Evaluating the efficiency of community-based HIV testing and counseling strategies to decrease HIV burden in sub-Saharan Africa

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Abstract

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Knowledge of one's HIV status is vital to accessing treatment and prevention yet only a fraction of individuals in sub-Saharan Africa are regularly tested for HIV. Community-based HIV testing and counseling (HTC), defined as HTC conducted outside of a healthcare facility, has the potential to achieve high population testing coverage and linkage to care. The studies within this dissertation describe effectiveness and efficiency (cost-effectiveness) of various modalities of community-based HTC. *Aim 1* presents a systematic review of community and facility-based HTC strategies in sub-Saharan Africa. *Aims 2 and 3* evaluate the cost-effectiveness of two types of community HTC interventions in western Kenya by incorporating primary cost and effectiveness data from randomized clinical trials into an HIV mathematical model. Specifically, *Aim 2* assesses the health and economic impact of implementing a home-based partner education and HIV testing (HOPE) intervention for pregnant women and their male partners. *Aim 3* evaluates the cost-effectiveness of scaling up provider notification services for sexual partners of recently diagnosed HIV-positive persons.

In *Aim 1*, we found that community HTC (including home, mobile, partner notification, key populations, campaign, workplace and self-testing) successfully reached target groups (men, young adults and first-time testers) with higher coverage than facility HTC. Community HTC also identifies HIV-positive individuals at higher CD4 counts who were likely to be earlier in their disease course. Combined with the potential of community HTC with facilitated linkage to achieve high linkage to treatment with similar retention rates as facility HTC, this suggests that scaling up community interventions can reduce the morbidity, mortality and transmission associated with late or non-initiation of ART. Of all modalities examined, home HTC attained the highest population coverage (70%, 95% CI = 58–79) while mobile HTC reached the highest proportion of men (50%, 95% CI = 47–54%). Self-testing reached the highest proportion of young adults (66%, 95% CI = 65–67%). As each HTC modality reaches distinct sub-populations, a combination of modalities (differing by setting) will likely be needed to achieve high ART coverage.

In *Aim 2*, we found that the incremental cost of adding the HOPE intervention to standard antenatal care was $31-37 USD per couple tested; task shifting intervention responsibilities to community health workers lowered the cost to $14-16 USD per couple tested. At 60% coverage of male partners, HOPE was projected to avert 6,987 HIV infections and 2,603 deaths in Nyanza province over 10 years with an incremental cost-effectiveness ratio (ICER) of $886 and $615 per DALY averted for the program and task-shifting scenario, respectively. The ICERs are below the threshold of Kenya's per capita gross domestic product ($1,358) and are therefore considered cost-effective. We conclude that the HOPE intervention can cost-effectively decrease HIV-associated morbidity and mortality in western Kenya by linking HIV-positive male partners to care.

In *Aim 3*, we found that implementing assisted partner services (aPS) or active tracing, exposure notification, and home HTC for sexual partners of newly diagnosed HIV-positive persons in western Kenya is projected to achieve 12% population coverage and reduce HIV infections by by 2.8% and HIV-related deaths by 1.5%. The incremental cost-effectiveness ratio (ICER) of implementing aPS is $1,703 USD (range $1,198-2,887) per disability-adjusted life year (DALY) averted. Task-shifting intervention activities from healthcare professionals to community health workers decreases the ICER to $1,302 (range $955-2,789) per DALY averted. The task-shifting scenario falls below Kenya's per capita gross domestic product (GDP) and is therefore considered very cost-effective while the full program cost scenario is considered cost-effective under the higher threshold of 3-times Kenya's per capita GDP. Intervention cost-effectiveness and HIV-related deaths averted among aPS partners increased with expanded ART initiation criteria.

We hope that this dissertation work will be useful in forming policy deliberations regarding implementation of community HTC in countries of sub-Saharan Africa.

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DEDICATION

To my mother.

CHAPTER 1: Introduction

Introduction

Despite the effectiveness of antiretroviral therapy (ART), HIV remains one of the world's most serious health challenges. Globally, there are approximately 2.3 million new HIV infections and 1.6 million HIV-related deaths annually, with 70% of incident infections occurring in sub-Saharan Africa.[1,2] In spite of high burden, only one-third of adults in sub-Saharan Africa have been tested for HIV in the past year.[3,4]

Facility-based HIV testing and counselling (HTC) has not achieved high coverage in sub-Saharan Africa (SSA) and will likely be insufficient to curb the epidemic. Barriers to facility HTC uptake include distance from clinic, long wait times, economic costs (transportation, lost wages, childcare), concerns about confidentiality, inconvenient hours, and lack of access to the healthcare system.[5] Community-based HTC (defined as HTC outside of a health facility) has the potential to overcome these barriers and achieve widespread testing coverage.[6,7] Modalities of community HTC are diverse and include: home, mobile, workplace, partner/index, and campaign testing. Community HTC has been shown to have high acceptability and requires minimal infrastructure allowing for easier scale up. Since community HTC enables easy access to testing, it can identify asymptomatic HIV-positive individuals at high CD4 counts. In contrast, individuals generally seek facility HTC when they are feeling ill, later in the course of their illness. Identifying HIV-positive persons at higher CD4 counts enables early ART initiation, which improves patient survival and reduces HIV transmission from virally suppressed individuals by up to 96%.[8,9] In KwaZulu-Natal, South Africa, an analysis found a 1.4% decline in HIV incidence for every 1% increase in ART coverage.[10] Additionally, modeling studies project substantial decreases in HIV incidence if high coverage of ART is started immediately

after diagnosis.[11-13] As countries shift their ART initiation criteria from a CD4 threshold to immediate treatment, efficient ways to identify HIV-positive persons will be crucial.

Community HTC has the potential to achieve high population testing coverage which can reduce stigma of testing. In addition, community HTC can reach underserved groups, including men, young adults, and key populations (commercial sex workers, men who have sex with men, and persons who inject drugs). Men are more likely to be lost at each step of the HIV treatment cascade. They are less likely to test for HIV, more likely to start ART at advanced disease and to interrupt treatment, all of which leads to increased morbidity and mortality.[14] Young adults (age 15 to 24 years) represent 39% of new infections in those over age 15 years[15] yet they have lower access to HTC and HIV care and poorer clinical outcomes than other age groups.[16] Key populations have an HIV prevalence up to eight times higher than the general population yet are marginalized which results in limited access to the healthcare system.[17,18] Increasing HTC and treatment coverage in these groups is critical to controlling the epidemic.

Community HTC modalities are diverse and acceptability and population reached differ by modality and can vary by setting and linkage strategy.[7] Further, each modality is associated with a different cost per person tested. Synthesizing the literature on HTC modalities can assist policymakers in determining the optimal combination of HTC modalities to implement in each country. As most countries have multiple and varying epidemics, UNAIDS recommends creating regional policies tailored to macro-epidemics rather than nation-wide approaches.[19] Summarizing the data on HTC can also inform parameters in mathematical models to project the long-term impact of HTC interventions.

As countries in SSA have limited budget to implement community HTC, it is important to examine the cost-effectiveness of different modalities. Previous studies have examined the

cost-effectiveness of home and mobile HTC, but other modalities are not well studied. One such strategy is home HTC for male partners of pregnant woman which has been shown to be successful in testing men; the recently completed HOPE intervention in Kisumu, Kenya found that 87% of male partners had been tested 6 weeks post-partum in the HOPE arm compared to 39% in the standard of care arm.[20] Further, couples HIV testing and status disclosure has been shown to increase women's adherence to both antiretroviral therapy (ART) and prevention of mother to child transmission (PMTCT) regimens.[21-23] Interventions for encouraging male partners to come to the ANC with their partner and undergo HTC have had varied success; a study in Uganda found that written invitations asking males to attend the ANC for HIV testing was no more effective than standard of care,[24] while other studies in Tanzania and South Africa found that a substantial proportion of men came to the clinic and underwent testing after receiving a letter of invitation (43% and 32%, respectively compared to control rates of <19% and 11%, respectively).[25,26] Therefore, home HTC for male partners may be a viable alternative in settings where encouraging males to attend ANC for testing has not been successful. Indeed, qualitative studies showed home HTC is preferred by both pregnant women (54%) and their male partners (68%) over ANC or VCT.[27]

Another promising HTC modality that requires further evaluation is partner notification services.[28] Partner services (PS), refers to efforts to identify sex partners of persons diagnosed with a sexually transmitted disease, notify them of their potential exposure, provide counseling, testing, and referral to treatment for those found positive. Types of partner services include passive referral—the index case is asked to notify their sexual partners of potential exposure and encourage them to seek HTC, provider notification or assisted partner services (aPS)—healthcare providers contact sexual partners directly and provide counseling and testing, or

contract referral—a mix of the previous two methods in which the index patient is given a certain amount of time to contact their partners, after which the healthcare provider conducts notification.[29] Partner services are widely implemented in high-income countries and growing evidence from sub-Saharan Africa shows PS is feasible and acceptable.[30] APS was recently scaled up by the Ministry of Health in Cameroon; index patients were given a choice of passive referral, assisted partner notification, or contract referral. The intervention achieved 66% coverage of reported sexual partners and HIV positivity was high (50%), with 86% of those found positive were enrolled in care.[30] Similarly, a PS trial with 3 arms in Malawi attained 51% coverage of partners in both the provider notification and contract referral arms compared to only 24% in the passive referral arm. Overall with 64% of partners tested HIV-positive.[31] The high HIV positivity found through APS interventions are similar to those reported in the literature of 45-50% prevalence in cohabitating partners of HIV-positive adults, the vast majority of whom are unaware of their status. APS can also be used as a prevention tool to target pre-exposure prophylaxis (PrEP) to HIV-negative persons who are at high risk of acquiring infection from a positive partner.[32] Although aPS has been shown to be effective in sub-Saharan Africa, its cost-effectiveness has not been well evaluated. Implementing partner services will require significant economic investment so it is crucial to evaluate efficiency to maximize use of limited resources. As conducting an aPS RCT for a sufficiently long time frame to collect clinical endpoints is not feasible, mathematical models can be used to synthesize epidemiologic and economic data and project the long-term health consequences (HIV infections and disability-adjusted life years (DALYs) averted) of implementing aPS over a 10 year time horizon. Modeling results can provide insight to decision makers as they choose which interventions to implement.

This dissertation comprehensively describes key characteristics of various modalities of community HTC and then focus specifically on the health and economic impacts of implementing two understudied forms of community HTC—Home HTC for male partners of pregnant women and assisted partner notification services (aPS). We hope that these papers will provide information to policymakers as they determine which HTC interventions to implement in the context of their country's HIV epidemic. We also hope to inform the WHO guidelines on community HTC and partner notification for sub-Saharan Africa.

Chapter 2: A systematic review and meta-analysis of community and facility-based approaches to address gaps in HIV testing and linkage in sub-Saharan Africa

We conducted a systematic review of HIV testing and counselling modalities, characterizing facility and community (home, mobile, index, key populations, campaign, workplace and self-testing) approaches by population reached (men, first time testers, young adults, key populations), HIV-positivity, CD4 count at diagnosis, linkage to care and cost. A large number of studies have been conducted in the past decade and this is the first paper to synthesize the literature on both facility and community HTC in SSA as well as the first to characterize the ability of each modality to reach young adults and men, and assess the literature on self-testing, an innovative low-cost method to test hard to reach populations.

Assessing linkage to care is also crucial as the success of HTC strategies is dependent on their ability to link persons to ART. We assess the effectiveness of community HTC with and without facilitated linkage to care strategies (i.e. counsellor home visits to encourage linkage). We also assess the difference in uptake between two types of facility testing: voluntary counselling and testing (VCT) and provider initiated testing counselling and (PITC). Since PITC is provider driven, it can provide a safety net for those who do not independently seek HTC.[33,34]

Chapter 3: Modeling the cost-effectiveness of home-based HIV testing and education (HOPE) for pregnant women and their male partners in Nyanza Province, Kenya

In Chapter 3, we assess the efficiency of adding the HOPE intervention to standard antenatal care in western Kenya. Pregnant and post-partum women in sub-Saharan Africa (SSA) have rates of HIV-acquisition that are more than two fold higher than in non-pregnant women.[35-38],[39] Additionally, HIV-positive pregnant women face a higher risk of maternal mortality and can transmit HIV to their infants.[40] Although pregnant women have high rates of HIV testing coverage, largely due to antenatal (ANC) testing, they are less likely to know the HIV status of their male partners. In Kenya during 2013, 88% of pregnant women were tested for HIV, while only 4.5% of their male partners underwent testing in the prior 12 months.[40,41] Home HTC for pregnant women and their male partners can address this gap by facilitating couples testing outside of the ANC. Increasing HIV testing in males reduces transmission to their female partners, while also averting morbidity and mortality in men associated with late ART initiation. However, home-based couples counseling for pregnant women is resource intensive and its cost-effectiveness has not been evaluated. We used a mathematical model to assess the cost-effectiveness of providing home-based partner education and HIV testing (HOPE) to couples as a part of routine antenatal care in western Kenya. We conducted a detailed in-country microcosting to estimate the cost per couple tested for scaling up the HOPE intervention under a program scenario of healthcare professionals and with a task-shifting scenario utilizing community health workers.

Chapter 4: Cost-effectiveness of implementing active partner notification for HIV in Kenya: A mathematical modeling analysis

In Chapter 4, we evaluate the efficiency of partner services for HIV prevention in SSA. While partner services are routinely utilized in developed countries, they have not been widely implemented in SSA. Similarly, although several studies have evaluated the cost-effectiveness of partner services in developed countries, we found only one such economic analysis in SSA.[29] This analysis was a static model that did not incorporate indirect benefits (herd immunity) generated by the intervention and only used a one year time horizon. Our economic evaluation uses a dynamic model that projects the long-term health and economic impact of implementing a large-scale aPS program in a low resource setting. We also conducted a micro-costing of the aPS randomized clinical trial in Kenya. By collecting costs prospectively and assessing staff time needed to perform different aspects of the intervention, we were able to accurately project the incremental cost per sexual partner tested. APS costs data from SSA are scarce in the published literature.

In SSA, where the primary driver of the HIV-epidemic is heterosexual transmission and 50% of HIV-positive persons do not know they are infected, aPS is a promising strategy to fill in testing gaps. APS can provide targeted HTC to those at high risk of HIV infection—sexual partners of persons diagnosed with HIV. APS can also serve as a vehicle for couples counseling and disclosure as well as PrEP if the partner is HIV-negative.

References

1. Montaner JS, Lima VD, Barrios R, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet 2010;376:532-9.
2. UNAIDS. The Gap Report. Accessed on 10/3/2015 from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf.
3. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. PLoS medicine 2011;8:e1001056.
4. Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society 2012;15:17383.
5. Musheke M, Ntalasha H, Gari S, et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in Sub-Saharan Africa. BMC public health 2013;13:220.
6. Paulin HN, Blevins M, Koethe JR, et al. HIV testing service awareness and service uptake among female heads of household in rural Mozambique: results from a province-wide survey. BMC public health 2015;15:1388.
7. Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. PLoS medicine 2013;10:e1001496.
8. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet 2010;375:2092-8.
9. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.
10. Tanser F, Barnighausen 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;339:966-71.
11. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet 2009;373:48-57.
12. Eaton JW, Johnson LF, Salomon JA, et al. HIV treatment as prevention: systematic comparison of mathematical models of the potential impact of antiretroviral therapy on HIV incidence in South Africa. PLoS medicine 2012;9:e1001245.
13. Ying R, Barnabas RV, Williams BG. Modeling the implementation of universal coverage for HIV treatment as prevention and its impact on the HIV epidemic. Curr HIV/AIDS Rep 2014;11:459-67.
14. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Tropical medicine & international health : TM & IH 2011;16:828-9.
15. Kurth AE, Lally MA, Choko AT, Inwani IW, Fortenberry JD. HIV testing and linkage to services for youth. Journal of the International AIDS Society 2015;18:19433.
16. MacPherson P, Munthali C, Ferguson J, et al. Service delivery interventions to improve adolescents' linkage, retention and adherence to antiretroviral therapy and HIV care. Tropical medicine & international health : TM & IH 2015;20:1015-32.
17. Wheeler T, Wolf RC, Kapesa L, Cheng Surdo A, Dallabetta G. Scaling-up HIV responses with key populations in West Africa. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S69-73.
18. Adebajo S, Eluwa G, Njab J, et al. Evaluating the effect of HIV prevention strategies on uptake of HIV counselling and testing among male most-at-risk-populations in Nigeria; a cross-sectional analysis. Sex Transm Infect 2015.
19. Honge B, Jespersen S, Medina C, et al. Hepatitis B virus surface antigen and anti-hepatitis C virus rapid tests underestimate hepatitis prevalence among HIV-infected patients. HIV Med 2014;15:571-6.

20. Krakowiak D, Kinuthia J, Osoti A, Asila V, Gone MA, Mark J, Sharma M, Barnabas RV. Male partner home HIV testing vs clinic invitation in pregnancy: A randomized trial. [Oral] Conference on Retroviruses and Opportunistic Infections (CROI), Boston, MA, February, 2016.
21. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis 2015;33:123-9.
22. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. AIDS and behavior 2010;14:558-66.
23. Rosenberg NE, Mtande TK, Saidi F, et al. Recruiting male partners for couple HIV testing and counselling in Malawi's option B+ programme: an unblinded randomised controlled trial. The lancet HIV 2015;2:e483-91.
24. Byamugisha R, Astrom AN, Ndeezi G, Karamagi CA, Tylleskar T, Tumwine JK. Male partner antenatal attendance and HIV testing in eastern Uganda: a randomized facility-based intervention trial. Journal of the International AIDS Society 2011;14:43.
25. Jefferys LF, Nchimbi P, Mbezi P, Sewangi J, Theuring S. Official invitation letters to promote male partner attendance and couple voluntary HIV counselling and testing in antenatal care: an implementation study in Mbeya Region, Tanzania. Reprod Health 2015;12:95.
26. Mohlala BK, Boily MC, Gregson S. The forgotten half of the equation: randomized controlled trial of a male invitation to attend couple voluntary counselling and testing. AIDS (London, England) 2011;25:1535-41.
27. Osoti AO, John-Stewart G, Kiarie JN, et al. Home-based HIV testing for men preferred over clinic-based testing by pregnant women and their male partners, a nested cross-sectional study. BMC infectious diseases 2015;15:298.
28. Hogben M, McNally T, McPheeters M, Hutchinson AB. The effectiveness of HIV partner counseling and referral services in increasing identification of HIV-positive individuals a systematic review. Am J Prev Med 2007;33:S89-100.
29. Rutstein SE, Brown LB, Biddle AK, et al. Cost-effectiveness of provider-based HIV partner notification in urban Malawi. Health policy and planning 2014;29:115-26.
30. Henley C, Forgwei G, Welty T, et al. Scale-up and case-finding effectiveness of an HIV partner services program in Cameroon: an innovative HIV prevention intervention for developing countries. Sexually transmitted diseases 2013;40:909-14.
31. Brown LB, Miller WC, Kamanga G, et al. HIV partner notification is effective and feasible in sub-Saharan Africa: opportunities for HIV treatment and prevention. Journal of acquired immune deficiency syndromes (1999) 2011;56:437-42.
32. Brown LB, Miller WC, Kamanga G, et al. Predicting partner HIV testing and counseling following a partner notification intervention. AIDS and behavior 2012;16:1148-55.
33. Silvestri DM, Modjarrad K, Blevins ML, Halale E, Vermund SH, McKinzie JP. A comparison of HIV detection rates using routine opt-out provider-initiated HIV testing and counseling versus a standard of care approach in a rural African setting. Journal of acquired immune deficiency syndromes (1999) 2011;56:e9-32.
34. Topp SM, Li MS, Chipukuma JM, et al. Does provider-initiated counselling and testing (PITC) strengthen early diagnosis and treatment initiation? Results from an analysis of an urban cohort of HIV-positive patients in Lusaka, Zambia. Journal of the International AIDS Society 2012;15:17352.
35. Leroy V, Van de Perre P, Lepage P, et al. Seroincidence of HIV-1 infection in African women of reproductive age: a prospective cohort study in Kigali, Rwanda, 1988-1992. AIDS (London, England) 1994;8:983-6.
36. Taha TE, Dallabetta GA, Hoover DR, et al. Trends of HIV-1 and sexually transmitted diseases among pregnant and postpartum women in urban Malawi. AIDS (London, England) 1998;12:197-203.

