourteen priority SSA countries were included, and some interventions took place in rural and/or urban settings. Where the information was presented, there were large differences in baseline circumcision rates. The included studies used a range of study designs, measured different VMMC outcomes, reported varying effect measures and it was not possible to calculate the absolute impact of intervention in all studies.

The strength of the evidence from the included studies is variable; some used historic controls making it impossible to separate the impact of the interventions from secular changes; most had much shorter follow-up than the anticipated two-years needed for men to move from awareness to completing the procedure [37]; a number of studies were underpowered. With reference to the HIV Prevention Cascade, service capacity and other supply factors were outside the scope of this review but may have been limiting factors during some studies potentially hampering the impact of the intervention. In addition, intervention effectiveness was mostly viewed in isolation within the included studies, which may have neglected potential synergism within wider demand creation programmes.

Finally, no comprehensive search of the grey literature was conducted, and conference abstracts were excluded to allow quality assessment of the included studies which may have excluded recent studies in this rapidly evolving field.

4.3 | Interpretation of results

This review adds to the growing body of evidence of the effectiveness of financial compensation at increasing VMMC uptake [23,24]. We found that higher compensation was associated with larger effect size; however, the observed absolute difference in uptake was small [31]. It is important that the value of financial incentives in future programmes is optimized to maximize cost-effectiveness. Carrasco *et al.* argue that it may be most cost-effective to introduce financial incentives in settings with an already high prevalence of VMMC to focus on men who would not have "accessed the services otherwise" [24].

Although none of the included studies report major concerns with financial incentives, coercive potential should be monitored as qualitative data suggest this has the potential to impede programme effectiveness [13,15]. The type of compensation should be considered; food or transport vouchers may increase the amount that can be given without coercion fears or social harms [31]; however, cash may have a higher perceived value and be more cost-effective [13].

Individual counselling is effective at increasing VMMC uptake when offered to men who had already taken the step of presenting to a VMMC facility [33]. Group education or awareness raising interventions delivered in the community are also effective [16,28]. Having time to process information between discussions allows for a natural decision-making process; reviewing topics can reinforce benefits and alleviate new concerns [28]. The design of counselling/education should also be considered in relation to the specific audience; group sessions may be more appropriate for younger men, who place greater value in peer acceptance and support particularly when delivered by people who had lived experience of VMMC [16,25].

Theories have suggested that role models, families and peers play a part in changing an individual's behaviour [38]. This review found that religious leaders could play a key role in disseminating information and appear to address the challenge of norms and social acceptability [30]. Carrasco *et al.* found that a key barrier to men undergoing VMMC was a negative perception that it is "practiced by other or foreign cultures and religions" [25]. The potential exists to work with other similarly influential community figures. A human-centred design approach for new programmes would encourage open dialogue at the community level to identify appropriate influencers and their training needs [39].

VMMC peer-referral schemes were not shown to increase VMMC uptake in this review. One key finding was that men did not want to refer their friends due to a reluctance to discuss potentially sensitive topics [21]. We argue that further research into this intervention is warranted, using a human-centred design approach, because we did not identify an appropriately powered RCT [22].

Studies across SSA, outside the scope of this review, have found that women can have a significant influence on decisions to become circumcised [25,40,41]. The influence a woman has over the decision to undergo VMMC varies across culture, religion and marital status [40]. Two studies in this review included women in the intervention [18,29]. Educating pregnant women about VMMC was unsuccessful at increasing demand; however, group education delivered to both partners was effective. Technology can increase the reach and reduce costs of demand creation programmes [17]. This review found that the content of an SMS message is important as "encouraging" messages had a greater impact compared to basic health promotion [33].

HIV prevention cascade and programme design

This review identified the need to undertake studies that are larger (to address the issues of underpowered research); have

longer follow-up (to allow for behavioural change); and that have consistent reporting of the impact of demand creation interventions. There is a need for consistency in outcome definitions, absolute and relative effects to allow more robust comparisons. Several of the studies included in this review did not report the observed absolute change in VMMC uptake and it is this absolute difference that is needed to populate the HIV Prevention Cascade to allow analysis of bottlenecks and inform the design of prevention programmes.

The impact of any lead-time needed for behavioural change means that despite adequate supply of VMMC services, it will take time to see an impact on VMMC targets. Effective demand creation should disrupt this cycle, shortening the period considerably by increasing exposure to accurate information, addressing concerns and offering incentives.

The studies included in this review predominantly assess the effectiveness of single interventions. However, it is plausible that synergy (or redundancy) may occur when interventions are combined into demand creation programmes. Furthermore, the synergistic potential of VMMC demand creation strategies may extend to other areas of HIV prevention and healthcare. For example, Weiss *et al*. found that post-intervention condom use increased after VMMC group education sessions, highlighting a potential for integration with sexual-risk reduction services [28]. We suggest that programmatic evaluations should draw on the HIV Prevention Cascade framework and consider applying a complex systems approach in recognition of the challenge of determining the contribution of individual interventions within the wider real-world sphere of HIV prevention [8,42].

5 | CONCLUSIONS

A range of demand creation interventions can increase VMMC uptake, the most acceptable and effective interventions appear to be financial incentives framed as fair compensation and programmes of education or counselling delivered by people who are influential in the community or have personal experience of VMMC. In this context, individual interventions are often components of larger programmes which need to be appropriate and acceptable in the setting and phase of the programme. This resonates with the growing interest in human based design approaches which adapt effective interventions to both the social context and individual preference.

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COMPETING INTERESTS

The authors declare no competing interests.

AUTHORS' CONTRIBUTIONS

H.W. conceived the study question and design. S.E. designed the systematic search and completed the initial search, data extraction and first draft as a student project under the supervision of H.W., T.R. and B.D. T.R. contributed to the qualitative analysis. B.D. undertook data extraction and quantitative analysis and co-authored the revised drafts. H.W. undertook data extraction and qualitative analysis and co-authored the revised draft. All authors edited and approved the final draft.

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REFERENCES

1. Global UNAIDS. AIDS update 2018: miles to go. ; 2018.
2. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. PLoS Med. 2005;2(11):e298.
3. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369(9562):643–56.
4. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369(9562):657–66.
5. Njeuhmeli E, Forsythe S, Reed J, Opuni M, Bollinger L, Heard N, et al. Voluntary medical male circumcision: modeling the impact and cost of expanding male circumcision for HIV prevention in eastern and southern Africa. PLoS Med. 2011;8(11):e1001132.
6. World Health Organisation. WHO progress brief. Voluntary medical male circumcision for HIV prevention. 2018.
7. Sgaier SK, Reed JB, Sundaram M, Brown A, Djimeu E, Ridzon R. Interventions to drive uptake of voluntary medical male circumcision-A collection of impact evaluation evidence. J Acquir Immune Defic Syndr. 2016;72 Suppl 4: S257–61.
8. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
9. Godfrey-Faussett P. The HIV prevention cascade: more smoke than thunder? Lancet HIV. 2016;3(7):e286–8.
10. Garnett GP, Hallett TB, Takaruza A, Hargreaves J, Rhead R, Warren M, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. Lancet HIV. 2016;3(7):e297–306.
11. Schaefer R, Gregson S, Fearon E, Hensen B, Hallett T, Hargreaves J. HIV prevention cascades: a unifying framework to replicate the successes of treatment cascades. Lancet HIV. 2019;6(1):60–6.
12. Kaufman MR, Smelyanskaya M, Van Lith LM, Mallalieu EC, Waxman A, Hatzhold K, et al. Adolescent sexual and reproductive health services and implications for the provision of voluntary medical male circumcision: results of a systematic literature review. PLoS ONE. 2016;11(3):e0149892.
13. Bazant E, Mahler H, Machaku M, Lemwayi R, Kulindwa Y, Gisenge Lija J, et al. A randomized evaluation of a demand creation lottery for voluntary medical male circumcision among adults in Tanzania. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S280–7.
14. DeCelles J, Hershow RB, Kaufman ZA, Gannett KR, Kombandeya T, Chaibva C, et al. Process evaluation of a sport-based voluntary medical male circumcision demand-creation intervention in Bulawayo, Zimbabwe. J Acquir Immune Defic Syndr. 2016;72:S304–8.
15. Evens E, Lanham M, Murray K, Rao S, Agot K, Omanga E, et al. Use of economic compensation to increase demand for voluntary medical male circumcision in Kenya: qualitative interviews with male participants in a randomized controlled trial and their partners. J Acquir Immune Defic Syndr. 2016;72: S316–20.
16. Kaufman ZA, DeCelles J, Bhauti K, Hershow RB, Weiss HA, Chaibva C, et al. A sport-based intervention to increase uptake of voluntary medical male circumcision among adolescent male students: results from the MCUTS 2 cluster-randomized trial in Bulawayo, Zimbabwe. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S292–8.
17. Leiby K, Connor A, Tsague L, Sapele C, Kaonga A, Kakaire J, et al. The impact of SMS-based interventions on VMMC uptake in Lusaka province, Zambia: a randomized controlled trial. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S264–72.

18. Semeere AS, Castelnuovo B, Bbaale DS, Kiragga AN, Kigozi J, Muganzi AM, et al. Innovative demand creation for voluntary medical male circumcision targeting a high impact male population: a pilot study engaging pregnant women at antenatal clinics in Kampala, Uganda. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S273–9.
19. Thirumurthy H, Masters SH, Rao S, Murray K, Prasad R, Zivin JG, et al. The effects of providing fixed compensation and lottery-based rewards on uptake of medical male circumcision in Kenya: a randomized trial. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S299–305.
20. Wilson N, Frade S, Rech D, Friedman W. Advertising for demand creation for voluntary medical male circumcision. J Acquir Immune Defic Syndr. 2016;72: S293–6.
21. Zanolini A, Bolton C, Lyabola L, Phiri G, Samona A, Kaonga A, et al. Feasibility and effectiveness of a peer referral incentive intervention to promote male circumcision uptake in Zambia. J Acquir Immune Defic Syndr. 2016;72 Suppl 4: S257–63.
22. Djimeu EW, Brown AN. Strength of evidence on demand creation for voluntary medical male circumcision from 7 impact evaluations in Southern and Eastern Africa. J Acquir Immune Defic Syndr. 2016;72 Suppl 4:S321–5.
23. Tamuzi J, Tshimwanga J, Muyaya L, Manwana E. Conditional cash transfers to promote male circumcision uptake in middle and low income countries: review. Int J Res. 2017;4(9):1831–40.
24. Carrasco MA, Grund JM, Davis SM, Ridzon R, Mattingly M, Wilkinson J, et al. Systematic review of the effect of economic compensation and incentives on uptake of voluntary medical male circumcision among men in sub-Saharan Africa. AIDS Care. 2018;30(9):1071–82.
25. Carrasco MA, Wilkinson J, Kasdan B, Fleming P. Systematic review of barriers and facilitators to voluntary medical male circumcision in priority countries and programmatic implications for service uptake. Glob Public Health. 2018;1–21.
26. Downe S, Finlayson K, Tuncalp Ö, Gülmezoglu A. Factors that influence the uptake of routine antenatal services by pregnant women: a qualitative evidence synthesis (Protocol). Cochrane Database Syst Rev. 2016;10:CD012392.
27. Wiysonge C, Kongnyuy E, Shey M, Muula A, Navti O, Akl E, et al. Male circumcision for prevention of homosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2011;6:CD007496.
28. Weiss SM, Zulu R, Jones DL, Redding CA, Cook R, Chitalu N. The Spear and Shield intervention to increase the availability and acceptability of voluntary medical male circumcision in Zambia: a cluster randomised controlled trial. Lancet HIV. 2015;2(5):e181–9.
29. Cook R, Jones D, Redding CA, Zulu R, Chitalu N, Weiss SM. Female partner acceptance as a predictor of men's readiness to undergo voluntary medical male circumcision in Zambia: the spear and shield project. AIDS Behav. 2016;20 (11):2503–13.
30. Downs JA, Mwakisole AH, Chandika AB, Lugoba S, Kassim R, Laizer E, et al. Educating religious leaders to promote uptake of male circumcision in Tanzania: a cluster randomised trial. Lancet. 2017;389:1124–32.
31. Thirumurthy H, Masters SH, Rao S, Bronson MA, Lanham M, Omanga E, et al. Effect of providing conditional economic compensation on uptake of voluntary medical male circumcision in Kenya: a randomized clinical trial. JAMA. 2014;312(7):703–11.
32. Thornton R, Godlonton S. Medical male circumcision: how does price affect the risk-profile of take-up? Prev Med. 2016;92:68–73.
33. Barnabas RV, van Rooyen H, Tumwesigye E, Brantley J, Baeten JM, van Heerden A, et al. Uptake of antiretroviral therapy and male circumcision after community-based HIV testing and strategies for linkage to care versus standard clinic referral: a multisite, open-label, randomised controlled trial in South Africa and Uganda. Lancet HIV. 2016;3(5):e212–20.
34. Marshall E, RainTaljaard R, Tsepe M, Monkwe C, Taljaard D, Hlatswayo F, et al. Obtaining a male circumcision prevalence rate of 80% among adults in a short time an observational prospective intervention study in the Orange Farm township of South Africa. Medicine. 2017;96(4):e5328.
35. Montague C, Ngcobo N, Mahlase G, Frohlich J, Pillay C, YendeZuma N, et al. Implementation of adolescent-friendly voluntary medical male circumcision using a school based recruitment program in rural KwaZulu-Natal, South Africa. PLoS ONE. 2014;9(5):e96468.
36. Miiro G, DeCelles J, Rutakumwa R, NakiyingiMiiro J, Muzira P, Ssembajjwe W, et al. Soccer-based promotion of voluntary medical male circumcision: a mixed-methods feasibility study with secondary students in Uganda. PLoS ONE. 2017;12(10):e0185929.
37. UNAIDS. Using market research for long-term sustainability of VMMC in Zimbabwe and Zambia. [cited 22 May 2017] Available at: http://www.unaids.org/en/resources/presscentre/featurestories/2016/October/20161019_VMMC
38. Bandura A. Social foundations of thought and action: a social cognitive theory. Englewood Cliffs, NJ: Prentice-Hall; 1986.
39. Sgaier SK, Eletskaya M, Engl E, Mugurungi O, Tambatamba B, Ncube G, et al. A case study for a psychographic-behavioral segmentation approach for targeted demand generation in voluntary medical male circumcision. Elife. 2017;6:e25923.
40. Osaki H, Mshana G, Wambura M, Grund J, Neke N, Kuringe E, et al. "If you are not circumcised, I cannot say yes": the role of women in promoting the uptake of voluntary medical male circumcision in Tanzania. PLoS ONE. 2015;10 (9):e0139009.
41. Lanham M, L'Engle KL, Loolpapit M, Oguma IO. Women's roles in voluntary medical male circumcision in Nyanza province, Kenya. PLoS ONE. 2012;7(9): e44825.
42. Rutter H, Savona N, Glonti K, Bibby J, Cummins S, Finegood DT, et al. The need for a complex systems model of evidence for public health. Lancet. 2017;390(10112):2602–4.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Inclusion criteria.
Appendix S2. Example search strategy for Medline.
Appendix S3. Exclusion criteria.
Appendix S4. Questions and results of MMAT.

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RESEARCH ARTICLE

Cash plus: exploring the mechanisms through which a cash transfer plus financial education programme in Tanzania reduced HIV risk for adolescent girls and young women

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Abstract

Introduction: Cash transfers have been promoted as a means to reduce HIV risk for adolescent girls and young women (AGYW) in sub-Saharan Africa. One of the main mechanisms whereby they are hypothesized to reduce risk is by deterring transactional sex. In this paper, we use qualitative methods to explore participant experiences, perspectives and reported behaviours of a cash transfer plus financial education programme among out of school, 15- to 23-year-old AGYWs in rural Tanzania with a focus on partner choice and transactional sex.

Methods: We conducted 60 in-depth interviews (IDIs) and 20 narrative timeline interviews with participants of the PEPFAR DREAMS Sauti/WORTH+ cash transfer programme between June 2017 and July 2018. Interviews were taped, transcribed and translated from Kiswahili to English. Transcripts were coded and analysed for key themes.

Results: We found that participants in a cash transfer plus programme discussed behaviours that could reduce HIV risk through decreasing their dependence on male sex partners. There appeared to be two main mechanisms for this. One, young women discussed the cash transfer providing for basic needs (e.g. food, toiletries) which appeared to reduce their dependence on male sex partners who previously provided these goods (e.g. transactional sex). This experience was more pronounced among the poorest participants. Two, young women discussed how the financial education/business development aspect of the programme empowered them to refuse some sex partners; unmarried women discussed these experiences more than married women. Social support from family and programme mentors appeared to strengthen young women's ability to successful start businesses, produce income and thus be less dependent on partners.

Conclusions: The cash transfer programme may have reduced AGYW engagement in transactional sex that occurred to meet basic needs (one form of transactional sex). The financial education/business development and mentorship elements of the programme appeared important in building AGYW agency, self-esteem and future orientation which may support AGYWs in refusing unwanted sex partners. Future cash plus programmes should consider adding or strengthening financial education and job skills training, mentorship and future orientation to see stronger and perhaps sustainable outcomes for HIV prevention.

Keywords: adolescents; HIV prevention; structural drivers; cash transfers; Africa; transactional sex

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1 | INTRODUCTION

Cash transfers are increasingly popular in Africa as part of many government social protection programmes with the aim of providing a social safety net for the most poor and vulnerable, allowing them to afford basic necessities such as food, shelter, education and medical care. In recent years, cash transfers have been identified as key strategy that could be leveraged to reduce HIV risk for adolescent girls and young women (AGYW) [1,2].

There are a number of mechanisms through which cash transfers have been hypothesized to reduce HIV risk for AGYW including increasing school attendance, reducing stress and depression, and increasing hope for the future [3,4]. One of the main mechanisms is by reducing their economic dependency on men, in particular, reducing their need to engage in transactional sex (defined as non-marital, non-commercial sexual relationships motivated by an implicit assumption that sex will be exchanged for material support or other benefits) [5-7].

Data on the efficacy of cash transfers in reducing HIV risk for AGYW are mixed. Of five studies that have evaluated the impact of cash transfers on HIV risk in AGYW, the two that measured HIV incidence found no impact on incidence, one study found an impact on HIV prevalence, one study found a reduction in transactional sex and two found AGYW were less

likely to report older partners [6-10]. Some factors which may explain differences in results include the background level of poverty in the study area and among the target recipients, the amount of the transfer and frequency, gender and power norms for women, cultural constructions of materials goods, success and relationships, and the background level of social protection in the study area. These studies have highlighted the complexity of structural interventions and the importance that contextual factors play in impacting the effect of cash transfer programmes on HIV risk. In addition, they have raised questions as to whether cash transfers alone are sufficient for HIV prevention [11]. In the prevention landscape, UNAIDS considers cash transfers as part of a combination package, addressing upstream/structural drivers of HIV risk [12].

Despite the mixed evidence, there are a number of cash transfer programmes in the field targeted to AGYW with the aim of reducing HIV risk. The President's Emergency Plan For AIDS Relief (PEPFAR) DREAMS partnership (Determined, Resilient, Empowered, AIDS free, Mentored and Safe women), is a large HIV prevention initiative designed to reduce HIV risk among AGYW in 10 countries in Africa and includes the provision of cash transfers in some countries [13]. In this paper, we use qualitative methods to explore participant experiences, perspectives and reported behaviours in a cash transfer plus financial education programme (Sauti/WORTH+) on out of school, 15- to 23-year-old AGYWs in rural Tanzania on HIV risk, in particular partner choice and transactional sex.

2 | METHODS

2.1 | Parent study – Sauti project

We conducted our assessment with participants who participated in a DREAMS cash transfer plus programme which was implemented by the Sauti Project. Sauti Project is USAID-funded programme that targets key and vulnerable populations with community-based HIV prevention and reproductive health services. Cash transfers of TZS 70,000 (approximately USD 31) were provided to AGYW every three months for 18 months. AGYW who attended at least 10 hours of a behaviour change and communication (BCC) curriculum were eligible to participate in the cash transfer. Girls who completed the 10-hour BCC curriculum, and were getting the cash, were offered the opportunity to participate in a small group financial literacy and individual savings and loan programme called WORTH+. The programme's theory of change was that AGYW would have more access to money thus being able to make healthier sexual decisions including reduced transactional sex, fewer older partners, fewer partners and more condom use. The cash transfer programme targeted AGYW aged 15 to 23 who were out of school.

2.2 | Recruitment and study sites

We recruited female participants (n = 80) through community-based social service organizations implementing the DREAMS project in northwest Tanzania. Participants were purposefully sampled from within selected study villages based on a vulnerability criteria (risky sexual behaviours) used by Sauti to identify adolescents for the DREAMS programme. We aimed to get an equal number of participants in the 15 to 19 and 20 to 23 age ranges and to sample more unmarried than married young women. Specifically, we recruited from Bulungwa village, Shinyanga municipal and Kahama. Locations are within three hours of each other and agriculture is the primary commerce. Bulungwa is more rural than the other two, with Shinyanga municipal being the district headquarters and Kahama having experienced rapid population boom with the existence of the Buzwagi gold mine at the edge of the town.

2.3 | Data collection

2.3.1 | In-depth interviews

We conducted 20 baseline interviews in June 2017 after the first cash transfer payments, and then again in June 2018. The 60 interviews included 20 follow-up interviews with baseline participants and 40 new interviews. Interviews broadly assessed the impact of the cash transfer on AGYWs lives and how the cash may have influenced sexual decision-making and partner choice.

2.3.2 | Narrative timeline interviews

We conducted narrative timeline interviews with 20 women [14,15]. These interviews asked AGYW to draw a timeline of sexual partnerships they had in the previous two years and to indicate the time when they received each cash transfer. Participants were then asked to discuss characteristics of each partner, including financial support, condom use, HIV testing and overall quality of the relationship. Interviewers probed about different qualities of each partner and how the cash may have impacted relationships.

All interviews were audio recorded and were conducted in Kiswahili by four trained female research assistants who were Swahili native speakers and experienced interviewers. Prior to the interviews, research assistants received refresher trainings on research ethics, the informed consent process, interview probing techniques and conducted pilot interviews with guides.

2.4 | Analyses

Interviews were transcribed verbatim and translated from Kiswahili to English. Transcriptions were checked for quality by two of the study team members. We used applied thematic analysis to analyse data from all methods. Applied thematic analysis is a systematic, inductive process of sorting content by codes and conveying the meaning through themes. All transcripts were coded using Dedoose, a qualitative data analysis software program. For each method, an initial transcript was coded by four researchers, and then compared code by code across researchers. Following this global comparison, approximately 20% of the rest of the transcripts were quality checked by another researcher to ensure consistency in coding. We used coded transcripts to develop matrices [16] which included a summary of participant responses for each thematic category allowing for comparisons across interviews. The four researchers convened to discuss emergent themes focusing on the relationship between cash transfer receipt and HIV risk. In our discussion, we use the following terms to describe how common each theme was: a few means not that many people discussed the issue, some means that more than

a few but less than half discussed the issue and many/most means more than half discussed the issue.

2.5 | Ethical review

We obtained Institutional Review Board (IRB) approval from The University of North Carolina and the National Institute for Medical Research in Tanzania. Informed consent was obtained prior to any interview or focus group session.

3 | RESULTS

Table 1 presents the demographic profile of the young women who participated in these interviews. Here, we present key themes on possible mechanisms through which cash transfer programmes may operate to reduce HIV risk for young women. The conceptual framework was developed after analysis of the data and is informed by our interpretation of the data and prior literature on how cash transfers reduce HIV risk (Figure 1). Solid lines are pathways discussed by young women in the interviews, dotted lines are theorized pathways that other literature and cash transfer studies have observed but we did not observe in this study. Below, we explore components of the conceptual framework as they relate to partner selection and provide information generated from the interviews to expand on the themes identified.

3.1 | Programme design played a key role in programme effects

The design of the cash transfer programme had an important influence on how cash was used and thus the potential of the programme to influence partner selection and thus HIV risk. The aim of the programme was to provide young women with money so that they could develop businesses, earn their own income and thus be less dependent on men. The vast majority of AGYW internalized this messaging as illustrated in the quote below:

> *"They advised us to open our business/plans, not to be influenced by men by whom we (Inhalation), for example, having needs for money, do not go to request a man but you satisfy your own needs" (17 years old, not married, no child, ID21N)*

> *I: Mhh did they tell you why you were given the money for? R: For the purpose of uplifting us so that we don't depend on men (21 years old, married, 1 child, ID16L)*

Table 1. Demographic characteristics of AGYW participants taking part in interviews

Variables	Total population % (n = 80)
Age in years	
15 to 19	47.5 (38)
20 to 24	52.5 (42)
Education	
Primary school or less	53.8 (43)
Some secondary school	12.5 (10)
Secondary school completed or more	33.8 (27)
Marital status	
Not married	65 (52)
Married	35 (28)
Children	
No	50 (40)
Yes	50 (40)
Residence	
Bulungwa	28.8 (23)
Kahama	28.8 (23)
Shinyanga	42.5 (34)

3.2 | Cash helped meet basic needs for the most vulnerable AGYW

AGYW talked about the cash addressing some of the immediate consequences of poverty such as food insecurity and access to basic needs (e.g. sanitary pads, soap). Some AGYW talked about how there was no money in their home for food at times and how the cash transfer allowed them to buy food. Thus, the cash appears to have helped provide for basic needs for some young women, especially the poorest.

> *"Eee sometimes when they [family] don't have money at home and there's no food, if I have money [the cash transfer] then I take care of them at home, I can buy flour, rice" (19 years old, not married, one child, ID18 L)*

AGYW who came from homes that were more financially stable discussed being able to use the money to develop or grow a business or spend on their own needs than young women who were more poor. In fact, for young women who were financially better off, they talked about family providing extra money to develop a business or grow an existing business or attend training courses which helped AGYW succeed in earning income.

