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Combination implementation for HIV prevention: moving from evidence to population-level impact

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We declare that we have no conflicts of interest.

Summary

The promise of combination HIV prevention—the application of multiple HIV prevention interventions to maximize population-level impact—has never been greater. However, to succeed in achieving significant reductions in HIV incidence, an additional concept needs to be considered —*combination implementation*. Combination implementation for HIV prevention is defined here as the pragmatic, localized application of evidence-based strategies to realize high sustained uptake and quality of HIV prevention interventions. This review explores diverse implementation strategies including HIV testing and counseling models, task shifting, linkage to and retention in care, antiretroviral therapy support, behavior change, demand creation, and structural interventions and discusses how they could be used in the provision of HIV prevention interventions such as medical male circumcision and treatment as prevention. Only through careful consideration of how to implement and operationalize HIV prevention interventions will the HIV community be able to move from clinical trial evidence to population-level impact.

Introduction

Recently, the term combination HIV prevention has been used to describe the application of multiple HIV prevention interventions to maximize population-level impact and potentially bring HIV epidemics under control.[1, 2] The landmark results of HPTN 052, a randomized controlled trial (RCT) demonstrating that antiretroviral therapy (ART) reduces HIV transmission to uninfected partners, established Treatment as Prevention (TasP) as one of the cornerstones of combination HIV prevention.[3] These findings followed studies of medical male circumcision (MMC) which had been clearly shown to reduce male HIV acquisition in three RCTs.[4–8] These data, along with studies demonstrating the effectiveness of condoms and some behavior change interventions,[9–17] the potential of Pre-Exposure Prophylaxis (PrEP),[18–21] and modeling suggesting the potential for reversing the HIV epidemic,[22–25] provide the impetus to test the effectiveness and impact of combined HIV prevention strategies.

This growing evidence-base has led to the initiation of several large-scale combination HIV prevention programs and trials.[26, 27] However, the success of these efforts will be dependent on achieving high sustained uptake and quality of interventions. While significant attention has been directed at *what* should make up the package of HIV prevention interventions,[2, 4, 26] there has been less discussion of *how*, i.e. what implementation strategies are needed to achieve broad and sustained population coverage.[28–31] To succeed in realizing HIV control, we propose an additional combination concept—*combination implementation* for HIV prevention.

We define combination implementation in this setting as the pragmatic, localized application of a package of evidence-based prevention interventions using optimized implementation and operational strategies to achieve high sustained uptake of good quality services. Combination implementation strategies which begin with a “know your epidemic approach” and best operationalize efficacious HIV prevention interventions will be needed to move from trial-based evidence of efficacy to population-level impact.[32–34] This narrative review explores a diverse group of potential implementation strategies to be incorporated into combination implementation efforts, focusing first on specific HIV prevention services and concluding with more cross-cutting issues, and discusses how these strategies could be used to fulfill the potential of combination HIV prevention in low and middle-income countries (LMIC).

Implementation Strategies for HIV Prevention Services

HIV Testing and Counseling (HTC)

HTC, the gateway to learning one's HIV serostatus, is a necessary component of all combination HIV prevention strategies. HTC may include pre-test counseling, risk-behavior assessment, informed consent, and post-test counseling based on test results to provide individually-tailored risk reduction messages. HTC alone may offer HIV prevention benefits through reduction of sexual risk behaviors, particularly among HIV-infected individuals.[35] Implementation models for HIV counseling and testing can be facility-based (either client or provider initiated),[36] mobile, workplace, or home-based.[37]

Facility-based HTC has been the standard model in most LMIC; however, this model by itself has been unable to attain high population coverage levels with the majority of people in LMIC still unaware of their serostatus.[38] Community-based mobile HTC where the "facility" typically moves into areas with limited access to HTC is a promising strategy (see Table 1). In some populations, this model appears to have provided coverage to about half of key target groups.[39] Workplace-based HTC also appears to offer an opportunity for increasing access.[40] However, definitive coverage levels within a community remain difficult to ascertain with any of these approaches. Furthermore, none appear able to achieve the near (90%) or universal HTC coverage which modeling has suggested is needed for significant decreases in HIV incidence.[23, 24]