37. Humphrey JH, Hargrove JW, Malaba LC, et al. HIV incidence among post-partum women in Zimbabwe: risk factors and the effect of vitamin A supplementation. AIDS (London, England) 2006;20:1437-46.
38. Kinuthia J, Kiarie JN, Farquhar C, et al. Cofactors for HIV-1 incidence during pregnancy and postpartum period. Curr HIV Res 2010;8:510-4.
39. Gray RH, Li X, Kigozi G, et al. Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study. Lancet 2005;366:1182-8.
40. WHO. Global Update on the health sector response to HIV, 2014 Accessed from: http://apps.who.int/iris/bitstream/10665/128494/1/9789241507585_eng.pdf?ua=1 on 10/16/2015.
41. UNAIDs. Kenya AIDS Response Progress Report, 2014. Accessed on 1/20/2016 from http://www.unaids.org/sites/default/files/country/documents/KEN_narrative_report_2014.pdf.

CHAPTER 2: A systematic review and meta-analysis of community and facility-based approaches to address gaps in HIV testing and linkage in sub-Saharan Africa

A systematic review and meta-analysis of community and facility-based approaches to address gaps in HIV testing and linkage in sub-Saharan Africa

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Abstract

HIV testing and counselling is the first crucial step for linkage to HIV treatment and prevention. However, despite high HIV burden in sub-Saharan Africa, testing coverage is low, particularly among young adults and men. Community-based HIV testing and counselling (testing outside of health facilities) has the potential to reduce coverage gaps, but the relative impact of different modalities is not well assessed. We conducted a systematic review of HIV testing and counselling modalities, characterizing facility and community (home, mobile, index, key populations, campaign, workplace and self-testing) approaches by population reached, HIV-positivity, CD4 count at diagnosis and linkage. Of 2,520 abstracts screened, 126 met eligibility criteria. Community HIV testing had high coverage and uptake and identified HIV-positive individuals at higher CD4 counts than facility testing. Mobile HIV testing reached the highest proportion of men of all modalities examined (50%, 95% CI = 47–54%) and home with self-testing reached the highest proportion of young adults (66%, 95% CI = 65–67%). Few studies evaluated HIV testing and counselling for key populations (commercial sex workers and men who have sex with men), but these interventions yielded high HIV positivity (38%, 95% CI = 19–62%) combined with the highest proportion of first-time testers (78%, 95% CI = 63–88%), indicating service gaps. Facilitated linkage (for example, counsellor follow-up to support linkage) achieved high linkage to care (95%, 95% CI = 87–98%) and ART initiation (75%, 95% CI = 68–82%). Expanding mobile HIV testing, self-testing and outreach to key populations with facilitated linkage can increase the proportion of men, young adults and high-risk individuals linked to HIV treatment and prevention.

Introduction

Globally, there are around 2.3-million new HIV infections annually, 80% of which occur in sub-Saharan Africa[1]. Despite the high burden, only one-third of adults in sub-Saharan Africa have been tested for HIV in the past year and less than 50% of HIV-positive individuals know their status[2,3]. Knowledge of one's serostatus is vital for accessing lifesaving anti-retroviral therapy (ART) and linking to HIV prevention. Conventional facility-based HIV testing and counselling (HTC) has not achieved high testing coverage in sub-Saharan Africa and will probably be insufficient to meet UNAIDS ambitious 90–90–90 targets — 90% of HIV-positive individuals knowing their status, 90% of HIV-positive individuals who are aware of their status on ART, and 90% of individuals on ART virally suppressed[4,5]. Barriers to facility testing include distance from clinic, long wait times, costs (transportation, lost wages and childcare), confidentiality concerns, low perceived risk and infrequent contact with the health-care system[6]. In addition, patients often present at facilities late in the course of their illness, increasing HIV morbidity, mortality and transmission[7]. Community-based HTC (conducted outside of a health facility) has the potential to overcome these barriers, achieve high coverage, and identify asymptomatic HIV-positive individuals at high CD4 counts[8,9]. In addition, community HTC may reach more men, young adults, and key populations than facility HTC. Community-based strategies also require minimal infrastructure allowing for easier scale up[10-12].

Community HTC modalities include: home, mobile, workplace, index partner/family members (sexual partners or family members of HIV-positive persons) and as part of a campaign. Uptake and demographics of population reached can vary widely by modality[9]. A large number of studies on HTC have been conducted in sub-Saharan Africa and a previous systematic review was completed in 2012, but facility testing was not included and uptake in

men and young adults was not assessed. In addition, several large-scale interventions have been published since 2012[11,13-15]. Recently, the World Health Organization's released guidelines that strongly recommend implementing community HTC[16]. As most countries have multiple and varying epidemics, UNAIDS recommends creating regional policies tailored to the macro-epidemic rather than nation-wide approaches.[17] Local policymakers will need to determine the optimal combination of community HTC interventions to increase testing in the context of their country's HIV epidemic.

To provide evidence for decision makers, we summarize the literature on community and facility-based HTC. We characterize each modality by population coverage, since high coverage is beneficial to both HIV-positive and -negative people. HTC can reduce risk behaviour in HIV-negative individuals, while providing a means to link them to primary prevention (including circumcision and pre-exposure prophylaxis (PrEP))[18-21]. We evaluate effectiveness in reaching men and young adults (both groups have a disproportionately high risk of HIV acquisition and poorer clinical outcomes once infected[22-24]) and targeted HTC for key populations (men who have sex with men (MSM), commercial sex workers (CSWs) and people who inject drugs (PWID)) — groups that generally have very high HIV prevalence and low access to health care[25]. We assess HIV positivity to characterize yield and examine CD4 count at diagnosis to identify modalities that have the potential to link infected persons to care earlier in their disease course. Estimates from our analysis can also be used as parameters in mathematical models to project the long-term impact of HTC interventions.

Methods

Inclusion criteria. We conducted a systematic literature review following Cochrane and PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines[26].

Studies were eligible for inclusion if they reported data on at least one of the following outcomes: coverage (individuals who accepted HTC/eligible target population); uptake (individuals who accepted HTC/individuals offered HTC); proportion of young adults (age <25 or <30 years**;** proportion of men; proportion of first-time testers; HIV positivity (number positive/total tested); proportion with a CD4 count of 350 cells μL^{-1} or less; proportion linked to care (those who had visited a clinic, obtained a CD4 count or initiated ART); proportion retained in care (individuals retained/individuals who initiated ART); or cost per person tested. The target population was defined as eligible population in the catchment area, either enumerated by the study (often the case for home HTC) or estimated (often the case for mobile and campaign HTC). For facility HTC, the target population was defined as people visiting the clinic, and for index partner or family members it was defined as all sexual partners or cohabitating family members listed by index patient. With the exception of HTC targeted to key populations, we excluded HTC studies not related to general population screening, including case reports and studies limited to antenatal or paediatric settings, or to patients with specific diseases (for example, tuberculosis). Observational (cross-sectional and cohort) studies and randomized trials were eligible for inclusion. Studies were included in the analyses more than once if they had different arms or multiple study sites (for example, urban and rural settings or different countries). If more than one wave of a survey or intervention was completed, only the most recent was used.

Search strategy. Literature searches were conducted with the help of a librarian on July 22, 2014 and updated on June 10, 2015. Briefly, we searched PubMed, EMBASE, Cochrane Library, Global Health Database, African Index Medicus, and conference abstracts (CROI, R4P, IAS) using MeSH terms for PubMed and comparable terms for other databases. Search terms included

"HIV Infections/diagnosis" AND "Africa South of the Sahara" AND ("mass screening" OR test OR tests OR testing OR screen* OR diagnosis OR “counseling”). Bibliographies of relevant papers were screened and authors were contacted for missing outcomes. Searches were limited to human studies published between 2000 and 2015. Full strategy is described in the Supplementary Information.

Definitions of HTC modalities. Community-based HTC was defined as that conducted outside of health facilities. Facility-based HTC modalities were conducted in health-care facilities (for example, clinics, hospitals, fixed stand-alone voluntary counselling and testing sites). Facility HTC was divided into two categories: voluntary counselling and testing (VCT), which is patient-initiated testing; and provider-initiated testing counselling (PITC), which is routine or opt-out HTC that is initiated by a provider. Community HTC modalities included home (offering HTC door-to-door to a catchment area), mobile (setting up a mobile van or container to provide HTC in a central area of a community), index partner or family member (offering HTC to individuals who may have been exposed to HIV by a sexual partner or who have an HIV-positive household member), campaign (short — generally one to two weeks — intensive community mobilization followed by mobile testing, often partnered with other health interventions), key populations (targeted to MSM, CSWs and PWID) and workplace (offered at a place of employment). We examined a subset of home and workplace HTC that used self-testing.

Data screening and extraction. M.S., R.Y. and R.V.B. screened abstracts for initial inclusion. Disagreements were adjudicated by reviewing the full text. M.S., R.V.B., R.Y. and G.T. reviewed papers for eligibility and used a standardized extraction form to characterize eligible studies (Supplemental Information 2). Study quality was rated low; moderate; or high; based on representativeness of underlying population, follow-up (present or absent), assessment of

outcomes, and number of outcomes presented. Costs were inflated to 2012 US dollars by converting to local currency units, multiplying by the ratio of each country's gross domestic product deflator (2012 deflator or base year deflator) and converting back to US dollars[27].

Statistical analysis. Random effects meta-analysis of single proportions with binomial exact confidence intervals (CI) was used to summarize results. Proportions were stabilized using the Freeman-Tukey double arcsine transformation unless the number of events was less than ten, in which case a logit transformation was used because of convergence issues. Heterogeneity was quantified using the I^2 statistic. For modalities with enough data (ten studies or more), trends were examined by year before 2005 (when the HIV rapid diagnostic test was introduced), country and facilitated linkage. Analyses were conducted in R software using the metaprop function in the meta package[28].

Results

We identified 126 eligible studies out of 2,520 abstracts (Supplementary Figure S0.a). Overall, 64% of studies were rated moderate or high quality (Supplementary Information 2). Most studies included in our analysis evaluated facility and home HTC. We identified far fewer studies on other types of community HTC: home with self-testing (n = 2), workplace with self-testing (n = 2), index partner/family member (n = 5), key populations (n = 5), campaign (n = 5) and workplace (n = 4). Forest plots of each outcome by modality are available in the Supplementary Information with pooled estimates presented here. I^2 values of pooled estimates varied from 90% to 100%, reflecting high heterogeneity in study designs and countries included (Supplementary Information). The countries represented varied by outcome with the greatest number reporting data for home and facility HTC coverage, uptake and tester demographics. Far fewer studies reported CD4 count at diagnosis and linkage to care outcomes; studies containing these data

were mainly conducted in South Africa, Kenya and Uganda. All home self-testing studies were conducted in Malawi and the most key population studies were conducted in Nigeria. Overall, the largest number of studies were conducted in South Africa.

Coverage and uptake

Coverage was reported in 19 home HTC studies[15,18,29-45], one mobile[13], two campaign[46,47], three index partner/family member[48-50], five facility VCT[51-55], and five facility PITC studies[56-61]. Overall, community HTC modalities achieved higher coverage than facility, with home (70%, 95% CI = 58–79) and campaign (76%, 95% CI = 49–95%) having the highest population coverage (Fig. 1). Home HTC consistently achieved high coverage across 19 studies, whereas campaign coverage was also high, but based on only two studies. Pooled coverage was 37% (95%, CI = 33–42%) for mobile HTC, from one study conducted in three countries (South Africa, Tanzania and Zimbabwe). Coverage of index HTC was heterogeneous depending on target group (family members compared with sexual partners) and type of contact tracing (active or passive referral). Figure 1 shows results for sexual partner tracing only (41%); full results are shown in Supplementary Figure S18. Facility VCT (15%, 95% CI = 9–21%) and PITC (18%, 95% CI = 18–31%) attained the lowest coverage.

Uptake was reported in 31 home HTC studies[5,14,15,18,27,29-38,40-45,53,62-74], two home with self-testing[11,75], two mobile[10,68], three index partner or family member[48-50], four campaign[46,47,76,77], three workplace[78-80], three facility VCT[54,56,81], and 11 facility PITC studies[56,57,59,60,81-87]. Overall, community modalities had high uptake (Fig. 1). Home HTC had a pooled uptake of 82% (95% CI = 76–87%) and home with self-testing had slightly lower uptake (69%, 95% CI = 59–78). Mobile and campaign had the highest uptake (both at97%). Index uptake was 89% (95% CI = 88–90%) for home testing of family members (Supplementary

Figure S10) and 52% for sexual partners (95% CI = 30–71%; Fig. 1). Uptake for facility VCT was defined as number tested divided by number referred for VCT by provider, for facility PITC it was defined as number tested divided by number offered PITC. We found higher uptake for people given routine PITC (73%, 95% CI = 55–87%) compared with those referred to on site VCT (26%, 95% CI = 15–39%).

Demographics of testers

The percentage of men out of total persons tested was reported in 25 home HTC studies[5,14,18,29,31,32,37,38,41-45,63,64,66,68-72,88-90], two home with self-testing[11,75], 10 mobile[10,13,68,72,91-99], 3 index partner[47,49,88], 3 campaign[46,47,76], 2 workplace[100,101], 20 facility VCT[52,54,61,64,81,88,89,92,93,95,96,98,102-107], and 13 facility PITC[58,60,82-84,86,99,108-113] (Fig. 2). Mobile had the highest percentage of men (50%, 95% CI = 47–54%), whereas home had the lowest for general population HTC (40%, 95% CI = 39–41%). Index partner testing had 41% men (95% CI = 23–61%), but varied greatly by tracing strategy; active tracing had 50% men whereas passive clinic referral had only 15% (Supplementary Figure S18). Facility VCT and PITC both had 42% men.

Percentage of participants reporting testing for the first time was included in 20 home HTC studies[5,14,18,29,31,32,38,41-44,63,65,66,68-72,88], 11 mobile[10,12,68,93-95,97,103,114], 3 campaign[46,47,77], 3 key populations[25,115,116], and 7 facility VCT[12,54,91,93,95,106], and 5 facility PITC[58,86,88,111,112]. Pooled percentages of first-time testers were higher for community than facility modalities (Fig. 2). Percentages varied by country, with South Africa consistently having the lowest percentage of first-time testers across modalities (Supplementary Figures S23–S27). Key population interventions had the highest proportion of first-time testers (83%, 95% CI = 71–91%), and mobile had the highest percentage among the general population (63%, 95% CI = 50–74%).

Home HTC had 58% first-time testers (95% CI = 48–67%), and campaign had 55% (95% CI = 20–91%), but was highly variable depending on the setting (Supplementary Figure S25). Facility VCT had 53% (95% CI = 40–66%) and PITC had 55% (95% CI = 48–62%) first-time testers.

The percentage of testers who were young adults testers <age 25 or <30 years) was reported in 17 home HTC studies[5,18,29-31,35,37,38,45,63,64,68-70,73,74,90,117], one home with self-testing[11], 13 mobile[10,12,13,68,91,93,95-97,103,107,114], two index partner[48,88], two campaign[47,77], 20 facility VCT[12,51,52,54,64,88,89,91-93,95,104-107,114,118-120], and six facility PITC[58,82,86,88,110,113]. Results varied considerably by study (Supplementary Figures S29–S35). Community HTC generally tested a higher proportion of young adults than facility modalities; home with self-testing had the largest percentage (66%, 95% CI = 65–67%), followed by mobile, and then home (Fig. 2). Campaign reported 31% young adults, but varied from 20–50% depending on study (Supplementary Figure S32). Facility VCT had 46% (95% CI = 39–53%) and PITC had 38% (95% CI = 39–53%).

HIV positivity and CD4 count of less than 350 cells μL^{-1} at diagnosis

Yield of HIV positive individuals (HIV positivity) was reported in 29 home studies[14,15,18,27,29-32,34,36,38,41-45,63,65,66,68,70-73,88,89], one home with self-testing[11], 12 mobile[10,13,68,72,92-95,97,98,103,107,114], five campaign[46,47,76,77,120], three workplace[79,80,121], four key population[12,115,116,122], four index partner[48-50,88], 27 facility VCT[54-56,64,81,84,88,91-93,95,98,102,104-107,114,118-120,123-127], and 17 facility PITC[56,57,59,60,81,83-88,99,110-113,126] studies. Community-based strategies for the general population had lower HIV positivity (6–11%) than facility HTC (18–20%), whereas targeted community HTC for key populations and sexual partners of index patients had the highest HIV yield (Fig. 3). HTC interventions targeting sexual partners of index cases had 28% positivity (95% CI = 13–50%), those for MSM had 24% (95% CI = 14–39%), for CSWs had 27% (95% CI = 12–51%), and interventions targeting PWIDs had the lowest positivity (3%, 95% CI = 1–15%). Index HTC

for family members had similar HIV yield to home and mobile HTC (9%, 95% CI = 5–14%) (Supplementary Figure S42). Forest plots of HIV positivity for each modality stratified by country are shown in Supplementary Figures S36–S44). HIV positivity for community HTC in the general population largely mirrored prevalence of the country where the study was conducted, with the exception of four countries with the highest prevalence: Mozambique, Swaziland, Botswana and Lesotho. These countries have adult HIV prevalence ranging from 22–27%[128], but HIV yield from home, mobile and campaign HTC was 5–12%. HIV positivity for facility VCT and PITC was generally higher than prevalence in the general population.

The proportion of individuals with CD4 count of less than 350 cells μL^{-1} at HIV diagnosis was reported in 7 home[14,38,42,43,65,72,73], 3 mobile[91,94,114], 3 campaign[46,47,76], 8 facility VCT[60,81,107,126,127,129-131] and 5 facility PITC studies[61,81,99,126,130]. Community-based strategies identified HIV-positive individuals at higher CD4 counts than facility HTC, with campaign having the lowest proportion with CD4 count less than 350 cells μL^{-1} (26%, 95% CI = 22–30%) (Fig. 3). Home (39%, 95% CI = 32–46%) and mobile (38%, 95% CI = 36–41%) had similar proportions of HIV-positive individuals with a CD4 count less than 350 cells μL^{-1}, whereas facility VCT (66%, 95% CI = 60–72%) and PITC (71%, 95% CI = 67–75%) had the highest proportion with low CD4 count.