> *"As for me when I requested her (mother) to help me buy a sewing machine, she accepted and told me she is in the process of inquiring so that we can buy." (18 years old, not married, no child, ID1N)*

For those who were very poor, some AGYW talked about having to spend the money for basic needs or emergencies instead of investing in starting a business.

> *"For me honestly when I receive the first installment I did not invest it into business. I only bought clothes and food" (16, unmarried, 1 child, ID101N)*

3.3 | Cash covered AGYW basic needs which reduced reliance on male partners

Girls discussed that the cash allowed them to buy small things that they could not previously afford prior to the cash transfer. Many unmarried young women talked about how the cash reduced their need to seek out male partners to cover their basic needs. The poorer young women talked about this more than young women who appeared better off financially.

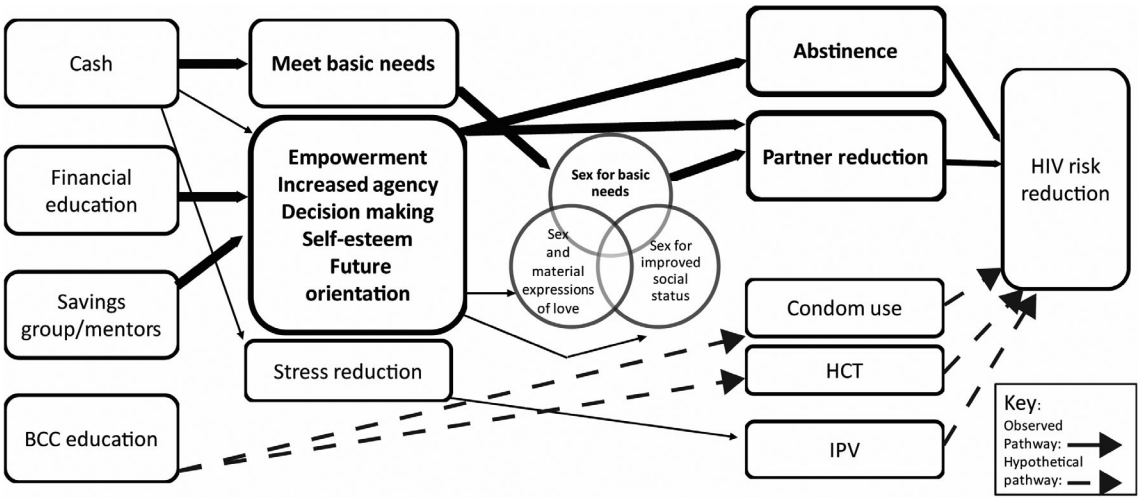

Figure 1. Conceptual framework on pathways through with the Sauti/WORTH+ cash transfer programme reduced HIV risk for AGYW. Solid lines, observed pathways, display pathways discussed by participants in the interviews. Dotted lines, hypothetical pathways, are those that the literature or other conceptual frameworks have endorsed. The transactional sex concepts are drawn from the conceptual framework by Stoebenau *et al*. Words and lines in bolder text are related to items that were more frequently discussed by participants in the interviews presented here. HCT, HIV counselling and testing; IPV, intimate partner violence.

"It [the cash transfer] helped us a lot to overcome the temptations [seeking out men] and to be able to afford our small needs . . . Because at first I was thinking on how to get my own money, but after getting this cash transfer it has reduced my stress on where to get the money. . . what will I do. . . but after receiving it has reduced it in one way or another" (18 years old, unmarried, no children, ID103N)

"Before I used to think of men. . .You find that I don't have any money. . .You find that I think about men a lot. But for now with the money being sent. . . I have opened a business. So now those thoughts are no longer in my mind." (21 years old, married, 1 child, ID8L)

Some young women when asked directly about how the cash influenced partner selection reported that it did not. This feeling was predominantly expressed by women who were already in committed relationships and younger women who had never been in a relationship.

"But like me it has changes my behavior to the extent that it has changed in terms of life and business wise..But not in partners" (24 years old, married, 1 child, ID16N).

A few married women did talk about engaging in extramarital relationships to get additional money to support their families and that the cash meant they did not have to seek out other partners to provide financial support; however, most transactional sex appeared to take place among unmarried women.

3.4 | Entrepreneurial skills enhanced future aspirations

Some young women talked about how the cash transfer coupled with business development skills supported stronger future aspirations. A few AGYW talked about going for job training or buying assets such as livestock or land that would provide income or financial security beyond the limited scope of the cash payments, showing a focus on the future.

"When I received a cash transfer for the first time I went to a certain woman with a sewing machine and begun to learn how to sew and the second time [second payment] I also used it there. . . The third time when I received I was given some money at home so I added to it and bought my own sewing machine" (18 years old, not married, no children, ID7N)

3.5 | Social support enhanced young women's entrepreneurial success

Young women talked about how social support from family and programme mentors helped them succeed in meeting their business goals. Many AGYW talked about the importance of family supporting them to meet their financial goals, and providing advice related to the cash and staying on track with meeting business and financial goals.

"I felt happy because after telling her [sister] that am doing a certain business then she advised me on how to use that money so I just knew she's still with me . . . until now she still advises me"(24 years old, not married, 1 child, ID9N)

Male partner support appeared common for married but not unmarried women. This seemed to be because married women lived with their husbands and made financial decisions with them. In most cases, married women talked about men being supportive of the cash as it was used for the household. Most unmarried young women reported not telling male partners about the cash because they felt the relationship was not serious enough to warrant discussing personal finances, they were worried they would lose financial support from partners or due to lack of trust of partners.

Many unmarried AGYW talked about stress reduction in their families from not having to ask mothers or other family members for money to pay for small, personal items (e.g. sanitary pads, lotion, oil). A few married women talked about how the cash reduced financial stress in the home which reduced tension and potentially violence from partners which ultimately may have improved relationship quality.

As part of the cash transfer programme, AGYW were encouraged to participate in savings groups and had mentors who advised them on how to develop a business and save. AGYW talked about the savings clubs providing financial support when they needed it (they could ask the group for money instead of men) and that it provided support in growing their business.

> *"My views about the group since I have seen its benefits. First, I can say that it helps when you're keeping your savings there because you can take a loan and do business on something that you know you'll make a profit and return the loan you took from the group. By doing so it eliminates [sexual] temptations because you may say that you'd want to do a certain business and maybe the starting capital is 100,000, and you do not have that money and maybe your parents also cannot help and you meet someone on the street and someone [sex partner] offers to give you 150,000. It helps to avoid such temptations." (19 years old, not married, no children, ID14NT)*

Young women talked about how programme mentors helped keep AGYW on task with the development of a business and savings. Some AGYW talked about how they spent the first payment on things not related to building a business but through guidance from programme mentors they were able to spend future payments on business development.

3.6 | Cash and business experience empowered AGYW which enabled them to refuse unwanted sex partners and abstain from sex

An important outcome of the cash and entrepreneurial training that young women talked about was that it allowed them to take care of themselves and meet their own small needs without having to depend on anyone else, be it family members or partners, which created a sense of empowerment, agency, self-reliance and pride.

> *"Because I wanted to reach my goals as a young person so I did not need to have a partner. After the organisation started sending me money I had faith in myself and believed I did not need anyone." (19 years old, married, no children, ID29N)*

Some young women discussed how this empowerment and self-esteem/pride that the programme fostered gave them the agency to say no to men who might offer them money. Financial independence empowered some young women to say no to partners they were not interested in.

> *"As in pride as in you have your own money as in even if someone talks to you, you really don't have time for them as in you just don't care. . .If you meet up with him and he tells you something then you can tell him to leave you alone but it's hard if you don't have money" (24 years old, married, children, ID16N).*

> *"We first get the money project and engage ourselves so a man just can't come from nowhere and I just love him and right now we are proud of something we also have money so a man can't stress me and I also I can look for that man who has a higher earning than me." (24 years old, not married, children, ID9N)*

For the few younger women who had not ever had sex, they talked more about the programme helping them to abstain from sex while for AGYW who had already had sex they talked more about refusing unwanted partners, thus reducing partner number. A few young women also talked about how they were too busy running a business and thinking about making money to have time for men. Overall, there was minimal discussion of condom use or other HIV prevention behaviours such as testing as a direct result of the cash transfer.

4 | DISCUSSION

In this qualitative study of a cash plus financial education programme among out of school AGYW in rural Tanzania, we found that provision of the cash transfer helped some young women meet basic needs which appeared to reduce transactional sex motivated by the need for food and basic goods. Importantly, the cash transfer plus financial education and savings groups appeared to increase AGYWs agency and self-esteem, empowering them to refuse some male sex partners, possibly reducing HIV risk.

One of the main hypotheses of how cash transfers may reduce HIV risk for AGYW is by reducing their financial dependence on men thereby reducing engagement in transactional sex [6,7]. We found that the Sauti/WORTH+ programme may have helped young women refuse sex with men for basic needs, likely the most poor. The assumption that small cash transfers will reduce transactional sex among AGYW relies on the assumption that transactional sex is motivated by poverty. However, using the conceptual framework by Stoebenau *et al.* describing motivators for transactional sex, sex for basic needs is only one reason why young women engage in transactional sex [5]. Depending on the context and background poverty level of an area, the ability of a cash transfer to reduce transactional sex may depend on the proportion of young women engaging in transactional sex to obtain basic needs. It seems less likely that a small cash transfer will have a strong impact on other motivations for engaging in transactional sex including desire for social status and sex and material expressions of love. Thus, we posit that cash transfer programmes will reduce HIV risk by helping provide for basic needs and this may have had a modest impact on one element of risky transactional sex, sex for basic needs thus reducing partner number (Figure 1).

A second and perhaps more important pathway through which a cash plus financial education/business development

programme could reduce AGYW's HIV risk is by increasing their agency and self-esteem (Figure 1). For many young women in this programme, this was the first time they had access to their own money to spend how they pleased. Elements of the programme that focused on building and running a business, making money and saving resulted in AGYW gaining courage to do new things, greater decision-making abilities and self-confidence they could provide for themselves and meet their future goals independent of a male partner. The business development and savings component appeared to help some young women think more about their future resulting in them saving to buy land, livestock or assets for their business. This benefit is something that cash alone programmes likely would not provide.

The confidence and agency gained from the programme by AGYW appeared to translate to some AGYW being able to have greater choice over sex partners. The empowerment agency and self-esteem gained appeared to have a direct impact on partner reduction or delayed coital debut/abstinence (Figure 1). It also may have had an indirect and small impact on transactional sex that is motivated by social status, where girls may have sex to obtain "commodities of modernity" which allow them to gain social status with peers [5]. Through improved self-esteem and future aspirations, it is possible AGYW may find confidence from within themselves and not from material goods. The other element of transactional sex addresses the interconnectedness of love and money in romantic relationships [17]. Traditional gender norms in many settings expect men to provide for women/family and women in turn reciprocate by providing sex and domestic services. We argue that women's increasing participation in provision of household needs may start to challenge traditional gender norms of male provision. The implication of these gradual shifts in gender roles is unclear and further research would be necessary to understand the effect on women's economic and sexual empowerment.

While the Sauti/Worth+ programme focused on out of school AGYW, it did not exclude married young women. However, the impact of the cash plus programme in reducing HIV risk for married women in this programme seemed minimal given most risk likely comes from male partners/husbands. It is unclear that including married women in cash transfer programmes to reduce HIV risk will have a major impact.

Social support from family and the programme mentors and participants appeared important in helping AGYW be more successful in achieving financial goals. The programme design of WORTH+ hypothesized that savings groups would provide social support from fellow AGYW. Importantly, programme mentors who lead the savings groups appeared important in helping young women set up businesses and stay on track with business development when they were struggling. It is possible that future programmes would benefit from further strengthening the mentorship piece. Finally, family and parents, appeared to play an important role in the financial and business decisions AGYWs contributing to their success and their role should be considered in future programming.

Sustainability of programme effects once cash transfer programmes end is an important consideration. The Sauti/WORTH+ project provided six payments to AGYW over 18 months. This is a relatively short period of time to build benefits that can extend beyond the programme end. For young women who were able to build a sustainable business, acquire job skill training or purchase assets, it is possible that programme effects may extend beyond the end of the programme while for those who did not and were reliant on male partners, it seems unlikely that any programme effects on partner reduction and transactional sex will be maintained.

The current thinking in the cash transfers for HIV prevention field is that cash alone will likely not reduce HIV risk for AGYW significantly [11,18]. Our findings support this view. This has led to the advocacy for "cash plus" programmes meaning that cash transfers should be packaged with other services, including mentorship, financial education, and health services. While the impacts of these programmes are still to be seen, from this qualitative exploration, it appears that future cash plus programmes should consider including financial education and savings groups and focus on unmarried AGYW. A key message in the Sauti/WORTH+ programme was that it was to make AGYW less financially dependent on men; AGYW internalized this message. Future programmes may want to consider similar clear, strong programme messaging. Adding programming around future orientation may also be important so AGYW can use the cash to advance long-term savings and business goals. In addition, strengthening AGYW mentorship could play a critical role in helping AGYW achieve financial and future life goals. Programme mentors who can provide training in key job and life skills could help AGYW transition from adolescence into adulthood more successfully.

4.1 | Limitations

There are a number of limitations of this study. As this is qualitative study, the purpose was to explore experiences with a cash transfer programme and possible influences on partner selection and thus we cannot draw any conclusions about the programme impact on HIV. Second, the Sauti/WORTH+ programme had strong messaging around reducing young women's reliance on male partners; thus, it is possible that social desirability bias influenced AGYW responses even though our research team were independent of the Sauti team. Along these lines, girls selected to participate in the interviews may not be representative of all girls in the programme. Third, few young women discussed how the programme influenced HIV prevention modalities such as condom use or HIV testing; however, we did not ask direct questions about this.

5 | CONCLUSIONS

Overall, we found that out of school AGYW in rural Tanzania who participated in a cash plus financial education programme discussed some possible pathways through which the programme may have reduced dependence on male partners. The pathways discussed included the cash providing for AGYWs basic needs that they previously acquired from male partners and also through increased empowerment, agency and self-esteem acquired from the financial education, savings groups and business development aspects of the programme. Future cash plus programme should consider including financial education/savings groups, mentorship and social support for AGYW, and more training on future goals and aspirations.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHORS' CONTRIBUTIONS

Audrey Pettifor conceptualized the study, developed the protocol and study guide, reviewed the transcripts, analysed the data, identified the themes and wrote the paper. Joyce Wamoyi conceptualized the study, developed the protocol and study guide, oversaw the field work, reviewed the transcripts, analysed the data, identified the themes and edited the paper. Peter Balvanz provided the study oversight and implementation, coded the transcripts, analysed the data, identified the themes and edited the paper. Margaret Gichane coded the transcripts, analysed the data, identified the themes and edited the paper. Suzanne Maman conceptualized the study, developed the protocol and study guide, reviewed the transcripts, analysed the data, identified themes and edited the paper.

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REFERENCES

1. Pettifor A, MacPhail C, Nguyen N, Rosenberg M. Can money prevent the spread of HIV? A review of cash payments for HIV prevention. AIDS Behav. 2012;16(7):1729–38.
2. Heise L, Lutz B, Ranganathan M, Watts C. Cash transfers for HIV prevention: considering their potential. J Int AIDS Soc. 2013;16:18615.
3. Handa S, Palermo T, Rosenberg M, Pettifor A, Halpern CT, Thirumurthy H. How does a national poverty programme influence sexual debut among Kenyan adolescents? Glob Public Health. 2017;12(5):617–38.
4. The Transfer Project. Ujana Salama: cash plus model on youth well-being and safe, healthy transitions. Chapel Hill, NC: Carolina Population Center; 2018.
5. Stoebenau K, Heise L, Wamoyi J, Bobrova N. Revisiting the understanding of "transactional sex" in sub-Saharan Africa: a review and synthesis of the literature. Soc Sci Med. 2016;168:186–97.
6. Cluver L, Boyes M, Orkin M, Pantelic M, Molwena T, Sherr L. Child-focused state cash transfers and adolescent risk of HIV infection in South Africa: a propensity-score-matched case-control study. Lancet Glob Health. 2013;1(6):e362–70.
7. Pettifor A, MacPhail C, Hughes JP, Selin A, Wang J, Gómez-Olivé FX, et al. The effect of a conditional cash transfer on HIV incidence in young women in rural South Africa (HPTN 068): a phase 3, randomised controlled trial. Lancet Glob Health. 2016;4(12):e978–88.
8. Baird SJ, Garfein RS, McIntosh CT, Özler B. Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet. 2012;379(9823):1320–9.
9. Handa S, Peterman A, Huang C, Halpern C, Pettifor A, Thirumurthy H. Impact of the Kenya cash transfer for orphans and vulnerable children on early pregnancy and marriage of adolescent girls. Soc Sci Med. 2015;141:36–45.
10. Abdool Karim Q, Leask K, Kharsany A, Humphries H. Impact of conditional cash incentives on HSV-2 and HIV prevention in rural South African high school students: results of CAPRISA 007 cluster randomized trial. International AIDS Conference. Vancouver, Canada; 2015.
11. Cluver LD, Orkin FM, Boyes ME, Sherr L. Cash plus care: social protection cumulatively mitigates HIV-risk behaviour among adolescents in South Africa. AIDS. 2014;28 Suppl 3:S389–97.
12. UNAIDS. Fast-tracking combination prevention. Geneva; 2015.
13. Presidents Emergency Fund for AIDS Relief (PEPFAR). DREAMS Core Package of Interventions Summary https://www.pepfar.gov/documents/organization/269309.pdf
14. Goldenberg T, Finneran C, Andes KL, Stephenson R. 'Sometimes people let love conquer them': how love, intimacy, and trust in relationships between men who have sex with men influence perceptions of sexual risk and sexual decision-making. Cult Health Sex. 2015;17(5):607–22.
15. Goldenberg T, Finneran C, Andes KL, Stephenson R. Using participant-empowered visual relationship timelines in a qualitative study of sexual behaviour. Glob Public Health. 2016;11(5–6):699–718.
16. Miles MB, Huberman A. Matrix displays: some rules of thumb. Qualitative data analysis: an expanded sourcebook. Thousand Oaks: Sage Publications; 1994.
17. Majola S. Love, Money, and HIV becoming a modern African woman in the age of AIDS. Oaklandm, CA: University of California Press; 2014.
18. Cluver LD, Orkin FM, Yakubovich AR, Sherr L. Combination social protection for reducing HIV-risk behavior among adolescents in South Africa. J Acquir Immune Defic Syndr. 2016;72(1):96–104.

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RESEARCH ARTICLE

Strengthening the scale-up and uptake of effective interventions for sex workers for population impact in Zimbabwe

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Abstract

Introduction: UNAIDS' goal of ending AIDS by 2030 is unreachable without better targeting of testing, prevention and care. Female sex workers (FSW) in Zimbabwe are at high risk of HIV acquisition and transmission. Here, we report on collated programme and research data from Zimbabwe's national sex work programme. We also assess the potential for wider population impact of FSW programmes by modelling the impact on HIV incidence of eliminating transmission through FSW (i.e. calculate the population attributable fraction of incidence attributable to sex work).

Methods: Descriptive analyses of individual-level programme data collected from FSW between 2009 and June 2018 are triangulated with data collected through 37 respondent driven sampling surveys from 19 sites in Zimbabwe 2011 to 2017. We describe programme coverage, uptake, retention and patterns of sex work behaviour and gaps in service provision. An individual-level stochastic simulation model is used to reconstruct the epidemic and then the incidence compared with the counter-factual trend in incidence from 2010 had transmission through sex work been eliminated from that date.

Results: Sisters has reached >67,000 FSW since 2009, increasing attendance as number of sites, programme staff and peer educators were increased. Over 57% of all FSW estimated to be working in Zimbabwe in 2017 (n = 40,000) attended the programme at least once. The proportion of young FSW reached has increased with introduction of the "Young Sisters programme." There are no clear differences in pattern of sex work across settings. Almost all women report condom use with clients at last sex (95%); however, consistent condom use with clients in the last month varies from 52% to 95% by site. Knowledge of HIV-positive status has increased from 48 to 78% between 2011 and 2016, as has prevalence of ART use among diagnosed women (29 to 67%). Although subject to uncertainty, modelling suggests that 70% (90% range: 32%, 93%) of all new infections in Zimbabwe from 2010 are directly or indirectly attributable to transmission via sex work.

Conclusions: It is feasible to increase coverage and impact of sex work programming through community-led scale-up of evidence-based interventions. Eliminating transmission through commercial sex would likely have a substantial impact on new infections occurring more widely across Zimbabwe.

Keywords: sex workers; HIV infection; Zimbabwe; Africa; HIV prevention; HIV testing

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1 | INTRODUCTION

The UNAIDS goal of eliminating HIV by 2030 is unreachable without targeting testing, prevention and care [1,2] more effectively. Despite 21 of 37 million people living with HIV (PLHIV) accessing antiretroviral therapy (ART) globally, 1.8 million new infections occurred in 2017, 980,000 in sub-Saharan Africa. The region's demographic transition, wherein 40% of the region's population is aged <15 years means that without substantial reductions in HIV incidence, the absolute number of new HIV infections in southern Africa will double in the next 20 years [3,4].

These figures hide disparity in risk of HIV acquisition by age, sex, geography and behaviour [1]. For example, odds of HIV infection among female sex workers (FSW) across sub-Saharan Africa (SSA) is 11 times higher than among adult women generally [5]. Suboptimal care-seeking among FSW is associated with poor health outcomes [6], contributing a substantial proportion of new infections in the broader population [7,8]. Modelling studies from around Africa suggest that previous assessments of transmission, which did not fully take into account indirect transmissions, greatly underestimated the likely contribution of sex work even in the generalized epidemics of SSA [7,8]. Furthermore, as treatment has become more widely available, thus reducing transmissions within the general population, the relative importance of transmission from commercial sex to overall numbers of new infections

may well have increased. Sex work interventions are highly cost effective [9] and calls to take programmes to scale have intensified in recent years [10,11].

Optimizing FSW programming requires maximizing FSW ownership and uptake of and engagement in prevention and treatment cascades [1,12,13]. Programmes need to build community empowerment to ensure that effective interventions (HIV testing, treatment for sexually transmitted infections, treatment for HIV-infected FSW, consistent condom use and pre-exposure prophylaxis (PrEP)) are taken to scale with sufficient intensity, and that they include the most vulnerable and difficult to reach, that is, young women [14]; recent entrants into sex work; and those with highest client load, inconsistent condom use and problematic drug or alcohol use [15].

In this paper, we collate programme and research evidence from Zimbabwe's national sex work programme "Sisters with a Voice" to (1) present the current impact that engagement in the Sisters programme has on HIV incidence, prevalence and control in FSW (based on programme and respondent driven sampling (RDS) survey data), (2) to describe the patterns and characteristics of sex work among FSW in Zimbabwe (based on RDS survey data), and (3) to assess the potential for wider population impact of sex worker programmes by modelling the impact on HIV incidence of eliminating transmission through FSW (i.e. calculate the population attributable fraction of incidence attributable to sex work).

2 | METHODS

2.1 | Sisters with a Voice programme

2.1.1 | Overview of the programme

Zimbabwe's national sex work programme, Sisters with a Voice, was established on behalf of Ministry of Health and Child Care and National AIDS Council in 2009. The programme expanded from five initial sites to 13 (2010) and then 36 sites (2013 to 2017), although five small sites recently closed due to funding constraints. Sites are located at major urban, town and highway hubs for sex work transmission (see Figure 1).

2.1.2 | Data collection and analysis

Since the start of the programme, comprehensive data have been collected from all women seeking clinical services and more recently (2016), from women engaged with community-based peer education.

At the first visit to the Sisters programme, women are assigned an alphanumeric unique identifier. Each time a woman visits the programme she is asked if she has attended previously and if so, her records are retrieved. The ID links consultations within and across sites, except where women provide false information. Prior to 2013, data were collected manually by nursing staff and single-entered into a Microsoft Access database. At all visits, information was collected on whether FSW had ever tested for HIV and the date and result of the most recent test, some self-reported and some conducted and recorded by the programme. Among women identified as living with HIV, data were collected at each visit on whether and when antiretroviral drugs (ARV) had been initiated and if these were currently being taken (although the Sisters programme does not itself provide ART). Since 2013 the same data have been collected using real time electronic data capture synced daily to secure cloud storage.

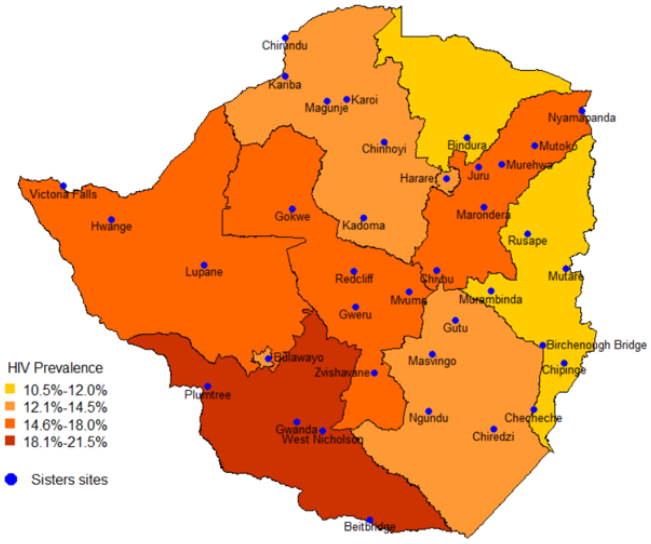

Figure 1. Map of general population HIV prevalence by province with location of Sisters sites superimposed.