Home-based HTC, especially when used in conjunction with point-of-care rapid HIV testing, retains many of the advantages of mobile HTC but may further improve access and allow for more accurate assessment of community-level coverage. Several small to large scale home-based HTC programs have been implemented with high rates of acceptance in both rural and urban communities (Table 1). Cost-effectiveness and observational studies have also found home-based HTC to be a better strategy for reaching populations with low-rates of prior testing and higher CD4 counts, critical populations to engage for combination HIV prevention interventions.[41, 42]

As early and comprehensive identification of serostatus is fundamental to the implementation of all HIV prevention interventions, home-based HTC as the primary implementation model may be the most effective of the HTC strategies to achieve high population levels of serostatus awareness. Mobile and workplace HTC appear to offer promising complementary approaches which will be appropriate to some settings. Finally, facility-based HTC, which makes services available on an ongoing basis, remains a critical basic health care service in most LMIC settings to promote combination HIV prevention.

Treatment as Prevention (TasP)-Linkage and Retention in Care

Numerous observational studies have demonstrated the challenges in engaging PLHIV across the entire spectrum of care,[43] both with initial linkage to care and subsequent retention, with estimates of only 59% being clinically staged after diagnosis and 25% of patients not retained in care one year after ART initiation.[44, 45] Barriers to engagement are numerous, ranging from site-specific transport challenges,[46] to more generalized stigma.[47] Combination HIV prevention programs will need to engage a high percentage of the population and address the particularly vexing issues of late presentation for HIV diagnosis and care.[48]

Unfortunately, the evidence base for interventions to link and retain PLHIV in care remains scarce. An RCT in rural Uganda found that community-based peer treatment supporters decreased lost to follow-up rates by 44%.[49] An observational study in Kenya found that provision of free cotrimoxazole improved retention of ART-ineligible clients over twofold

compared to historical controls.[50] Patient tracers in South Africa have been used to successfully return patients to care.[51] However, little evidence exists on how to engage largely asymptomatic HIV-infected populations with higher CD4 counts or how to best identify and engage acutely HIV-infected patients. Improved recognition and diagnosis of people with acute HIV infection using such strategies as pooled HIV RNA testing and improving provider awareness may offer some implementation strategies to address this challenging population,[52, 53] but more research in this area is needed.

Point of care (POC) CD4 testing, with a growing evidence-base validating its performance, offers substantial promise for clinical staging at the time of diagnosis, thus facilitating immediate entry into appropriate care and treatment services.[54–56] A small RCT of POC CD4 at HIV testing in South Africa reported a twofold improvement in linkage to care.[57] An observational study in Mozambique found an 80% reduction in early lost to follow-up.[58] The implementation evidence base for this maturing technology needs continued validation,[59, 60] and POC CD4 technology development and field trials should be a research priority provided CD4 cell count remains one of the standards for determining ART eligibility.[61] Provocatively, a treatment for all model of TasP whereby all PLHIV would qualify for ART regardless of CD4 cell count is one scale-up strategy that would remove the need for eligibility assessment and largely obviate much of the need for CD4 testing.[23]

While the evidence base for strategies to optimize engagement in care continues to mature, existing program models which have demonstrated success may provide reasonable starting points for combination HIV prevention activities.[62, 63] These successful programs often involve task shifting, decentralization with community and/or home-based services, frequently incorporate patient tracing services and recruit PLHIV in the engagement and retention of their peers.[44, 59, 63–68] Novel community-based programs with good programmatic outcomes have included self-forming groups of patients,[69] the use of handheld technology to support task shifting to PLHIV,[70] incorporation of electronic medical records,[71] and emphasizing pre-ART care services.[72]