Linkage and retention in care for HIV-positive individuals

Linkage to care was defined as visiting a clinic for community HTC and returning to the clinic to obtain CD4 count results (or enrolling in pre-ART care) for facility HTC. Linkage was reported for ten home[14,15,29,34,41-43,65,72,132], six mobile[72,91,92,94,133-135], two campaign[76,77], eight facility VCT[56,81,84,91,92,123,126,136] and five facility PITC studies[60,84,87,111,126]. Home and campaign interventions achieved a high proportion of individuals linked (95%, 95% CI = 87–98%) when

paired with facilitated linkage to care strategies (for example lay-counsellor follow up to encourage clinic visit); interventions without facilitated linkage achieved lower proportions of HIV positive individuals visiting a clinic (26%, 95% CI = 18–36%) (Fig. 4). Mobile HTC achieved 37% (95% CI = 24–51%) linkage; rates were highest in two intervention conducted in South Africa, one which used incentivized monetary recruitment and another which used a call centre to encourage linkage after HTC[94,134] . Linkage to care from facility VCT was 61% (95% CI = 48–72%) and from PITC was 55% (95% CI = 39–71%) (Fig. 4). Time from HTC to linkage to care ascertainment varied by study (ranging from 1 to 12 months); the method of ascertainment (participant self-report or clinic record) also varied.

Four home HTC studies reported ART initiation among those eligible[14,41,43,65]. Similar to linkage to care, ART initiation was higher in home interventions with facilitated linkage (76%, 95% CI = 26–82%) compared with those without facilitated linkage (16%, 95% CI = 12–20%) (Fig. 5). ART initiation rates after home HTC with facilitated linkage were similar to those achieved through facility HTC. Initiation among those eligible was 64% (95% CI = 54–72%) in facility VCT and 70% (95% CI = 61–78%) in facility PITC with three studies reporting initiation rates for VCT[61,126,130] and four for facility PITC[60,81,84,87,111]. Self-testing showed an ART initiation rate of 29% (95% CI = 17–45%), although this number is among all HIV-positive individuals and is not restricted to those who are ART eligible since POC CD4 counts were not conducted[11] (Supplementary Figure S55).

One study reported retention in care at12 months after ART initiation for home HTC[14] and two studies for both facility VCT and PITC reported retention — one at 6 months[60] and one at 12 months[130]. Not surprisingly, linkage rates were higher in the 6 month compared with the 12 month retention study (Supplementary Figure S59). Retention was highest for home HTC,

although the sample size was small (93%, 95% CI = 83–97%) (Fig. 5). Facility VCT achieved 53% (95% CI = 32–71%) retention, and PITC retention achieved 64% (95% CI = 32–90%).

Cost per person tested

The average cost per person tested (2012 US dollars) for community HTC was $27.38 for mobile, $16.60 for index, $11.17 for campaign and $8.58 for home HTC[88,93,103,137-141] (Supplementary Table S2 and Figure S61). The cost per person tested was highest for stand-alone VCT ($36.78)[88,93,142] whereas hospital and clinic HTC had similar costs ($12.56 and $12.32, respectively)[81,88,93,140,142-147] (Supplementary Table S3 and Figure S62). Costs were dependent on the country where the study was conducted, which costs were included (start-up or ongoing only) and the intervention scale.

Discussion

Across modalities, community HTC successfully reached target groups (men, young adults and first-time testers) with higher coverage than facility HTC. High uptake of community HTC reflects population acceptability of testing outside of health-care facilities. Community HTC identified HIV-positive individuals with higher CD4 counts who were likely to be earlier in their disease course. Combined with the potential of community HTC with facilitated linkage to achieve high linkage to treatment with similar retention rates as facility HTC, this suggests that scaling up community interventions could reduce the morbidity, mortality and transmission associated with late or non-initiation of ART. Although community interventions test a large number of HIV-negative individuals, HTC can reduce risky sexual behaviour[74] and provide a means to link uninfected persons to primary prevention. This is particularly crucial for young women, who have high HIV incidence and can benefit from PrEP[21]. Preventing HIV infections averts future treatment costs as well as morbidity. A recent modelling study found that ART

scale-up should be combined with primary prevention such as PrEP to achieve maximum HIV reduction[148]. High coverage of HTC can also reduce stigma around testing.

Each HTC modality reaches distinct sub-populations and a combination of strategies will probably be necessary to achieve high ART coverage. Mobile and campaign HTC had high uptake (97%), as individuals who present at a mobile van or during a campaign are probably seeking out testing, but home HTC also achieved high uptake among people at home who were offered testing (82%). Home HTC also attained high population coverage, probably because offering testing door-to-door removes substantial barriers, including eliminating the need to actively seek out HIV testing[149]. However, home HTC is less likely to reach men and young adults. A recent home HTC intervention in Botswana reached 85% of women in the target population compared with just 50% of men[150]. This may be because women are more likely to be home at the times when the intervention is conducted.

Campaign HTC has the potential to attain high coverage in large catchment areas and identify HIV-positive individuals at high CD4 counts (one-third of newly diagnosed HIV-positive individuals had a CD4 count of less than350 cells μL^{-1} compared with two-thirds or more for facility HTC). The multidisease focus of campaigns may reduce stigma of HIV testing interventions. Our results suggest that campaign HTC can be a successful strategy for countries seeking to increase overall testing coverage in a short time frame.

Home HTC with self-testing reached the greatest proportion of young adults of all modalities examined[11] and is a promising strategy to achieve high uptake[151]. Young adults (age 15 to 24 years) represent 39% of new infections in those over 15-years old[23], but have lower access to HTC and HIV care and poorer clinical outcomes than other age groups[24]. Home HTC with self-testing had slightly lower coverage and reached fewer first-time testers than home HTC

administered by counsellors. The World Health Organization recommends HIV self-testing as an option for individuals who are unable or unwilling to receive counsellor-administered HTC. However, supervision improves interpretation of results[151] and a reactive self-test should not be considered a definitive diagnosis, as standard testing is needed to confirm results. More studies evaluating linkage to care following a positive self-test are needed[16].

Mobile HTC is the most effective strategy for reaching men, a target group in sub-Saharan Africa. Men are more likely to be lost at each step of the HIV treatment cascade; they are less likely to undergo testing, more likely to start ART at an advanced disease stage and more likely to interrupt treatment — all of which leads to increased morbidity and mortality[22]. Qualitative studies highlight men's preference to test outside of facilities[152], so scale up of community interventions can meet this need. Future studies could investigate HTC at predominantly male workplaces, nightclubs or bars.

HIV testing of sexual partners through active contact tracing is an efficient high yield method that should be scaled up. HIV positivity was high (55%) and the intervention attained a high coverage (41%). The HIV prevalence we report is similar to that found in the literature — 45–50% in cohabitating partners of HIV-positive adults, most of whom are unaware of their status[48]. Interestingly, high coverage of males was achieved only through active contact tracing, whereas passive tracing identified more women (Supplementary Figure S18).

Facilitated linkage strategies are a key component of successful community-based HTC. Persons testing at an HIV facility generally have higher rates of linking to care and initiating ART than those who test outside the health-care system. However, we report that high linkage rates (comparable with, or higher than, facility HTC) can be achieved with community HTC when individuals are followed-up to encourage linkage.

Although scaling up community HTC with facilitated linkage is important, the benefits of improving facility HTC coverage should not be overlooked. Consistent with previous studies, our analysis finds opt-out facility PITC had much greater uptake than referring patients to VCT[56]. However, coverage of PITC in health facilities is low, demonstrating missed opportunities to identify HIV-positive individuals and to link them to care. For example, a Ugandan hospital reported only 50% of inpatients with HIV-related diagnoses were tested for HIV before leaving the hospital[86]. PITC is an underused strategy in sub-Saharan Africa and scaling up testing would provide a safety net for those who do not independently seek HTC[61,112]. Because PITC identifies mainly symptomatic HIV-positive persons at low CD4 counts as well as those with health-care access, it should be coupled with other modalities to maximize population coverage.

Our review identified gaps where additional evidence is needed. A large proportion of CD4 count and linkage data came from South Africa, with Uganda and Kenya also well represented. South Africa has the lowest percentage of first-time testers, reflecting the successful scale-up of HTC. There are fewer studies from other parts of sub-Saharan Africa, which may limit how much the pooled estimates can be generalized. Also, few studies followed patients longitudinally and measured linkage to care, ART initiation, retention and viral suppression. In addition, although many studies evaluated home HTC, more data are needed for other community modalities, including campaign and workplace.

Data were also limited for key populations. Despite having an HIV prevalence up to eight times higher than the general population, interventions for key populations are scarce and scale up is urgently needed[115,153]. Key population interventions can reduce the spread of HIV in the general population[154]. Currently, numerous policy barriers exist that restrict the availability and

access of HIV-related services for MSM and CSWs, including police harassment and criminal laws[155]. Only three HTC interventions were targeted to MSM and only one was targeted to CSWs and PWIDs. Most key population HTC studies were from Nigeria, so data are needed from other parts of sub-Saharan Africa. We report a high HIV positivity combined with a high proportion of first-time testers in MSM and CSW groups, highlighting the need for service expansion. We found a lower HIV prevalence in PWIDs compared with MSM and CSW groups, reflecting sexual transmission as the main mode of HIV spread in sub-Saharan Africa. Successful HTC programmes for key populations are community-based (particularly mobile), as many high-risk groups are marginalized and do not have access to conventional health systems[122]. Community-based HTC for MSM and PWIDs have been shown to have higher acceptance and greater HIV yield than clinic referral for HTC[115]. In addition, self-testing is a potential strategy to reach key populations, as it demonstrates high acceptability and is considered convenient and private[156].

Costs of community-based and facility-based HTC vary by modality, country, scale of intervention, linkage strategy and costs included. Generally, community-based HTC and integrated facility HTC costs were comparable. However, stand-alone HTC had the highest cost per person tested indicating integrated HTC may be more cost-efficient than stand-alone services (Supplementary Table S3).

The limitations of our analysis included the heterogeneity across studies, which may not be accurately reflected in the pooled estimates. Differences in study design, geographical location (country, urban or rural area) and intervention year added to the heterogeneity. To address this, we used random effects meta-analysis and stratified on key variables (year <2005, country and facilitated linkage). In addition, large numbers of HIV-positive individuals were lost

to follow up in studies that reported linkage so we considered these persons unlinked in our analyses. If individuals linked at another clinic, our estimates may be conservative[157]. Furthermore, assessment of linkage to care differed by study (self-report or clinic records review), as did time to linkage assessment, which varied from 1 to 12 months after HTC. In addition, CD4 count at diagnosis and ART uptake among those with eligible CD4 counts could only be assessed in community HTC interventions employing point-of-care CD4, as studies that report CD4 only for those visiting a clinic would not provide accurate denominators. Only studies reporting linkage to care among those eligible for ART were included in our main analysis. Also, estimates of coverage vary in their precision because some studies conducted population enumeration and others used census estimates of the catchment area. Finally, proportion of first-time testers, men and young adults tested are crude measures of relative uptake. For example, for home HTC, it is not possible to discern whether 40% of those tested being men reflects a lower coverage of men, or a greater coverage of women, or a combination of the two. Future studies reporting the number of men, first-time testers and young adults offered testing compared with those accepting testing would increase the accuracy of these measures. Our findings on uptake, HIV positivity and CD4 count at diagnosis are similar to a previously published meta-analysis[9].

This analysis characterizes linkage and populations reached by HTC modalities to inform policymakers who are charged with addressing gaps in testing. Facility HTC, although important, is unlikely to be sufficient to curb the HIV epidemic since many people in sub-Saharan Africa do not have regular access to health care. Scaling a combination of community HTC, mobile testing to reach men, self-testing to reach young adults and outreach to high-risk

populations, as appropriate to the local epidemic setting, is crucial to achieve high knowledge of serostatus and linkage to HIV treatment and prevention in sub-Saharan Africa.

References

1. UNAIDS 2013 Report on the Global AIDS Epidemic . Available from: http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport. Accessed on 22/5/15.
2. Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society 2012;15:17383.
3. UNAIDS World AIDS Day Report 2012. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2434_WorldAIDSday_results_en_1.pdf. Accessed on 25/5/15.
4. Fast-Track: Ending the AIDS Epidemic by 2030. Joint United Nations Programme on HIV/AIDS, 2014. at http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf.)
5. Fylkesnes K, Sandoy IF, Jurgensen M, Chipimo PJ, Mwangala S, Michelo C. Strong effects of home-based voluntary HIV counselling and testing on acceptance and equity: a cluster randomised trial in Zambia. Social science & medicine (1982) 2013;86:9-16.
6. Musheke M, Ntalasha H, Gari S, et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in Sub-Saharan Africa. BMC public health 2013;13:220.
7. Siedner MJ, Ng CK, Bassett IV, Katz IT, Bangsberg DR, Tsai AC. Trends in CD4 count at presentation to care and treatment initiation in sub-Saharan Africa, 2002-2013: a meta-analysis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2015;60:1120-7.
8. Paulin HN, Blevins M, Koethe JR, et al. HIV testing service awareness and service uptake among female heads of household in rural Mozambique: results from a province-wide survey. BMC public health 2015;15:1388.
9. Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. PLoS medicine 2013;10:e1001496.
10. van Rooyen H, McGrath N, Chirowodza A, et al. Mobile VCT: reaching men and young people in urban and rural South African pilot studies (NIMH Project Accept, HPTN 043). AIDS and behavior 2013;17:2946-53.
11. MacPherson P, Lalloo DG, Webb EL, et al. Effect of optional home initiation of HIV care following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: A randomized clinical trial. JAMA - Journal of the American Medical Association 2014;312:372-9.
12. Ahmed S, Delaney K, Villalba-Diebold P, et al. HIV counseling and testing and access-to-care needs of populations most-at-risk for HIV in Nigeria. AIDS care 2013;25:85-94.
13. Coates TJ, Kulich M, Celentano DD, et al. Effect of community-based voluntary counselling and testing on HIV incidence and social and behavioural outcomes (NIMH Project Accept; HPTN 043): a cluster-randomised trial. The Lancet Global health 2014;2:e267-77.
14. Barnabas RV, van Rooyen H, Tumwesigye E, et al. Initiation of antiretroviral therapy and viral suppression after home HIV testing and counselling in KwaZulu-Natal, South Africa, and Mbarara district, Uganda: a prospective, observational intervention study. The lancet HIV 2014;1:e68-e76.
15. Genberg BL, Naanyu V, Wachira J, et al. Linkage to and engagement in HIV care in western Kenya: an observational study using population-based estimates from home-based counselling and testing. The Lancet HIV 2015;2:e20-e6.
16. WHO. Consolidated guidelines on HIV testing services. Accessed on 27 July 2015 from: http://www.who.int/hiv/pub/guidelines/hiv-testing-services/en/.
17. UNAIDS. The Gap Report. Accessed on 10/3/2015 from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf.
18. Sekandi JN, Sempeera H, List J, et al. High acceptance of home-based HIV counseling and testing in an urban community setting in Uganda. BMC public health 2011;11:730.

19. Rosenberg NE, Westreich D, Barnighausen T, et al. Assessing the effect of HIV counselling and testing on HIV acquisition among South African youth. AIDS (London, England) 2013;27:2765-73.
20. Barnabas, R. V., H. van Rooyen, E. Tumwesigye, J. Brantley, M. Krows, A. van Heerden, B. Turyamureeba, J. Hughes, J. Baeten and C. Celum (2015). Community-based HIV testing and linkage effectively delivers combination HIV prevention: Results from a multisite randomized trial 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015). Vancouver, BC, Canada.
21. Baeten J, Heffron R, Kidoguchi L, et al. Near Elimination of HIV Transmission in a Demonstration Project of PrEP and ART. 2015 Conference on Retroviruses and Opportunistic Infections. Seattle, February 23-24, 2015. Abstract 24.
22. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Tropical medicine & international health : TM & IH 2011;16:828-9.
23. Kurth AE, Lally MA, Choko AT, Inwani IW, Fortenberry JD. HIV testing and linkage to services for youth. Journal of the International AIDS Society 2015;18:19433.
24. MacPherson P, Munthali C, Ferguson J, et al. Service delivery interventions to improve adolescents' linkage, retention and adherence to antiretroviral therapy and HIV care. Tropical medicine & international health : TM & IH 2015;20:1015-32.
25. Mine M, Chishala S, Makhaola K, Tafuma TA, Bolebantswe J, Merrigan MB. Performance of rapid HIV testing by lay counselors in the field during the behavioral and biological surveillance survey among female sex workers and men who have sex with men in Botswana. Journal of acquired immune deficiency syndromes (1999) 2015;68:365-8.
26. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ (Clinical research ed) 2009;339:b2700.
27. Uwimana J, Zarowsky C, Hausler H, Jackson D. Training community care workers to provide comprehensive TB/HIV/PMTCT integrated care in KwaZulu-Natal: lessons learnt. Tropical medicine & international health : TM & IH 2012;17:488-96.
28. RStudio (2015). RStudio: Integrated development environment for R (Version 0.98.1103) [Computer software]. Boston, MA. Retrieved May 20, 2014. Available from http://www.rstudio.org/.
29. Bigogo G, Amolloh M, Laserson KF, et al. The impact of home-based HIV counseling and testing on care-seeking and incidence of common infectious disease syndromes in rural western Kenya. BMC infectious diseases 2014;14:376.
30. Gonzalez R, Munguambe K, Aponte J, et al. High HIV prevalence in a southern semi-rural area of Mozambique: a community-based survey. HIV medicine 2012;13:581-8.
31. Helleringer S, Kohler HP, Frimpong JA, Mkandawire J. Increasing uptake of HIV testing and counseling among the poorest in sub-Saharan countries through home-based service provision. Journal of acquired immune deficiency syndromes (1999) 2009;51:185-93.
32. Kimaiyo S, Were MC, Shen C, et al. Home-based HIV counselling and testing in western Kenya. East African medical journal 2010;87:100-8.
33. Kranzer K, McGrath N, Saul J, et al. Individual, household and community factors associated with HIV test refusal in rural Malawi. Tropical medicine & international health : TM & IH 2008;13:1341-50.
34. Medley A, Ackers M, Amolloh M, et al. Early uptake of HIV clinical care after testing HIV-positive during home-based testing and counseling in western Kenya. AIDS and behavior 2013;17:224-34.
35. Michelo C, Sandoy IF, Dzekedzeke K, Siziya S, Fylkesnes K. Steep HIV prevalence declines among young people in selected Zambian communities: population-based observations (1995-2003). BMC public health 2006;6:279.
36. Molesworth AM, Ndhlovu R, Banda E, et al. High accuracy of home-based community rapid HIV testing in rural Malawi. Journal of acquired immune deficiency syndromes (1999) 2010;55:625-30.