We estimated the proportion of FSW "in the programme" who for each month since 2009 fell into one of five statuses: (1) Never tested for HIV; (2) HIV negative and not tested in the last six months; (3) HIV negative and tested in the last six months; (4) HIV positive and not on ART; (5) HIV positive and on ART. FSW were considered to be "in the programme" at a given time point if they had (1) had a visit within the last six months or (2) had a visit more than six months prior and in addition have another visit recorded at a future timepoint, beyond 31 December 2017. We used both self-reported HIV testing data and results and HIV tests conducted by the programme.

2.1.3 | Research data

Research has been integral to the development, expansion and evaluation of the programme, with respondent driven sampling surveys conducted through three studies conducted at 19 sites: in 2011 and 2015 (repeat surveys conducted in three sites), 2013 and 2016 (repeat surveys conducted in 14 sites including one site surveyed in 2011/15 surveys) and 2017 (three additional survey sites including Harare and Bulawayo), showing a mean HIV prevalence of 58% (range 44% to 82%) [16-19]. HIV incidence has been estimated from analysis of programme data between 2009 to 2013 at 10% per annum and 7% in 18 to 24 year olds [20,21].

2.1.4 | Synthesis of research data

Data from the three RDS survey studies conducted in 19 sites [19,22,23] (17 on highways or in towns around mines, army camps plus Harare and Bulawayo) provide a picture of sex work in Zimbabwe. In all surveys, eligible FSW had exchanged sex for money in the past 30 days, were aged ≥18, and had been working in the interview site for at least six months

(30 days for Harare, Bulawayo and one rural site). In each site, we conducted mapping, followed by purposive selection of "seeds" representing a mix of ages, sex work types and geographic locations. We interviewed seeds and gave them two coupons to distribute to peers. Women receiving a coupon could attend an interview and were subsequently given two coupons for their peers. Five to seven iterations of this process ("waves") were performed, excluding the seeds. Participants were given US$5 compensation for their time, and US $2 for each participant recruited. Checks were included to ensure coupons were genuine and minimize repeat participation. Interviewer-administered questionnaire data were collected on tablet computers and included demographics, sex work, sexual behaviour, HIV prevention and care uptake and on personal network size for RDS adjustment. A finger-prick blood-sample was collected from each FSW for HIV antibody testing, and for two studies (17 sites), measurement of HIV viral load.

Relevant data from the surveys were merged and patterns of sex work and related behaviours and treatment cascade indicators analysed descriptively across surveys. We explored differences by type of Sisters site (rural, highway, town, city, Bulawayo and Harare). Although women were recruited anonymously, all provided information combining initials and date of birth to create a "check-identifier" to minimize risk of duplicate enrolment. Within the combined dataset we identified seven participants who had similar "check-identifiers" but their questionnaire responses suggested they were different FSW. One FSW likely took part in surveys at two different sites. As the check-identifier was not "fail safe" data were retained from her participation in both surveys. We looked at changes in HIV cascade indicators among 2011, 2013 and 2015/6/7.

Our approach to RDS analysis has been described in detail elsewhere [19,22]. We followed guidance to assess evidence of bias in our operationalization of RDS [24]. We used the RDS-II method for analysis: dropping seed responses and weighting each woman in each site by the inverse of her network size, that is, the number of other women she could have recruited [25]. Data were pooled across surveys and weighted for size of site (not study) and weighted using site-normalized inverse degree weights. All analyses were at the cluster (site) level.

2.2 | Modelling

2.2.1 | *Overview of the existing HIV synthesis model*

The HIV Synthesis model has been used to assess (potential) effectiveness and/or cost effectiveness of a range of interventions in SSA, including HIV self-testing [26], a vaccine [27], a cure [28], ART monitoring [29,30] and drug resistance testing [31]. It is an individual-based model of HIV transmission, progression and the effect of ART in adults. Each time the model is run it simulates values of variables for the number of short term condomless sex partners, presence of a long term condomless sex partner, HIV testing, HIV acquisition and additionally, in PLHIV, viral load, CD4 count, use of specific ART drugs, adherence to ART, resistance to specific drugs and risk of HIV-related death, each updated in three-month time steps from 1989. It is informed by extensive cohort and survey data from within and outside Zimbabwe. A woman is designated a condomless sex FSW if she has at least three condomless sex partners in a three-month period in the past year. We further consider that a proportion of women are FSW but that they always use condoms (and thus have no possibility of acquisition or transmission of HIV) [32].

2.2.2 | *Calibration of the model*

For this paper, the model was calibrated to data from Zimbabwe. Data items to which the model is calibrated are HIV prevalence, HIV incidence, number of HIV tests performed per year, PLHIV with known status, number receiving ART, number on second line, proportion with viral suppression, proportion with resistance, number of pregnant women and number of FSW [32]. The data from RDS surveys are used to inform the calibration in respect of the number of FSW as well as prevalence among FSW and we have further compared the model outputs with observed sex worker programme data on the cascade of HIV care [32].

2.3 | Ethical issues

All research studies had ethical approval from the Medical Research Council of Zimbabwe (MRCZ) and collaborating universities (University College London, London School of Hygiene and Tropical Medicine and Liverpool School of Tropical Medicine). All participants provided written informed consent obtained according to principles of good clinical practice. Approval of secondary data analysis of programme data has been provided by MRCZ.

3 | RESULTS

3.1 | Programme attendance

By September 2018 over 67,000 women had been seen at least once, for 194,000 clinic visits. As service provision is scaled up, the number of women reached (and reached repeatedly) increases (see Table 1, Figure 2a). The proportion of young women has increased since the development of the "Young Sisters" programme in 2014 supported by teen peer educators [33] and scaled up across the programme from 2016. In 2017, the last year for which full statistics are available, over 24,000 women were reached with clinical services (57% of all FSW estimated in Zimbabwe). Self-reported condom use has increased over time. In 2017, 65% of attendees reported condom use at last sex and 52% reported consistent condom use with all clients in the past month. Of note, services intensified in the major cities during 2017, peer educator numbers increased, including those aged <25 from 13 to over 70, allowing more intensive outreach within the cities. This had an impact on number of FSW reached and the proportion of young women reached (see Figure 2b for FSW of all ages in Harare and 2c for FSW <25 for sites overall).

In Figures 2a,b,c, the pattern of engagement with Sisters services is shown over time. While attendance has increased overall (Figure 2a), funding gaps led to temporary reductions in service provision. There was a six-month funding gap in the second and third quarters of 2012. 2013 was an election year, resulting in some temporary clinic closures. In 2014, funding

Table 1. Sisters programme implementation by year showing number of clinics operating, intensity of clinical service provision, numbers and age of peer educators

Year of program operation	# Static sites[a]	# Out-reach sites[b]	# Peer educators	# Sites young sisters program	# Peer educators aged <25	# FSW seen	% FSW < 25	% FSW < 20	# FSW seen first time	% FSW first time <25	% First time FSW < 20	# Reached by community mobilization	% FSW aware of HIV status[c]	% Consistent condom use last month	% Condom use at last sex with client	Comment on implementation
2009	1	4[d]	41	0	NA	322	25.8	6.5	322	25.8	6.5	NA	23.9	38.4	NA	
2010	3	13[d]	131	0	NA	3394	22.3	5.8	3196	22.2	5.9	NA	44.6	35.5	NA	
2011	3	13[d]	131	0	NA	5083	21.0	5.8	3642	22.2	6.4	NA	58.9	35.4	40.6	
2012	3	13[d]	131	0	NA	4021	22.3	7.4	2442	25.1	8.9	NA	67.1	44.7	69.8	Funding interrupted for four months
2013	6	27[d]	100	0	NA	6151	23.7	7.3	4255	25.0	7.8	NA	69.6	35.1	57.7	Election year slowed programme implementation
2014	6	30[e]	170	3	NA	13,045	23.7	7.8	9895	25.9	8.8	4560	72.8	28.0	69.8	
2015	6	30[e]	170	3	NA	16,688	23.8	7.5	10,539	27.8	9.5	17,186	75.9	24.2	74.3	
2016	6	30[e]	184	9	54	18,539	25.5	7.8	10,657	32.9	11.5	21,885	75.3	51.4	70.1	Funding to 18 outreach sites withdrawn for four months
2017	6	30[e]	280	24	90	24,563	30.0	11.7	15,638	38.5	16.7	13,348	69.3	51.9	64.6	Supplemental funding for activities in five main cities
2018	10	20[e]	191	30	65	10,731	28.2	9.5	5066	38.4	15.0	2485	73.7	59.4	64.8	January to June only. Delayed implementation – donor funding transition

[a]static sites sited in government clinics, open all day Monday to -Friday; [b]outreach sites in small towns, mines highways, sited in government clinics; [c]aware of HIV positive status or tested HIV negative within six months when attended clinic; [d]open one day each fortnight. Peer educators on site in between; [e]open one day per week, peer educators on site in between.

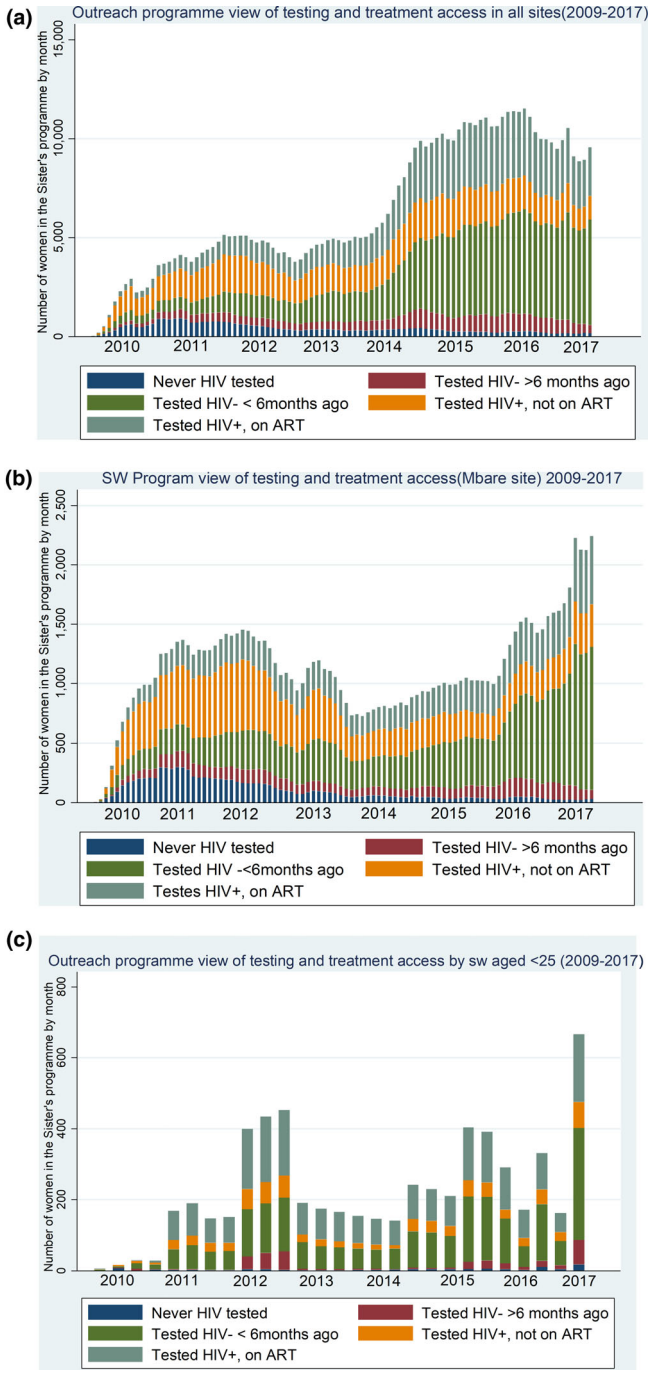

Figure 2. Outreach programme view of testing and treatment access in (a) all sites 2009 to 2017 (b) Mbare, Harare 2009 to 2017. (c) all sites by FSW aged <25 years 2009 to 2017.

increased, allowing 30 Sisters outreach sites to be opened weekly instead of bimonthly, but at the end of 2016 and again in 2017 18 outreach sites were closed due to funding restrictions.

In Harare (Figure 2b) the Sisters clinic was moved out of the City of Harare (Mbare) clinic and into the Central Business District between 2013 and 2016 due to space concerns, reducing acceptability of the clinic to FSW. Attendance returned to previous levels when the clinic relocated back to Mbare. When services in Harare were intensified in 2016/7 there was greatly increased attendance. Recruiting younger peer educators and specifically targeting younger FSW has resulted in an increase in the number and proportion of younger women seen.

The increased engagement of FSW attending the Sisters programme with testing and treatment is striking (Figures 2a,b,c). In 2009, the majority of those diagnosed HIV positive were not on treatment (eligibility for ART was determined by CD4 count), and around one-third had never tested for HIV. By 2017, almost all had tested previously, among those who previously tested negative the majority had tested within the last six months, and among those testing positive an increasing proportion were on ART across all sites.

3.2 | Pattern of Sex Work

A total of 6096 women were recruited into 3 studies at 19 sites between 2011 and 2017. Table 2 shows their characteristics and patterns of work by location.

Between 20% and 28% of FSW were aged <25 and the majority had some education; those from rural areas were less educated. Most had dependent children and the majority in all sites other than Bulawayo were divorced or separated. In terms of behaviour, 11% to 19% started selling sex below age 18 (defined as child abuse by UN agencies), 7% to 19% had worked as FSW for less than a year, most meet clients in bars or on the street, and 14% to 36% had over 10 clients in the previous week. Women typically received under US$5 per sex act although those in towns (but not cities) more often reported receiving US$5-10. There are some differences in characteristics/behaviours among FSW working in different settings but no clear patterns.

Data on service use across the 17 sites that have data for all cascade steps are presented in Figure 3. Engagement with care has increased over time. In 2015/6/7 FSW LHIV, 78% were aware of their diagnosis, 85% of those reported being on ART and 82% of those reporting ART were virologically suppressed. Among FSW LHIV overall 66% had a viral load <1000 copies/mL. Among HIV negative FSW, 76% reported having tested within the preceding six months.

3.3 | Using modelling to predict potential for averting new infections through targeting FSW

Figure 4 presents historical data and projections of HIV incidence with and without condomless transactional sex after 2010. This was done by first reconstructing the epidemic as it has played out and then re-running the re-construction but eliminating condomless sex work, based on the assumption that condomless sex work corresponds to a woman having more than three different condomless partners in a three-month period. It thus involves assuming that all women with multiple partners at this level or beyond are FSW [34]. Figure 4 indicates the potential course of the HIV epidemic had transmission via sex work ceased from 2010. The comparator (black line) conveys the actual epidemic as it has played out and takes into account the increased prevention, diagnosis and successful use of ART in this period. Overall there is an estimated 70% (90% uncertainty bound 32% to 93%) of

Table 2. Characteristics of female sex workers and their pattern of work by type of geographic location

	Rural (3 sites) (N = 609) n (%)	Highway (3 sites) (N = 615) n (%)	Towns (9 sites) (N = 1953) n (%)	Cities (2 sites) (N = 614) n (%)	Bulawayo (N = 808) n (%)	Harare (N = 1497) n (%)
Age (years)						
Mean (SD)	33 (9.4)	32 (8.6)	32 (8.5)	34 (9.7)	32 (9.3)	31 (8.0)
Median (IQR)	32 (11)	31 (11)	31 (11)	33 (14)	31 (13)	31 (11)
Education						
None	28 (3.7)	18 (3.9)	64 (2.4)	19 (2.6)	7 (0.7)	28 (1.8)
Primary	188 (40.3)	150 (26.3)	544 (27.6)	169 (22.8)	186 (24.2)	410 (28.9)
Secondary	387 (55.8)	444 (69.5)	1339 (70.0)	424 (74.3)	607 (73.8)	1056 (69.1)
Tertiary	6 (0.2)	2 (0.3)	6 (0.1)	2 (0.3)	8 (1.3)	2 (0.2)
Marital status						
Divorced/separated	408 (78.9)	434 (71.6)	1226 (63.0)	370 (58.6)	394 (48.1)	1026 (70.3)
Widowed	136 (17.6)	99 (15.6)	358 (12.0)	130 (19.2)	108 (13.1)	217 (13.8)
Never been married	63 (3.4)	78 (12.4)	335 (23.7)	109 (21.7)	285 (36.7)	240 (14.8)
Married/cohabiting	2 (0.1)	4 (0.4)	33 (1.3)	5 (0.5)	21 (2.1)	14 (1.1)
Number of children <18 years						
0	93 (17.2)	100 (15.5)	306 (17.2)	72 (11.6)	158 (23.4)	196 (12.9)
1 to 2	313 (46.1)	283 (47.0)	1065 (58.1)	348 (61.7)	367 (43.2)	765 (53.9)
≥3	203 (36.7)	232 (37.5)	582 (24.7)	194 (26.7)	283 (33.4)	536 (33.2)
Women aged <25 years with dependent children						
No	25 (23.6)	36 (30.3)	92 (23.3)	22 (15.0)	79 (42.4)	72 (20.1)
Yes	80 (76.4)	79 (69.7)	270 (76.7)	91 (85.0)	140 (57.6)	140 (79.9)
Age at first selling sex (years)						
Mean (SD)	26 (7.7)	26 (39.8)	26 (23.1)	25 (7.2)	24 (7.2)	25 (6.6)
Median (IQR)	25 (10)	24 (8)	24 (9)	24 (9)	23 (10)	24 (9)
Duration in sex work (years)						
Mean (SD)	8 (6.8)	8 (6.6)	7 (6.4)	9 (7.7)	7 (7.3)	7 (5.7)
Median (IQR)	5 (7)	5 (8)	5 (7)	6 (10)	5 (8)	5 (6)
Venue for client recruitment						
Bars/nightclubs/other venue	342 (80.9)	293 (56.9)	1365 (81.5)	411 (71.6)	675 (84.8)	939 (63.7)
By telephone	24 (1.6)	37 (6.1)	120 (13.8)	50 (12.1)	22 (2.1)	12 (0.8)
In the market place/street	126 (16.0)	143 (26.7)	252 (4.4)	71 (16.0)	89 (11.2)	501 (32.8)
Other	98 (1.5)	58 (10.3)	139 (0.3)	15 (0.3)	21 (1.9)	39 (2.7)
Number of clients in the last week						
Mean (SD)	7 (8.2)	8 (8.2)	8 (8.7)	12 (13.5)	8 (8.3)	14 (15.4)
Median (IQR)	5 (7)	5 (7)	5 (7)	7 (11)	5 (7)	10 (15)
Currently have a steady partner						
No	221 (45.1)	206 (31.9)	722 (23.9)	286 (49.7)	262 (33.3)	793 (52.8)
Yes	388 (54.9)	409 (68.1)	1231 (76.1)	328 (50.3)	546 (66.7)	704 (47.2)
Price per client – short time						
<$5	548 (93.5)	471 (76.6)	1218 (24.3)	359 (55.3)	596 (74.7)	1389 (93.8)
>$5 to $10	56 (6.2)	127 (21.1)	616 (68.8)	169 (36.5)	196 (24.0)	91 (5.2)
>$10 to $20	2 (0.2)	11 (2.1)	47 (6.2)	28 (7.0)	11 (1.3)	15 (1.0)
>$20	1 (0.1)	1 (0.2)	8 (0.7)	2 (1.2)	0 (0.0)	0 (0.0)
Proportion of income generated through sex work						
<25%	46 (9.6)	31 (4.2)	133 (2.4)	39 (2.4)	86 (6.6)	238 (14.9)
25% to 50%	103 (6.7)	108 (16.2)	255 (11.2)	75 (13.0)	80 (7.9)	210 (14.1)
>50% to 99%	195 (13.6)	233 (39.6)	528 (27.8)	177 (32.4)	173 (21.7)	258 (17.9)
100%	265 (70.1)	243 (40.0)	1031 (58.6)	469 (52.2)	469 (63.8)	791 (53.1)
Relationship with other female sex workers						
Good	425 (57.6)	429 (72.2)	1294 (67.7)	454 (72.5)	559 (66.5)	559 (58.2)
Neither good nor bad	147 (36.2)	160 (24.3)	489 (20.9)	121 (19.6)	208 (28.8)	208 (33.8)
Bad or no relationship	36 (6.2)	26 (3.4)	168 (11.4)	39 (7.9)	41 (4.7)	41 (8.0)

Table 2. (*Continued*)

	Rural (3 sites) (N = 609) n (%)	Highway (3 sites) (N = 615) n (%)	Towns (9 sites) (N = 1953) n (%)	Cities (2 sites) (N = 614) n (%)	Bulawayo (N = 808) n (%)	Harare (N = 1497) n (%)
Frequency of alcohol use in past 12 months						
Never	216 (28.1)	256 (42.6)	692 (33.8)	194 (29.8)	172 (21.4)	406 (26.5)
Once a month or less	71 (15.2)	66 (9.2)	191 (9.2)	84 (19.5)	70 (8.9)	165 (12.2)
2 to 4 times per month	54 (6.3)	61 (9.5)	312 (20.7)	129 (22.3)	87 (12.1)	185 (13.5)
2 to 3 times per week	124 (25.9)	121 (21.0)	334 (15.4)	82 (12.4)	261 (33.8)	399 (26.6)
4 or more times per week	144 (24.5)	111 (17.7)	421 (20.9)	125 (16.0)	125 (23.8)	342 (21.2)
Experience of physical violence from steady partner						
No	322 (46.9)	314 (49.5)	1055 (64.2)	327 (52.4)	422 (58.4)	708 (47.1)
Yes	287 (53.1)	301 (50.5)	898 (35.8)	287 (47.6)	386 (41.6)	789 (52.9)
Experience of physical violence from client						
No	464 (72.0)	433 (72.2)	1432 (82.5)	450 (76.1)	566 (74.9)	952 (66.2)
Yes	145 (28.0)	182 (27.8)	520 (17.5)	164 (23.9)	242 (25.1)	545 (33.8)
Ever been raped						
No	570 (72.0)	550 (72.2)	1805 (82.5)	581 (76.1)	690 (74.9)	1225 (66.2)
Yes	39 (28.0)	65 (27.8)	148 (17.5)	31 (23.9)	118 (25.1)	272 (27.8)
Experience of violence from police in the past 12 months						
No	568 (97.1)	547 (91.7)	1671 (93.0)	550 (92.3)	729 (90.3)	1297 (87.4)
Yes	40 (2.9)	67 (8.3)	265 (7.0)	63 (7.7)	78 (9.7)	196 (12.6)
Condom use at last sex with client						
No	26 (5.2)	20 (4.1)	57 (2.9)	28 (5.7)	31 (4.9)	57 (3.5)
Yes	583 (94.8)	595 (95.9)	1885 (97.1)	584 (94.3)	776 (95.1)	1439 (96.5)
Condom-less sex with client in the past month						
No	400 (93.4)	333 (52.4)	1117 (70.9)	384 (72.6)	670 (83.0)	1255 (81.5)
Yes	173 (6.6)	266 (47.6)	684 (29.1)	220 (27.4)	138 (17.0)	242 (18.5)

infections attributable to sex work. In this analysis model the maximum number of FSW in 2017 was 203,000 (median 116,000 FSW, median 47,000 condomless sex FSW). If we restrict to runs for which the number of FSW is below 110,000 (median number of FSW 90,000, condomless sex FSW 39,000), an estimated 72% (90% uncertainty bound 32% to 89%) of infections were attributable to sex work.

Moreover, compared with a scenario in which the epidemic and programme continues as currently, with the same rate of HIV testing, ART initiation and retention, current rate of circumcision to 2030, there would be 85% less new infections in 2030 had transmission through sex work been eliminated from 2010.

4 | DISCUSSION

We describe trends over time in key characteristics of FSW engagement in services in the context of a national FSW programme supported by peer-led mobilization and empowerment and general scale up of ART. These suggest the potential feasibility of virtually eliminating HIV transmissions through commercial sex in Zimbabwe. We show that this would likely have substantial impact on the Zimbabwe epidemic more generally. Increasing coverage and intensity of service delivery by strengthening community involvement and empowerment alongside increasing numbers of programme staff led to concomitant increases in coverage, status awareness and uptake and optimal use of ART. In our recently published SAPPH-IRe trial of a targeted combination prevention intervention between 2013 and 2016 [22] there were substantial gains in engagement in both arms; more intensive service provision in the intervention arm was associated with greater community mobilization of women (twice as many new HIV infections were diagnosed), although there was no significant difference by arm in the proportion of all FSW with VL <1000 copies/mL. The proportion of HIV positive FSW with VL <1000 copies/mL rose from 50% in 2013 to 68% to 73% in 2016, suggesting that increasing FSW programme coverage and intensity in the context of a well-functioning national ART programme can have a substantial impact on the proportion of FSW with infectious HIV. Of note, the rate of virological suppression at endline in the SAPPH-IRe trial compares favourably with data from ZIMPHIA which found that 65% of all HIV positive women were virologically suppressed [35].