Treatment as Prevention-Treatment Support

ART patients will need to indefinitely adhere to treatment at high levels for TasP to succeed.[73] Implementation strategies to promote and support adherence include the use of peer treatment supporters (variably called expert patients, peer health workers, or lay/community health workers) which have shown some improvement in adherence and virologic outcomes (see Table 3).[49, 73] They may also confer survival benefits,[13] though the evidence base remains small. Integration of HIV treatment with tuberculosis or primary care services have also demonstrated their potential to improve patient-oriented outcomes such as time to ART initiation.[74–76] Food support has been found to have some benefits in improving adherence in pilot studies,[77] but the large-scale implementation and sustainability of such interventions is daunting.[78] Directly observed therapy studies have had unconvincing results, and they remain difficult to scale-up at a population-level.[13, 79–81]

New technologies have shown promise in supporting ART adherence. One RCT in Kenya demonstrated that mobile phone alert coupled to provider support decreased the risk of virologic failure by 16%.[82] Another Kenyan RCT utilized a text-message reminder (SMS) and observed 13–16% improved adherence.[83] However, failure of an alarm device in a third Kenyan study demonstrated how local assessment of technological strategies must be ongoing,[84] and that reminders alone without patient support may be insufficient.[85] Additional evaluations of electronic reminders and support in other populations would significantly add to these early reports.

Routine laboratory monitoring appears not to be a prerequisite for TasP implementation, which should be reassuring to programs with limited laboratory support.[86] However, laboratory monitoring does have clinical and survival benefits.[87–89] In particular, monitoring of HIV viral load, the best proxy for infectiousness at the individual and community level, may have substantial TasP benefits through earlier regimen switching in cases of ART treatment failure and by preventing unnecessary regimen changes.[90] Targeted viral load strategies which only conduct viral load testing in high-risk patients based on laboratory, e.g. CD4, and/or behavioral characteristics, e.g. adherence assessments, may be a less initially costly strategy but needs further evaluation of impact.[91]

Pragmatic application of lay health worker, technology, and laboratory support, tailored to the local epidemic and treatment dynamics, will be needed to assist with implementing TasP.[92, 93] Continued evaluation of these support strategies and their effectiveness in supporting PLHIV on ART, especially when used in combination, will be enlightening.

Medical Male Circumcision (MMC)

In settings of moderate to high HIV prevalence and low male circumcision rates, MMC will be a critical component of combined HIV prevention. MMC scale-up has proceeded at variable paces throughout LMIC.[94] No RCT evidence could be found supporting one type of scale-up strategy versus another. However, several observational studies provide examples of potential approaches (Table 4). South Africa has demonstrated an effective model using community-based outreach and mobilization,[95] and Tanzania's MMC campaign approach has exceeded original targets.[96] Efforts in Kenya have found significant early success through government led, task-shifting initiatives.[97] Task-shifting of MMC appears to be safe with adverse event rates similar between non-physician clinicians and doctors and specialists.[98]

Non-surgical male circumcision devices, such as the Shang Ring and PrePex, are currently undergoing evaluations of safety and acceptability to determine what role they may play in accelerating MMC scale-up efforts and addressing human resource shortages.[99] These new devices are promising and innovative; however, their relative benefits and adverse effects compared to each other and to surgical methods require further evaluation. MMC efforts may also need to be cognizant of seasonal demands and adjust their supply appropriately.[100] Finally, uptake of MMC among higher risk men remains suboptimal, and innovative, targeted strategies addressing this difficult to engage population are needed.[94]

Prevention of Mother to Child Transmission (PMTCT)

Significant progress in scaling up PMTCT has been made over the past several years.[38] New antiretroviral prophylaxis methods are increasingly efficacious, but coverage level remains below target goals.[101] While PMTCT implementation strategies are not well represented in the scientific literature, some approaches have shown promise. These approaches include the adoption of task shifting, integrating PMTCT services into the larger context of care for the mother and family, adopting system improvement methods, and empowering mothers to self-administer PMTCT.[102–105]