37. Negin J, Wariero J, Mutuo P, Jan S, Pronyk P. Feasibility, acceptability and cost of home-based HIV testing in rural Kenya. Tropical medicine & international health : TM & IH 2009;14:849-55.
38. Ng'ang'a A, Waruiru W, Ngare C, et al. The status of HIV testing and counseling in Kenya: results from a nationally representative population-based survey. Journal of acquired immune deficiency syndromes (1999) 2014;66 Suppl 1:S27-36.
39. Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet 2007;369:643-56.
40. Shisana O, Stoker D, Simbayi LC, et al. South African national household survey of HIV/AIDS prevalence, behavioural risks and mass media impact —detailed methodology and response rate results. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde;94:283-8.
41. Tumwebaze H, Tumwesigye E, Baeten JM, et al. Household-based HIV counseling and testing as a platform for referral to HIV care and medical male circumcision in Uganda: a pilot evaluation. PloS one 2012;7:e51620.
42. Tumwesigye E, Wana G, Kasasa S, Muganzi E, Nuwaha F. High uptake of home-based, district-wide, HIV counseling and testing in Uganda. AIDS patient care and STDs 2010;24:735-41.
43. van Rooyen H, Barnabas RV, Baeten JM, et al. High HIV testing uptake and linkage to care in a novel program of home-based HIV counseling and testing with facilitated referral in KwaZulu-Natal, South Africa. Journal of acquired immune deficiency syndromes (1999) 2013;64:e1-8.
44. Wachira J, Ndege S, Koech J, Vreeman RC, Ayuo P, Braitstein P. HIV testing uptake and prevalence among adolescents and adults in a large home-based HIV testing program in Western Kenya. Journal of acquired immune deficiency syndromes (1999) 2014;65:e58-66.
45. Welz. Continued very high prevalence of HIV infection in rural KwaZulu-Natal, South Africa: a population- based longitudinal study. 2007.
46. Chamie G, Kwarisiima D, Clark TD, et al. Uptake of community-based HIV testing during a multi-disease health campaign in rural Uganda. PloS one 2014;9:e84317.
47. Lugada E, Millar D, Haskew J, et al. Rapid implementation of an integrated large-scale HIV counseling and testing, malaria, and diarrhea prevention campaign in rural Kenya. PloS one 2010;5:e12435.
48. Lugada E, Levin J, Abang B, et al. Comparison of home and clinic-based HIV testing among household members of persons taking antiretroviral therapy in Uganda: results from a randomized trial. Journal of acquired immune deficiency syndromes (1999) 2010;55:245-52.
49. Brown LB, Miller WC, Kamanga G, et al. HIV partner notification is effective and feasible in sub-Saharan Africa: opportunities for HIV treatment and prevention. Journal of acquired immune deficiency syndromes (1999) 2011;56:437-42.
50. Armbruster B, Helleringer S, Kalilani-Phiri L, Mkandawire J, Kohler HP. Exploring the relative costs of contact tracing for increasing HIV case finding in sub-Saharan countries. Journal of acquired immune deficiency syndromes (1999) 2011;58:e29-36.
51. Bwambale FM, Ssali SN, Byaruhanga S, Kalyango JN, Karamagi CA. Voluntary HIV counselling and testing among men in rural western Uganda: implications for HIV prevention. BMC public health 2008;8:263.
52. Cawley C, Wringe A, Isingo R, et al. Low rates of repeat HIV testing despite increased availability of antiretroviral therapy in rural Tanzania: findings from 2003-2010. PloS one 2013;8:e62212.
53. Fylkesnes K, Siziya S. A randomized trial on acceptability of voluntary HIV counselling and testing. Tropical medicine & international health : TM & IH 2004;9:566-72.
54. Isingo R, Wringe A, Todd J, et al. Trends in the uptake of voluntary counselling and testing for HIV in rural Tanzania in the context of the scale up of antiretroviral therapy. Tropical medicine & international health : TM & IH 2012;17:e15-25.

55. MacPherson P, Lalloo DG, Choko AT, et al. Suboptimal patterns of provider initiated HIV testing and counselling, antiretroviral therapy eligibility assessment and referral in primary health clinic attendees in Blantyre, Malawi. Tropical medicine & international health : TM & IH 2012;17:507-17.
56. Dalal S, Lee CW, Farirai T, et al. Provider-initiated HIV testing and counseling: increased uptake in two public community health centers in South Africa and implications for scale-up. PloS one 2011;6:e27293.
57. Fetene NW, Feleke AD. Missed opportunities for earlier HIV testing and diagnosis at the health facilities of Dessie town, North East Ethiopia. BMC public health 2010;10:362.
58. Kayigamba FR, Bakker MI, Lammers J, et al. Provider-initiated HIV testing and counselling in Rwanda: acceptability among clinic attendees and workers, reasons for testing and predictors of testing. PloS one 2014;9:e95459.
59. Kharsany AB, Karim QA, Karim SS. Uptake of provider-initiated HIV testing and counseling among women attending an urban sexually transmitted disease clinic in South Africa - missed opportunities for early diagnosis of HIV infection. AIDS care 2010;22:533-7.
60. Topp SM, Chipukuma JM, Chiko MM, Wamulume CS, Bolton-Moore C, Reid SE. Opt-out provider-initiated HIV testing and counselling in primary care outpatient clinics in Zambia. Bulletin of the World Health Organization 2011;89:328-35a.
61. Topp SM, Li MS, Chipukuma JM, et al. Does provider-initiated counselling and testing (PITC) strengthen early diagnosis and treatment initiation? Results from an analysis of an urban cohort of HIV-positive patients in Lusaka, Zambia. Journal of the International AIDS Society 2012;15:17352.
62. Angotti N, Bula A, Gaydosh L, Kimchi EZ, Thornton RL, Yeatman SE. Increasing the acceptability of HIV counseling and testing with three C's: convenience, confidentiality and credibility. Social science & medicine (1982) 2009;68:2263-70.
63. Cherutich P, Kaiser R, Galbraith J, et al. Lack of knowledge of HIV status a major barrier to HIV prevention, care and treatment efforts in Kenya: results from a nationally representative study. PloS one 2012;7:e36797.
64. Chirawu P, Langhaug L, Mavhu W, Pascoe S, Dirawo J, Cowan F. Acceptability and challenges of implementing voluntary counselling and testing (VCT) in rural Zimbabwe: evidence from the Regai Dzive Shiri Project. AIDS care 2010;22:81-8.
65. Dalal W. Home-Based HIV Testing and Counseling in Rural and Urban Kenyan Communities. 2013.
66. Doherty T, Tabana H, Jackson D, et al. Effect of home based HIV counselling and testing intervention in rural South Africa: cluster randomised trial. BMJ (Clinical research ed) 2013;346:f3481.
67. Hensen B, Lewis JJ, Schaap A, et al. Factors associated with HIV-testing and acceptance of an offer of home-based testing by men in rural Zambia. AIDS Behav 2015;19:492-504.
68. Maheswaran H, Thulare H, Stanistreet D, Tanser F, Newell ML. Starting a home and mobile HIV testing service in a rural area of South Africa. Journal of acquired immune deficiency syndromes (1999) 2012;59:e43-6.
69. Mutale W, Michelo C, Jurgensen M, Fylkesnes K. Home-based voluntary HIV counselling and testing found highly acceptable and to reduce inequalities. BMC public health 2010;10:347.
70. Naik R, Tabana H, Doherty T, Zembe W, Jackson D. Client characteristics and acceptability of a home-based HIV counselling and testing intervention in rural South Africa. BMC public health 2012;12:824.
71. Nyigo V, Kilale A, Kilima S, et al. Magnitude of HIV infection among older people in Mufindi and Babati districts of the Tanzania mainland. HIV/AIDS - Research and Palliative Care 2014;6:75-9.
72. Parker LA, Jobanputra K, Rusike L, et al. Feasibility and effectiveness of two community-based HIV testing models in rural Swaziland. Tropical medicine & international health : TM & IH 2015;20:893-902.

73. Shapiro AE, Variava E, Rakgokong MH, et al. Community-based targeted case finding for tuberculosis and HIV in household contacts of patients with tuberculosis in South Africa. American journal of respiratory and critical care medicine 2012;185:1110-6.
74. Wolff B, Nyanzi B, Katongole G, Ssesanga D, Ruberantwari A, Whitworth J. Evaluation of a home-based voluntary counselling and testing intervention in rural Uganda. Health policy and planning 2005;20:109-16.
75. Choko AT, Desmond N, Webb EL, et al. The uptake and accuracy of oral kits for HIV self-testing in high HIV prevalence setting: a cross-sectional feasibility study in Blantyre, Malawi. PLoS medicine 2011;8:e1001102.
76. Granich R, Muraguri N, Doyen A, Garg N, Williams BG. Achieving universal access for human immunodeficiency virus and tuberculosis: potential prevention impact of an integrated multi-disease prevention campaign in kenya. AIDS research and treatment 2012;2012:412643.
77. Labhardt ND, Motlomelo M, Cerutti B, et al. Home-based versus mobile clinic HIV testing and counseling in rural Lesotho: a cluster-randomized trial. PLoS medicine 2014;11:e1001768.
78. Corbett EL, Dauya E, Matambo R, et al. Uptake of workplace HIV counselling and testing: a cluster-randomised trial in Zimbabwe. PLoS medicine 2006;3:e238.
79. Van der Borght SF, Schim van der Loeff MF, Clevenbergh P, et al. Long-term voluntary counseling and testing (VCT) uptake dynamics in a multicountry HIV workplace program in sub-Saharan Africa. AIDS care 2010;22:195-205.
80. Bemelmans M, van den Akker T, Pasulani O, et al. Keeping health staff healthy: evaluation of a workplace initiative to reduce morbidity and mortality from HIV/AIDS in Malawi. Journal of the International AIDS Society 2011;14:1.
81. Bassett IV, Giddy J, Nkera J, et al. Routine voluntary HIV testing in Durban, South Africa: the experience from an outpatient department. Journal of acquired immune deficiency syndromes (1999) 2007;46:181-6.
82. Abdurahman S, Seyoum B, Oljira L. Factors affecting acceptance of provider-initiated hiv testing and counseling services among outpatient clients in selected health facilities in harar town, Eastern Ethiopia. HIV/AIDS - Research and Palliative Care 2015;7:157-65.
83. LaCourse SM, Chester FM, Matoga M, et al. Implementation of Routine Counselor-Initiated Opt-Out HIV Testing on the Adult Medical Ward at Kamuzu Central Hospital, Lilongwe, Malawi. Journal of acquired immune deficiency syndromes (1999) 2015;69:e31-5.
84. Leon N, Mathews C, Lewin S, Osler M, Boulle A, Lombard C. A comparison of linkage to HIV care after provider-initiated HIV testing and counselling (PITC) versus voluntary HIV counselling and testing (VCT) for patients with sexually transmitted infections in Cape Town, South Africa. BMC health services research 2014;14:350.
85. Moodley J, Bryan M, Tunkyi K, Khedun SM. A clinical audit of provider-initiated hiv counselling and testing in a gynaecological ward of a district hospital in kwazulu-natal, South Africa. South African Journal of Obstetrics and Gynaecology 2014;20:8-11.
86. Wanyenze RK, Nawavvu C, Namale AS, et al. Acceptability of routine HIV counselling and testing, and HIV seroprevalence in Ugandan hospitals. Bulletin of the World Health Organization 2008;86:302-9.
87. Waxman MJ, Kimaiyo S, Ongaro N, Wools-Kaloustian KK, Flanigan TP, Carter EJ. Initial outcomes of an emergency department rapid HIV testing program in western Kenya. AIDS patient care and STDs 2007;21:981-6.
88. Menzies N, Abang B, Wanyenze R, et al. The costs and effectiveness of four HIV counseling and testing strategies in Uganda. AIDS (London, England) 2009;23:395-401.
89. Mulogo EM, Abdulaziz AS, Guerra R, Baine SO. Facility and home based HIV Counseling and Testing: a comparative analysis of uptake of services by rural communities in southwestern Uganda. BMC health services research 2011;11:54.

90. Wachira J, Kimaiyo S, Ndege S, Mamlin J, Braitstein P. What is the impact of home-based HIV counseling and testing on the clinical status of newly enrolled adults in a large HIV care program in Western Kenya? Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2012;54:275-81.
91. Bassett IV, Regan S, Luthuli P, et al. Linkage to care following community-based mobile HIV testing compared with clinic-based testing in Umlazi Township, Durban, South Africa. HIV medicine 2014;15:367-72.
92. Bassett IV, Regan S, Mbonambi H, et al. Finding HIV in Hard to Reach Populations: Mobile HIV Testing and Geospatial Mapping in Umlazi Township, Durban, South Africa. AIDS and behavior 2015.
93. Grabbe KL, Menzies N, Taegtmeyer M, et al. Increasing access to HIV counseling and testing through mobile services in Kenya: strategies, utilization, and cost-effectiveness. Journal of acquired immune deficiency syndromes (1999) 2010;54:317-23.
94. Kranzer K, Govindasamy D, van Schaik N, et al. Incentivized recruitment of a population sample to a mobile HIV testing service increases the yield of newly diagnosed cases, including those in need of antiretroviral therapy. HIV medicine 2012;13:132-7.
95. Mabuto T, Latka MH, Kuwane B, Churchyard GJ, Charalambous S, Hoffmann CJ. Four models of HIV counseling and testing: utilization and test results in South Africa. PloS one 2014;9:e102267.
96. Meehan SA, Naidoo P, Claassens MM, Lombard C, Beyers N. Characteristics of clients who access mobile compared to clinic HIV counselling and testing services: a matched study from Cape Town, South Africa. BMC health services research 2014;14:658.
97. Morin SF, Khumalo-Sakutukwa G, Charlebois ED, et al. Removing barriers to knowing HIV status: same-day mobile HIV testing in Zimbabwe. Journal of acquired immune deficiency syndromes (1999) 2006;41:218-24.
98. Sweat M, Morin S, Celentano D, et al. Community-based intervention to increase HIV testing and case detection in people aged 16-32 years in Tanzania, Zimbabwe, and Thailand (NIMH Project Accept, HPTN 043): a randomised study. The Lancet infectious diseases 2011;11:525-32.
99. Van Rie A, Clouse K, Hanrahan C, et al. High uptake of systematic HIV counseling and testing and TB symptom screening at a primary care clinic in South Africa. PloS one 2014;9:e105428.
100. Kalibala S, Tun W, Cherutich P, Nganga A, Oweya E, Oluoch P. Factors associated with acceptability of HIV self-testing among health care workers in Kenya. AIDS and behavior 2014;18 Suppl 4:S405-14.
101. Pant Pai N, Behlim T, Abrahams L, et al. Will an unsupervised self-testing strategy for HIV work in health care workers of South Africa? A cross sectional pilot feasibility study. PloS one 2013;8:e79772.
102. Arendt V, Mossong J, Zachariah R, et al. Clinical screening for HIV in a health centre setting in urban Kenya: an entry point for voluntary counselling, HIV testing and early diagnosis of HIV infection? Tropical doctor 2007;37:45-7.
103. Bassett IV, Govindasamy D, Erlwanger AS, et al. Mobile HIV screening in Cape Town, South Africa: clinical impact, cost and cost-effectiveness. PloS one 2014;9:e85197.
104. Creek TL, Alwano MG, Molosiwa RR, et al. Botswana's Tebelopele voluntary HIV counseling and testing network: use and client risk factors for HIV infection, 2000-2004. Journal of acquired immune deficiency syndromes (1999) 2006;43:210-8.
105. Fiscus SA, Pilcher CD, Miller WC, et al. Rapid, real-time detection of acute HIV infection in patients in Africa. The Journal of infectious diseases 2007;195:416-24.
106. Mwangi M, Kellogg TA, Dadabhai SS, et al. Factors Associated with Uptake of HIV Test Results in a Nationally Representative Population-Based AIDS Indicator Survey. The open AIDS journal 2014;8:7-16.
107. van Schaik N, Kranzer K, Wood R, Bekker LG. Earlier HIV diagnosis--are mobile services the answer? South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 2010;100:671-4.

108. Abdallah TM, Ali AA, Adam I. Provider-initiated HIV testing and counseling among tuberculosis patients in Kassala, Eastern Sudan. Journal of infection and public health 2012;5:63-6.
109. Ansa GA, Walley JD, Siddiqi K, Wei X. Delivering TB/HIV services in Ghana: a comparative study of service delivery models. Transactions of the Royal Society of Tropical Medicine and Hygiene 2014;108:560-7.
110. Bondo M, Modiba MC, Becker P. HIV infection in general surgical patients at the Ga-Rankuwa/MEDUNSA complex South Africa. East African medical journal 2001;78:395-7.
111. Kiene SM, Bateganya M, Wanyenze R, Lule H, Nantaba H, Stein MD. Initial outcomes of provider-initiated routine HIV testing and counseling during outpatient care at a rural Ugandan hospital: risky sexual behavior, partner HIV testing, disclosure, and HIV care seeking. AIDS patient care and STDs 2010;24:117-26.
112. Silvestri DM, Modjarrad K, Blevins ML, Halale E, Vermund SH, McKinzie JP. A comparison of HIV detection rates using routine opt-out provider-initiated HIV testing and counseling versus a standard of care approach in a rural African setting. Journal of acquired immune deficiency syndromes (1999) 2011;56:e9-32.
113. O'Laughlin KN, Kasozi J, Walensky RP, et al. Clinic-based routine voluntary HIV testing in a refugee settlement in Uganda. Journal of acquired immune deficiency syndromes (1999) 2014;67:409-13.
114. Nglazi MD, van Schaik N, Kranzer K, Lawn SD, Wood R, Bekker LG. An incentivized HIV counseling and testing program targeting hard-to-reach unemployed men in Cape Town, South Africa. Journal of acquired immune deficiency syndromes (1999) 2012;59:e28-34.
115. Adebajo S, Eluwa G, Njab J, et al. Evaluating the effect of HIV prevention strategies on uptake of HIV counselling and testing among male most-at-risk-populations in Nigeria; a cross-sectional analysis. Sex Transm Infect 2015.
116. Charurat ME, Emmanuel B, Akolo C, et al. Uptake of treatment as prevention for HIV and continuum of care among HIV-positive men who have sex with men in Nigeria. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S114-23.
117. Nyblade LC, Menken J, Wawer MJ, et al. Population-based HIV testing and counseling in rural Uganda: participation and risk characteristics. Journal of acquired immune deficiency syndromes (1999) 2001;28:463-70.
118. Arthur GR, Ngatia G, Rachier C, Mutemi R, Odhiambo J, Gilks CF. The role for government health centers in provision of same-day voluntary HIV counseling and testing in Kenya. Journal of acquired immune deficiency syndromes (1999) 2005;40:329-35.
119. Gresenguet G, Sehonou J, Bassirou B, et al. Voluntary HIV counseling and testing: experience among the sexually active population in Bangui, Central African Republic. Journal of acquired immune deficiency syndromes (1999) 2002;31:106-14.
120. Hood JE, MacKellar D, Spaulding A, et al. Client characteristics and gender-specific correlates of testing HIV positive: a comparison of standalone center versus mobile outreach HIV testing and counseling in Botswana. AIDS and behavior 2012;16:1902-16.
121. Corbett EL, Makamure B, Cheung YB, et al. HIV incidence during a cluster-randomized trial of two strategies providing voluntary counselling and testing at the workplace, Zimbabwe. AIDS (London, England) 2007;21:483-9.
122. Mulongo S, Kapila G, Hatton T, et al. Applying innovative approaches for reaching men who have sex with men and female sex workers in the Democratic Republic of Congo. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S248-51.
123. Appiah LT, Havers F, Gibson J, Kay M, Sarfo F, Chadwick D. Efficacy and acceptability of rapid, point-of-care HIV testing in two clinical settings in Ghana. AIDS patient care and STDs 2009;23:365-9.