Community empowerment of FSW is a critical component of effective programming and has been UNAIDS best practice for well over a decade [36]. Optimizing programme impact requires that empowered FSW know about and are motivated to use services, that there are acceptable, accessible comprehensive services in place and FSW accessing these services are supported to fully engage with them [12]. We can consider the extent of programme activity in the context of an estimate of the size of the FSW population in Zimbabwe. In a separate study, we have combined size estimation data from 20 sites and extrapolated from programme data in a further

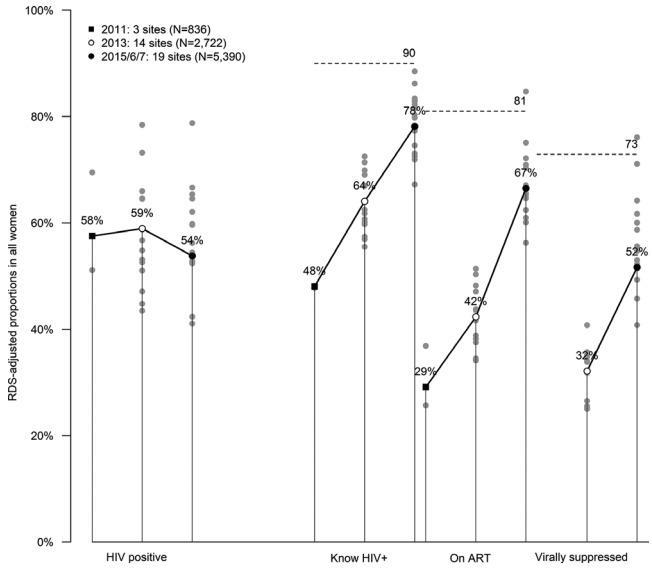

Figure 3. Engagement of female sex workers in the HIV care cascade 2011, 2013, 2015/6/17.
The treatment cascades for the three time point arms are illustrated, with the left of each bar showing results for 2011, the middle for 2013 and the right 2016. The cascades are shown for all women included in the relevant surveys, with the 90:90:90 targets indicated with horizontal dotted lines. All values were adjusted with RDS-II. The dots represent the value of cascade indicator for each site surveyed in that year.

16**,** to estimate that there are 40,000 (plausibility bounds 28,000 to 59,000) women working as sex workers in Zimbabwe (1.23% (plausibility bounds 0.86% to 1.79%) of adult female population (Fearon *et al*., unpublished data) with around 20,000 (50%) in Harare and Bulawayo. In 2017, over 24,000 FSW engaged with the national programme, 60% of the estimated sex work population; 8677 were in Harare and Bulawayo, which is 43% of the estimated populations in those cities.

Although attendees' mean number of clinical contacts with the programme has increased to three, it falls short of quarterly visits recommended by WHO [37]. If the "optimal ratio" of peer educator to FSW is 1:50 to provide sufficient community support for service engagement [38], for example, then 280 peer educators rather than the current 70 are required in Harare. Of note, a government, donor and implementor panel convened in 2017 to inform national size estimation estimated that the location of Sisters programme sites provides the potential for access to between 75% and 85% of all FSW nationally (Fearon *et al*., unpublished data), although since then six sites have closed due to funding constraints. Thus, extending the capacity of existing sites plus establishing new sites at hotspots not currently covered is needed. In addition, training of health care providers within government services to ensure that they are FSW friendly is critical. As condomless sex is commonly reported (and more commonly with regular partners and among programme attendees, perhaps reflecting less social desirability bias in this setting) [39] scaling and supporting optimal use of PrEP is increasingly urgent; proportionately few HIV negative FSW (<15% by July 2018) are on PrEP (personal communication Emily Gwavava). Extending services to ensure that regular partners of FSW can access HIV and STI testing and treatment as well as condoms is critical.

Intensifying community engagement and empowerment, using microplanning, and initiating self-help groups to build trust, social cohesion and community ownership (with the aim that self help groups transition over time to become FSW-led community-based organizations) could further increase effectiveness of prevention and care programmes [12,40,41]. Peer-led microplanning, which provides regular, risk-differentiated, individual peer support has potential to improve service uptake, including regular repeat HIV testing, and adherence to

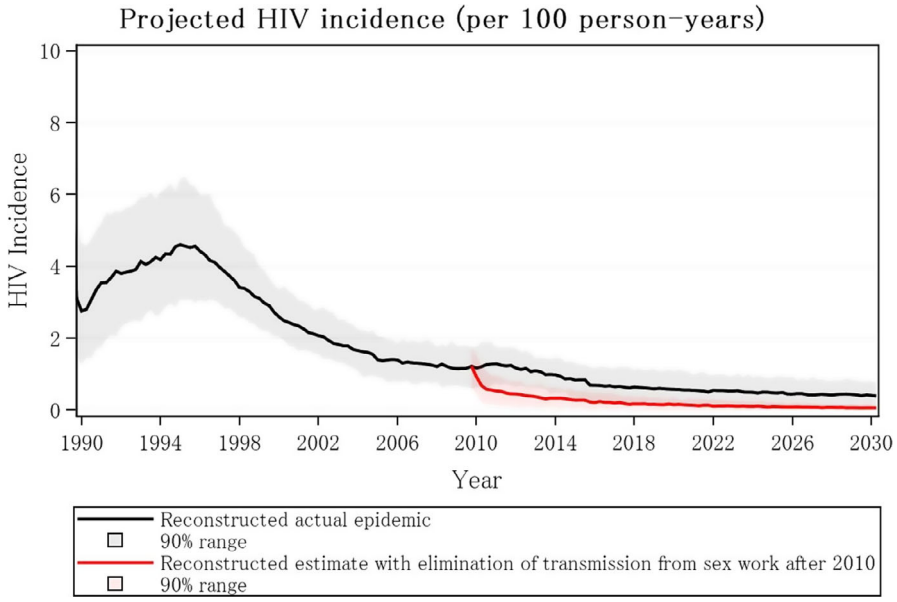

Figure 4. Projected HIV incidence among general population in Zimbabwe with (red line) and without (black line) elimination of transmission in either direction between sex workers and clients from 2010.

PrEP and ART. Despite considerable gains, further scale-up and intensification of targeted programming in partnership with FSW is needed to maximize impact and likely cost effectiveness.

This study has many strengths. It triangulates individual-level programme data from over 67,000 FSW collected over nine years with representative survey data from across Zimbabwe between 2011 and 2017 plus other research data. This allows us to convincingly show that with increasing coverage and intensity of service provision supported by increasing community ownership, HIV status awareness and engagement with the treatment cascade has improved. In addition, these analyses have allowed us to identify gaps in service provision, uptake and use that can be targeted. These data have been used to inform the HIV Synthesis model for Zimbabwe, so we can assess in broad terms the potential impact of eliminating direct and indirect acquisition and transmission of HIV resulting from commercial sex transactions in Zimbabwe and the region more broadly. We plan to further develop the model to inform programme targeting and regional policy.

Study limitations include the self-reporting of testing and ART initiation in programme and survey data, and some 10% of programme variables are missing. Our use of respondent-driven sampling to recruit FSW might have been subject to bias. Refusal rates are difficult to document with this design. Our analyses suggested little evidence of bias, but were not definitive. We have not thus far been able to identify longitudinal data on frequency of transitions into and out of sex work, and little is known about the life course of sex work and how this varies according to sex work typologies that can be reflected in the model. We are not clear on what proportion of all women with three or more condomless sex partners in a three-month period identify as FSW, who the others are, and how to reach them. For this reason, our estimate of 70% of new infections after 2010 attributable to sex work is associated with considerable uncertainty, even beyond that captured by the uncertainty bounds we present which represent variation over model runs with different input parameter values. Nevertheless, there is little uncertainty over the fact that this attributable fraction is substantial. Additionally, our model does not explore differentiated targeting according to level of vulnerability. Using mathematical modelling in Kenya [7], Steen *et al*. found that reaching only high activity FSW with interventions had similar population impact to reaching all FSW.

Another data gap relates to behaviour of men, specifically those who have high numbers of condomless sex partners. We have little knowledge of what types of partnerships these are, what proportion are transactional, including what proportion are with self-identified FSW.

5 | CONCLUSIONS

Prevention efforts need to be intensified if new HIV infections are to be reduced to 2030 targets. Modelling suggests that "eliminating" HIV transmissions through commercial sex by maximizing engagement with treatment and prevention services would have considerable impact on the number of new infections in Zimbabwe over the next 12 years and beyond. Further work to refine the model and explore impact and cost effectiveness of various targeting approaches is planned. We present evidence that it is possible to attain high uptake and coverage, but that this is dependent on extent and sustainability of resources. Regular, risk-differentiated, individual peer support through microplanning coupled with community empowerment has the potential to optimize service use to maximize programme impact.

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COMPETING INTERESTS

No competing interests to declare.

AUTHORS' CONTRIBUTIONS

F.C. drafted the paper. S.C. and S.M. undertook analyses of respondent driven sampling surveys and of programme data. E.F. and C.D. provided statistical support. T.M. oversaw programme implementation. L.B.M. undertook modelling. J.B., R.S., O.M. and J.H. provided insights into analyses. L.M.B., V.C. and A.P. devised HIV synthesis model. All authors have been integral to design of studies included here and programme data collection. All authors commented on manuscript draft.

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REFERENCES

1. Global HIV Prevention Coalition. HIV Prevention 2020 Road Map: accelerating HIV prevention to reduce new infections by 75%. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2017.
2. Joint United Nations Programme on HIV/AIDS, UNAIDS. Ending AIDS: Progress towards the 90-90-90 targets. Global AIDS Update. Geneva: UNAIDS, 2017Contract No.: JC2900E.
3. Canning D, Raja S, Yazbeck A. Africa's demographic transition: dividend or disaster? World Bank. 2015.
4. Bekker L-G, Alleyne G, Baral S, Cepeda J, Daskalakis D, Dowdy D, et al. Advancing global health and strengthening the HIV response in the era of the Sustainable Development Goals: the International AIDS Society & Lancet Commission. Lancet. 2018;392(10144):312–58.
5. Baral S, Beyrer C, Muessig K, Poteat T, Wirtz AL, Decker MR, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infect Dis. 2012;12(7):538–49.
6. Mountain E, Mishra S, Vickerman P, Pickles M, Gilks C, Boily M-C. Antiretroviral therapy uptake, attrition, adherence and outcomes among HIV-infected female sex workers: a systematic review and meta-analysis. PLoS One. 2014;9(9):e105645.
7. Steen R, Hontelez JA, Veraart A, White RG, de Vlas SJ. Looking upstream to prevent HIV transmission: can interventions with sex workers alter

the course of HIV epidemics in Africa as they did in Asia? AIDS. 2014;28(6):891–9.
8. Boily MC, Pickles M, Alary M, Baral S, Blanchard J, Moses S, et al. What really is a concentrated HIV epidemic and what does it mean for West and Central Africa? Insights from mathematical modeling. J Acquir Immune Defic Syndr. 2015;68 Suppl 2:S74–82.
9. Wilson D. HIV Programs for sex workers: lessons and challenges for developing and delivering programs. PLoS Med. 2015;12(6):e1001808.
10. Steen R, Wheeler T, Gorgens M, Mziray E, Dallabetta G. Feasible, efficient and necessary, without exception – working with sex workers interrupts HIV/STI transmission and brings treatment to many in need. PLoS One. 2015;10(10):e0121145.
11. Shannon K, Crago A-L, Baral SD, Bekker L-G, Kerrigan D, Decker MR, et al. The global response and unmet actions for HIV and sex workers. Lancet. 2018;392(10148):698–710.
12. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
13. UNAIDS. UNAIDS 2016-21 strategy: on the fast-track to end AIDS. Geneva: UNAIDS, 2015.
14. Inter-Agency Working Group on Key Populations. HIV and young key populations: technical briefs. Geneva: UNAIDS; 2015.
15. Chersich M, Bosire W, King'ola N, Temmerman M, Luchters S. Effects of hazardous and harmful alcohol use on HIV incidence and sexual behaviour: a cohort study of Kenyan female sex workers. Global Health. 2014;10(1):22.
16. Cowan F, Davey C, Mushati P, Mtetwa S, Chiyaka T, Chabata S, et al., editors. Results of the SAPPH-IRe Trial: a cluster randomised trial of a combination intervention to empower female sex workers in Zimbabwe to link and adhere to antiretrovirals for treatment and prevention. 21st International AIDS Conference 2016; Durban, South Africa.
17. Cowan FM, Mtetwa S, Davey C, Fearon E, Dirawo J, Wong-Gruenwald R, et al. Engagement with HIV prevention treatment and care among female sex workers in Zimbabwe: a respondent driven sampling survey. PLoS One. 2013;8(10):e77080.
18. Cowan FM, Davey CB, Fearon E, Mushati P, Dirawo J, Cambiano V, et al. The HIV care cascade among female sex workers in Zimbabwe: results of a population-based survey from the sisters antiretroviral therapy programme for prevention of HIV, an integrated response (SAPPH-IRe) trial. J Acquir Immune Defic Syndr. 2017;74(4):375–82.
19. Ndori-Mharadze T, Fearon E, Busza J, Dirawo J, Musemburi S, Davey C, et al. Changes in engagement in HIV prevention and care services among female sex workers during intensified community mobilization in 3 sites in Zimbabwe, 2011 to 2015. J Int AIDS Soc. 2018;21 Suppl 5:e25138.
20. Hargreaves JR, Mtetwa S, Davey C, Dirawo J, Chidiya S, Benedikt C, et al. Cohort analysis of programme data to estimate HIV incidence and uptake of HIV-related services among female sex workers in Zimbabwe, 2009-14. J Acquir Immune Defic Syndr. 2016;72(1):e1–8.
21. Hensen B, Chabata S, Floyd S, Chiyaka T, Mushati P, Birdthistle I, et al., editors. HIV prevalence and risk factors for prevalent HIV among young women who sell sex in Zimbabwe: results from a respondent driven survey conducted for an impact evaluation of DREAMS. AIDS Impact; 2017; Cape Town.
22. Cowan FM, Davey C, Fearon E, Mushati P, Dirawo J, Chabata S, et al. Targeted combination prevention to support female sex workers in Zimbabwe accessing and adhering to antiretrovirals for treatment and prevention of HIV (SAPPH-IRe): a cluster-randomised trial. Lancet HIV. 2018;5(8):e417–26.
23. Personal communication.
24. Gile KJ, Johnston LG, Salganik MJ. Diagnostics for respondent-driven sampling. J R Stat Soc Ser A Stat Soc. 2015;178(1):241–69.
25. Volz E, Heckathorn D. Probability based estimation theory for respondent driven sampling. J Official Stat. 2008;24(1):79–97.
26. Cambiano V, Ford D, Mabugu T, Napierala Mavedzenge S, Miners A, Mugurungi O, et al. Assessment of the potential impact and cost-effectiveness of self-testing for HIV in low-income countries. J Infect Dis. 2015;212(4):570–7.
27. Phillips AN, Cambiano V, Nakagawa F, Ford D, Lundgren JD, Roset-Bahmanyar E, et al. Potential future impact of a partially effective HIV vaccine in a southern African setting. PLoS One. 2014;9(9):e107214.
28. Phillips AN, Cambiano V, Revill P, Nakagawa F, Lundgren JD, Bansi-Matharu L, et al. Identifying key drivers of the impact of an HIV cure intervention in sub-Saharan Africa. J Infect Dis. 2016;214(1):73–9.
29. Phillips AN, Pillay D, Garnett G, Bennett D, Vitoria M, Cambiano V, et al. Effect on transmission of HIV-1 resistance of timing of implementation of viral load monitoring to determine switches from first to second-line antiretroviral regimens in resource-limited settings. AIDS. 2011;25(6):843–50.
30. Phillips A, Shroufi A, Vojnov L, Cohn J, Roberts T, Ellman T, et al. Sustainable HIV treatment in Africa through viral-load-informed differentiated care. Nature. 2015;528(7580):S68–76.
31. Phillips AN, Cambiano V, Nakagawa F, Revill P, Jordan MR, Hallett TB, et al. Cost-effectiveness of public-health policy options in the presence of pretreatment NNRTI drug resistance in sub-Saharan Africa: a modelling study. Lancet HIV. 2018;5(3):e146–54.
32. Bansi-Matharu L, Cambiano V, Apollo T, Yekeye R, Dirawo J, Musemburi S, et al. 90-90-90 by 2020? Estimation and projection of the adult HIV epidemic and ART programme in Zimbabwe – 2017 to 2020. J Int AIDS Soc. 2018;21(11):e25205.
33. Integrating HIV/STD prevention in the school setting. UNAIDS Position Paper. August1997.
34. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV pre-exposure prophylaxis (PrEP) for all populations: a systematic review and meta-analysis. AIDS. 2016;30(12):1973–83.
35. Ministry of Health and Child Care. Zimbabwe population-based HIV impact assessment (ZIMPHIA) 2015–16: first report. Harare, Zimbabwe: Ministry of Health and Child Care; July2017.
36. Kerrigan D, Kennedy CE, Morgan-Thomas R, Reza-Paul S, Mwangi P, Win KT, et al. A community empowerment approach to the HIV response among sex workers: effectiveness, challenges, and considerations for implementation and scale-up. Lancet. 2015;385(9963):172–85.
37. World Health Organisation. Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organisation; 2014.
38. Foundation BMG. Micro-planning in peer led outreach programs – a handbook. New Dehli: Bill & Melinda Gates Foundation; 2013.
39. Fearon E, Phillips A, Mtetwa S, Chabata ST, Mushati P, Cambiano V, et al. How can programmes better support female sex workers to avoid HIV infection in Zimbabwe? A prevention cascade analysis. J Acquir Immune Defic Syndr. 2019 Feb 7. doi: 10.1097/QAI.0000000000001980. [Epub ahead of print].
40. Blanchard JF, Bhattacharjee P, Kumaran S, Ramesh BM, Kumar NS, Washington RG, et al. Concepts and strategies for scaling up focused prevention for sex workers in India. Sex Transm Infect. 2008;84 Suppl 2:ii19–23.
41. Vassall A, Pickles M, Chandrashekar S, Boily M-C, Shetty G, Guinness L, et al. Cost-effectiveness of HIV prevention for high-risk groups at scale: an economic evaluation of the Avahan programme in South India. Lancet Global Health. 2014;2(9):e531–40.

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RESEARCH ARTICLE

The role of costing in the introduction and scale-up of HIV pre-exposure prophylaxis: evidence from integrating PrEP into routine maternal and child health and family planning clinics in western Kenya

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Abstract

Introduction: Understanding the cost of strategies to reach and deliver pre-exposure prophylaxis (PrEP) to priority populations is essential to assess the cost-effectiveness and budget impact of HIV prevention programmes. Providing PrEP through maternal and child health and family planning clinics offers a promising strategy to reach women in high HIV burden settings. We estimated incremental costs and explored the cost drivers of integrating PrEP delivery into routine maternal and child health and family planning services in Kenya.

Methods: We conducted a costing study from the provider perspective within the PrEP Implementation for Young Women and Adolescents programme in western Kenya. We identified all within- and above-facility activities supporting PrEP delivery and measured clinical service time using time-and-motion studies. We obtained input costs from programme budgets, expenditure records and staff interviews. We estimated changes in costs if creatinine testing were postponed from initiation to first follow-up visit and if PrEP were prioritized to clients at high HIV risk using a behavioural risk assessment tool. We also projected costs under Ministry of Health (MOH) implementation assuming MOH salaries and programme supervision. We estimated annual numbers of PrEP visits from programme data abstracted from 16 facilities between November 2017 and June 2018. We report the cost per client-month of PrEP dispensed in 2017 USD.

Results: For an annual programme output of 24,005 screenings, 4198 PrEP initiations and 4427 follow-up visits, the average cost per client-month of PrEP dispensed in the study was $26.52. Personnel, drugs and laboratory tests comprised 43%, 25% and 14% of programme costs respectively. Postponing creatinine testing and prioritizing PrEP delivery to clients at high HIV risk reduced total programme costs by 8% and 14% respectively. In the MOH scenario assuming no changes in outputs, the projected cost per client-month of PrEP dispensed decreased to $16.54 and total programme costs decreased by 38%.

Conclusions: Incremental PrEP costs are sensitive to the service delivery strategy used to engage priority populations. Postponing creatinine testing and prioritizing PrEP delivery to clients at high HIV risk may reduce costs. Context-specific cost data are crucial to assess the cost-effectiveness and affordability of PrEP delivery models.

Keywords: HIV; PrEP; women; prevention; cost-effectiveness; health economics; cost analysis

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | INTRODUCTION

Despite remarkable progress in expanding access to antiretroviral therapy (ART), an estimated 200,000 women aged 15 to 24 in sub-Saharan Africa were newly infected with HIV in 2017 [1]. Pre-exposure prophylaxis (PrEP) prevents HIV infection and offers promise as a female-controlled HIV prevention strategy [2,3]. Effective models for PrEP delivery to young women are needed to maximize population-level benefits. Budgets have competing demands, and evidence on the cost, affordability and potential impact of PrEP programmes is necessary to guide policy decisions about the choice and implementation of prevention interventions [4].

PrEP programmes that achieve widespread coverage and adherence among individuals at high risk of acquiring HIV infection (priority populations) will maximize population-level impact [5-11]. However, the cost and yield of engaging priority populations will vary across settings, affecting cost-effectiveness and budget impact conclusions [12]. While several studies have projected the potential cost-effectiveness of PrEP delivery in sub-Saharan Africa, few service delivery models for identifying and providing PrEP to priority populations have been defined that could substantiate the costs assumed in modelling studies [13-18]. Primary costing studies of PrEP delivery are sparse, and research describing how costs vary across outreach and service delivery strategies is limited [19-21].

Integrating PrEP into other medical and nonmedical services may be an efficient strategy for reaching priority populations. For example, offering PrEP to women through maternal and child health (MCH) or family planning (FP) programmes may have low incremental costs. Pregnant and postpartum women in sub-Saharan Africa have high HIV incidence, and recent evidence suggests that HIV risk may be elevated in pregnancy and postpartum periods [22-24]. However, no prior studies have estimated the cost of delivering PrEP to women through MCH and FP clinics. A previous modelling study of PrEP administration to pregnant and breastfeeding women varied PrEP programme costs per patient-year from $80 to $720 per year, reflecting large uncertainty in the absence of data [25].

We present the results from a costing study for the PrEP Implementation for Young Women and Adolescents (PrIYA) programme, an implementation project delivering PrEP in 16 MCH and FP clinics in western Kenya. We estimated the incremental cost of integrating PrEP delivery into routine MCH and FP services. Furthermore, we explored the cost implications of service delivery modifications such as timing of creatinine monitoring and prioritized delivery to women identified as having high risk for HIV infection.

2 | METHODS

2.1 | Study setting

The PrIYA programme is an implementation project to evaluate PrEP delivery strategies to young women through MCH and FP clinics in Kenya [26]. PrIYA is part of the DREAMS Innovation Challenge funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and managed by JSI Research & Training Institute, Inc. In collaboration with Department of Health and Sanitation, Kisumu County and the Kenya National AIDS and STI Control Programme (NASCOP), PrIYA has been implemented in 16 facilities (nine public hospitals, four mission hospitals, one private hospital, one health centre and one dispensary) in Kisumu County and involves centralized supervision and administration by programme staff. This region has an estimated adult HIV prevalence of 16% and high incidence of HIV among pregnant women [27,28]. Women attending MCH and FP clinics are screened by nurses for behavioural risk factors for HIV and willingness to consider PrEP. All medically eligible (HIV-negative and creatinine clearance <50 mL/min by national guidelines) women who are interested in PrEP are offered same-day PrEP initiation and can return to the same clinic for monthly follow-up visits and refills [29]. PrEP is delivered either by the same nurse providing routine MCH and FP services or by a separate nurse in an adjoining room. Nurses perform point-of-care creatinine testing at initiation and dispense medication directly to clients. Additional programme details have been described elsewhere [30]. The PrIYA protocol was approved by the University of Washington Human Subjects Division and the Kenyatta National Hospital/University of Nairobi Ethical Review Committee. Participants provided oral informed consent.

2.2 | Costs

We estimated the incremental economic cost of PrEP delivery from the provider perspective following the principles outlined in the Global Health Cost Consortium Reference Case [31]. We categorized costs as either fixed (constant irrespective of programme output over the course of one year) or variable (costs directly related to programme output). To estimate variable costs, we measured resource use at a sample of eight facilities representative of clinic size, ownership (public, mission or private), and type (MCH vs FP). For each PrEP clinical activity (behavioural screening and counselling, initiation, and follow-up visits), we measured the cost of drugs, clinical personnel, laboratory testing and other supplies. We estimated clinical personnel unit costs using time-and-motion studies and multiplying the average time spent in each activity (in minutes) by the cost per minute (including both salary and benefits). For supplies and commodity costs, we observed resource use for each activity and multiplied the relevant quantity by input costs obtained from programme budgets or centralized price lists. Drug costs for oral co-formulated tenofovir disoproxil fumarate/emtricitabine ($6.75 per 30 days) included the cost of purchase from the manufacturer as well as central storage and distribution costs. Fixed costs included centralized start-up costs (microplanning and training), capital (equipment, furniture), overheads (e.g. building costs, transportation and airtime) and administrative and supervisory personnel supporting PrEP delivery. We annualized start-up and capital costs over the expected useful life (assumed to be five years or fewer) using a discount rate of 3% [31]. We allocated building space based on the proportion of all MCH or FP visits that included a PrEP encounter. We multiplied the average size of the room in which PrEP screening and initiation were conducted by a rental rate estimated from nearby commercial properties. This analysis excludes the cost of any research activities that would not be part of routine PrEP service delivery.

We calculated programme-level average unit costs for each clinical activity (screening, initiation and follow-up visits) by allocating fixed costs to each activity and adding the activity's average variable cost. Fixed costs that could not be assigned exclusively to a single activity were apportioned using hourly rate allocation based on clinical service time [32]. We adjusted all costs to 2017 currency using GDP deflators and converted to US dollars (USD) using the 2017 average exchange rate (1 USD = KSh 103.40) [33]. We analysed costs in Excel 2018 (Microsoft, Redmond, USA). Additional details about the costing methodology, including the Excel file used for the analysis, are available in the Supporting Information.

2.3 | Programme volume

We used data collected as part of routine monitoring to estimate the numbers of women screened, initiated and dispensed PrEP over a one-year period. Study staff abstracted standardized client records in all 16 facilities from 20 November 2017 to 15 June 2018. We extrapolated programme volume to one year assuming no changes in the pattern of visits. We analysed programme volume using R version 3.5.1 [34]. Further details are available in the Supporting Information.