Combination HIV prevention programs will likely want to include PMTCT as a core prevention component, not only for the benefit of reducing HIV transmission to infants, but also to leverage PMTCT to increase access to other services for the mother and family.[105, 106] PMTCT serves as a critical entry point into the health care system for both HIV-negative and positive individuals.[76] For HIV-negative individuals, the opportunity to access this service increases engagement in care and offers counseling opportunities and seronegative appropriate interventions. For HIV-infected individuals, a variety of other

prevention interventions may apply beyond PMTCT, such as ART and couples counseling. Recently, Option B+, whereby pregnant HIV-infected women are started on triple-drug ART regardless of CD4 count at time of diagnosis and continued for life, has gained interest for its clinical and programmatic benefits and may represent a compelling strategic component of PMTCT and TasP efforts.[107, 108] Tight integration of PMTCT in combination HIV prevention programs may therefore have synergistic benefits with other prevention interventions and careful evaluations of the impact of integrated programs should be encouraged.

Behavior Change and Condoms

Combination HIV prevention will not succeed without significant and sustained individual and community-level HIV risk reduction behavior change.[109] One challenge to selection of implementation strategies is the mixed evidence for behavior change interventions.[8–12, 110, 111] Additionally, it has been difficult to disentangle the varied contributions of other drivers of HIV incidence from specific changes in behavior.[112] Nevertheless, behavior change counseling interventions aimed at increasing condom access and use and decreasing sexual partners and activity have some demonstrated successes which can guide local implementation approaches, such as a 33% reduction in risk behavior prevalence in a 5-country study.[113, 114] Notably, the biomedical intervention arms of HIV prevention RCTs typically included concomitant behavioral change interventions, a further argument for integration.

Counseling strategies addressing partner risk behaviors and promoting condom use have become standard of care for most HIV prevention efforts, and they will likely need to continue as foundational components of most combination HIV prevention programs. In particular, discordant couples are an important population to target HIV prevention efforts using facilitated disclosure[115] and couples counseling strategies.[16, 116, 117] Peers may again play an important role here as they are economical and relatively effective behavior change agents.[110] The effectiveness of condoms is well established,[17] and ensuring adequate supply and access will aid HIV prevention efforts. Creating demand for condoms and sustaining their use will be difficult,[11] and ongoing evaluations of behavior change implementation strategies are needed.

Pre-Exposure Prophylaxis (PrEP)

The evidence-base for oral and vaginal PrEP continues to evolve, with current results mixed.[19–21, 118,119] Implementation science evidence for PrEP remains limited due to minimal field experience with efficacious PrEP interventions.[120] The reasons for discordant results of some PrEP trials remain uncertain and further analyses will be helpful in informing important implementation issues such as the role of adherence in determining intervention efficacy. While modeling studies have shown that efficacious and widely implemented oral PrEP could result in a cost-effective and significant impact on HIV incidence,[121] given the current level of uncertainty about population-level effectiveness, oral PrEP may not be a core component of most current combination HIV prevention activities. However, in select groups such as discordant couples where the HIV-infected partner is not on ART or high risk populations such as sex workers and their clients and men who have sex with men (MSM), PrEP may play an important role. Demonstration projects are needed to provide further evidence that this biomedical intervention can be applied at significant scale to assist in the control of generalized HIV epidemics.[122]

Cross-cutting Strategies for Combination HIV Prevention

Task Shifting

Task shifting is the rational redistribution of tasks among health workforce teams from higher trained providers to those who require less training.[68] It is a direct respons to the health worker human resource crisis in LMIC which is a substantial barrier to implementation of combination HIV prevention.[123, 124] Multiple observational task shifting studies have focused on shifting ART care from physicians to nurses and have typically demonstrated that task shifting can be accomplished without significant differences in quality of care.[125–129] A number of mostly observational studies have also addressed task shifting and MMC.