124. Kouassi-M'Bengue A, Boni CC, Ouattara D, et al. Co-infection of HIV and HBV in voluntary counseling and testing center in Abidjan. Asian Pacific Journal of Tropical Disease 2011;1:275-8.
125. Akhigbe RE, Bamidele JO. Prevalence and pattern of utilization of voluntary counseling and testing services and HIV infection in Ogbomoso, southwestern Nigeria. Journal of natural science, biology, and medicine 2013;4:163-6.
126. Kikaya V, Skolnik L, Garcia MC, Nkonyana J, Curran K, Ashengo TA. Voluntary medical male circumcision programs can address low HIV testing and counseling usage and ART enrollment among young men: lessons from Lesotho. PloS one 2014;9:e83614.
127. Govender S, Otwombe K, Essien T, et al. CD4 counts and viral loads of newly diagnosed HIV-infected individuals: implications for treatment as prevention. PloS one 2014;9:e90754.
128. World Bank Development Indicators. Prevalence of HIV, (% of total population ages 15-49). Accessed on 07/07/2015 from http://data.worldbank.org/indicator/SH.DYN.AIDS.ZS/countries?display=default.
129. Agaba PA, Meloni ST, Sule HM, et al. Patients who present late to HIV care and associated risk factors in Nigeria. HIV medicine 2014;15:396-405.
130. Clouse K, Hanrahan CF, Bassett J, Fox MP, Sanne I, Van Rie A. Impact of systematic HIV testing on case finding and retention in care at a primary care clinic in South Africa. Tropical medicine & international health : TM & IH 2014;19:1411-9.
131. Haskew J, Turner K, Ro G, Ho A, Kimanga D, Sharif S. Stage of HIV presentation at initial clinic visit following a community-based HIV testing campaign in rural Kenya. BMC public health 2015;15:16.
132. Naik R, Doherty T, Jackson D, et al. Linkage to care following a home-based HIV counselling and testing intervention in rural South Africa. Journal of the International AIDS Society 2015;18:19843.
133. Govindasamy D, van Schaik N, Kranzer K, Wood R, Mathews C, Bekker LG. Linkage to HIV care from a mobile testing unit in South Africa by different CD4 count strata. Journal of acquired immune deficiency syndromes (1999) 2011;58:344-52.
134. van Zyl MA, Brown LL, Pahl K. Using a call center to encourage linkage to care following mobile HIV counseling and testing. AIDS care 2015;27:921-5.
135. Larson BA, Schnippel K, Ndibongo B, et al. Rapid point-of-care CD4 testing at mobile HIV testing sites to increase linkage to care: an evaluation of a pilot program in South Africa. Journal of acquired immune deficiency syndromes (1999) 2012;61:e13-7.
136. Larson BA, Brennan A, McNamara L, et al. Lost opportunities to complete CD4+ lymphocyte testing among patients who tested positive for HIV in South Africa. Bulletin of the World Health Organization 2010;88:675-80.
137. Terris-Prestholt F, Kumaranayake L, Foster S, et al. The role of community acceptance over time for costs of HIV and STI prevention interventions: analysis of the Masaka Intervention Trial, Uganda, 1996-1999. Sexually transmitted diseases 2006;33:S111-6.
138. Kahn JG, Harris B, Mermin JH, et al. Cost of community integrated prevention campaign for malaria, HIV, and diarrhea in rural Kenya. BMC health services research 2011;11:346.
139. Sharma M, Van Rooyen H, Celum C, Baeten J, Levin C, Barnabas R. The Cost of Community Based HIV Counseling and Testing and Linkage to Care in Rural South Africa: Estimates from the Linkages Randomized Control Trial. Research for Prevention (R4P), Capetown, SA, November, 2014.
140. Mulogo EM, Batwala V, Nuwaha F, Aden AS, Baine OS. Cost effectiveness of facility and home based HIV voluntary counseling and testing strategies in rural Uganda. African health sciences 2013;13:423-9.
141. McConnel CE, Stanley N, du Plessis JA, et al. The cost of a rapid-test VCT clinic in South Africa. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 2005;95:968-71.
142. Sweat M, Gregorich S, Sangiwa G, et al. Cost-effectiveness of voluntary HIV-1 counselling and testing in reducing sexual transmission of HIV-1 in Kenya and Tanzania. Lancet 2000;356:113-21.

143. Aliyu HB, Chuku NN, Kola-Jebutu A, Abubakar Z, Torpey K, Chabikuli ON. What is the cost of providing outpatient HIV counseling and testing and antiretroviral therapy services in selected public health facilities in Nigeria? Journal of acquired immune deficiency syndromes (1999) 2012;61:221-5.
144. Obure CD, Vassall A, Michaels C, et al. Optimising the cost and delivery of HIV counselling and testing services in Kenya and Swaziland. Sex Transm Infect 2012;88:498-503.
145. Forsythe S, Arthur G, Ngatia G, Mutemi R, Odhiambo J, Gilks C. Assessing the cost and willingness to pay for voluntary HIV counselling and testing in Kenya. Health policy and planning 2002;17:187-95.
146. Hausler HP, Sinanovic E, Kumaranayake L, et al. Costs of measures to control tuberculosis/HIV in public primary care facilities in Cape Town, South Africa. Bulletin of the World Health Organization 2006;84:528-36.
147. Thielman NM, Chu HY, Ostermann J, et al. Cost-effectiveness of free HIV voluntary counseling and testing through a community-based AIDS service organization in Northern Tanzania. Am J Public Health 2006;96:114-9.
148. Stover J, Hallett TB, Wu Z, et al. How can we get close to zero? The potential contribution of biomedical prevention and the investment framework towards an effective response to HIV. PloS one 2014;9:e111956.
149. Sabapathy K, Van den Bergh R, Fidler S, Hayes R, Ford N. Uptake of home-based voluntary HIV testing in sub-Saharan Africa: a systematic review and meta-analysis. PLoS medicine 2012;9:e1001351.
150. Novitsky V, Bussmann H, Okui L, et al. Estimated age and gender profile of individuals missed by a home-based HIV testing and counselling campaign in a Botswana community. J Int AIDS Soc 2015;18:19918.
151. Choko AT, MacPherson P, Webb EL, et al. Uptake, Accuracy, Safety, and Linkage into Care over Two Years of Promoting Annual Self-Testing for HIV in Blantyre, Malawi: A Community-Based Prospective Study. PLoS medicine 2015;12:e1001873.
152. Leblanc NM, Andes KL. An exploration of men's knowledge, attitudes, and perceptions of HIV, HIV risk, and willingness to test for HIV in Yendi District, Northern Ghana. The Journal of the Association of Nurses in AIDS Care : JANAC 2015;26:281-95.
153. Wheeler T, Wolf RC, Kapesa L, Cheng Surdo A, Dallabetta G. Scaling-up HIV responses with key populations in West Africa. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S69-73.
154. Bekker LG, Johnson L, Cowan F, et al. Combination HIV prevention for female sex workers: what is the evidence? Lancet 2015;385:72-87.
155. Duvall S, Irani L, Compaore C, et al. Assessment of policy and access to HIV prevention, care, and treatment services for men who have sex with men and for sex workers in Burkina Faso and Togo. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S189-97.
156. Figueroa C, Johnson C, Verster A, Baggaley R. Attitudes and Acceptability on HIV Self-testing Among Key Populations: A Literature Review. AIDS and behavior 2015;19:1949-65.
157. Nsanzimana S, Kanters S, Remera E, et al. HIV care continuum in Rwanda: a cross-sectional analysis of the national programme. The lancet HIV 2015;2:e208-15.

Figure 1. Pooled coverage and uptake of HIV testing and counselling modalities.

Coverage is defined as total number of people tested/total number of people in the target population. Uptake is defined as total number of people tested/total number of people offered testing. Bars indicate 95% confidence intervals of random effects meta-analyses. *n*, sample size.

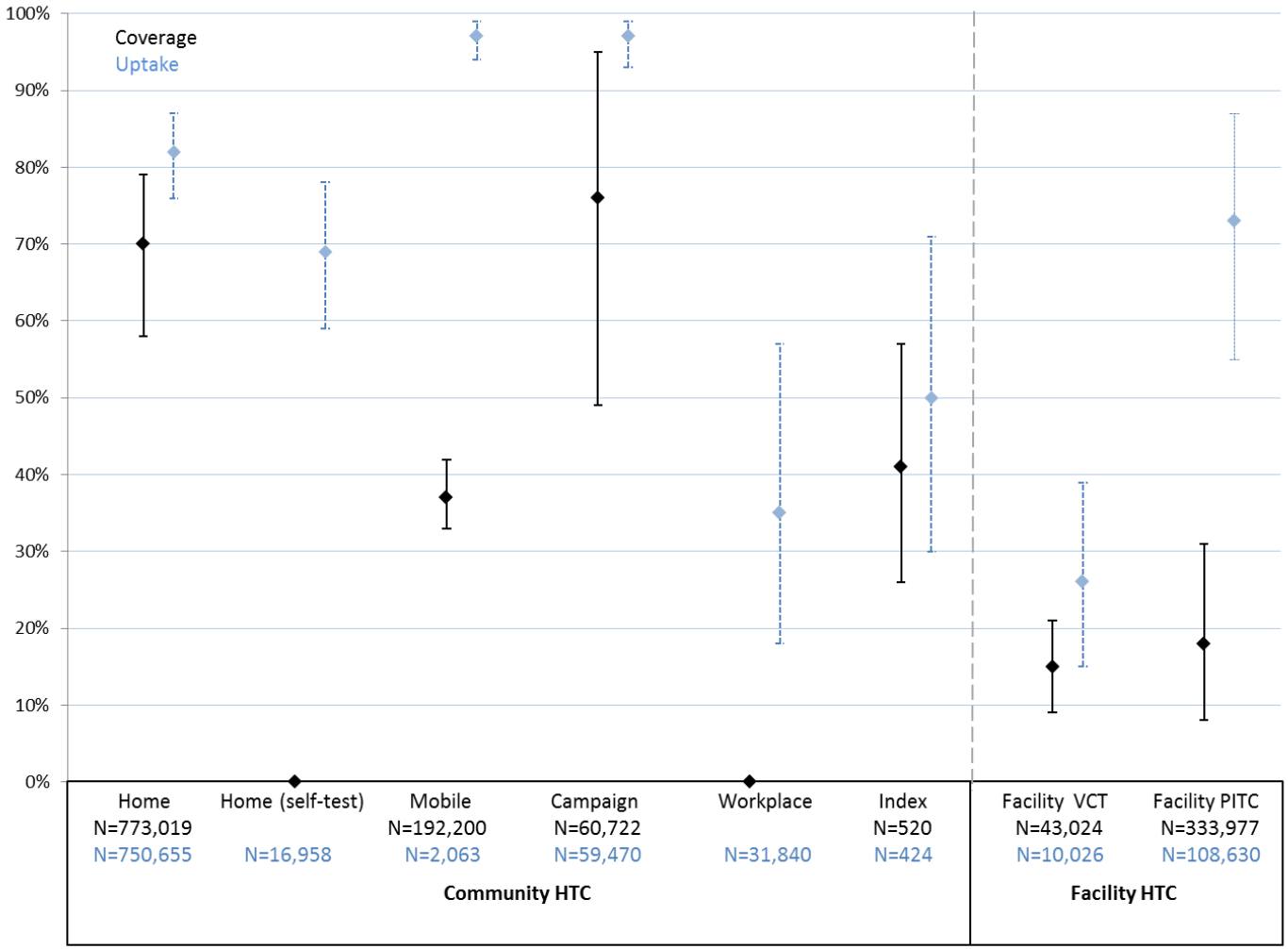

Figure 2. Pooled percentage of men, young adults and first-time testers by HIV testing and counselling modality.
Bars indicate 95% confidence intervals of random effects meta-analyses. *n*, sample size.

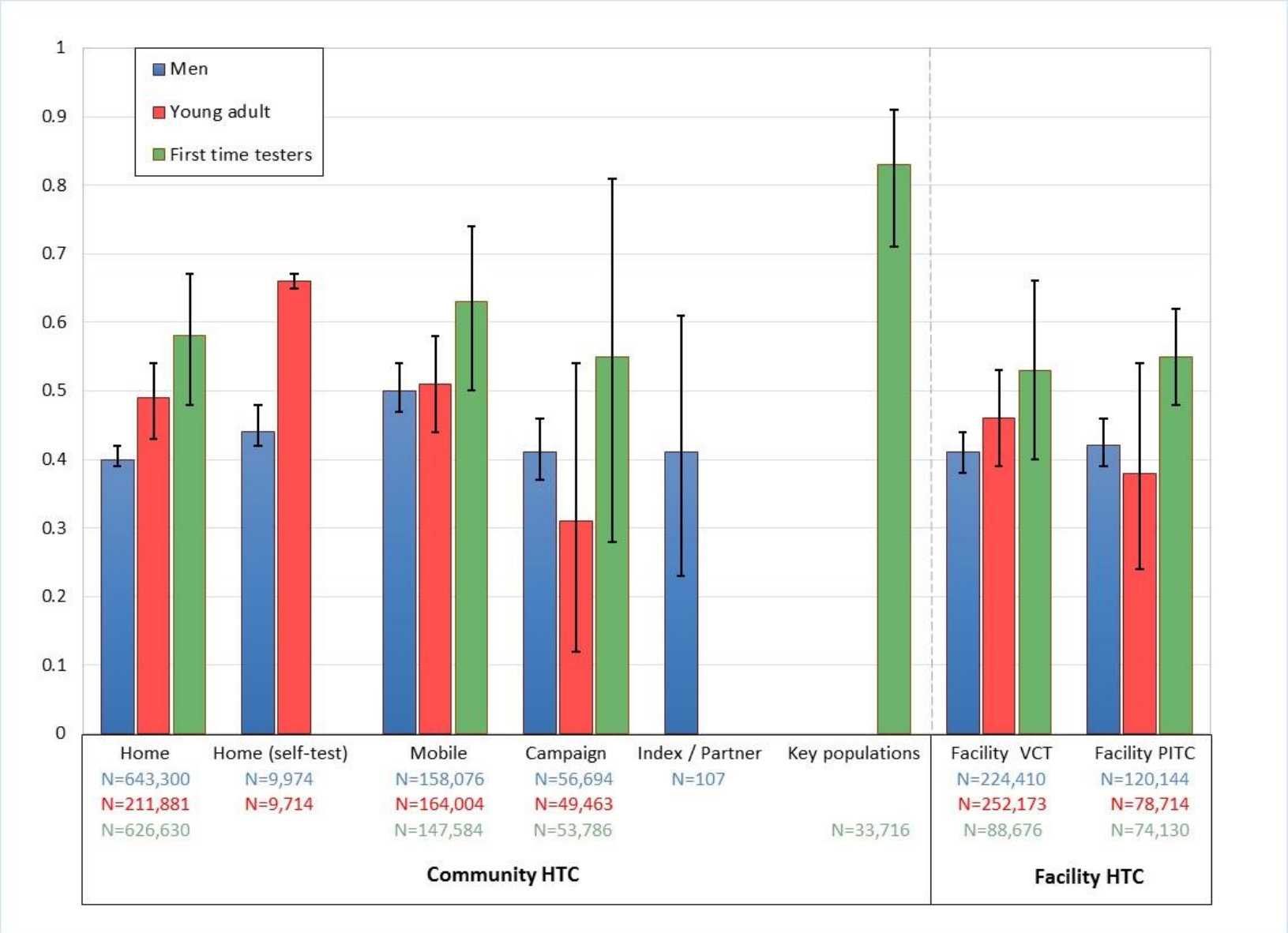

Figure 3. Pooled HIV positivity and proportion of newly diagnosed HIV positivity with CD4 count of 350 cells μL^{-1} or less by HIV testing and counselling modality.

Bars indicate 95% confidence intervals of random effects meta-analyses. *n*, sample size.

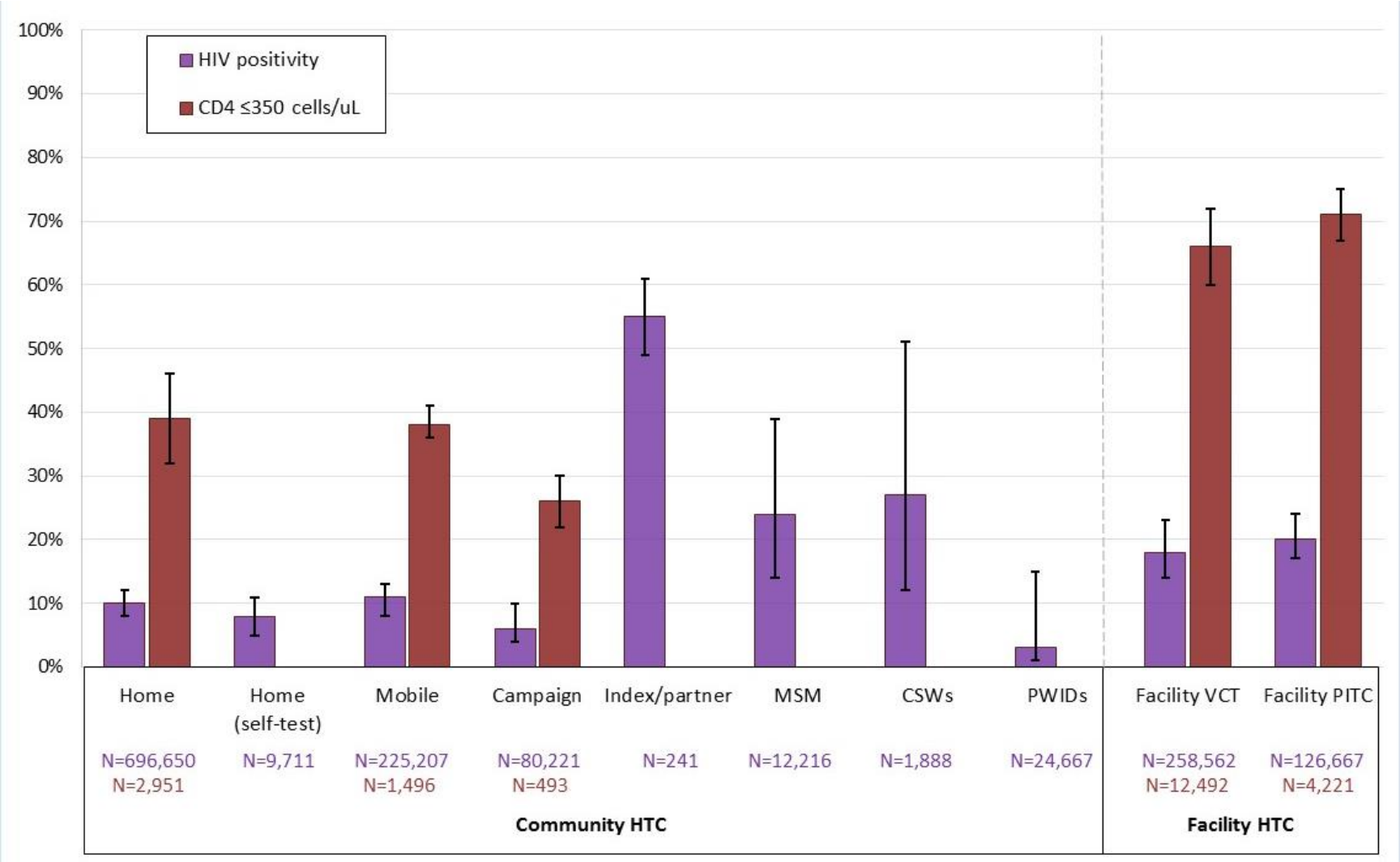

Figure 4. Linkage to care after community and facility HIV testing and counselling
Bars indicate 95% confidence intervals of random effects meta-analyses. *n*, sample size.