2.4 | Cost metrics

We estimated the total programme cost (across 16 facilities) by multiplying the number of screening, initiation and follow-up visits by their respective average unit costs and summing the total. We then calculated the cost per client-month of PrEP dispensed as follows:

$$\text{Cost per client-month of PrEP dispensed} = \frac{\text{Total programme cost}}{\text{\# months of PrEP dispensed}}$$

2.5 | Scenarios

To evaluate the potential cost ramifications of different delivery scenarios, we projected costs incurred under the following conditions: (1) postponing creatinine testing to the first follow-up visit rather than initiation; (2) restricting PrEP initiation to clients identified as having high risk for acquiring HIV; and (3) if the programme were entirely implemented through the Ministry of Health (MOH).

The first scenario (postponing creatinine testing) is motivated both by the low prevalence (8/4007) of ineligible creatinine tests among PrIYA clients at initiation as well as the considerable proportion of clients who choose to discontinue PrEP within a month after initiating. This scenario is expected to decrease programme costs by reducing the number of creatinine tests conducted. For the second scenario, we categorized clients as having high risk of HIV infection based on reporting at least one of the following risk factors assessed at their first PrEP screening visit: (1) current partner with unknown or positive HIV status; (2) positive rapid plasma regain syphilis test; or (3) reporting at least one of the following in the prior six months: (a) exchanging sex for money or other favours; (b) diagnosis or treatment for a sexually transmitted infection; (c) forced to have sex against will; (d) experiencing intimate partner violence; (e) sharing needles while engaging in injection drug use; or (f) using post-exposure prophylaxis more than twice. Assessment of these specific risk factors for PrEP consideration is recommended as part of national guidelines [29]. This scenario is expected to decrease total programme costs by reducing the number of clients who initiate and continue on PrEP.

In the third scenario, we revised costs to reflect a programme implemented entirely through the MOH. First, we adjusted clinical personnel salaries to reflect government cadre-specific salary scales (including benefits). Second, we estimated the cost of facility, sub-county and county supervisory activities that are planned to subsume PrIYA administrative staff responsibilities. Last, we replaced the cost of the point-of-care assay used in PrIYA with the average facility price for creatinine testing. These projections assume no changes in programme output. We conducted a sensitivity analysis under the MOH scenario to explore how costs might change with varying uptake and retention, assuming constant fixed costs.

3 | RESULTS

3.1 | Overall programme costs and unit costs

For an annual programme output of 24,005 screenings, 4198 PrEP initiations, and 4427 follow-up visits, the estimated total annual programme cost as implemented was $204,253 (Table 1). Personnel (43%), drugs (25%) and laboratory tests (14%) comprised the largest cost categories. Supervision and administration accounted for nearly two-thirds of personnel costs. The average cost per client-month of PrEP dispensed was $26.52. The unit costs of PrEP screening, initiation and follow-up encounters were $2.91, $19.18 and $12.16 respectively (Table 2).

3.2 | Cost implications of service delivery modifications

Table 3 shows the estimated impact of postponing creatinine testing to the first follow-up visit or prioritizing PrEP initiation to clients at high risk of HIV infection on the total programme cost and cost per month of PrEP dispensed. Postponing creatinine testing would reduce the annual number of tests by

Table 1. Total programme cost and average cost per client-month of PrEP dispensed (2017 USD)

	Total annual cost (USD)	Average cost per client-month of PrEP dispensed (USD)
Variable		
Personnel (clinical)	37,535	4.87
Drugs	51,997	6.75
Laboratory testing	27,830	3.61
Other supplies	3,616	0.47
Sub-total	120,978	15.71
Fixed		
Microplanning	1,366	0.18
Training	2,898	0.38
Personnel (supervision and administration)	50,924	6.61
Capital (e.g. creatinine machines, furniture)	3,925	0.51
Overhead (e.g. building, airtime, transportation)	24,162	3.14
Sub-total	83,275	10.81
Summary	204,253	26.52

Table 2. Unit cost breakdown by clinical activity (2017 USD)

	Screening	Initiation	Follow-up[a]
Variable unit cost			
Personnel (clinical)	0.91	1.47	2.14
Drugs	0.00	6.75	5.34
Laboratory testing	0.00	5.76	0.83
Other supplies	0.02	0.32	0.41
Sub-total	0.93	14.30	8.71
Fixed unit cost	1.98	4.88	3.45
Total unit cost (variable + fixed)	2.91	19.18	12.16
Number	24,005	4,198	4,427
Total annual cost	69,876	80,525	53,852

[a]Follow-up unit costs are weighted averages of the costs of visits with (79%) and without (21%) PrEP dispensation.

two-thirds (from 4198 to 1370) and decreases estimated programme costs by 7.5%, resulting in a cost of $24.53 per client-month of PrEP dispensed. Clients at high risk for HIV infection (at least one baseline risk factor) accounted for 34% of screening encounters but 68% of PrEP initiations. The most common risk factor was having a partner of unknown status (89% of clients with at least one baseline risk factor). Restricting PrEP initiation to clients at high risk of HIV lowered total programme costs by 14%. Under this scenario, the cost per client-month of PrEP dispensed only to clients with high risk of HIV infection was $31.88.

3.3 | Projected costs under MOH implementation

We projected how programme costs might change under Kisumu County MOH implementation assuming no changes in outputs. Substituting public-sector clinical staff salaries for PrIYA nurse salaries decreased the cost per client-month of PrEP dispensed from $26.52 to $25.92 (Table 4). Using the estimated cost of planned MOH supervision in place of PrIYA administration lowered the cost per client-month of PrEP dispensed from $25.92 to $18.00. Replacing the cost of the point-of-care creatinine assay with facility creatinine prices further decreased the cost per client-month of PrEP dispensed to $16.54. Overall, we estimated the total programme cost under the MOH scenario to be $127,421, which constitutes a 38% decrease compared to PrIYA implementation, and the average cost per client-month of PrEP dispensed decreased to $16.54. The largest cost components were drugs (41%), personnel (33%) and laboratory tests (15%) (Figure 1 and Figure S3). Overall personnel costs were 52% lower under the assumption that project coordinator staff activities would be subsumed under existing facility and above-facility supervisory structures.

We evaluated the sensitivity of costs under the MOH scenario to assumptions about programme output. Doubling both the proportion of screening encounters that result in an initiation (from 17% as observed to 34%) and the average number of follow-up visits within a year among clients with at least one follow-up visit (from 2.6 as observed to 5) increases estimated programme costs by 224% and lowers the cost per client-month of PrEP dispensed to $12.96. In comparison, halving both uptake and retention increases the cost per client-month of PrEP dispensed to $25.31 while reducing total programme costs by 42%.

Table 3. Estimated cost implications of service delivery modifications

Scenario	Total annual cost (USD)	Cost per client-month of PrEP dispensed (USD)
As implemented	204,253	26.52
Postponed creatinine[a]	188,932	24.53
Prioritized delivery to clients at high risk for HIV infection[b]	175,793	31.88[c]

[a]Creatinine testing postponed from initiation to first follow-up visit; [b]High risk is defined as having at least one of the following risk factors at baseline: Current partner with unknown or positive HIV status, positive rapid plasma reagin syphilis test, or reporting at least one of the following in the prior six months: exchanging sex for money or other favours, diagnosis or treatment for a sexually transmitted infection, forced to have sex against will, experiencing intimate partner violence (IPV), sharing needles while engaging in injection drug use, using post-exposure prophylaxis more than twice; [c]Unit cost is calculated by dividing the total programme cost by the number of person-months of PrEP dispensed to clients at high risk of HIV infection.

4 | DISCUSSION

We explored the relationship between costs and service delivery strategies using primary data from an implementation study of integrating PrEP into MCH and FP clinics, as part of the DREAMS Innovation Challenge funded by PEPFAR.

Table 4. Cost projections under Ministry of Health (MOH) implementation assuming constant output

Scenario	Total annual cost (USD)	Cost per client-month of PrEP dispensed (USD)
As implemented	204,253	26.52
With public-sector clinical staff salaries	199,613	25.92
With MOH supervision[a] and public-sector clinical staff salaries	138,609	18.00
With facility creatinine testing[b], MOH supervision[a], and public-sector clinical staff salaries	127,421	16.54

[a]PrIYA administrative staff responsibilities are subsumed into routine facility, sub-county and county supervision; [b]Using prices for facility-based creatinine testing instead of a point-of-care assay.

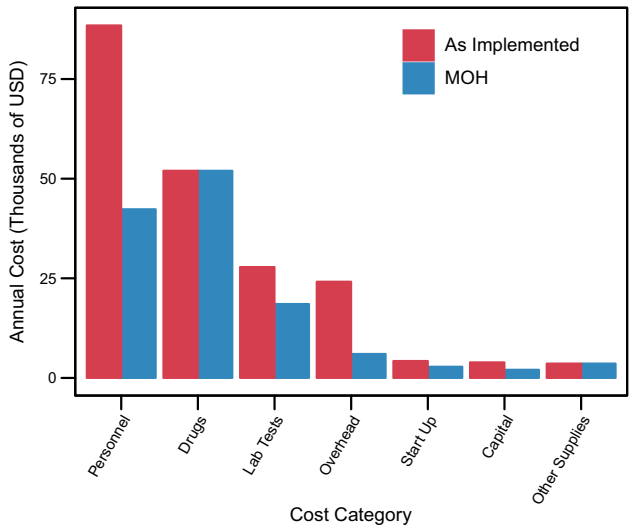

Figure 1. Total annual programme cost (2017 USD) by category as implemented and in the Ministry of Health (MOH) scenario. The MOH scenario assumes public sector clinical staff salaries instead of study salaries; study administrative staff responsibilities are subsumed into routine facility, sub-county, and county supervision; and facility-based creatinine testing instead of point-of-care.

Offering PrEP to women through MCH and FP clinics as done in this study would cost on average $26.52 per client-month of PrEP dispensed, with personnel and drugs accounting for 43% and 25% of programme costs respectively. In comparison, an analysis of PrEP delivery to female sex workers and men who have sex with men (MSM) in Nairobi that found that drugs accounted for 15-19% of total costs [20]. The Nairobi study estimated higher unit costs ($33 to 44 per client-month of PrEP dispensed) than our study despite similar drug unit costs. The difference in the two programme costs may reflect the increased resources used in outreach efforts needed to contact FSW and MSM compared to a clinic-based strategy that integrated PrEP within existing services. However, our estimated unit costs are higher than analyses among FSW and MSM conducted in South Africa, which estimated costs per client-month of $17-18 [10,19]. This programme had substantially lower drug costs (<$5 per month) as well as high uptake and retention, both of which contributed to lower unit costs. Additional efforts are needed to better understand differences between delivery strategies and to standardize cost reporting.

Prioritizing PrEP delivery to clients at high risk for HIV infection can reduce total costs if these clients are easily identified. In our study, total programme costs decrease by 14% if initiation occurs only among clients with baseline behavioural risk factors. Clients with baseline risk factors were more likely to initiate PrEP, demonstrating that risk prioritization is to some extent occurring as these clients self-select to initiate PrEP when universally offered [26]. Eighty-nine percent of clients with a baseline risk factor had a partner with unknown HIV status, highlighting that increasing partner testing could improve client risk assessment. Given the low cost of HIV self-test kits ($2 as negotiated by the Bill and Melinda Gates Foundation), providing HIV self-test kits to promote partner testing might be an efficient method for refining client decisions about PrEP [35,36]. The utility of these strategies will depend on the how well risk can be evaluated by both client and provider. An ongoing randomized trial using an HIV risk assessment tool designed for peripartum women and self-testing to guide PrEP delivery among pregnant women will help evaluate the potential impact of this strategy [37,38]. In the process of risk assessment, it is also important that PrEP delivery programmes do not stigmatize women or suggest they are the primary population responsible for HIV prevention. Validated and context-specific risk assessment tools for a range of populations, including men, are needed to guide prevention programmes.

Creatinine testing consumed significant resources, and previous studies of reducing the frequency of kidney function monitoring have not shown harm [39]. Due to high numbers of clients discontinuing PrEP after initiation, deferral of creatinine testing from initiation to the first follow-up visit would save an estimated 7.5% of overall programme costs. Notably, only 0.2% of clients in the programme had creatinine clearance measured at less than 50 mL/min at initiation (the NASCOP threshold for PrEP ineligibility). Postponing creatinine testing by one month does not present a major departure from Kenya national guidelines, which recommend baseline and then annual testing but permit PrEP delivery without testing if laboratory facilities are unavailable [29].

Implementation projects are essential for demonstrating the impact and costs of strategies for introducing PrEP to at-risk populations; however, their costs may not reflect typical MOH settings. Our analysis projects overall programme costs could decrease by 38% under routine MOH implementation. This large potential cost reduction is consistent with previous PrEP costing studies that have compared observed costs to projections in an MOH scenario. A demonstration project of PrEP as a bridge to ART among serodiscordant couples in Uganda reported estimated unit costs of $408 (as studied) and $92 (MOH scenario) per couple per year [40]. However, the projected costs in the MOH scenario were highly sensitive to assumptions about programme volume. The degree to which unit costs will change will depend on how programme output is affected by changes in staff and supervision.

Within a facility-based setting, additional service delivery modifications may affect PrEP costs. For example, providing multiple months of PrEP prescription for established clients could improve retention by requiring fewer visits, as has been demonstrated in some ART programmes [41,42]. Additionally, task shifting PrEP screening counselling to HTS counsellors may reduce costs and alleviate nurse time burden. HIV testing provides a natural entry point for discussions about HIV prevention and PrEP use, as PrEP initiation is contingent upon a negative test and behavioural assessment. While task shifting HIV services has demonstrated efficiency gains across a wide variety of settings [43,44], it is possible that programme output would be affected. Implementation studies are needed to evaluate the utility of these models.

Our analysis has several limitations. The baseline behavioural risk factors used to classify clients are not based on a validated risk score and may not fully capture HIV risk. The unit cost of client-month of PrEP dispensed reflects neither the client's true HIV risk nor drug adherence, both of which are crucial parameters for cost-effectiveness studies. In addition, our assumption of constant volume with reduced costs under MOH implementation may be unrealistic. Programme output may decrease without PrIYA clinical staff and

programme support. Alternatively, PrEP uptake and retention may increase over time with expanded community awareness and sensitization, and counselling time may decrease as clients become more familiar with the intervention. Improving demand generation, messaging and support strategies will be critical to increasing PrEP usage in this population [3,45]. We did not address whether additional MOH clinical staff would be required to support PrEP initiation, which would add human resource costs. Last, the 16 facilities involved in PrIYA were primarily hospitals in urban and semi-urban environments that may benefit from economies of scale. These facilities may not be representative of all MCH and FP clinics in western Kenya, so caution must be taken in generalizing these cost estimates to other settings. We were not able to address facility-level variation in PrEP service delivery costs given the centralized implementation of the programme; further research under routine conditions is needed to identify facility-level drivers of service delivery costs.

Despite these limitations, cost projections are useful to evaluate the relative impact that programme modifications may have on budgets. Benefits of offering PrEP through MCH and FP services include potential economies of scope and convenient access to a priority population, without ancillary outreach activities to needed reach them. However, the degree to which women perceive themselves at risk and choose to take PrEP as part of routine MCH and FP services will critically affect costs, coverage and impact. While our study focused on a PrEP delivery strategy for women, ongoing cost data collection efforts nested in implementation science evaluations are needed to provide up-to-date evidence on the costs of delivery strategies to reach other priority populations, including adolescents, serodiscordant couples, FSW and MSM. Such data will be critical for understanding the potential success of PrEP programmes at the country level and will serve as invaluable inputs to mathematical models that aim to produce more accurate estimates of potential cost-effectiveness.

5 | CONCLUSIONS

MCH and FP services offer a potential PrEP delivery platform to efficiently reach large numbers of at-risk women in high HIV burden settings. Postponing creatinine testing and prioritizing PrEP delivery to clients at high HIV risk are potential strategies to reduce costs. Sub-population-specific costing studies are needed to evaluate the costs of delivering PrEP to priority populations in other settings. Cost-effectiveness studies of PrEP scale-up need context-specific costing data in order to accurately inform policy.

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COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHORS' CONTRIBUTION

DAR, CL and RVB designed and conducted the study with contributions from FA, HL, JK, JP, AB, JMB and GJS. GBG and SF provided insight into the interpretation of the results and assisted with writing the manuscript. DAR wrote the first draft of the manuscript. All authors have read and approved the final manuscript.

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REFERENCES

1. UNAIDS. UNAIDS estimates. 2018 [cited 2018 Sep 15]. Available at: http://aidsinfo.unaids.org/
2. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. AIDS. 2016;30:1973–83.
3. Celum CL, Delany-Moretlwe S, McConnell M, van Rooyen H, Bekker L-G, Kurth A, et al. Rethinking HIV prevention to prepare for oral PrEP implementation for young African women. J Int AIDS Soc. 2015;18:20227.
4. Mugo NR, Ngure K, Kiragu M, Irungu E, Kilonzo N. The preexposure prophylaxis revolution; from clinical trials to programmatic implementation. Curr Opin HIV AIDS. 2016;11:80–6.
5. Pretorius C, Stover J, Bollinger L, Bacaër N, Williams B. Evaluating the cost-effectiveness of pre-exposure prophylaxis (PrEP) and its impact on HIV-1 transmission in South Africa. PLoS One. 2010;5:e13646.
6. Anderson S-J, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. Lancet. 2014;384:249–56.
7. Hallett TB, Baeten JM, Heffron R, Barnabas R, de Bruyn G, Cremin Í, et al. Optimal uses of antiretrovirals for prevention in HIV-1 serodiscordant heterosexual couples in South Africa: a modelling study. PLoS Med. 2011;8:e1001123.
8. Cremin I, Alsallaq R, Dybul M, Piot P, Garnett G, Hallett TB. The new role of antiretrovirals in combination HIV prevention: a mathematical modelling analysis. Wolters Kluwer Heal AIDS. 2013;27:447–58.
9. Schnure M, Kripke K, Forsythe S, Hamilton M, Dent J, Reidy M, et al. Oral Pre-Exposure Prophylaxis (PrEP) modeling for strategic planning: results from thirteen countries. 22nd Int. AIDS Conf., Amsterdam: 2018.
10. Meyer-Rath G, Jamieson L, Leuner R, Johnson L. Finding the right target population for PrEP: the cost-effectiveness of pre-exposure prophylaxis provision to female and male adolescents and young women in South Africa. 9th IAS Conf. HIV Sci., Paris; 2017.
11. McGillen JB, Anderson S-J, Hallett TB. PrEP as a feature in the optimal landscape of combination HIV prevention in sub-Saharan Africa. J Int AIDS Soc. 2016;19:21104.
12. Cremin Í, Hallett TB. Estimating the range of potential epidemiological impact of pre-exposure prophylaxis. AIDS. 2015;29:733–8.
13. Gomez GB, Borquez A, Case KK, Wheelock A, Vassall A, Hankins C. The cost and impact of scaling up pre-exposure prophylaxis for HIV prevention: a systematic review of cost-effectiveness modelling studies. PLoS Med. 2013;10:e1001401.
14. Cambiano V, Miners A, Phillips A. What do we know about the cost–effectiveness of HIV preexposure prophylaxis, and is it affordable? Curr Opin HIV AIDS. 2016;11:56–66.
15. Cremin I, Morales F, Jewell BL, O'Reilly KR, Hallett TB. Seasonal PrEP for partners of migrant miners in southern Mozambique: a highly focused PrEP intervention. J Int AIDS Soc. 2015;18:19946.

16. Mitchell KM, Lépine A, Terris-Prestholt F, Torpey K, Khamofu H, Folayan MO, et al. Modelling the impact and cost-effectiveness of combination prevention amongst HIV serodiscordant couples in Nigeria. AIDS. 2015;29:2035–44.
17. Nichols BE, Baltussen R, van Dijk JH, Thuma PE, Nouwen JL, Boucher CAB, et al. Cost-effectiveness of PrEP in HIV/AIDS control in Zambia: a stochastic league approach. J Acquir Immune Defic Syndr. 2014;66:221–8.
18. Nichols BE, Boucher CAB, van Dijk JH, Thuma PE, Nouwen JL, Baltussen R, et al. Cost-Effectiveness of Pre-Exposure Prophylaxis (PrEP) in preventing HIV-1 infections in rural Zambia: a modeling study. PLoS One. 2013;8:e59549.
19. Eakle R, Gomez GB, Naicker N, Bothma R, Mbogua J, Cabrera Escobar MA, et al. HIV pre-exposure prophylaxis and early antiretroviral treatment among female sex workers in South Africa: results from a prospective observational demonstration project. PLOS Med. 2017;14:e1002444.
20. Cremin I, McKinnon L, Kimani J, Cherutich P, Gakii G, Muriuki F, et al. PrEP for key populations in combination HIV prevention in Nairobi: a mathematical modelling study. Lancet HIV. 2017;4:e214–22.
21. Ying R, Sharma M, Heffron R, L Celum C, M Baeten J, Katabira E, et al. Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda. J Int AIDS Soc. 2015;18:20013.
22. Drake AL, Wagner A, Richardson B, John-Stewart G. Incident HIV during pregnancy and postpartum and risk of mother-to-child HIV transmission: a systematic review and meta-analysis. PLoS Med. 2014;11:e1001608.
23. Thomson KA, Hughes J, Baeten JM, John-Stewart G, Celum C, Cohen CR, et al. Increased risk of HIV acquisition among women throughout pregnancy and during the postpartum period: a prospective per-coital-act analysis among women with HIV-infected partners. J Infect Dis. 2018;218:16–25.
24. WHO. WHO expands recommendation on oral pre-exposure prophylaxis of HIV infection (PrEP). WHO; 2018.
25. Price JT, Wheeler SB, Stranix-Chibanda L, Hosek SG, Watts DH, Siberry GK, et al. Cost-effectiveness of pre-exposure HIV prophylaxis during pregnancy and breastfeeding in Sub-Saharan Africa. J Acquir Immune Defic Syndr. 2016;72:S145–53.
26. Kinuthia J, Pintye J, Mugwanya KK, Serede M, Sila J, Abuna F, et al. High PrEP uptake among kenyan pregnant women offered PrEP during antenatal care. Boston, Massachussetts: Conf. Retroviruses Opportunistic Infect; 2018.
27. National AIDS and STI Control Programme. Kenya HIV Estimates. 2018.
28. Kinuthia J, Drake AL, Matemo D, Richardson BA, Zeh C, Osborn L, et al. HIV acquisition during pregnancy and postpartum is associated with genital infections and partnership characteristics. AIDS. 2015;29:2025–33.
29. Kenya Ministry of Health. Guidelines on use of antiretroviral drugs for treating and preventing HIV infection in Kenya. 2016.
30. Pintye J, Kinuthia J, Roberts DA, Wagner AD, Mugwanya K, Abuna F, et al. Integration of PrEP services into routine antenatal and postnatal care: experiences from an implementation program in Western Kenya. J Acquir Immune Defic Syndr. 2018; 79(5):590–595.
31. Vassall A, Sweeney S, Kahn J, Gomez GB, Bollinger L, Marseille E, et al. Reference case for estimating the costs of global health services and interventions. 2017.
32. Finkler SA, Ward DM, David M, Baker JJ. Essentials of cost accounting for health care organizations. Burlington, MA: Jones and Bartlett Publishers; 2007.
33. OANDA. Average Exchange Rates. n.d. [cited 2018 Sep 10]. Available at: https://www.oanda.com/currency/average
34. R Core Team. R: a language and environment for statistical computing. 2018.
35. Masters SH, Agot K, Obonyo B, Napierala Mavedzenge S, Maman S, Thirumurthy H. Promoting partner testing and couples testing through secondary distribution of HIV self-tests: a randomized clinical trial. PLOS Med. 2016;13:e1002166.
36. Ngure K, Heffron R, Mugo N, Thomson KA, Irungu E, Njuguna N, et al. Feasibility and acceptability of HIV self-testing among pre-exposure prophylaxis users in Kenya. J Int AIDS Soc. 2017;20:21234.
37. John-Stewart G. PrEP Implementation for Mothers in Antenatal Care (PrIMA). ClinicalTrialsGov n.d. [cited 2048 Sep 10]. Available at: https://clinicaltrials.gov/ct2/show/NCT03070600
38. Pintye J, Drake AL, Kinuthia J, Unger JA, Matemo D, Heffron R, et al. A risk assessment tool for identifying pregnant and postpartum women who may benefit from pre-exposure prophylaxis (PrEP). Clin Infect Dis. 2016;64:ciw850.
39. Mugwanya KK, Baeten JM, Wyatt C, Mugo NR, Celum CL, et al. Frequency of monitoring kidney function in HIV-uninfected persons using daily oral tenofovir disoproxil fumarate pre-exposure prophylaxis. J Acquir Immune Defic Syndr. 2018:77(2):206–211.
40. Ying R, Sharma M, Heffron R, Celum CL, Baeten JM, Katabira E, et al. Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda. J Int AIDS Soc. 2015;18:20013.
41. Grimsrud A, Barnabas RV, Ehrenkranz P, Ford N. Evidence for scale up: the differentiated care research agenda. J Int AIDS Soc. 2017;20:22024.
42. Prust ML, Banda CK, Nyirenda R, Chimbwandira F, Kalua T, Jahn A, et al. Multi-month prescriptions, fast-track refills, and community ART groups: results from a process evaluation in Malawi on using differentiated models of care to achieve national HIV treatment goals. J Int AIDS Soc. 2017;20:21650.
43. Seidman G, Atun R. Does task shifting yield cost savings and improve efficiency for health systems? A systematic review of evidence from low-income and middle-income countries. Hum Resour Health. 2017;15:29.
44. Callaghan M, Ford N, Schneider H. A systematic review of task- shifting for HIV treatment and care in Africa. Hum Resour Health. 2010;8:8.
45. Eakle R, Venter F, Rees H. Pre-exposure prophylaxis (PrEP) in an era of stalled HIV prevention: can it change the game? 2018;15:29.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Overview diagram of costing methodology.