Task shifting has been tested in a small number of RCTs (Table 2).[130] A study of home-based HIV care provided by field officers found them to be as effective as a clinic-based strategy with similar rates of virologic failure.[131] Home-based care supported by trained PLHIV resulted in similar patient-oriented outcomes and less frequent clinic visits compared to clinic-based care alone.[132] Another RCT demonstrated that nurse-monitored care was non-inferior to doctor-monitored care.[133, 134] The small number of participants in these studies is a limitation. However, early results from a larger cluster RCT shifting care to nurses in South Africa are also promising and final reporting should add substantively to the evidence-base.[134, 135]

Task shifting will be required beyond service scale-up and will need to include long-term activities such as adherence counseling and patient support as health systems move towards a more chronic care model for PLHIV. Combination HIV prevention will also require a complex and large-scale ongoing assessment of individual-level risk factors. Educational and support strategies for less highly trained workers will need to be strengthened and evaluated. Novel approaches to improve worker efficiency and the quality of services delivered may be required. For example, mobile electronic decision-making support for patient screening and triage to HIV prevention and care have been successfully piloted in Uganda as well as in Kenya in rural settings.[70, 136] These mobile technologies for health care (mHealth) may be appropriate components of combination HIV prevention implementation strategies.[92]

Given the scale of the human resource needs for combination HIV prevention, task shifting will be an important component of many implementation activities. Task shifting also represents an opportunity to involve PLHIV directly in combination HIV prevention activities,[15] including training them as prevention and treatment supporters.[137] The evidence base for task shifting is still being developed but early findings should be reassuring to implementers pragmatically moving forward with task shifting efforts. Important issues such as maintaining quality, safety, high retention, and developing and maintaining training capacity will benefit from careful monitoring, evaluation, and further operational research.[138–140] Task shifting alone may also not be sufficient to address all the human resource requirements for combination HIV prevention, and a general scale-up of provider capacity in LMIC would be ideal.[141]

Structural Interventions and Demand Creation

The use of structural interventions such as individual or community-based financial incentives to create demand and uptake of HIV prevention interventions is an area of growing interest.[142] There have been clear successes in other fields with incentive-based programs.[143] In the field of HIV, an RCT in Malawi found that cash transfer programs may have reduced HIV infections among young women.[144] Incentive interventions to increase participation in HTC have also been successfully piloted.[145, 146] Supply-side strategies such

as pay for performance and provider and facility-level incentives have shown promise for other health conditions, but evaluations of their application to HIV-related interventions remains limited.[147]

With a promising but still limited evidence base, the use of financial incentives or compensation for time and travel in combination HIV prevention programs could be considered provided rigorous evaluation procedures are concurrently implemented to provide ongoing demonstration of effectiveness. An issue of concern is whether compensation should be commensurate with actual costs imposed upon the intervention recipient and not constitute an incentive per se for interventions such as MMC. Appropriate compensation may be best determined by community advisory boards familiar with local costs. Structural interventions focused on food insecurity to improve adherence to ART have also shown some impact in pilot studies,[77] but population-level implementation of food support poses significant financial and sustainability challenges.

Increasing supply of combination HIV prevention services will be inadequate for controlling the HIV epidemic if demand for these interventions is not also increased. The MMC experience offers some insights into how to create demand. A variety of community mobilization strategies in Tanzania appeared to successfully increase demand with the program exceeding initial MMC targets.[96] Mass communication has also demonstrated some successes in HIV prevention to generate demand.[14] Systematic approaches utilizing mixed methods and economic evaluations provide a potential framework for approaching the challenging issue of demand creation.[148] In particular, strategies to involve men in prevention and care activities are needed as men typically have lower ART coverage and higher mortality.[149] More rigorous evaluations of demand creation are needed with appropriate counterfactuals to allow for better assessments of impact.