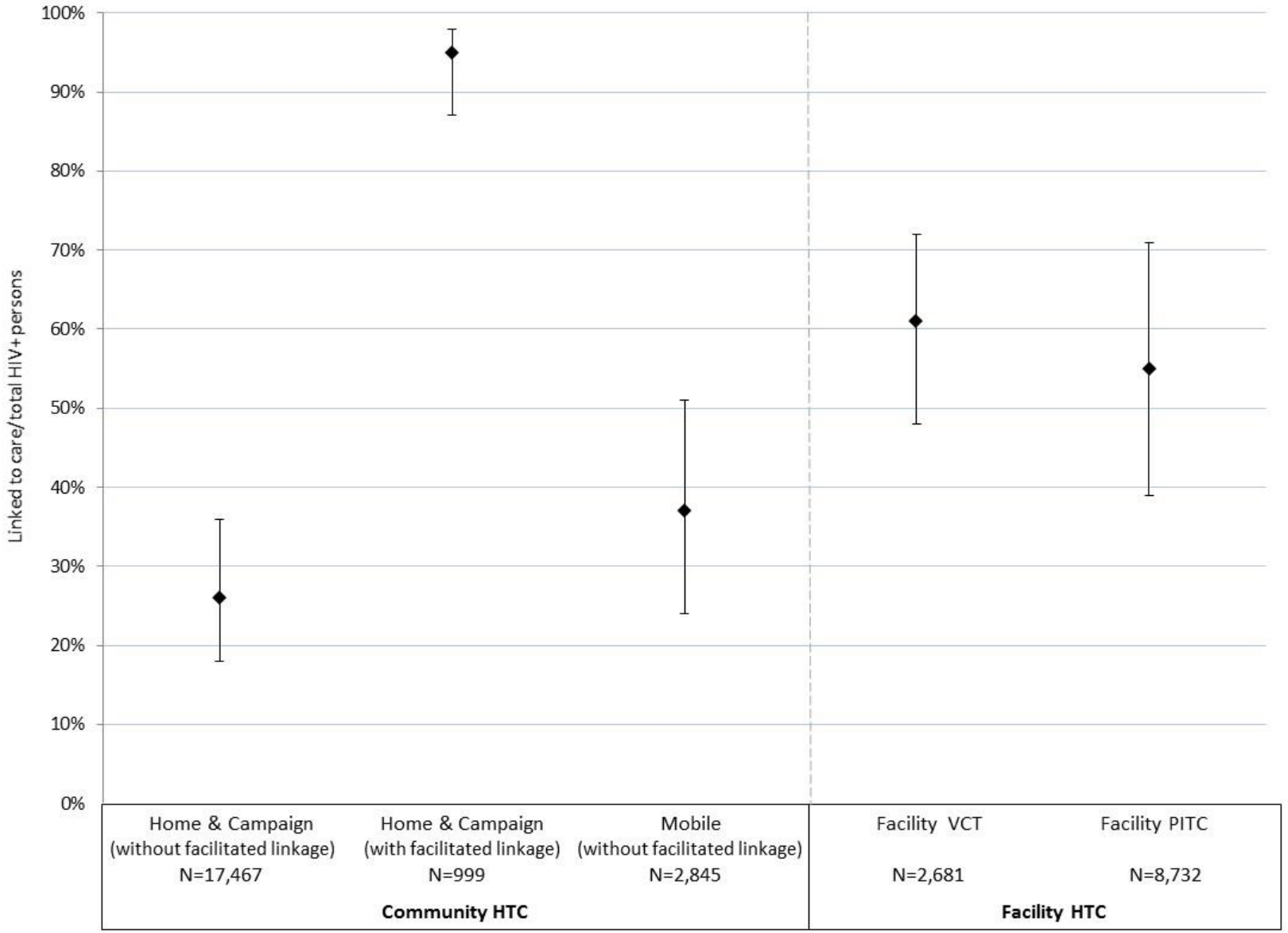

Figure 5. Pooled percentage initiated ART between those eligible and retained in care among those who initiated ART.
Bars indicate 95% confidence intervals of random effects meta-analyses. *n*, sample size.

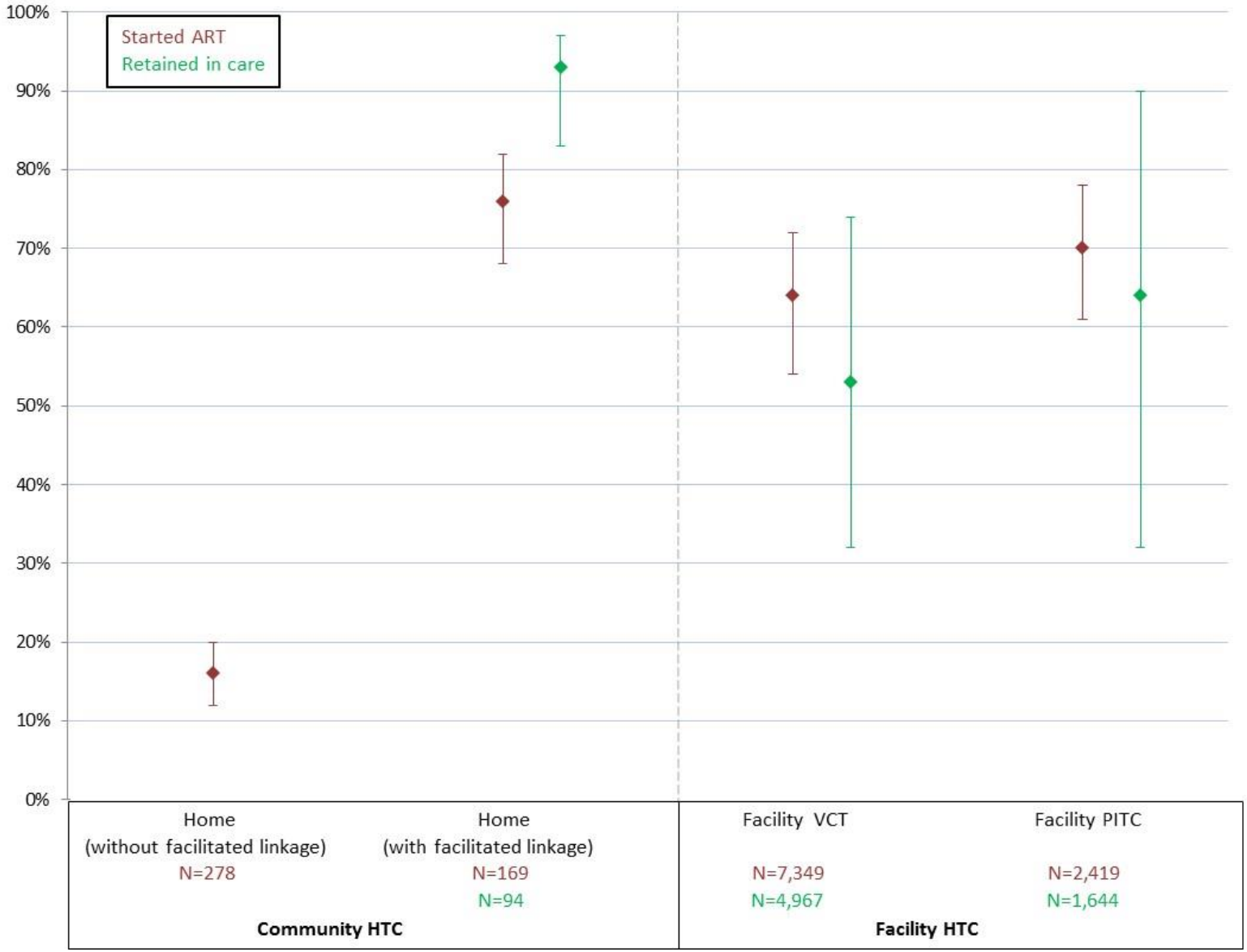

Table 1. Summary of HIV testing and counselling coverage and tester demographics

Parameter	Home		Mobile		Self-testing (home)		Campaign		Index		Key populations		Facility VCT		Facility PITC	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Coverage (accepted/ target population)	70	58–79	37	33–42			76	49–95	41	26–57			15	9–21	18	8–31
Uptake (accepted/ offered)	82	76–87	97	94–99	69	59–78	97	93–99	50	31–71			26	15–39	73	55–87
Young adult (age <25 or 30)	49	43–54	51	44–58	66	65–67	31	12–54					46	39–53	38	24–54
Men	40	39–42	50	47–54	44	42–48	41	37–46	41	23–61			41	38–44	42	39–46
First-time testers	58	48–67	63	50–74			55	28–81			83	71–91	53	40–66	55	48–62
CD4 ≤350 cells μl^{-1}	39	32–46	38	36–41			26	22–30					66	60–72	71	67–75
HIV positivity	10	8–12	11	8–13	8	5–11	6	4–10	55	49–61	16	9–26	18	13–23	20	17–24

CI, confidence interval; PITC, provider-initiated testing counselling; VCT, voluntary counselling and testing

Supplemental Appendix

Accompanying the manuscript:

Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa

Monisha Sharma, Roger Ying, Gillian Tarr, and Ruanne Barnabas

Background: HIV testing and counseling (HTC) is the critical first step for linking to lifesaving ART and reducing further transmission. Despite high HIV burden in sub-Saharan Africa, less than 50% of HIV-positive persons are aware of their status, with youth and men least likely to be tested. HTC scale-up is urgently needed to reach the UNAIDS target of 90% of HIV-positive persons knowing their status. Community-based HTC (testing outside of health facilities) has the potential to achieve widespread coverage, but whether community testing modalities address gaps in population coverage has not been reviewed.

Methods: Following Cochrane Guidelines, we searched Pubmed, EMBASE, Cochrane Library, Global Health Database, African Index Medicus, and conference abstracts using MeSH terms including "HIV Infections/diagnosis" AND “testing/screening/diagnosis” published from 2000 to 2015. We identified and screened 2,520 abstracts; 126 studies met eligibility criteria for inclusion. We characterized facility and community (home, mobile, index, key populations, workplace and self-testing) testing modalities by population reached, e.g. coverage, first-time testers, men, youth and high-risk groups, as well as HIV-positivity, CD4 count at diagnosis, linkage to care, ART initiation, retention in care, and cost per person tested when available.

Results: We found community HTC achieves high population coverage (70% for home (95% CI: 58-79%) and 76% for campaign (95% CI: 49-95%)) and identified HIV-positive persons at higher CD4 counts than facility HTC. Approximately one-third of HIV-positive individuals diagnosed in community HTC had CD4≤350 cells/μL compared to two-thirds in facility. Mobile reached the highest proportion of men (50%, 95% CI: 47-54%). Home with self-testing reached the highest proportion of young adults (66%, 95% CI: 65-67%). HTC for commercial sex workers and men who have sex with men yielded high HIV positivity combined with a high proportion of first-time testers, indicating a need for service expansion. Community HTC with facilitated linkage (e.g. counselor follow-up to encourage clinic visits) achieved high linkage to care, 95% (95% CI: 87-98%) and ART initiation 75% (95% CI: 68-82%).

Conclusion: Each HTC modality reaches distinct populations and scaling up a combination of strategies is critical to reducing the spread of HIV. Facilitated linkage to care is critical to the success of community HTC.

Table S1: HTC definitions

Community HTC	Definition	Number studies identified
Home	**Door-to-door in a catchment area**	**N=37**
Mobile	**Mobile van/container in central area of community**	**N=17**
Index partner/family member	**HTC for persons potentially HIV exposed by sexual partner or HTC for family members of HIV-positive persons**	**N=5**
Campaign	**Short (1-2 weeks) intensive HTC, often multi-disease**	**N=5**
Key populations	**Targeted HTC to MSM, CSWs and PWID**	**N=5**
Workplace	**Offered at a place of employment**	**N=6**
Facility HTC	Definition	Number studies identified
Facility VCT	**Client initiated voluntary HTC**	**N=37**
Facility provider initiated testing and counseling (PITC)	**Provider initiated, routine, or systematic HTC**	**N=21**

PubMed Strategy

The Pubmed search strategy is divided into two parts (A and B) that were combined using "OR".

Part A – 2012-2014 publications – community and non-community based approaches to testing = 442 references

("HIV Infections/diagnosis"[Majr:NoExp] OR "Acquired Immunodeficiency Syndrome/diagnosis"[Majr] OR "HIV Seropositivity/diagnosis"[Majr] OR "AIDS Serodiagnosis"[Majr] OR "HIV Infections/prevention and control"[Majr:NoExp] OR "Acquired Immunodeficiency Syndrome/prevention and control"[Majr] OR "HIV Seropositivity/prevention and control"[Majr]) AND "Africa South of the Sahara"[Mesh] AND ("mass screening"[mesh] OR test OR tests OR testing OR screen* OR diagnosis OR diagnoses OR diagnostic* OR serodiagnos* OR "counseling"[mesh] OR "Sensitivity and Specificity"[mesh]) AND ("2012/01/01"[PDat] : "2014/12/31"[PDat])

AND

("Health Care Evaluation Mechanisms"[mesh] OR "Empirical Research"[mesh] OR "clinical trial"[publication type] OR "comparative study"[publication type] OR "evaluation studies"[publication type] OR "meta-analysis"[publication type] OR "multicenter study"[publication type] OR "validation studies"[publication type] OR "review"[publication type])

Part B – focused on non-community approaches (terms in green) 2000-2011 = 675 references

("HIV Infections/diagnosis"[Majr:NoExp] OR "Acquired Immunodeficiency Syndrome/diagnosis"[Majr] OR "HIV Seropositivity/diagnosis"[Majr] OR "AIDS Serodiagnosis"[Majr] OR "HIV Infections/prevention and control"[Majr:NoExp] OR "Acquired Immunodeficiency Syndrome/prevention and control"[Majr] OR "HIV Seropositivity/prevention and control"[Majr]) AND "Africa South of the Sahara"[Mesh] AND ("mass screening"[mesh] OR test OR tests OR testing OR screen* OR diagnosis OR diagnoses OR diagnostic* OR serodiagnos* OR "counseling"[mesh] OR "Sensitivity and Specificity"[mesh]) AND ("2000/01/01"[PDat] : "2011/12/31"[PDat])

AND

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AND

("Health Facilities"[mesh] OR "Health Personnel"[mesh] OR "Prenatal Diagnosis"[mesh] OR "Family Planning Services"[mesh] OR "Prisons"[mesh] OR Facility OR facilities OR provider OR providers OR antenatal OR prenatal OR prison* OR jail OR jails OR voluntary OR VCT OR clinic OR clinics OR pharmacy OR pharmacies OR "medical center" OR "medical centers" OR hospital OR hospitals OR "health center" OR "health centers" OR office OR offices OR physician* OR nurse OR nurses OR pharmacist* OR doctor OR doctors OR inpatient* OR outpatient*)

Supplementary PubMed search for unindexed (primarily 2014) references

Strategy: 348 references

((((test[ti] OR tests[ti] OR testing[ti] OR tested[ti] OR screen*[ti] OR counsel*[ti] OR prevent*[ti] OR surveill*[ti] OR diagnos*[ti] OR service*[ti] OR program*[ti] OR campaign*[ti]) AND (test OR tests OR testing OR tested OR screen* OR counsel*) AND (hiv OR "human immunodeficiency virus" OR "acquired immunodeficiency" OR "acquired immune deficiency" OR aids[ti]) AND (africa OR african OR cameroon OR chad OR congo OR guinea OR gabon OR burundi OR djibouti OR eritrea OR ethiopia OR kenya OR rwanda OR somalia OR sudan OR tanzania OR uganda OR angola OR botswana OR lesotho OR malawi OR mozambique OR namibia OR swaziland OR zambia OR zimbabwe OR benin OR "burkina faso" OR "cape verde" OR "ivory coast" OR "cote d'ivoire" OR gambia OR ghana OR liberia OR mali OR mauritania OR niger OR nigeria OR senegal OR "sierra leone" OR togo) AND (community OR home OR homes OR house OR houses OR door OR mobile OR campaign* OR bar OR workplace OR business* OR church OR churches OR worship* OR temple* OR active OR school OR schools OR highway* OR brothel* OR bathhouse* OR festival* OR outreach OR van OR vans OR bicycle* OR tent OR tents OR Facility OR facilities OR provider OR providers OR antenatal OR prenatal OR "family planning" OR prison* OR jail OR jails OR voluntary OR VCT OR clinic OR clinics OR pharmacy OR pharmacies OR "medical center" OR "medical centers" OR hospital OR hospitals OR "health center" OR "health centers" OR office OR offices OR physician* OR nurse

OR nurses OR pharmacist* OR doctor OR doctors OR inpatient* OR outpatient*) AND ("2013"[PDat] : "2014"[PDat])) NOT medline[sb]

Comparable Embase search strategies (excluding references found in PubMed)

Divided into two parts that were combined using "OR"

This yields 301 references that are not included among the indexed PubMed references.

Part A – 2012-2014 publications – community and non-community based approaches to testing.