Figure S2. Map of PrIYA health facilities in Kisumu County, Kenya.

Figure S3. Percentage of total programme cost across cost categories as implemented and under Ministry of Health (MOH) scenario.*

Table S1. Input costs of key PrEP delivery components (2017 USD)

Table S2. Time (minutes) for clinical service delivery components estimated from time-and-motion studies

Table S3. Total annual programme cost and unit cost per client-month of PrEP dispensed (2017 USD) in Ministry of Health (MOH) scenario*

Table S4. Unit cost breakdown by clinical activity (2017 USD) under Ministry of Health (MOH) scenario*

Table S5. 5% Discount rate

Table S6. 10% Discount rate

Table S7. 15% Discount rate

Data S1. Cost Calculations Spreadsheet.

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RESEARCH ARTICLE

HIV prevention programme cascades: insights from HIV programme monitoring for female sex workers in Kenya

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Abstract

Introduction: HIV prevention cascades have emerged as a programme management and monitoring tool that outlines the sequential steps of an HIV prevention programme. We describe the application of an HIV combination prevention programme cascade framework to monitor and improve HIV prevention interventions for female sex workers (FSWs) in Kenya.

Methods: Two data sources were analysed: (1) annual programme outcome surveys conducted using a polling booth survey methodology in 2017 among 4393 FSWs, and (2) routine programme monitoring data collected by (a) 92 implementing partners between July 2017 and June 2018, and (b) Learning Site in Mombasa (2014 to 2015) and Nairobi (2013). We present national, sub-national and implementing partner level cascades.

Results: At the national level, the population size estimates for FSW were 133,675 while the programme coverage targets were 174,073. Programme targets as denominator, during the period 2017 to 2018, 156,220 (90%) FSWs received peer education and contact, 148,713 (85%) received condoms and 83,053 (48%) received condoms as per their estimated need. At the outcome level, 92% of FSWs used condoms at the last sex with their client but 73% reported consistent condom use. Although 96% of FSWs had ever tested for HIV, 85% had tested in the last three months. Seventy-nine per cent of the HIV-positive FSWs were enrolled in HIV care, 73% were currently enrolled on antiretroviral therapy (ART) and 52% had attended an ART clinic in the last month. In the last six months, 48% of the FSWs had experienced police violence but 24% received violence support. National and sub-national level cascades showed proportions of FSWs lost at each step of programme implementation and variability in programme achievement. Hotspot and sub-population level cascades, presented as examples, demonstrate development and use of these cascades at the implementation level.

Conclusions: HIV prevention programme cascades, drawing on multiple data sources to provide an understanding of gaps in programme outputs and outcomes, can provide powerful information for monitoring and improving HIV prevention programmes for FSWs at all levels of implementation and decision-making. Complexity of prevention programmes and the paucity of consistent data can pose a challenge to development of these cascades.

Keywords: key population; HIV prevention; Kenya; cascade; monitoring

Additional Supporting Information may be found online in the Supporting Information tab for this article.

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1 | INTRODUCTION

Despite the progress made by prevention programmes globally, the decline in new HIV infections among adults has slowed in the past decade [1]. According to UNAIDS, HIV prevention services are not being provided on an adequate scale, with sufficient intensity, nor reaching those most in need [2]. Combination prevention for key populations (KPs) has been identified as a key pillar in the UNAIDS HIV Prevention Road Map 2020 [3]. Approximately 40% of new HIV infections in 2017 occurred among KPs including female sex workers (FSWs), men who have sex with men (MSM), people who inject drugs (PWID) and transgender persons [2]. Kenya's HIV epidemic is driven by sexual transmission and is generalized, meaning it affects all sections of the population [4]. However, a disproportionate number of new infections occur among KPs [4], estimated at 33% of new infections annually in Kenya [5]. HIV prevalence in Kenya among FSWs is 29.3%, MSM 18.2% and PWID 18.7% [6] compared to an estimated national adult HIV prevalence of 4.8% [7].

For HIV prevention efforts to have an impact, increased emphasis on evidence-driven programme design and implementation, strategic and iterative programme monitoring, and rigorous evaluation of outcomes are required [8]. Cascade analysis has been used in measuring success in HIV care and this strategy has been translated to HIV prevention programmes recently with the development of HIV prevention cascades [9]. A prevention cascade defines important steps in a comprehensive prevention programme, provides estimates of the proportions of populations engaged or lost at each step and provides a framework for planning further actions to improve programmes [10]. Prevention cascades take into account the linkage between various programme elements [11] and offer insights for programme implementers and national decision makers on how best to analyse bottlenecks and develop solutions to improve programme outcomes for a more effective HIV prevention response [12].

However, challenges to the design and implementation of prevention cascades are complexity of prevention programmes and the paucity of consistent data. HIV prevention programmes are not as linear as HIV testing and treatment programmes, making it more difficult to define a prevention cascade as a series of sequential steps [12]. There is an array of different prevention needs for different populations and the context in which these populations live and work, and the barriers that they experience [13], adding complexity to the definition of prevention processes as a single cascade. Moreover, the monitoring of HIV prevention programmes requires the incorporation of combination prevention approach, capturing behavioural, biomedical and structural interventions outcomes at scale [14]. In addition, the use of aggregate level data may mask heterogeneity in population and thus more detailed and nuanced information on specific sub-populations that are not being reached is required [15]. While the cascade analysis helps identify gaps, unless there are consistent processes to understand and analyse the bottlenecks that are causing these gaps, programmes cannot identify opportunities to address them at all levels of programme design and implementation [16]. While current HIV prevention cascades use a demand and supply framework [10,14], we demonstrate the application of an HIV prevention programme cascade to measure globally recommended HIV programme outcomes [17]. This involves an embedded process of analysis which deliberately avoids predetermined assumptions for loss along the cascade and instead uses data to identify gaps and further explores opportunities by conducting continuous iterative refinement of interventions to address the gaps identified [16]. This approach builds on our team's previous work in India [18] and this paper demonstrates the application of this approach and learnings in the Kenyan context.

In this paper, we use data from the Kenya KP HIV Prevention Programme, led by the National AIDS and STI Control Programme (NASCOP), Ministry of Health, covering 32 out of the 47 counties (sub-national geographical and administrative units) in the country. KP behaviours are criminalized in Kenya which increases their vulnerability to stigma, discrimination and violence [19]. The Kenya KP programme recommends implementation of combination prevention interventions in accordance with global guidance [17,20]. The FSW programme has been scaled up to reach over 156,220 FSWs in 32 counties [21]. Since 2018, the KP programme has been using an HIV prevention programme cascade approach on a quarterly and annual basis for monitoring and management [22]. The aim of this paper is to describe the application of an HIV prevention programme cascade framework to monitor and improve HIV prevention interventions with FSWs and the utility of this approach for decision-making at the national, sub-national and implementation levels in Kenya.

2 | METHODS

2.1 | Data sources

We used two data sources to characterize HIV prevention programme cascades:

2.1.1 | Annual programme outcome surveys

NASCOP has been conducting annual outcome surveys with KPs using polling booth survey (PBS) methodology [23] which is designed to minimize the reporting bias which can be seen with face-to-face interview methods [24,25]. A PBS is a group interview method in which participants' responses are unlinked and anonymous. As previously described elsewhere [23], a two-stage, stratified cluster sampling methodology was used to recruit FSWs for the PBS. For the first stage of sampling in each study site, hotspots were selected as the primary sampling units (PSUs). A "hotspot" was defined as any physical location where FSWs meet their clients. At the second stage, respondents were randomly selected from the PSUs. We used data from a PBS conducted in 2017 among 4393 FSW in 13 counties [26].

2.1.2 | Routine programme monitoring data

Kenya conducted size estimation of FSWs in 2012 in 32 counties using a geographic mapping approach [27] and estimated approximately 133,675 FSWs (range 76,674 to 208,711) [28]. Ninety-two KP implementing partners in Kenya collected routine monitoring data on a monthly basis using standard NASCOP reporting tools [29]. Routine programme monitoring data collected by these implementing partners between July 2017 and June 2018 were used to develop national and county level cascades. We also used data from NASCOP Learning Sites [30] for HIV Prevention for FSWs implemented between 2013 and 2014 in Nairobi and implemented between August 2014 and July 2015 in Mombasa to characterize a hotspot-based programme cascade and sub-population level programme cascade desegregated by age at implementation partner level respectively.

2.2 | Data analysis

We used both data sources described above to determine programme inputs, outputs and outcomes to develop national programme prevention cascades. Size estimation data and programme coverage targets, as established by donors to the implementing partners, for the period were used as programme inputs. The coverage target of FSWs as per Kenya AIDS Strategic Framework 2014/15 to 2018-18 is 90% of estimated FSW population [4] and programme coverage is defined as the proportion of FSWs that receive a defined set of services that address their risk and vulnerability [20]. To arrive at the programme outputs, we aggregated the data for the period to arrive at an annual figure and used it as a

numerator against the programme coverage targets (the denominator). Following indicators were used: (i) received peer education and contacts; (ii) received condoms; and (iii) received condoms as per estimated need. Condom need was calculated as 76 condoms per month for FSWs on an average, derived from evidence on client volume per month per FSW in 2017. 2017 PBS data were analysed for programme outcomes: (1) behavioural outcomes: (a) condom use at last sex with any paying client and (b) any occasion when had sex with any paying client without using a condom in the last one month; (2) biomedical outcomes: (a) ever tested for HIV; (b) tested for HIV in the past three months; (c) ever enrolled in care (among all FSWs living with HIV (PLHIV)); (d) currently on antiretroviral therapy (ART) (all PLHIV); and (e) ever missed an appointment in the last one month (this indicator was used as a proxy indicator to measure adherence to ART); (3) structural outcomes: (a) arrested or beaten up by police in the last six months and (b) received any support when experienced violence. Similar indicators were used to analyse and develop HIV prevention programme cascades for implementation partners at the hotspot/peer educator level and sub-population level. Tables S1,S2,S3 show the indicators and data used for analysis.

2.3 | Ethical approval

Ethical approval was received from the Kenyatta National Hospital-University of Nairobi Ethical Review Committee, approval number P647/11/2017, to conduct secondary data analysis of the programme monitoring data, including the annual programme outcome surveys (PBS).

3 | RESULTS

3.1 | HIV prevention programme cascade at the national level

Figure 1 shows that the national size estimate of FSWs was 133,675 (range 76,674 to 208,711) and the programme coverage target was 174,073 FSWs. Out of the total programme coverage target, in the year 2017 to 2018, 90% of the FSWs received peer education and contact, 85% of the FSWs received condoms and 48% of the FSWs received condoms as per their estimated need. Although 92% of the FSWs reported using condoms with paying clients in the last sex act, 73% used condoms consistently in the last month. Among the FSW respondents, 96% reported receiving an HIV test in their lifetime, and 85% had tested for HIV in the last three months. Among those FSWs who were HIV positive, 79% were enrolled in HIV care, 73% were currently enrolled with an ART centre and 52% visited the ART clinic in the last one month. While 48% of FSWs had experienced police violence in the past six months, 24% received support to address this violence.

3.2 | HIV prevention programme cascade at the sub-national level

Figures 2 (Nairobi), 3 (Mombasa), 4 (Kiambu) and 5 (Kisumu) present HIV prevention programme cascades across four counties to depict sub-national variability in cascades. Out of the total programme coverage target in the year 2017 to 2018, 117% of the FSWs in Nairobi, 84% in Mombasa, 74% in Kiambu and 68% in Kisumu received peer education and contact every quarter. All the FSWs in Nairobi, 83% in Mombasa, 72% in Kiambu and 67% in Kisumu received condoms every quarter, and 50% of FSWs in Nairobi, 58% in Mombasa, 33% in Kiambu and Kisumu, respectively, received condoms as per their estimated need. In Nairobi, 91% of the FSWs, 92% in Mombasa, 91% in Kiambu and 92% in Kisumu reported using condoms with paying clients in the last sex act; 78% in Nairobi, 69% in Mombasa, 76% in Kiambu and 84% in Kisumu used condoms consistently in the last month. Among the respondents, 82% in Nairobi, 85% in Mombasa, 89% in Kiambu and 80% in Kisumu had tested for HIV in the last three months and among those who were HIV positive, 75% in Nairobi, 53% in Mombasa, 72% in Kiambu and 90% in Kisumu were enrolled in HIV care, 65% in Nairobi, 47% in Mombasa, 65% in Kiambu and 85% were currently enrolled with an ART centre, and 45% in Nairobi, 27% in Mombasa, 42% in Kiambu and 64% in Kisumu visited the ART clinic in the last one month. Among the FSWs, 56% in Nairobi, 43% in Mombasa, 53% in Kiambu and 31% in Kisumu had experienced police violence in the past six months, and 24% of FSWs in Nairobi, 17% in Mombasa, 27% in Kiambu and 22% in Kisumu received support to address this violence.

3.3 | HIV prevention programme cascade for implementation partner at the hot spot/peer educator level

Figure 6 shows an example of a prevention cascade at the hotspot level developed by one peer educator in Learning Site in Nairobi. In the Kenya programme, a FSW peer educator is responsible for 60 to 80 FSWs in 1 to 3 hotspots [31]. As shown in Figure 6, out of the 80 FSWs who were estimated to be available in a hotspot, the peer educator was able to enrol 30 FSWs in the programme. However, in the reporting month, she met and provided information to 45 FSWs (56%) in the hotspot, 30 (38%) received condoms from her, 13 FSWs (16%) attended the clinic and all 13 received HIV testing services in the clinic. After development of this cascade, the FSW peer educator used this visual communication to assess the reasons why proportions of FSWs in the hotspot were lost at each step of programme delivery as stated in the figure.

3.4 | HIV prevention programme cascade for implementation partner at the sub-population level

At the implementation level, we also examined microlevel data using this approach to understand the profiles of those who were lost to follow-up at different implementation steps. Figure 7 shows one such cascade analysis among FSWs in Learning Site in Mombasa, disaggregated by age. Out of 7281 FSWs registered in the Learning Site, 2619 (36%) were <24 years. During the reporting period, among the registered FSWs < 24 years versus those who were >24 years, we found that 71% versus 88% received peer education and contact, 54% versus 77% received condoms and 19% versus 27% received condoms as per their estimated need. 45% FSW < 24 years versus 54% of the FSWs > 24 years were enrolled in the project clinic, 23% versus 34% received STI screening and 18% versus 25% received HIV testing services.

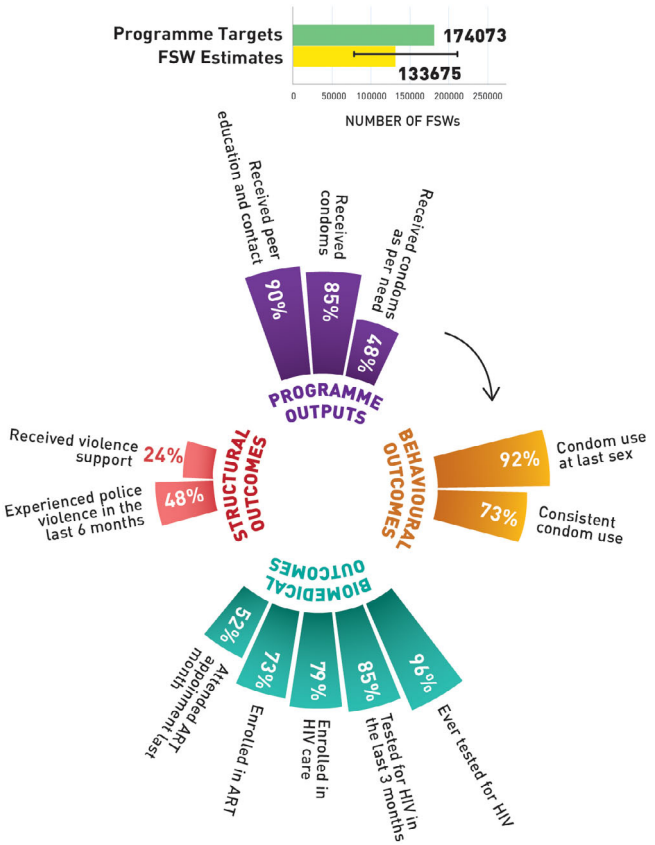

Figure 1. HIV prevention programme cascades, FSW, Kenya.
FSW, female sex worker; ART, antiretroviral treatment.

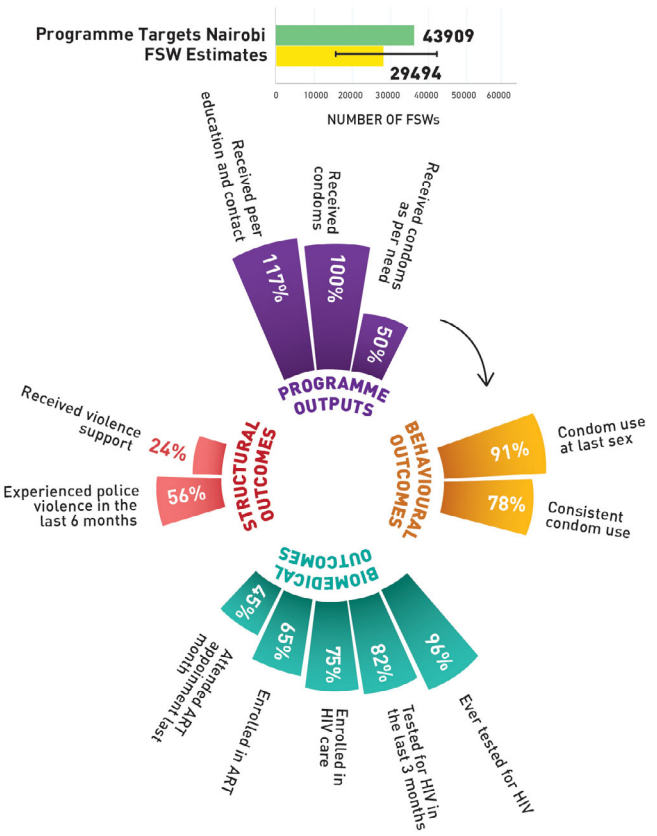

Figure 2. HIV prevention programme cascade for FSW, Nairobi County, Kenya.
FSW, female sex worker; ART, antiretroviral treatment.

4 | DISCUSSION

The recognized need for effective and efficient HIV programmes for KPs call for the development and use of effective monitoring methods that can provide timely and actionable information about programme progress and gaps [32]. A combination prevention approach emphasizes a multisectoral view that includes behavioural, biomedical and structural interventions [12]. Using data from Kenya, we have tried to illustrate the development and use of HIV prevention programme cascades at both the macro (national and subnational) and micro (implementation) levels for HIV combination prevention programmes for FSWs. The embedded analysis provides important findings for programme design, delivery and optimization.

At the national level, we found that the programme coverage targets were within the upper FSW size estimates range. Across programme outputs, there were high levels of coverage of FSWs by peer education and condom distribution (>80%) but there were also consistent gaps between the estimated need for condoms and the actual number of condoms distributed. In terms of programme outcomes, condom use at last sex act was high at 92%, (although slightly lower than the global target of 95% [33]) but, levels of consistent condom use needed improvement. Evidence shows that only when need is substantially met and the supplies are adequate, then programmes can try to understand other reasons for inconsistent condom use [34]. There is need for FSW programmes in Kenya to prioritize addressing condom supply and distribution gaps. Rates of HIV testing were high, but linkage to care, and ART initiation and adherence needed improvement. This emphasizes the need to devise not only differentiated ART service delivery approaches for FSWs, but also to address individual-level and structural barriers, such as stigma, discrimination, violence and drug-use, to initiate and adhere to ART programme [35]. Experience of police violence in the past six months was high and the proportion of FSWs receiving violence support was very low, pointing to the need to strengthen structural interventions. Violence is a structural barrier that decreases the ability of FSWs to access services or adopt protective behaviours [36]. An effective violence prevention and response programme not only impacts FSWs at an individual level, but improves collective agency and challenges power dynamics at the community level [37]. Commonly, structural components to an HIV programme are not included in a standard HIV prevention cascades and hence not measured; yet they are critical part of a comprehensive HIV prevention programme and standard global guidance.

At the sub-national level, the analysis of county-level variability provides valuable information for prioritization of counties for support. While coverage of FSWs with peer education and condom distribution was high in Mombasa and Nairobi (>80%), these outputs needed improvement in Kisumu and Kiambu counties. Condoms distributed did not meet the estimated need, and this was particularly evident in Kisumu and

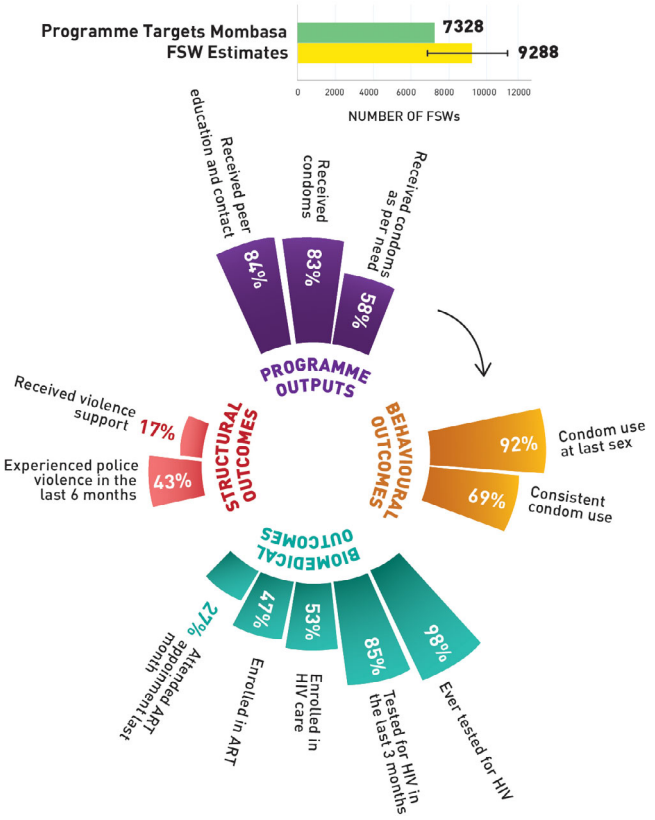

Figure 3. HIV prevention programme cascade for FSW, Mombasa County, Kenya.
FSW, female sex worker; ART, antiretroviral treatment.

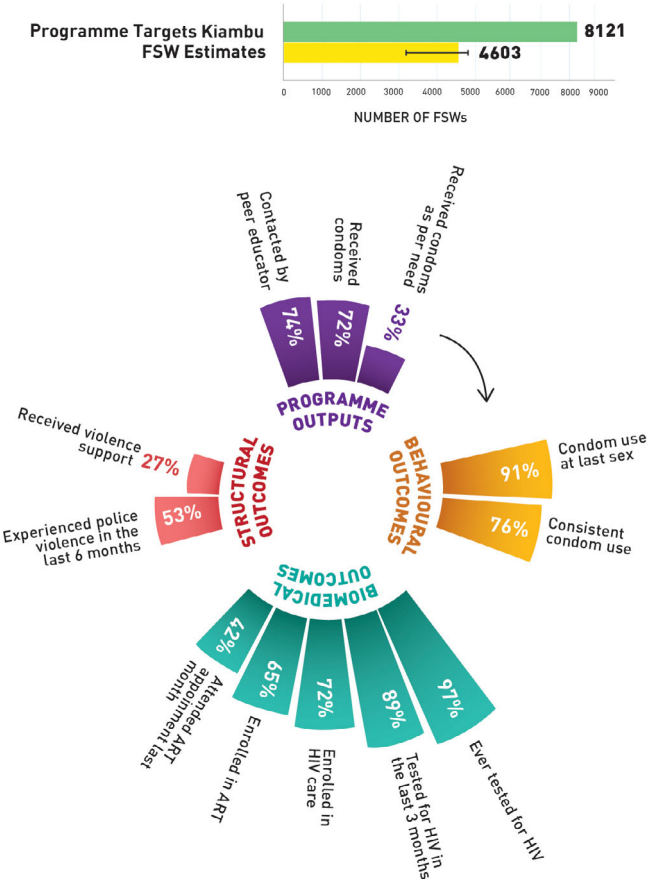

Figure 4. HIV prevention programme cascade for FSW, Kiambu County, Kenya.
FSW, female sex worker; ART, antiretroviral treatment.

Kiambu counties. Linkage to care and ART was poor in all counties except Kisumu. Adherence to ART was poor across the counties, and was particularly low in Mombasa. Levels of police violence were very high, with over 40% of FSWs experiencing violence in three of the counties and violence support was very low across all counties. The analysis shows that while all counties needed support in certain common areas, specific counties needed specific support like behavioural interventions in Kisumu county, linkage to ART for HIV-positive FSWs in Mombasa and violence response mechanisms in Nairobi and Kiambu counties.

The KP Programme Manager in Kenya uses this analysis and information to guide programme improvement and design. This analysis is shared on a quarterly basis at the KP Technical Working Group and quarterly donor meetings to help the stakeholders understand programme gaps and jointly look for solutions to address the gaps. National-level technical strategies are devised to address key gaps. Technical support is provided to the priority counties and the implementing partners from the KP Technical Support Unit (TSU) based at NASCOP as and when necessary to address the gaps.

Implementation-level prevention programme cascades can be analysed in multiple ways. At the hotspot level, a peer educator through the cascade analysis identified the gaps to be low enrolment of the FSWs in the hotspot and lower visits to the clinic. Using the cascade, she analysed the reasons for these gaps and devised strategies to enrol more FSWs in the hotspot and motivate them to visit the clinics. Engaging frontline workers, particularly peer educators, in cascade analysis is an important step in building ownership and accountability among the frontline community staff [33], and ensuring that all KPs receive required services. Previously in India and now in Kenya, this analysis has been referred to as opportunity gap analysis [16,18,38].