Key Populations

Key populations for HIV-infection include, but are not limited to, sex workers and their clients, MSM, and injection drug users (IDUs).[150] The importance of these populations as critical target groups for HIV prevention efforts is increasingly being recognized.[151–156] Combination HIV prevention efforts require a “know your epidemic” approach which acknowledges that these often disadvantaged and marginalized populations may be important drivers of local and national epidemics and may be particularly vulnerable to HIV infection.[33] Modeling demonstrating the importance of key local epidemiologic risk groups in ongoing HIV transmission highlight the importance of targeting prevention interventions for these populations to ensure the success of TasP.[25]

A variety of implementation strategies could be emphasized with key populations. The use of needle-syringe distribution for IDUs is a proven HIV prevention intervention but remains largely underutilized in sub-Saharan Africa and field experience is limited.[154] Sex workers would benefit from many interventions suitable for generalized populations but also have certain interventions which are specific to their population such as community mobilization and empowerment activities.[157] MSM are subject to discrimination and barriers to prevention and care access,[45] and outreach efforts and the application of established prevention interventions will be needed.[150] Peers may again play a significant role in engaging these groups in prevention and care. However, the evidence-base for implementing HIV prevention interventions among key populations in Africa remains sparse with structural, cultural, and legal barriers impeding efforts to reach these populations.[150] Stigma and human rights violations faced by these populations may greatly impede adoption of HIV prevention interventions, and antidiscrimination laws and ensuring health service inclusiveness are important considerations for comprehensive implementation plans.[158] Efforts to understand the role these groups play in population-level HIV dynamics and

designing and evaluating targeted implementation strategies, evaluated with appropriate rigorous research designs, should be important components of many combination HIV prevention programs.

Discussion

This review has sought to broadly consider a variety of evidence-based implementation strategies which could be incorporated in a combination implementation approach to realize the combination HIV prevention goals of reduced HIV incidence. A large number of strategies were identified though the evidence-base for many strategies is limited. Furthermore, there is a scarcity of evidence on how best to combine different implementation strategies and what the benefits and trade-offs of different combinations might entail. Nevertheless, sufficient experience exists to guide the early design of combination HIV prevention programs and trials, and these initiatives will clearly benefit from rigorous implementation science and operational research evaluations to inform this rapidly evolving field.[32, 34, 159] While randomized study designs will have a significant role in evaluating combination implementation and prevention initiatives,[26] mixed methods and modeling studies of non-randomized studies will also be of critical importance.[111]

In designing combination HIV prevention programs, many organizations will begin with an initial assessment of local HIV transmission dynamics and resources for HIV prevention and treatment. Programs will then ideally be developed to reflect these local conditions, layering in prevention interventions with implementation and operational strategies. Evaluation frameworks using mixed methods, iterative processes, and patient-oriented outcomes will greatly assist in comprehensively assessing program impact. These evaluations and sustaining high uptake of combination HIV prevention will require significant resources, and the global community will need to make a commensurate financial commitment if these goals are to be realized.

Evaluations will need to carefully consider and monitor for the potentially synergistic or antagonistic effects of combining biomedical and behavioral interventions as well as multiple implementation strategies. Learning from the benefits and unintended consequences of combination approaches will be important lessons derived from current programs and trials. Given limited evidence that exists for certain strategies and some interventions, it will be important for implementers to remain flexible enough to alter their approaches as they begin receiving evaluation results. The ability to make ongoing, data-driven programmatic course corrections may not just be a luxury of combination HIV prevention efforts but a necessity.

This review has several important limitations. While a systematic process was performed to search for relevant manuscripts, the objective of this narrative review was not focused on a single strategy or intervention. Narrative reviews are appropriate when broadly summarizing a complex, multidisciplinary, and far-ranging topic such as combination implementation for HIV prevention, but may be subject to more biases than systematic reviews.[160] Our literature search was not exhaustive, and other relevant evidence likely exists to inform this topic. Inclusion of articles required author judgments on whether an implementation strategy was relevant to combination HIV prevention efforts and may be subject to error or disagreement. The division of the paper into implementation strategies for HIV prevention services and cross-cutting strategies was primarily for didactic purposes, and certain strategies, e.g. text messaging, could be classified in both sections. This review sought primarily to introduce the concept of combination implementation and provide an overview of potential components. Further discussions, insights, and research will be needed to more

comprehensively explore and better understand the multifaceted issues surrounding this concept.