(((('Human immunodeficiency virus infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 1 infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 2 infection'/mj/dm_di,dm_pc OR 'Acquired immune deficiency syndrome'/mj/dm_di,dm_pc) AND (screening/exp OR counseling/exp/mj OR test OR tests OR testing OR screen* OR diagnosis OR diagnoses OR diagnostic* OR serodiagnos*)) OR 'HIV Test'/exp/mj) AND 'Africa south of the Sahara'/exp *AND ('Clinical Study'/exp OR 'methodology'/exp OR 'Controlled Study'/exp OR 'Comparative Study'/exp OR 'Feasibility Study'/de OR 'Observational Study'/de OR 'Pilot Study'/de OR 'Prevention Study'/de OR 'Validation Study'/de OR 'Health Care Quality'/exp OR 'review'/exp)* AND (2012:py OR 2013:py OR 2014:py) AND ([embase]/lim NOT [medline]/lim)

Part B – focused on non-community approaches 2000-2011

((('Human immunodeficiency virus infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 1 infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 2 infection'/mj/dm_di,dm_pc OR 'Acquired immune deficiency syndrome'/mj/dm_di,dm_pc) AND (screening/exp OR counseling/exp/mj OR test OR tests OR testing OR screen* OR diagnosis OR diagnoses OR diagnostic* OR serodiagnos*)) OR 'HIV Test'/exp/mj) AND 'Africa south of the Sahara'/exp *AND ('Clinical Study'/exp OR 'methodology'/exp OR 'Controlled Study'/exp OR 'Comparative Study'/exp OR 'Feasibility Study'/de OR 'Observational Study'/de OR 'Pilot Study'/de OR 'Prevention Study'/de OR 'Validation Study'/de OR 'Health Care Quality'/exp OR 'review'/exp)* AND ('Health Care Facility'/exp OR 'Health Care Personnel'/exp OR 'Family Planning'/exp OR 'Prenatal Care'/exp OR 'Prison'/exp OR Facility OR facilities OR provider OR providers OR antenatal OR prenatal OR prison* OR jail OR jails OR voluntary OR VCT OR clinic OR clinics OR pharmacy OR pharmacies OR "medical center" OR "medical centers" OR hospital OR hospitals OR "health center" OR "health center" OR office OR offices OR physician* OR nurse OR nurses OR pharmacist* OR doctor OR doctors OR inpatient* OR outpatient*) AND (2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py) AND ([embase]/lim NOT [medline]/lim)

Additional search for published from 2014-2015 conducted on June 20th 2015

Search strategy for key populations only: 28 references

africa south of the sahara[mh] AND (hiv infections/pc[mh] OR hiv infections/di[mh]) AND (mass screening[mh] OR screen OR test[tw] OR tests[tw] OR testing[tw] OR diagno*[tw] OR counseling[mh] OR counsel*) AND (drug users[mh] OR injection drug* OR homosexual* OR homosexuality OR sex workers[mh] OR sex worker* OR transgender* OR prostitut* OR "men who have sex with men" OR vulnerable populations[mh] OR vulnerable population* OR most at risk*) AND 2014:2015[dp]*

Part A –2015 publications – community and non-community based approaches to testing = 103 references

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Supplementary PubMed search for unindexed (primarily 2015) references

Strategy: 404 references

((((test[ti] OR tests[ti] OR testing[ti] OR tested[ti] OR screen*[ti] OR counsel*[ti] OR prevent*[ti] OR surveill*[ti] OR diagnos*[ti] OR service*[ti] OR program*[ti] OR campaign*[ti]) AND (test OR tests OR testing OR tested OR screen* OR counsel*) AND (hiv OR "human immunodeficiency virus" OR "acquired immunodeficiency" OR "acquired immune deficiency" OR aids[ti]) AND (africa OR african OR cameroon OR chad OR congo OR guinea OR gabon OR burundi OR djibouti OR eritrea OR ethiopia OR kenya OR rwanda OR somalia OR sudan OR tanzania OR uganda OR angola OR botswana OR lesotho OR malawi OR mozambique OR namibia OR swaziland OR zambia OR zimbabwe OR benin OR "burkina faso" OR "cape verde" OR "ivory coast" OR "cote d'ivoire" OR gambia OR ghana OR liberia OR mali OR mauritania OR niger OR nigeria OR senegal OR "sierra leone" OR togo) AND (community OR home OR homes OR house OR houses OR door OR mobile OR campaign* OR bar OR workplace OR business* OR church OR churches OR worship* OR temple* OR active OR school OR schools OR highway* OR brothel* OR bathhouse* OR festival* OR outreach OR van OR vans OR bicycle* OR tent OR tents OR Facility OR facilities OR provider OR providers OR antenatal OR prenatal OR "family planning" OR prison* OR jail OR jails OR voluntary OR VCT OR clinic OR clinics OR pharmacy OR pharmacies OR "medical center" OR "medical centers" OR hospital OR hospitals OR "health center" OR "health centers" OR office OR offices OR physician* OR nurse OR nurses OR pharmacist* OR doctor OR doctors OR inpatient* OR outpatient*) AND ("2014/05/01"[PDat] : "2015"[PDat])) NOT medline[sb]

Comparable Embase search strategies (excluding references found in PubMed)

Divided into two parts that were combined using "OR"

This yields 119 references that are not included among the indexed PubMed references.

Part A – 2014-2015 publications – community and non-community based approaches to testing.

((('Human immunodeficiency virus infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 1 infection'/mj/dm_di,dm_pc OR 'Human immunodeficiency virus 2 infection'/mj/dm_di,dm_pc OR 'Acquired immune deficiency syndrome'/mj/dm_di,dm_pc) AND (screening/exp OR counseling/exp/mj OR test OR tests OR testing OR screen* OR diagnosis OR diagnoses OR diagnostic* OR serodiagnos*)) OR 'HIV Test'/exp/mj) AND 'Africa south of the Sahara'/exp *AND ('Clinical Study'/exp OR 'methodology'/exp OR 'Controlled*

Study'/exp OR 'Comparative Study'/exp OR 'Feasibility Study'/de OR 'Observational Study'/de OR 'Pilot Study'/de OR 'Prevention Study'/de OR 'Validation Study'/de OR 'Health Care Quality'/exp OR 'review'/exp) AND (2014:py OR 2015:py) AND ([embase]/lim NOT [medline]/lim)

Flow chart of review process: Figure S0.a

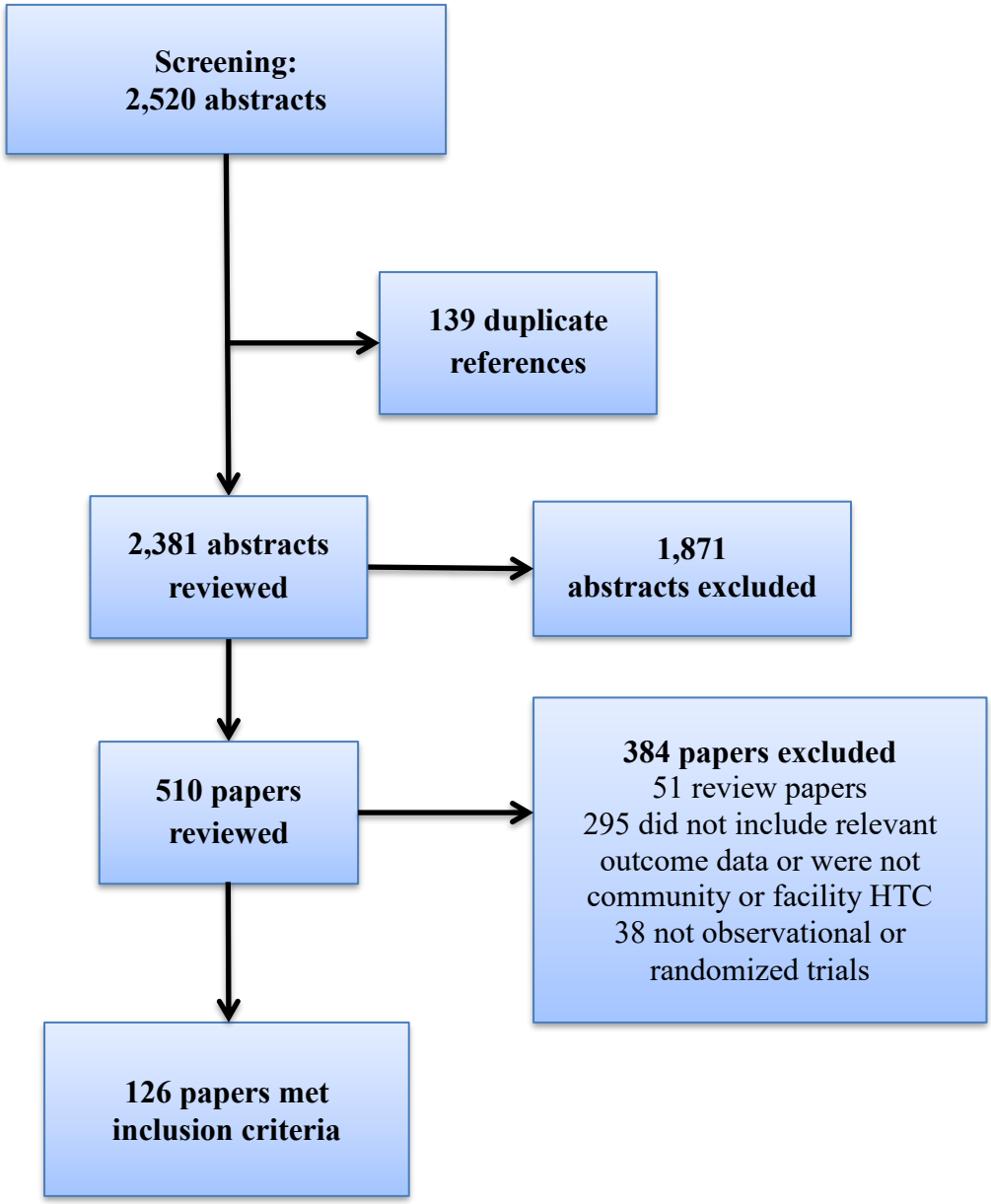
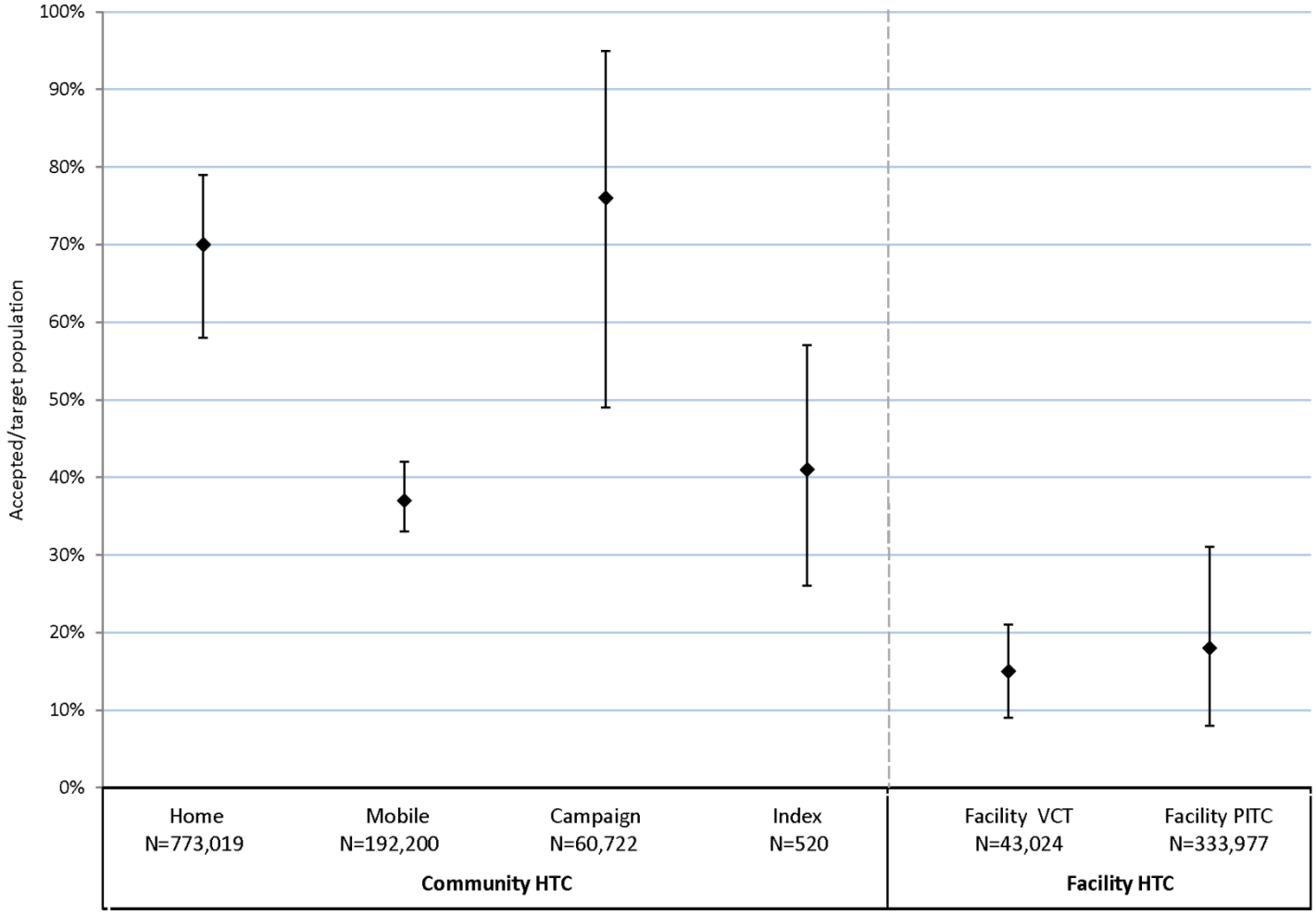
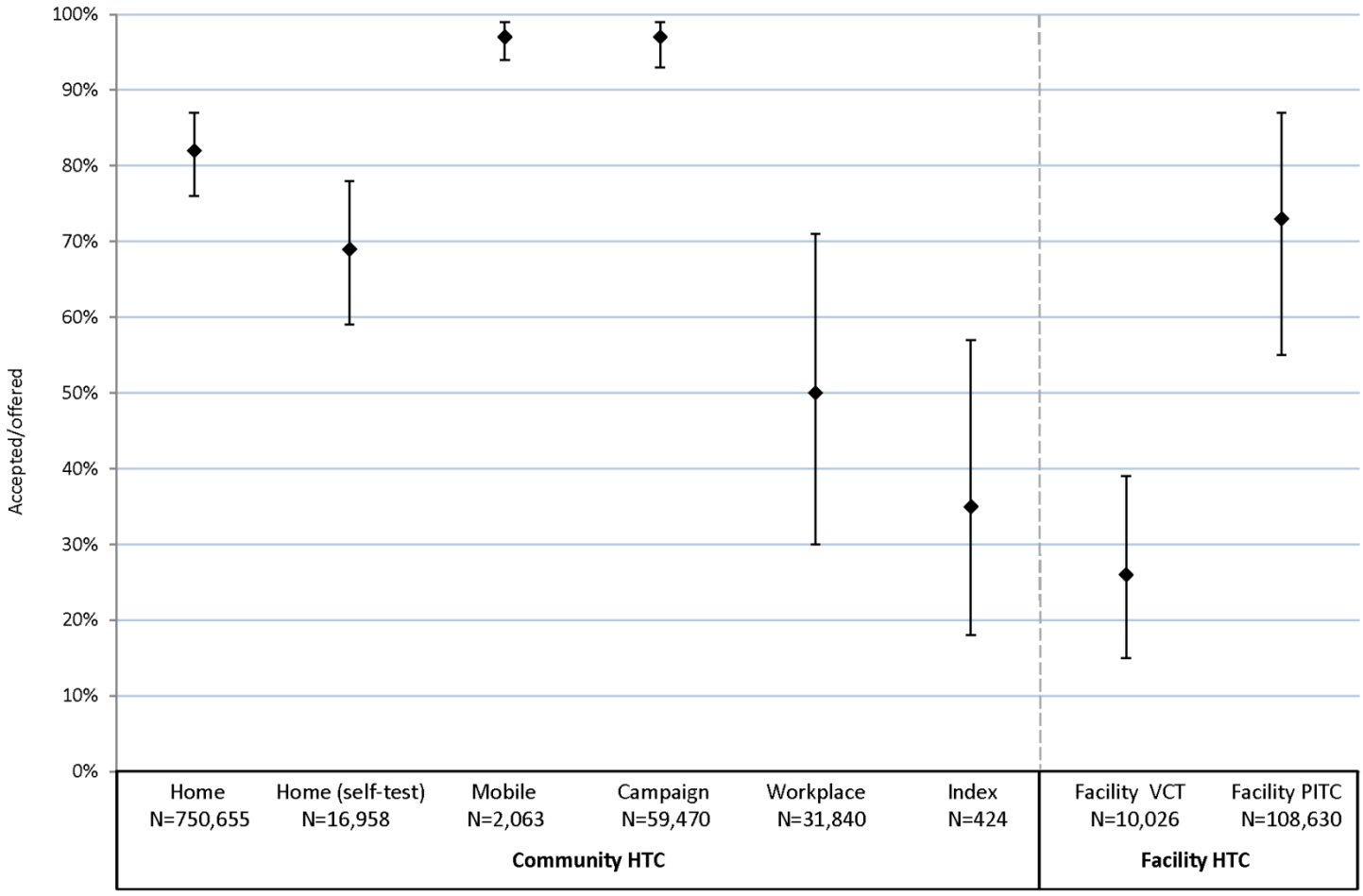


Figure S0.b: Pooled coverage of HTC modalities.*



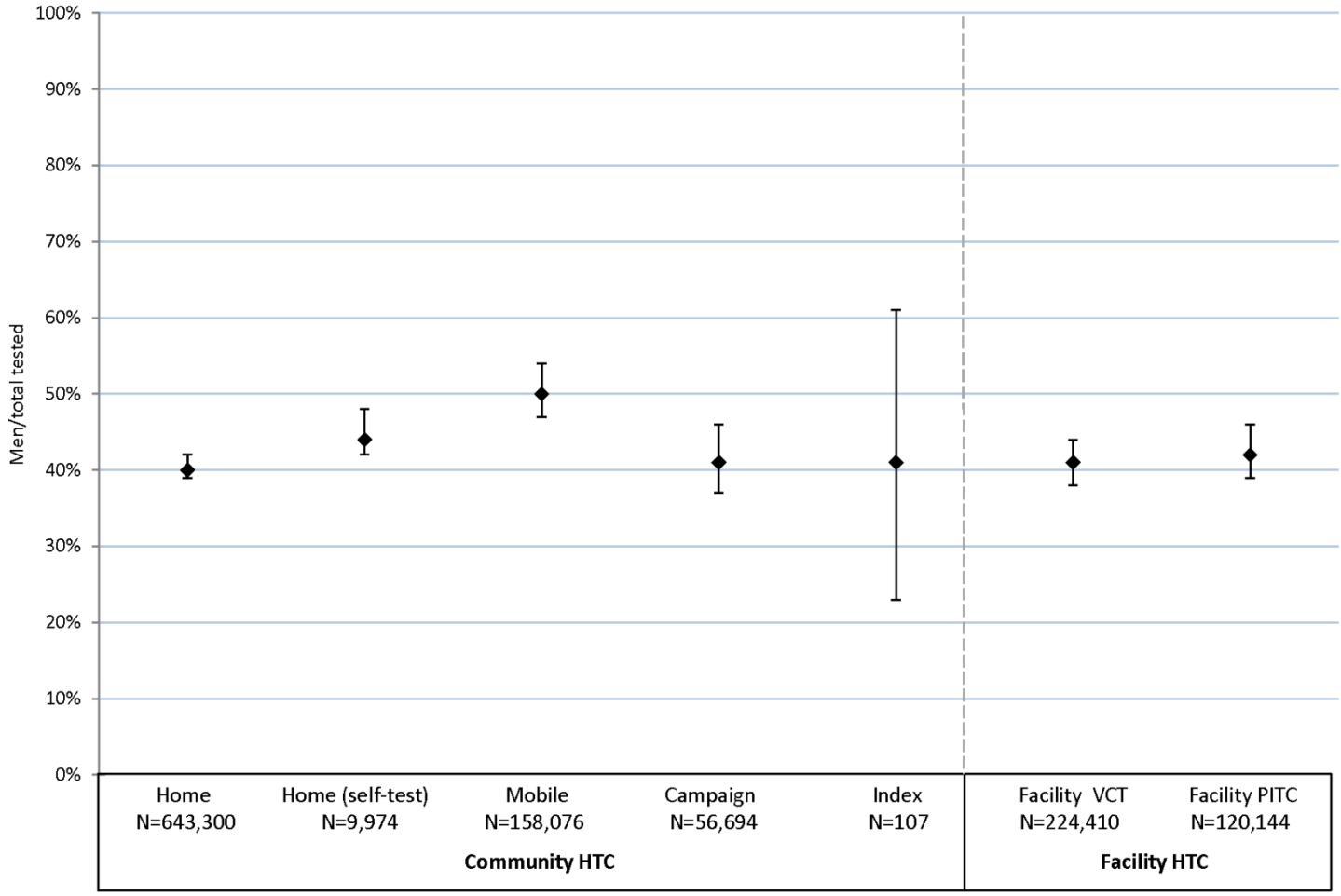
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.c: Pooled uptake of HTC modalities*