Using a prevention programme cascade for FSW sub-population (desegregated data of FSWs by age), the Learning Site was able to better understand the difference between sub-populations and their access and uptake of prevention services. The analysis shows that the enrolment of FSWs below 24 years was lower in the programme generally and even among those who were enrolled, a higher proportion of them were lost at each step of service delivery. This important heterogeneity often gets missed when examining programme "averages" or overall outcomes. Our findings are similar to an analysis conducted in the "Transitions" study [39] in Mombasa, which identified that only 26% of young FSWs reported being contacted by any programme [40]. This "programme access gap," when examined further, showed that by the second year in sex work, only 15% of young FSWs had been contacted by programmes [40]. The challenges of reaching young FSWs have been also highlighted in other published literature from Africa [41]. This analysis highlights the importance of disaggregating data by relevant characteristics to unmask the nuanced

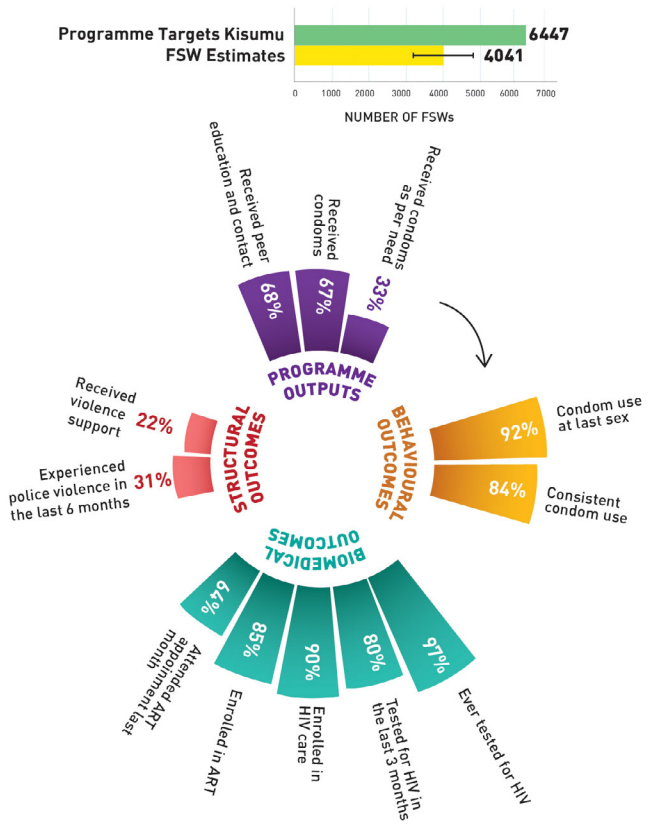

Figure 5. HIV Prevention programme cascade for FSW, Kisumu County, Kenya.
FSW, female sex worker; ART, antiretroviral treatment.

gaps that occur in sub-populations [42] to prioritize reaching the unreached.

HIV prevention programme cascades are useful for visualizing progress, but need to be designed to follow programme logic. Our approach measures performance and identifies gaps across HIV combination prevention programme, geographies (national, sub-national and hotspot) and sub-populations, by tracking inputs, key outputs and outcomes on a regular basis. This requires clear definitions of programme numerators and denominators to understand reach and coverage, and as we have demonstrated, multiple data sources can be utilized [43]. Prevention programme cascades should include simple, flexible and visual tools that facilitate analysis within this framework [16]. Decentralized analysis by frontline workers can lead to early identification of programme challenges and stimulate local problem-solving [33].

A limitation to our study is that our data only allows for cross-sectional cascades rather than cohort cascades, so we are unable to follow progression over time through the cascades. Another limitation of the study is paucity of data related to structural interventions and hence only one metric (violence) was used in this context. Lack of availability of recent KP size estimates is also a limitation as the size estimates may have been outdated in 2018. Nevertheless, there are many strengths to our approach. It uses routinely collected monitoring data from two sources to generate cascades across key outputs and outcomes for an combination HIV prevention programme with FSWs. The cascades also emphasize the need to embed an analytical process at the macro- and microlevels which involves managers at the national and local levels, and peer educators at the hotspot level. The tools and methods are simple to use, inexpensive, replicable, and have been applied on a large scale.

5 | CONCLUSIONS

Prevention programme cascades serve as an effective framework to track and monitor the important programme outputs and outcomes at all levels of combination programming with FSWs. We propose in future to advance beyond linear HIV cascades to the generation and use of cascades to measure

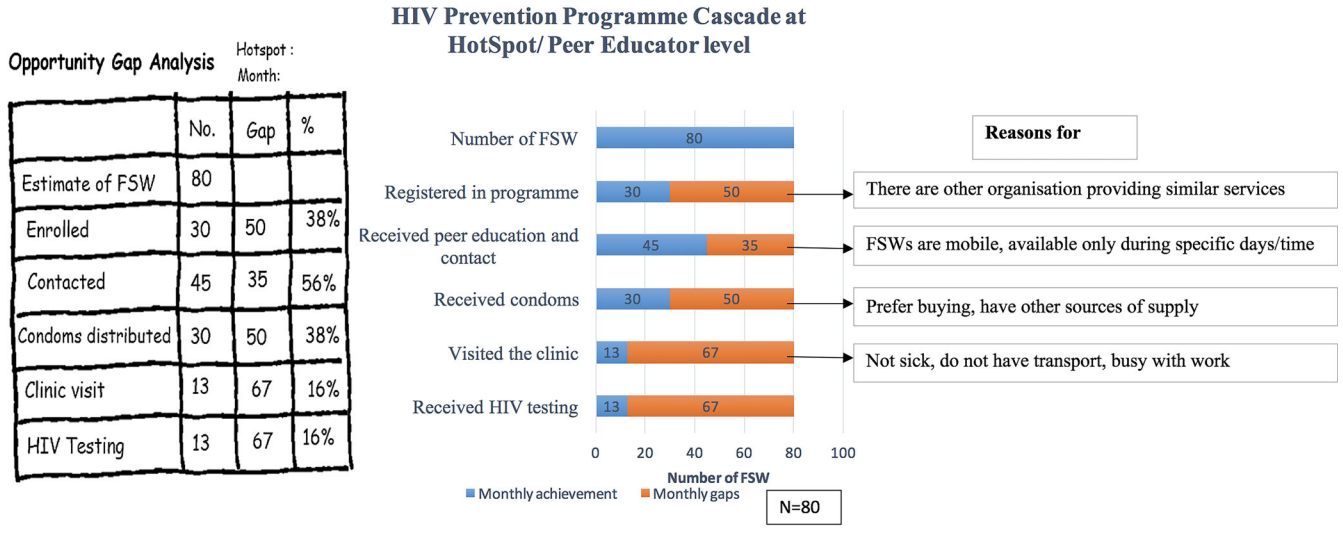

Figure 6. HIV prevention programme cascade for implementing partner at hot spot level, Learning site, Nairobi.
FSW, female sex worker.

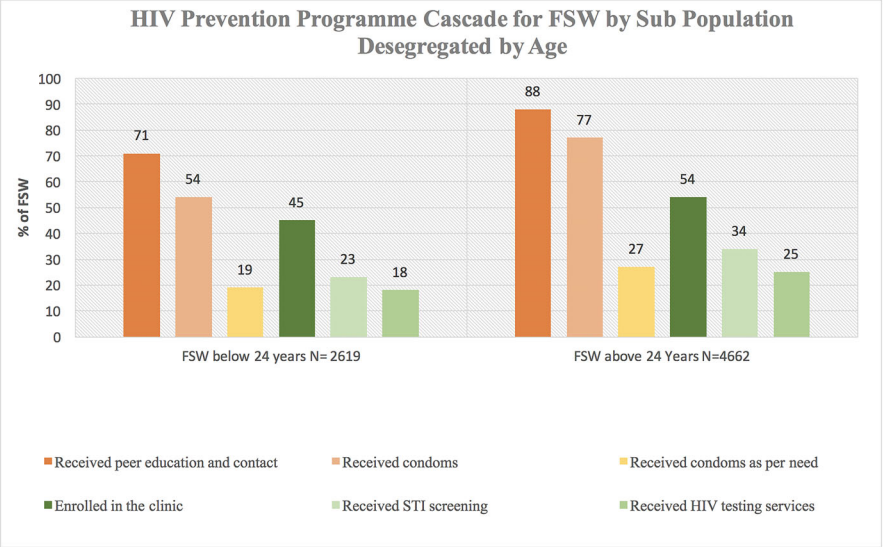

Figure 7. HIV prevention programme cascade for FSW, Mombasa Learning Site.
FSW, female sex worker; STI, Sexually Transmitted Infections.

outputs and outcomes across combination prevention programming, using data from multiple sources to capture heterogeneity across prevention interventions. Adaptation of some of these learnings in the context of other KPs like MSM and PWID and another countries or programme would have to take in account the HIV epidemic, the need of the populations and context of that country or programme, so as to fit the relevant contexts and needs.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

PB, HKM, MB, SM and JB conceptualized the paper. PB wrote the first draft of the paper, and HKM, MB, JB, SM, SI and SM contributed in writing different sections of the paper and reviewing the drafts. HKM and PB generated the data and managed the data collection process. JM, JK and SK supported in data collection and analysis. PB, MB, SM, SM, SKI and JB analysed various elements of the data. All co-authors reviewed the paper and made revisions.

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DISCLAIMER

None.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS. Prevention gap report. Geneva: UNAIDS; 2016 [Accessed 2018 August 2]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf
2. Joint United Nations Programme on HIV/AIDS. Miles to go. Closing gaps, breaking barriers, righting injustices. Global AIDS Update. Geneva: UNAIDS; 2018 [Accessed 2018 August 2]. Available from: http://www.unaids.org/en/20180718_GR2018
3. Joint United Nations Programme on HIV/AIDS. HIV prevention 2020 road map. Geneva: Joint United Nations Programme on HIV/AIDS; 2017.
4. National AIDS Control Council (NACC). Kenya AIDS strategic framework 2013/4-2018/19. Nairobi: Government of Kenya; 2014.
5. National AIDS Control Council (NACC). Kenya AIDS response progress report, 2016. Nairobi: Government of Kenya; 2017.
6. National AIDS and STI Control Programme (NASCOP). 2010-2011 Integrated biological and behavioural surveillance survey among key populations in Nairobi and Kisumu, Kenya. Nairobi: Government of Kenya, Ministry of Public Health and Sanitation; 2014.
7. National AIDS Control Council (NACC). Kenya HIV estimates 2017. Nairobi: Government of Kenya; 2018.
8. Isbell MT, Kilonzo N, Mugurungi O, Bekker LG. We neglect primary HIV prevention at our peril. Lancet HIV. 2016;3(7):e284–5.
9. Amico RK. Developing a HIV prevention cascade, current approaches and future direction. International Conference on HIV Treatment and Prevention

Adherence. Washington, DC: International Association of Providers in AIDS Care; 2015.
10. Garnett GP, Hallett TB, Takaruza A, Hargreaves J, Rhead R, Warren M, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. Lancet HIV. 2016;3(7):e297–306.
11. USAID, PEPFAR, Health Policy Plus. Best practices in cascade analytics and costing as steps to 95-95-95. Presented at Webinar Series: Five Ways to Accelerate Progress Toward the 95-95-95 Goals, February 2018.
12. Godfrey-Faussett P. The HIV prevention cascade: more smoke than thunder. Lancet HIV. 2016;3(7):e286–8.
13. Bauer GR, Travers R, Scanlon K, Coleman TA. High heterogeneity of HIV-related sexual risk among transgender people in Ontario, Canada: a province-wide respondent-driven sampling survey. BMC Public Health. 2012;12:292.
14. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
15. Blanchard J. What happened to the other 90s? The unintended consequences of test and treat interventions for key populations. Dublin: IUSTI; 2018.
16. Thompson L, Bhattacharjee P, Anthony J, Shetye M, Moses S, Blanchard J. A systematic approach to the design and scale-up of targeted interventions for HIV prevention among urban female sex workers. Bangalore, India: Karnataka Health Promotion Trust, University of Manitoba and World Bank; 2012.
17. World Health Organization, United Nations Population Fund, Joint United Nations Programme on HIV/AIDS, Global Network of Sex Work Projects, World Bank, United Nations Development Programme. Implementing comprehensive HIV/STI programmes with sex workers: practical approaches from collaborative interventions. Geneva: World Health Organization; 2013 [Accessed 2018 August 2]. Available from: http://www.nswp.org/sites/nswp.org/files/SWIT_en_UNDP%20logo.pdf
18. Blanchard JF, Bhattacharjee P, Kumaran S, Ramesh BM, Kumar NS, Washington RG, et al. Concepts and strategies for scaling up focused prevention for sex workers in India. Sex Transm Infect. 2008;84 Suppl II:ii19–23.
19. National AIDS Control Council (NACC) and National AIDS and STI Control Programme (NASCOP). Policy for prevention of HIV infections among key populations in Kenya. Nairobi: Government of Kenya; 2016.
20. National AIDS & STI Control Programme (NASCOP). National guidelines for HIV/STI programming with key populations. Nairobi: Government of Kenya, 2014 [Accessed 2018 August 15]. Available from: http://www.icop.or.ke/wp-content/uploads/2016/10/KP-National-Guidelines-2014-NASCOP.pdf
21. National AIDS and STI Control Programme (NASCOP). Quarterly programme monitoring report, June 2018. Nairobi: Government of Kenya; 2017.
22. National AIDS and STI Control Programme (NASCOP). Minutes of the key population. Technical Working Group Meeting, Nairobi, Kenya: NASCOP; March 2018.
23. Bhattacharjee P, McClarty LM, Musyoki H, Anthony J, Kioko J, Kaosa S, et al. Monitoring HIV prevention programme outcomes among key populations in Kenya: findings from a national survey. PLoS ONE. 2015;10(8):e0137007.
24. Béhanzin L, Diabaté S, Minani I, Lowndes CM, Boily MC, Labbé AC, et al. Assessment of HIV related risky behaviour: a comparative study of face-to-face interviews and polling booth surveys in the general population of Cotonou, Benin. Sex Transm Infect. 2013;89:595–601.
25. Lowndes CM, Jayachandran AA, Banandur P, Ramesh BM, Washington R, Sangameshwar BM, et al. Polling booth surveys: a novel approach for reducing social desirability bias in HIV-related behavioural surveys in resource-poor settings. AIDS Behav. 2012;16:1054–62.
26. National AIDS and STI Control Programme (NASCOP). Third National Behavioural Assessment of key populations in Kenya, polling booth survey report. Nairobi: Ministry of Health, Government of Kenya; 2018.
27. National AIDS Control Council (NACC) and National AIDS and STI Control Programme (NASCOP). Geographic mapping of most at risk populations for HIV in Kenya. Nairobi: Ministry of Health; Government of Kenya; 2012.
28. National AIDS and STI Control Programme (NASCOP). Kenya most at risk populations size estimate consensus. Nairobi: National AIDS and STI Control Programme, Government of Kenya; 2013 [accessed 2018 August 25]. Available from: http://www.aidsinfoonline.org/kpatlas/document/KEN/KEN_2012_PSE_Report_FSW_MSM_PWID.pdf
29. National AIDS and STI Control Programme (NASCOP). Key population data collection tools in Kenya: a reference guide. Nairobi: Ministry of Health, Government of Kenya; 2014.
30. McClarty LM, Bhattacharjee P, Isac S, Emmanuel F, Kioko J, Njiraini M, et al. Key programme science lessons form an HIV prevention "Learning Site" for sex workers in Mombasa Kenya. Sex Transm Infect. 2018;94(5):346–52. https://doi.org/10.1136/sextrans-2017-053228.
31. Bhattacharjee P, Musyoki H, Prakash R, Malaba S, Dallabetta G, Wheeler T, et al. Miscroplanning at scale with key populations in Kenya: optimizing peer educator ratios for programme outreach and HIV/ATI service utilization. PLoS ONE. 2018;13(11):e0205056.
32. Steen R, Wheeler T, Gorgens M, Mziray E, Dallabetta G. Feasible, efficient and necessary, without exception – working with sex workers interrupts HIV/STI transmission and brings treatment to many in need. PLoS ONE. 2015;10(10):e0121145. https://doi.org/10.1371/journal.pone.0121145.
33. Dehne KL, Dallabetta G, Wilson D, Garnett GP, Laga M, Benomar E, et al. HIV Prevention 2020: a framework for delivery and a call for action. Lancet HIV. 2016;3(7):e323–32.
34. Weiner R, Fineberg M, Dube B, Goswami P, Mathew S, Dallabetta G, et al. Using a cascade approach to assess condom uptake in female sex workers in India: a review of the Avahan data. BMC Public Health. 2018;18:897.
35. Mountain E, Mishra S, Vickerman P, Pickles M, Gilks C, Boily MC. Antiretroviral therapy uptake, attrition, adherence and outcomes among HIV-infected female sex workers: a systematic review and meta-analysis. PLoS ONE. 2014;9(9):e105645. https://doi.org/10.1371/journal.pone.0105645One.
36. Decker MR, Wirtz AL, Pretorius C, Sherman SG, Sweat MD, Baral SD, et al. Estimating the impact of reducing violence against female sex workers on HIV epidemics in Kenya and Ukraine: a policy modeling exercise. Am J Reprod Immunol. 2013;69 Suppl 1:122–32.
37. Blanchard AK, Mohan HL, Shahmanesh M, Prakash R, Isac S, Ramesh BM, et al. Community mobilization, empowerment and HIV prevention among female sex workers in south India. BMC Public Health. 2013;13:234.
38. National AIDS and STI Control Programme (NASCOP). Microplanning in learning site. Case study. Nairobi: Ministry of Health, Government of Kenya; 2015.
39. Becker ML, Bhattacharjee P, Blanchard JF, Cheuk E, Isac S, Musyoki HK, et al. Vulnerabilities at first sex and their association with lifetime gender-based violence and HIV prevalence among adolescent girls and young women engaged in sex work, transactional sex, and casual sex in Kenya. J Acquir Immune Defic Syndr. 2018;79(3):296–304.
40. Mishra S, Ma H. The prevalence and timing of unmet HIV prevention and care needs of adolescent girls and young women (AGYW) in Mombasa, Kenya. Nairobi: Maisha Webinar, National AIDS Control Council (NACC); 2018.
41. Busza J, Mtetwa S, Mapfumo R, Hanisch D, Wong-Gruenwald R, Cowan F. Underage and underserved: reaching young women who sell sex in Zimbabwe. AIDS Care. 2016;28 Suppl 2:14–20.
42. UN Women. Turning promises into action: gender equality in the 2030 agenda for sustainable development. New York: UN Women; 2018.
43. Parker C. Use it or lose it: how Avahan used data to shape its HIV prevention efforts in India. New Delhi, India: Bill & Melinda Gates Foundation; 2008.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Annual programme outcome survey (polling booth survey data) HIV prevention programme cascade: national and sub-national levels, programme outcomes (Figures 1,2,3,4,5).

Table S2. Routine programme monitoring data, national and sub-national HIV prevention programme cascades: national and sub-national levels, programme outputs (Figures 1,2,3,4,5).

Table S3. Routine programme monitoring data, National AIDS and STI Control Programme (NASCOP) learning site, Mombasa HIV prevention programme cascade: implementation level desegregated by age Figure 7).

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COMMENTARY

Application of the HIV prevention cascade to identify, develop and evaluate interventions to improve use of prevention methods: examples from a study in east Zimbabwe

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Abstract

Introduction: The HIV prevention cascade could be used in developing interventions to strengthen implementation of efficacious HIV prevention methods, but its practical utility needs to be demonstrated. We propose a standardized approach to using the cascade to guide identification and evaluation of interventions and demonstrate its feasibility for this purpose through a project to develop interventions to improve HIV prevention methods use by adolescent girls and young women (AGYW) and potential male partners in east Zimbabwe.

Discussion: We propose a six-step approach to using a published generic HIV prevention cascade formulation to develop interventions to increase motivation to use, access to and effective use of an HIV prevention method. These steps are as follows: (1) measure the HIV prevention cascade for the chosen population and method; (2) identify gaps in the cascade; (3) identify explanatory factors (barriers) contributing to observed gaps; (4) review literature to identify relevant theoretical frameworks and interventions; (5) tailor interventions to the local context; and (6) implement and evaluate the interventions using the cascade steps and explanatory factors as outcome indicators in the evaluation design. In the Zimbabwe example, steps 1-5 aided development of four interventions to overcome barriers to effective use of pre-exposure prophylaxis (PrEP) in AGYW (15-24 years) and voluntary medical male circumcision in male partners (15-29). For young men, prevention cascade analyses identified gaps in motivation and access as barriers to voluntary medical male circumcision uptake, so an intervention was designed including financial incentives and an education session. For AGYW, gaps in motivation (particularly lack of risk perception) and access were identified as barriers to PrEP uptake: an interactive counselling game was developed addressing these barriers. A text messaging intervention was developed to improve PrEP adherence among AGYW, addressing reasons underlying lack of effective PrEP use through improving the capacity ("skills") to take PrEP effectively. A community-led intervention (community conversations) was developed addressing community-level factors underlying gaps in motivation, access and effective use. These interventions are being evaluated currently using outcomes from the HIV prevention cascade (step 6).

Conclusions: The prevention cascade can guide development and evaluation of interventions to strengthen implementation of HIV prevention methods by following the proposed process.

Keywords: HIV prevention cascade; HIV prevention interventions; adolescent girls and young women; young men; Zimbabwe

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1 | INTRODUCTION

HIV prevention cascades may facilitate identification and understanding of gaps in use of primary HIV prevention methods and identification and evaluation of interventions to address the gaps [1-4].

While HIV treatment cascades – describing the steps required to achieve viral suppression [5] – have aided design of interventions to improve treatment programmes (e.g. in Uganda [6]) and cascades are utilized in prevention of mother-to-child HIV transmission programmes [7], formulations of the HIV prevention cascade have been largely theoretical and its utility in identifying appropriate interventions remains to be demonstrated [1-4,8-14]. We present a standardized approach to using the prevention cascade to guide identification, development and evaluation of interventions to increase effective use of HIV prevention methods. We demonstrate the feasibility of this approach by describing the development and pilot testing of interventions to reduce HIV risk among adolescent girls and young women (AGYW) in Manicaland, east Zimbabwe – moving prevention cascades from theory into practice.

2 | DISCUSSION

2.1 | HIV prevention cascade framework

Our preferred HIV prevention cascade framework – developed through multiple consultations [15] – focuses on three domains for prevention method use in a priority at-risk population: motivation, access and effective use (Figure 1A). Effective use is the uptake and adherence required to achieve close to the maximum level of protection against HIV infection afforded by the method. The gap between access and effective use reflects lack of capacity to use the method effectively. Justification of this framework is available [4]. Key features and advantages are as follows: (1) it is generic so can be applied for any primary prevention method(s) or population; (2) effective use – the endpoint of the cascade – is closely aligned with impact (HIV infections averted); (3) it provides a simple core cascade for high-level monitoring and advocacy; (4) ease of application to combination HIV prevention; and (5) it reflects that multiple barriers work together limiting effective use of HIV prevention methods.

2.2 | Standard approach to using the HIV prevention cascade to develop interventions

We propose a series of steps to be followed in using the HIV prevention cascade to identify and evaluate potentially effective interventions to improve use of HIV prevention methods and reduce HIV incidence in an at-risk population:

1. Measure the HIV prevention cascade for the chosen population and method(s)
2. Examine the three steps in the cascade to identify gaps in use of the method(s), thereby identifying broad targets for interventions
3. Use the best available data on the factors contributing to the gaps identified in the cascade (the sub-bars in Figure 1A) to establish which specific barriers should be targeted to increase effective use of the method(s)
4. Review the literature to identify theoretical frameworks and interventions that have potential to reduce the factors identified as barriers to effective use
5. Tailor the interventions to the local epidemiological and socio-economic context
6. Implement the interventions, including the steps and explanatory factors in the HIV prevention cascade as outcomes in the evaluation design

The prevention cascade supports the identification of intervention targets but does not impose specific intervention designs.

2.3 | Practical examples from Manicaland

2.3.1 | Setting and epidemiological context

The HIV prevention cascade is guiding research to develop interventions to reduce HIV incidence in AGYW in Manicaland by increasing effective use of HIV prevention methods including voluntary medical male circumcision (VMMC) in male partners and oral pre-exposure prophylaxis (PrEP) in AGYW.

Manicaland is a rural [16] province that has been identified as an HIV transmission "hotspot" [17] and is a priority area in the Zimbabwe National HIV and AIDS Strategic Plan [18]. Adult (15+) HIV prevalence declined from over 25% in the late 1990s to 11% in 2015-2016 [19]. HIV incidence fell from 1.8% in the mid-2000s to under 1% among females and 0.5% among males [20], partially due to behaviour change [21,22]. HIV prevalence among AGYW (5.4%) in Manicaland is nearly double that of young men (2.9%) [23]. HIV incidence among AGYW remains high (1.4% 2009 to 2013) [20]. AGYW in Manicaland commonly have sexual relationships with older men while condom use is low [24]. Oral PrEP is only available in small-scale research projects [25]. Zimbabwe is a priority country in the DREAMS programme [26]. Manicaland is a priority for PrEP introduction for key populations, including AGYW [27]. VMMC uptake in Manicaland has been slow [28].

2.3.2 | Selection of interventions

The study (Manicaland Study) commenced in July 2018 to identify and test interventions to reduce multi-level barriers preventing AGYW at risk of HIV infection and potential male partners from using efficacious prevention methods. The study is being implemented in eight sites in Manicaland representing different socio-economic strata; VMMC and PrEP were selected being relatively new methods of HIV prevention with high efficacy and potential to contribute more to the overall impact of combination prevention in Zimbabwe.