In summary, HIV prevention and treatment has arrived at a pivotal moment when combination efforts may result in significant enough population-level impact to reverse the epidemic and drive it toward elimination. For these efforts to succeed, evidence-based combination implementation strategies will need to be concurrently applied, evaluated, and refined. The need for rigorous implementation science and operational research to inform combination HIV prevention efforts has never been more urgent.

Search strategy and selection criteria

References for this review were identified through searches of PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials using the terms “operations research”, “operational research”, “implementation research”, and “implementation science”, limited by “HIV” and “AIDS” terms without language restrictions. We also reviewed bibliographies of pertinent articles and hand-searched high impact journals in the field and authors’ archives. Included papers were those conducted in low and middle-income countries from January 2000 (approximate beginning of treatment era in low and middle-income countries) to July 2012 which directly evaluated an implementation strategy relevant to combination HIV prevention. Papers on systematic reviews and randomized controlled trials were included, as well as observational studies if trial evidence was lacking. We emphasized in the text studies most relevant to sub-Saharan Africa, the setting for several combination HIV prevention trials.

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Table 1

Examples of mobile and home-based HIV testing and counseling models.

Reference	Model	Setting	N tested	% Accepting	HIV Prevalence
Morin 2006[161]	Mobile	12 Marketplaces	1,099	-	29·2%
Grabbe 2010[162]	Mobile	Multiple Provinces	47,539	-	9·0%
Sweat 2011[39, 163]	Mobile	32 Communities	16,129	-	5·9%
Maheswaran 2012[164]	Mobile, Home	1 Subdistrict	1013 (M) 1585 (H)	92% (H)	16·4% (M) 18·2% (H)
Matovu 2005[165]	Home	1 District	6,602	62%	10·7%
Were 2006[166]	Home	2 Districts	2,348	99%	7·5%
Negin 2009[167]	Home	1 Village	1,984	62%	8·2%
Kimaiyo 2010[167, 168]	Home	294 Villages	101,167	73%	3·0%
Lugada 2010[169]	Home	5 Districts	2,678	56%	7·1%
Tumwesigye 2010[136]	Home	1 District	264,966	94%	4·3%
Sekandi 2011[170]	Home	1 Urban Division	408	69%	7·4%

Table 2

Randomized controlled trials of task shifting and AIDS care.

Reference	Country	N	Description	Outcome Summary
Jaffar 2009[131]	Uganda	859	Home-based Field Officers vs. Facility-based Care	No differences in virologic or mortality outcomes.
Selke 2010[132]	Kenya	208	Home Assessments by PLHIV vs. Standard of Care	No differences in virologic and immunologic outcomes. Fewer clinic visits in intervention arm.
Sanne 2010[133]	South Africa	812	Nurse vs. Doctor management of ART	Non-inferior treatment failure, mortality, and retention outcomes.

Table 3

Randomized controlled trials of treatment support interventions.

Reference	Country	Description	N	Outcome Summary
Lester 2010[82]	Kenya	Text messages with provider support	538	Improved adherence and virologic outcomes.
Chang 2010[49]	Uganda	Peer treatment supporters	1336	Improved virologic and lost to follow-up outcomes.
Nachega 2010[13]	South Africa	Treatment supporters and directly observed therapy	274	No effect on virologic outcomes, improved survival.
Pop-Eleches 2011[83]	Kenya	Text message reminders	431	Improved adherence, fewer treatment interruptions.
Chung 2011[84]	Kenya	Counseling, Alarm Device	400	Counseling improved adherence and virologic outcomes. Alarm had no effect.

Table 4

Models of male circumcision scale-up.

Reference	Country	Key Features	Time Period	Estimated Coverage	N Circumcised
Lissouba 2010[95]	Orange Farm, South Africa	Task-shifting, Single facility	2008–2009	39%	14,011
Mwandi 2011[97]	Nyanza, Kenya	Government-led, Task-shifting, Static and mobile sites, Diathermy	2008–2011	50–55%	287,026
Mahler 2011[96]	Iringa, Tanzania	Task-shifting, Community mobilization, Facility-based	2010 (6 weeks)	-	10,352