Data collected between 1998 and 2013 in a general-population cohort study (Manicaland Cohort) [20] were used to measure the preliminary HIV prevention cascades [2,4] (step 1) and identify gaps in motivation, access, and effective use of PrEP and VMMC in AGYW and their male sexual partners (step 2). Cohort data were analysed to establish which specific barriers to effective use of these methods should be targeted by interventions (step 3). These analyses arranged existing Manicaland Cohort data into this framework. Interventions were identified using behavioural economics and community psychology literature (step 4), and developed and tailored to the local context (step 5) using information from previous studies [24,29], including qualitative analyses [30,31]. These interventions are being pilot tested using a cluster-randomized controlled trial design with matched intervention and control clusters in each of the study sites. Indicators based on the HIV prevention cascade are being used as outcomes in this evaluation study. Further details are available at https://clinicaltrials.gov (NCT03565575 and NCT03565588).

The study includes three individual-based interventions, in eight study sites, and a community-based intervention implemented in two of these sites. The study addresses individual- and community-level barriers to HIV prevention use – recognizing that HIV prevention behaviour is influenced by multiple factors acting at different levels [32-34].

Intervention 1: Increasing young men's motivation for and access to VMMC

Increasing effective use of VMMC helps to reduce HIV incidence in AGYW by reducing exposure to HIV infection from their male partners. VMMC is central in Zimbabwe's HIV prevention programme, but only 10% of men (15-49) are

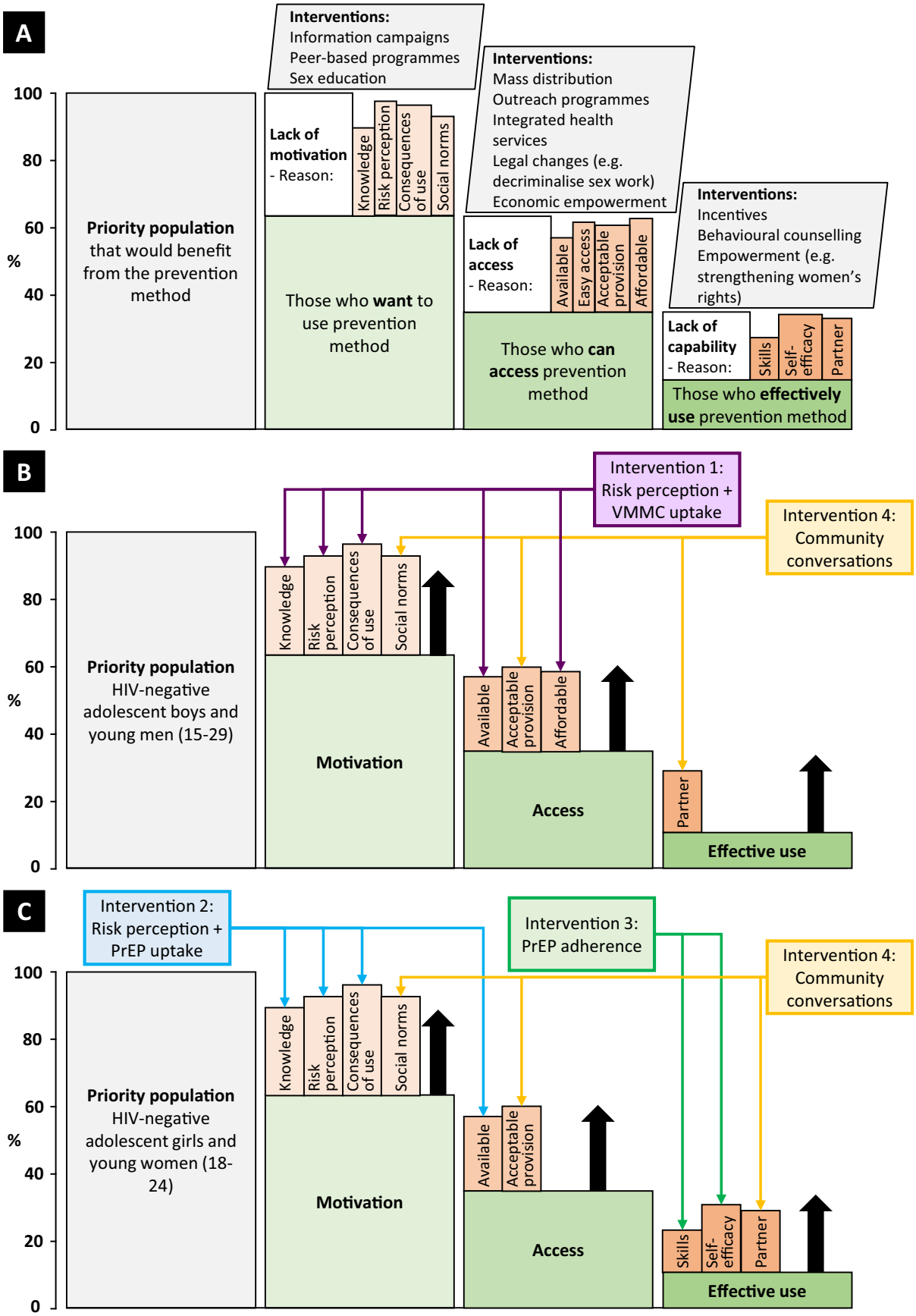
A
Interventions:
Information campaigns
Peer-based programmes
Sex education
Interventions:
Mass distribution
Outreach programmes
Integrated health services
Legal changes (e.g. decriminalise sex work)
Economic empowerment
Interventions:
Incentives
Behavioural counselling
Empowerment (e.g. strengthening women's rights)
100
80
60
%
40
20
0
Priority population that would benefit from the prevention method
Lack of motivation - Reason:
Knowledge
Risk perception
Consequences of use
Social norms
Those who want to use prevention method
Lack of access - Reason:
Available
Easy access
Acceptable provision
Affordable
Those who can access prevention method
Lack of capability - Reason:
Skills
Self-efficacy
Partner
Those who effectively use prevention method
B
Intervention 1: Risk perception + VMMC uptake
Intervention 4: Community conversations
Priority population HIV-negative adolescent boys and young men (15-29)
Knowledge
Risk perception
Consequences of use
Social norms
Motivation
Available
Acceptable provision
Affordable
Access
Partner
Effective use
C
Intervention 2: Risk perception + PrEP uptake
Intervention 3: PrEP adherence
Intervention 4: Community conversations
Priority population HIV-negative adolescent girls and young women (18-24)
Knowledge
Risk perception
Consequences of use
Social norms
Motivation
Available
Acceptable provision
Access
Skills
Self-efficacy
Partner
Effective use

Figure 1. The generic HIV prevention cascade framework used in this study (A) to guide the design of interventions to improve HIV prevention use among adolescent boys and young men (15-29) (B) and adolescent girls and young women (18-24) (C)
The generic prevention cascade includes the core steps of the cascade (green) and the major reasons underlying gaps in the core steps (orange), which provide links to interventions to improve motivation, access, and effective use. The specific interventions referred to in (A,B) are an education session by a circumcised health worker and financial incentives to take up voluntary medical male circumcision (VMMC) (intervention 1), an interactive counselling game to improve risk perception and pre-exposure prophylaxis (PrEP) uptake (intervention 2), weekly text message reminders to improve PrEP adherence (intervention 3), and community conversation (intervention 4).

circumcised in Manicaland [23] and uptake is off-track to meet national targets [28].

Previous HIV prevention cascade analysis using Manicaland Cohort data found that low VMMC uptake in the study population was largely due to low risk perception for HIV infection, suggesting gaps in motivation and poor local availability [2]. Motivation for VMMC uptake can be affected by negative perceptions of its consequences. Transport costs and lost income were identified as important barriers to access (Figure 1B).

An intervention was developed where HIV-negative young men (15-29) participate in an education session on HIV risks and reducing these risks through VMMC, run by a circumcised male "role-model." They are randomized to receive a fixed financial reward or the opportunity to participate in a lottery (with financial rewards) upon VMMC uptake. Participants receive a contribution towards transport costs for accessing VMMC and are referred to participating study clinics offering VMMC. The education session aims to increase motivation by improving HIV risk perception, knowledge and perceptions about consequences of VMMC. The financial incentive increases motivation by creating more positive consequences for uptake. Previous behavioural economics research showed lottery tickets may be more effective in increasing motivation than fixed financial rewards as individuals overweight small probability events [35]. For access to VMMC, the education session and referral provide information about local availability; the financial incentives and contribution towards transport costs improve its affordability.

Organizing the follow-up data in the prevention cascade framework aids evaluation by providing data on possible reasons why the intervention may have failed to improve uptake. Changes in the HIV prevention cascade for VMMC will be compared between a baseline and follow-up survey six months later, for men in the intervention and control groups using HIV risk perception and VMMC uptake as primary outcomes.

Intervention 2: Increasing motivation and access for PrEP use among AGYW

No prior measurements of the HIV prevention cascade for PrEP were available for AGYW in the study population. Since PrEP is a new method of HIV prevention in Zimbabwe and is not widely available [25], it was assumed that motivation, access and effective use would be low at the outset.

Earlier analyses of Manicaland Cohort data on risk among AGYW indicated unprotected sexual relationships with older men contribute to their high HIV incidence [24]. Preliminary analyses of the HIV prevention cascade for other prevention methods among AGYW found gaps in perceptions about personal HIV infection risks [2,4]. Lack of risk perception indicates lack of motivation to use HIV prevention methods. Evidence from population-based trials on PrEP in sub-Saharan Africa suggests low risk perception may limit PrEP use along with doubt about using antiretroviral drugs (ARVs) for prevention [36-38].

An intervention was designed whereby HIV-negative AGYW (18-24) play an interactive counselling game [39], addressing optimistic beliefs about HIV infection risks – particularly around sexual relations with older men – and providing information on the nature, effectiveness, tolerability and local availability of PrEP. Participants can choose to be contacted by a nurse to discuss PrEP further and a referral letter to participating study clinics where PrEP services are available. The intervention aims to adjust HIV risk perception and improve PrEP uptake by targeting barriers in motivation and access to use (Figure 1C). Gaps in motivation are addressed by improving knowledge of the method and consequences of its use and increasing risk perception accuracy. Previous studies showed that providing disaggregated information on HIV risks can adjust risk perception and behaviour [39,40]. Information on and referrals to local PrEP services address gaps in access.

Evaluation will compare the HIV prevention cascades for PrEP for AGYW in the intervention and control groups after six months using HIV risk perception and uptake of PrEP (confirmed by ARV presence in blood samples [41-43]) as primary outcomes.

Intervention 3: Increasing effective use of PrEP by AGYW

Effective use of PrEP requires continuous adherence – not just uptake – to provide protection against HIV infection. It is anticipated that this will be a challenge for AGYW [44]. AGYW may have difficulties remembering to take PrEP daily and could lack salience about the risks and consequences of HIV infection.

An intervention was designed to improve PrEP adherence among AGYW who are on PrEP whereby they receive unidirectional, personalized text messages, acting as "nudges." Text messaging "nudges" have been shown to improve ART adherence [45]. This intervention addresses the likely gaps in personal capacity to use PrEP effectively, specifically limited salience of HIV risk (Figure 1C), thus improving the "skills" required to adhere consistently. Knowledge of these reminders may improve the self-perceived ability to adhere to PrEP (self-efficacy).

This intervention will be evaluated by randomizing AGYW on PrEP into intervention and control groups. Effective use of PrEP (adherence assessed through self-reports and ARV presence in blood samples) will be compared in the two groups after six months.

Intervention 4: Improving social support for young people's use of HIV prevention methods

Some factors contributing to gaps in the cascade lie outside of the individual's control, including influences by partners, peers, families, healthcare providers and social structures [32]. Prevention cascade analysis of the study population showed social norms and partner disapproval represent barriers to condom use [4]. Individual-level interventions may have limited impact in increasing effective VMMC and PrEP use if the local social environment is not supportive.

A community conversations (CCs) intervention [46] is being implemented in two study sites to address community-level barriers contributing to the HIV prevention cascades for VMMC and PrEP. CCs are a community-led capacity-building process where community members identify, plan, implement and evaluate their own actions to break down community-level barriers to engagement with HIV prevention methods. CCs are expected to improve motivation for HIV prevention method use by creating and fostering supportive social norms (Figure 1B,C). Partner approval – an important factor for PrEP use [47] and VMMC [48] – is being addressed. Creating more prevention-positive social norms in a community may encourage health workers to adopt less stigmatizing attitudes towards HIV prevention use by young people, making provision of HIV prevention services more acceptable and improving access.

Survey and qualitative data will be analysed to evaluate whether the CCs intervention impacted the specific barriers to motivation, access and effective use of PrEP and VMMC by AGYW and young men in the study populations. Prevention cascades will be constructed and compared for VMMC and PrEP in the intervention and control groups between the two CCs sites and the remaining six sites to assess the effectiveness of CCs.

3 | CONCLUSIONS

We have outlined a generic approach to using the HIV prevention cascade to identify, develop and evaluate interventions and demonstrated feasibility of application using the example of a study testing interventions to strengthen implementation of VMMC and PrEP services in Manicaland.

When developing interventions, a central benefit of the HIV prevention cascade framework is that it underscores the multitude of factors to be addressed potentially limiting effective use of prevention methods. As with PrEP in Manicaland, the prevention cascade framework is useful for organizing evidence from other methods and settings to guide thinking about barriers to be addressed in implementing a new method. While the cascade highlights bottlenecks and areas that require interventions to improve progress through the cascade, it does not determine the most suitable interventions – these must be based on theoretical frameworks, local circumstances and evidence from similar settings.

When evaluating interventions, outcomes and process indicators can be defined corresponding to steps and reasons underlying gaps in the HIV prevention cascade, providing a standardized basis to compare intervention and control groups and over time. Cascade analysis can be useful for interpretation of trial results and identifying reasons for the success or failure of interventions. The HIV prevention cascade does not measure the impact of interventions. This is possible – as planned in the Manicaland Study – by mathematical modelling to generate estimates of population-level impact. The cascade is being used in evaluating the implementation of individual and combination HIV prevention methods to estimate the overall impact of the interventions on HIV incidence.

In the Manicaland Study, the HIV prevention cascade is being measured and interpreted using data from population surveys and qualitative investigations. Other data sources – for example, routinely collected health data – could also be used (see [4] for further discussion).

Evaluation of the aforementioned interventions has not been completed. Nevertheless, the study demonstrates the HIV prevention cascade framework can be used to improve development and evaluation of HIV prevention interventions by setting targets to be addressed to remove bottlenecks in prevention use. The framework can be used for multiple settings, populations and HIV prevention methods as it is generic and adaptable by design, although the risk of stigmatizing specific populations (e.g. AGYW) should be considered. As the HIV treatment cascade has aided a range of policy, programmes and research at multiple levels, we believe this cascade can provide a framework to identify gaps in prevention efforts and targets for interventions. We encourage this approach to inform the intervention development and believe this framework can support global efforts to reduce HIV incidence.

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COMPETING INTERESTS

S.G. declares shareholding in pharmaceutical companies (GSK and Astra Zeneca). R.T. declares personal fees received for consultancy for the International Decision Support Initiative. The authors declare no further potential competing interests.

AUTHORS' CONTRIBUTIONS

All authors have been involved in the design of the Manicaland Study, led by TBH and SG, LM and RS wrote the article, with input from all authors. All authors have read and approved the final manuscript.

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REFERENCES

1. Amico KR. Developing an "HIV prevention cascade": current approaches and future directions. 10th International Conference on HIV Treatment and Prevention Adherence, Miami; 2015.
2. Garnett GP, Hallett TB, Takaruza A, Hargreaves J, Rhead R, Warren M, et al. Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study. Lancet HIV. 2016;3(7):e297–306.
3. Hargreaves JR, Delany-Moretlwe S, Hallett TB, Johnson S, Kapiga S, Bhattacharjee P, et al. The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring. Lancet HIV. 2016;3(7):e318–22.
4. Schaefer R, Gregson S, Fearon E, Hensen B, Hallett TB, Hargreaves JR. HIV prevention cascades: a unifying framework to replicate the successes of treatment cascades. Lancet HIV. 2019;6(1):e60–6.
5. Haber N, Pillay D, Porter K, Bärnighausen T. Constructing the cascade of HIV care: methods for measurement. Curr Opin HIV AIDS. 2016;11(1):102.
6. Amanyire G, Semitala FC, Namusobya J, Katuramu R, Kampiire L, Wallenta J, et al. Effects of a multicomponent intervention to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised trial. Lancet HIV. 2016;3(11):e539–48.
7. Hamilton E, Bossiky B, Ditekemena J, Esiru G, Fwamba F, Goga AE, et al. Using the PMTCT cascade to accelerate achievement of the global plan goals. J Acquir Immune Defic Syndr. 2017;75 Suppl 1:S27–35.
8. San Francisco Department of Public Health. The jurisdictional HIV prevention plans for the San Francisco metropolitan statistical area 2012-2016. San Francisco: San Francisco Department of Public Health; 2013.
9. Liu A, Colfax G, Cohen S, Bacon O, Kolber M, Amico KR, et al. The spectrum of engagement in HIV prevention: proposal for a PrEP cascade. 7th International Conference on HIV Treatment and Prevention Adherence, Miami; 2012.
10. Wilton J, Kain T, Fowler S, Hart TA, Grennan T, Maxwell J, et al. Use of an HIV-risk screening tool to identify optimal candidates for PrEP scale-up among men who have sex with men in Toronto, Canada: disconnect between objective and subjective HIV risk. J Int AIDS Soc. 2016;19(1):20777.
11. Kelley CF, Kahle E, Siegler A, Sanchez T, Del Rio C, Sullivan PS, et al. Applying a PrEP continuum of care for men who have sex with men in Atlanta, Georgia. Clin Infect Dis. 2015;61(10):1590–7.
12. Horn T, Sherwood J, Remien RH, Nash D, Auerbach J, HIV Prevention Continuum Working Group ftTAG. Towards an integrated primary and secondary HIV prevention continuum for the United States: a cyclical process model. J Int AIDS Soc. 2016;19(1):21263.
13. McNairy ML, El-Sadr WM. A paradigm shift: focus on the HIV prevention continuum. Clin Infect Dis. 2014;59 Suppl 1:S12–5.
14. Johnson J. Toward comprehensive HIV prevention service delivery in the United States: an action plan. Washington, DC; New York, NY: The Foundation for AIDS Research; Treatment Action Group; 2015.
15. Manicaland Centre for Public Health Research. HIV prevention cascades: stakeholder consultation meeting and workshop. 2017 [cited 2018 Oct 30]. Available from: http://www.manicalandhivproject.org/uploads/4/7/1/9/4719905/hpc_consultation_workshop_report_final.pdf.
16. Zimbabwe National Statistics Agency (ZIMSTAT). Inter-censal demographic survey, 2017. Harare: ZIMSTAT; 2017.
17. Ministry of Healt and Child Care (MOHCC) Zimbabwe, National AIDS Council Zimbabwe, Centers for Disease Control and Prevention USA, UNAIDS. Smart investment to end HIV AIDS in ZIMBABWE based on hotspot analysis. Harare: MOHCC; 2015.
18. Ministry of Healt and Child Care (MOHCC) Zimbabwe, National AIDS Council Zimbabwe. Extended Zimbabwe national HIV and AIDS strategic plan (ZNASP) 2015-2020. Harare: MOHCC; 2015.
19. Ministry of Healt and Child Care (MOHCC) Zimbabwe. Zimbabwe Population-Based HIV Impact Assessment (ZIMPHIA) 2015-16: first report. Harare: MOHCC; 2017.
20. Gregson S, Mugurungi O, Eaton J, Takaruza A, Rhead R, Maswera R, et al. Documenting and explaining the HIV decline in east Zimbabwe: the Manicaland General Population Cohort. BMJ Open. 2017;7(10):e015898.
21. Gregson S, Garnett GP, Nyamukapa CA, Hallett TB, Lewis JJ, Mason PR, et al. HIV decline associated with behavior change in eastern Zimbabwe. Science. 2006;311(5761):664–6.
22. Gregson S, Nyamukapa C, Schumacher C, Mugurungi O, Benedikt C, Mushati P, et al. Did national HIV prevention programs contribute to HIV decline in Eastern Zimbabwe? Evidence from a prospective community survey. Sex Transm Infect. 2011;38(6):475–82.
23. Zimbabwe National Statistics Agency (ZIMSTAT), ICF International. Zimbabwe Demographic and Health Survey 2015: final report. Rockville, MD: ZIMSTAT and ICF International; 2016.
24. Schaefer R, Gregson S, Eaton JW, Mugurungi O, Rhead R, Takaruza A, et al. Age-disparate relationships and HIV incidence in adolescent girls and young women: evidence from Zimbabwe. AIDS. 2017;31(10):1461–70.
25. Ministry of Health and Child Care Zimbabwe. Implementation plan for HIV pre-exposure prophylaxis in Zimbabwe 2018-2020. Harare: Ministry of Health and Child Care Zimbabwe; 2018.
26. U.S. President's Emergency Plan for AIDS Relief (PEPFAR). DREAMS partnership: fact sheet. Washington, DC: PEPFAR; 2017.
27. Pangaea Global. Oral PrEP introduction: Zimbabwe rollout analysis [Online]. 2017 [cited 2018 Oct 7]. Available from: https://www.prepwatch.org/wp-content/uploads/2017/04/Zim_Rollout_Analysis_Feb2017.pdf
28. Zimbabwe MoHaCCM, National AIDS Council Zimbabwe. Global AIDS response progress report 2017: Zimbabwe Country report. Harare: MOHCC; 2017.
29. Schaefer R, Thomas R, Nyamukapa C, Maswera R, Kadzura N, Gregson S. Accuracy of HIV Risk Perception in East Zimbabwe 2003-2013. AIDS Behav. 2018; 10.1007/s10461-018-2374-0. [Epub ahead of print]
30. Rhead R, Skovdal M, Takaruza A, Maswera R, Nyamukapa C, Gregson S. The multidimensionality of masculine norms in east Zimbabwe: implications for HIV prevention, testing and treatment. AIDS. 2019;33(3):537–46.
31. Skovdal M, Campbell C, Madanhire C, Mupambireyi Z, Nyamukapa C, Gregson S. Masculinity as a barrier to men's use of HIV services in Zimbabwe. Global Health. 2011;7:13.
32. Kaufman MR, Cornish F, Zimmerman RS, Johnson BT. Health behavior change models for HIV prevention and AIDS care: practical recommendations for a multi-level approach. J Acquir Immune Defic Syndr. 2014;66 Suppl 3: S250–8.
33. Campbell C, Cornish F. Towards a "fourth generation" of approaches to HIV/AIDS management: creating contexts for effective community mobilisation. AIDS Care. 2010;22 Suppl 2:1569–79.
34. Gupta GR, Parkhurst JO, Ogden JA, Aggleton P, Mahal A. Structural approaches to HIV prevention. Lancet. 2008;372(9640):764–75.
35. Tversky A, Kahneman D. Judgment under uncertainty: heuristics and biases. Science. 1974;185(4157):1124.
36. van der Straten A, Stadler J, Montgomery E, Hartmann M, Magazi B, Mathebula F, et al. Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa. PLoS ONE. 2014;9(2):e89118.
37. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367:411–22.
38. Corneli AM, Deese J, Wang M, Taylor D, Ahmed K, Agot K, et al. FEM-PrEP: adherence patterns and factors associated with adherence to a daily oral study product for pre-exposure prophylaxis. J Acquir Immune Defic Syndr. 2014;66(3):324–31.
39. Datta S, Burns J, Maughan-Brown B, Darling M, Eyal K. Risking it all for love? Resetting beliefs about HIV risk among low-income South African teens. J Econ Behav Organ. 2015;118:184–98.
40. Dupas P. Do teenagers respond to HIV risk information? Evidence from a field experiment in Kenya. Am Econ J Appl Econ. 2011;3(1):1–34.
41. Jung BH, Rezk NL, Bridges AS, Corbett AH, Kashuba ADM. Simultaneous determination of 17 antiretroviral drugs in human plasma for quantitative analysis with liquid chromatography-tandem mass spectrometry. Biomed Chromatogr. 2007;21:1095–104.
42. Marzinke MA, Breaud A, Parsons TL, Cohen MS, Piwowar-Manning E, Eshleman SH, et al. The development and validation of a method using high resolution mass spectrometry (HRMS) for the qualitative detection of antiretroviral agents in human blood. Clin Chim Acta. 2014;433:157–68.
43. Matta MK, Burugula L, Pilli NR, Inamadugu JK, Rao S. A novel LC-MS/MS method for simultaneous quantification of tenofovir and lamivudine in human plasma and its application to a pharmacokinetic study. Biomed Chromatogr. 2012;26:1202–9.
44. Eakle R, Gomez GB, Naicker N, Bothma R, Mbogua J, Cabrera Escobar MA, et al. HIV pre-exposure prophylaxis and early antiretroviral treatment among female sex workers in South Africa: results from a prospective observational demonstration project. PLoS Med. 2017;14(11):e1002444.
45. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet. 2010;376(9755):1838–45.

46. Nigatu YT, Abera S, Mekonnen MG, Melesse WN. The role of the community conversation approach in facilitating HIV/AIDS competence and utilisation of testing services in Africa: the case of Ethiopia. Afr J AIDS Res. 2015;14(4):295–301.
47. Thomson KA, Baeten JM, Mugo NR, Bekker L-G, Celum CL, Heffron R. Tenofovir-based Oral PrEP Prevents HIV Infection among Women. Curr Opin HIV AIDS. 2016;11(1):18–26.
48. Westercamp N, Bailey RC. Acceptability of Male circumcision for prevention of HIV/AIDS in Sub-Saharan Africa: a review. AIDS Behav. 2007;11(3):341–55.

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