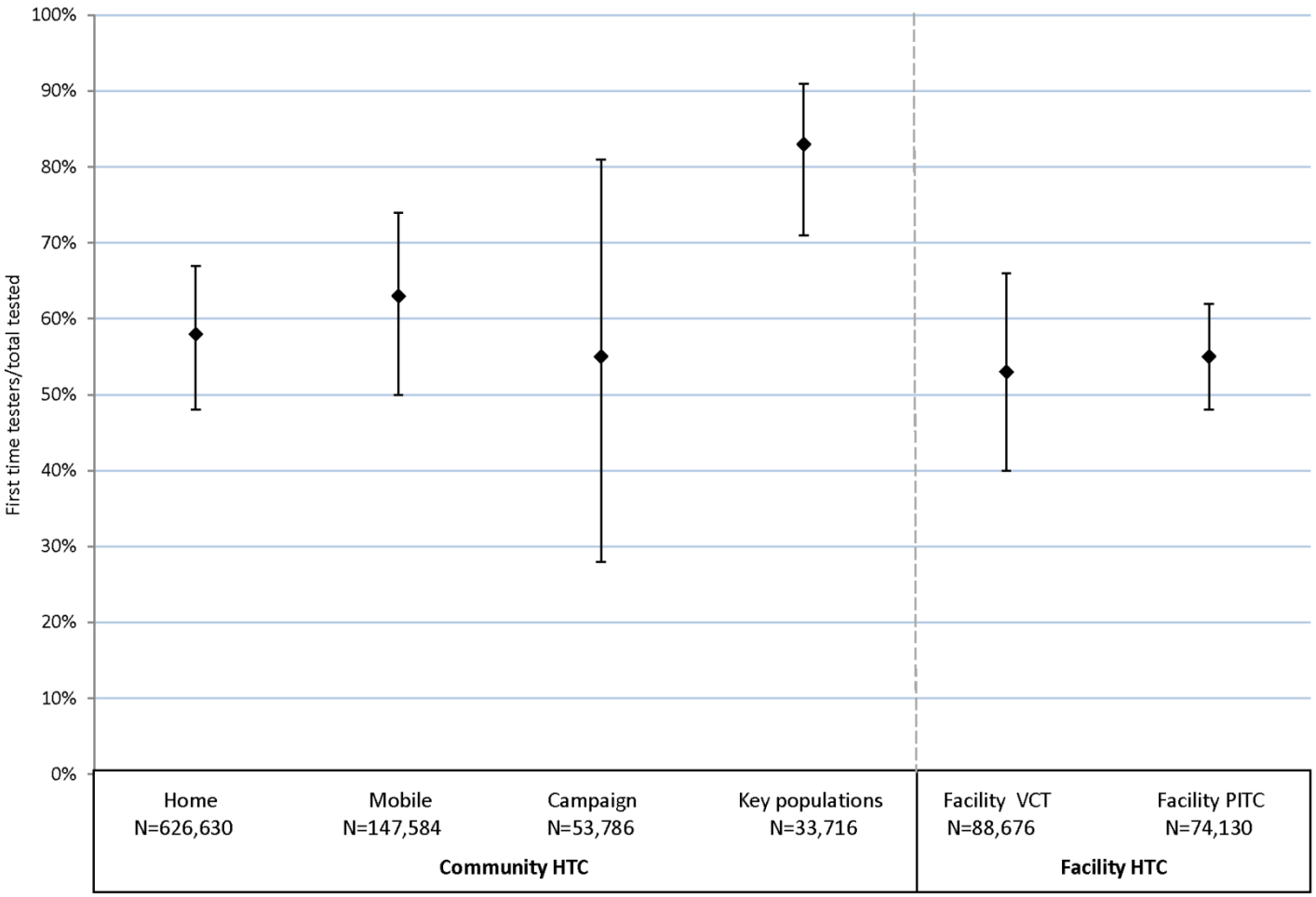
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.d: Pooled percentage men in HTC modalities*



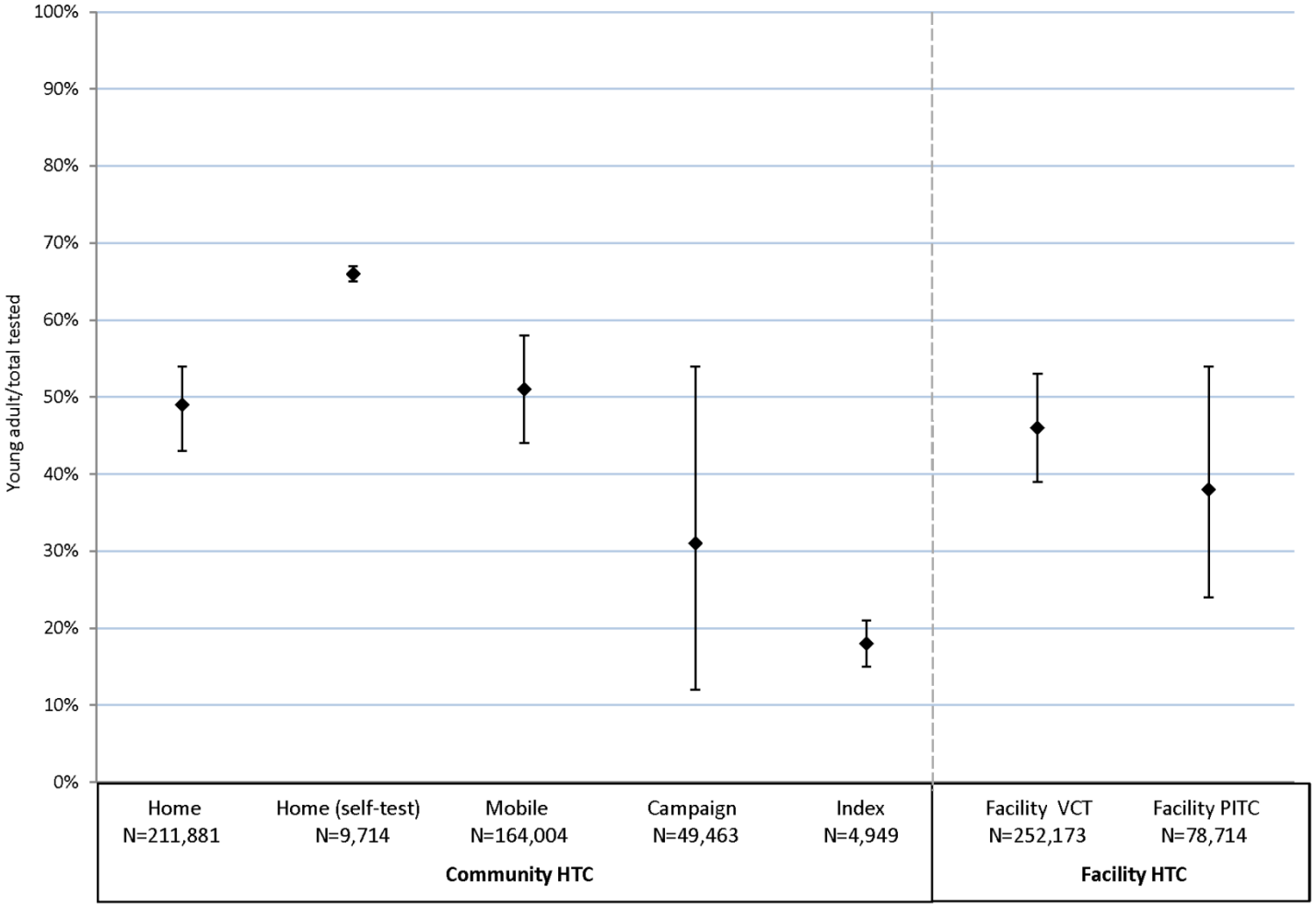
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.e: Pooled percentage first time testers in HTC modalities*



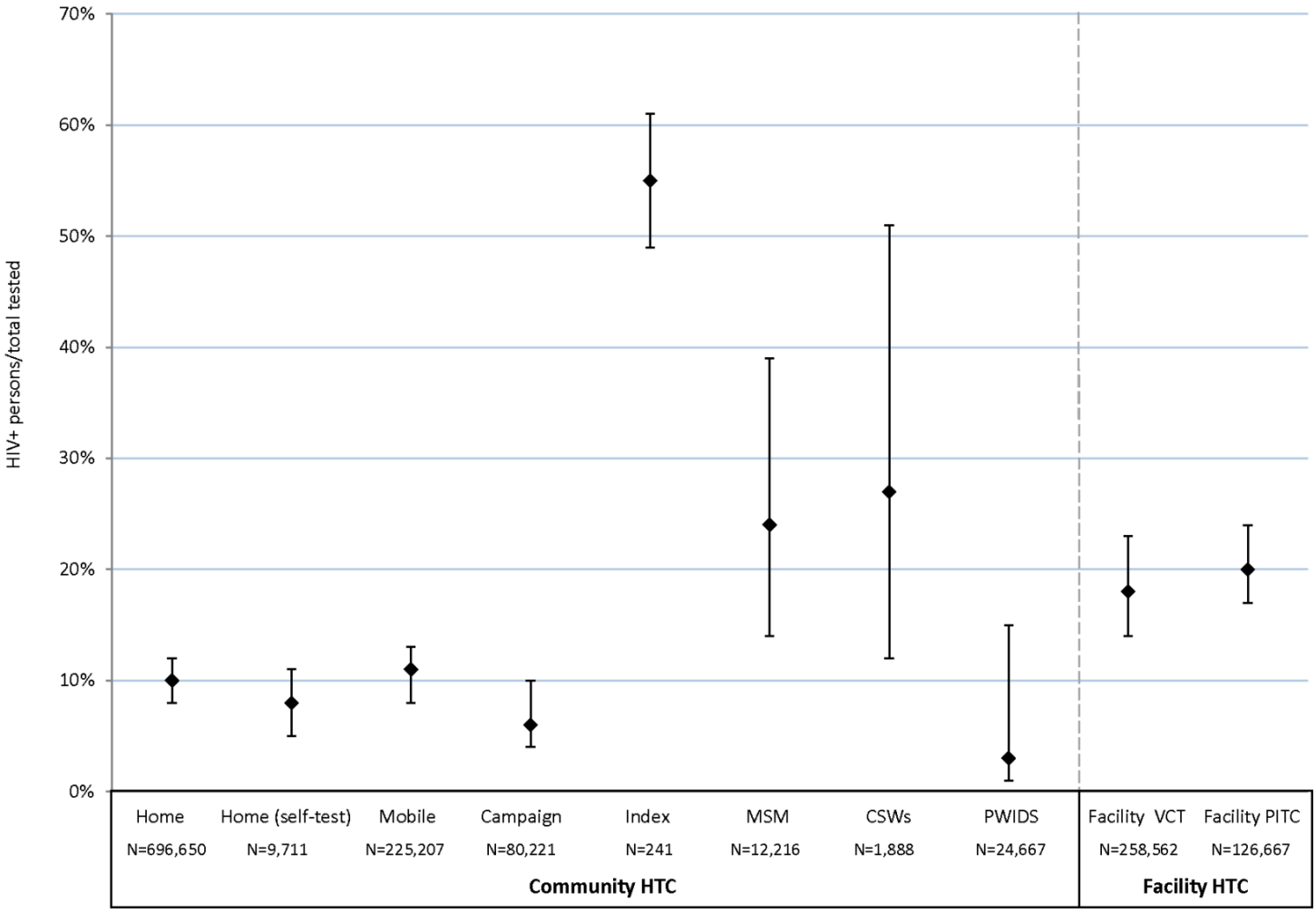
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.f: Pooled percentage young adult (<25 or 30 years of age) in HTC modalities*



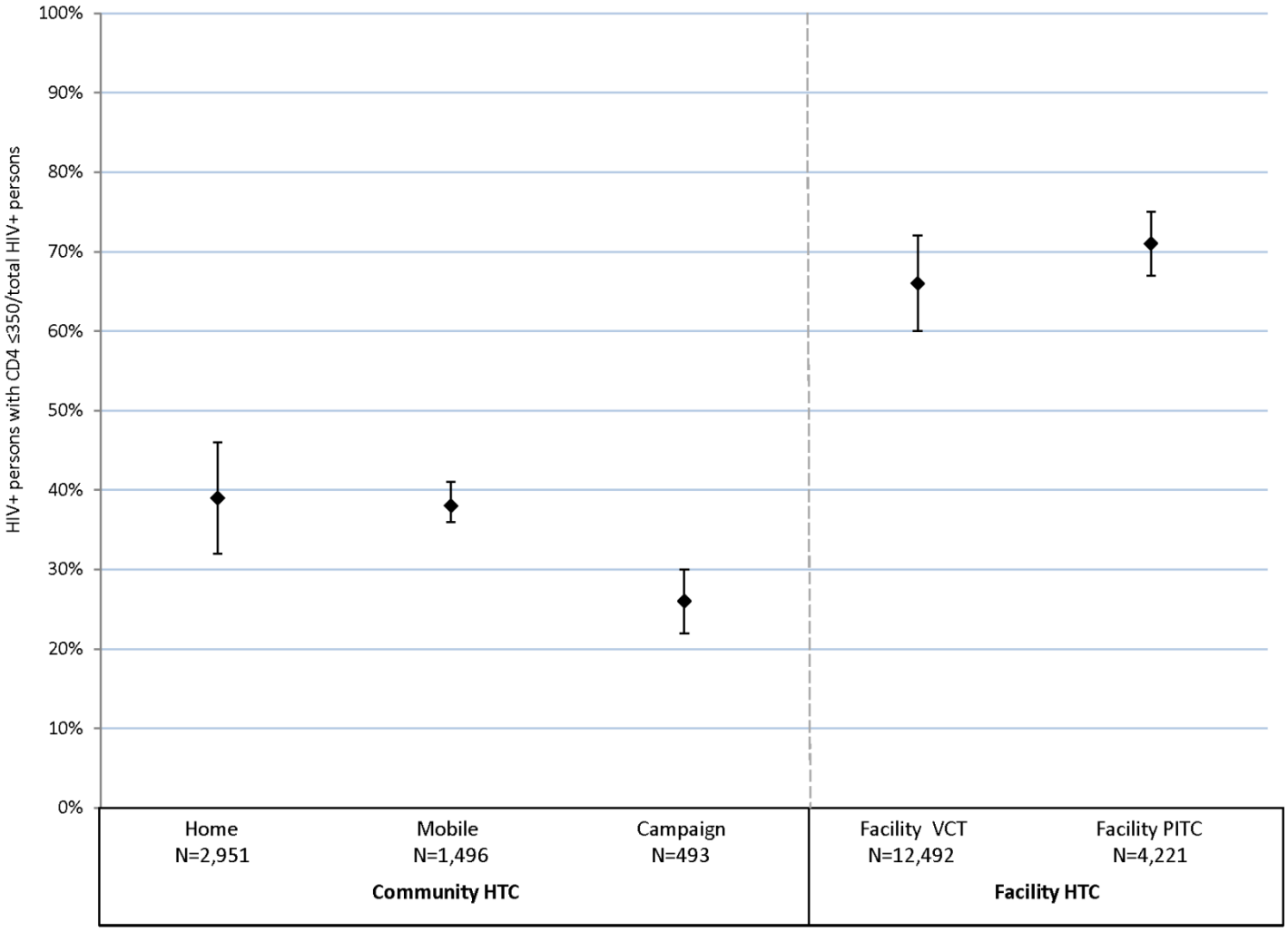
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.g: Pooled HIV positivity in HTC modalities*



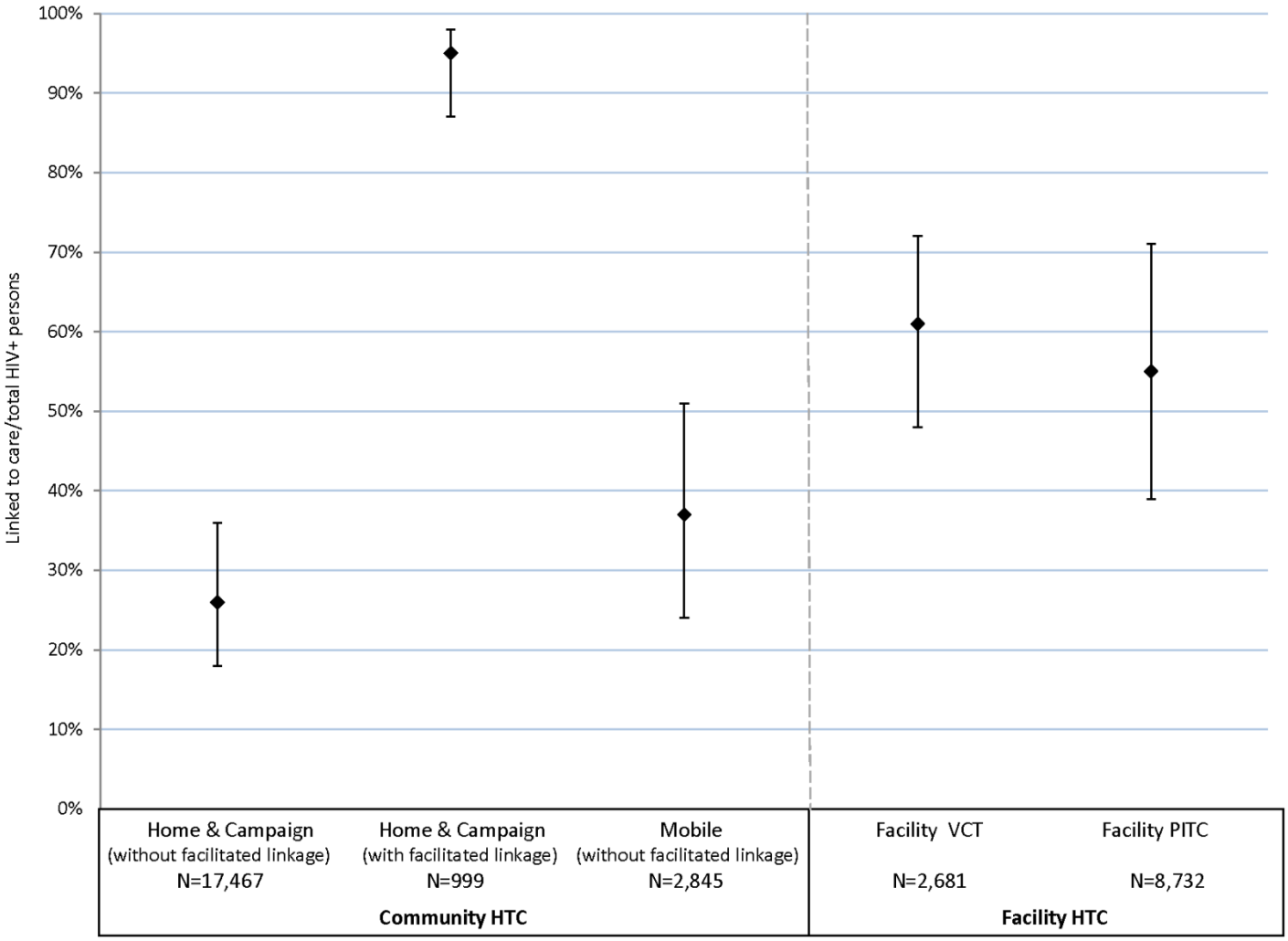
*Bars indicate 95% confidence intervals of random effects meta-analyses. Index: Testing of sexual partners of newly diagnosed HIV-positive index cases. PWIDS: Persons who inject drugs.

Figure S0.h: Pooled proportion newly diagnosed HIV+ with CD4 count≤350 cells/μL in HTC modalities*



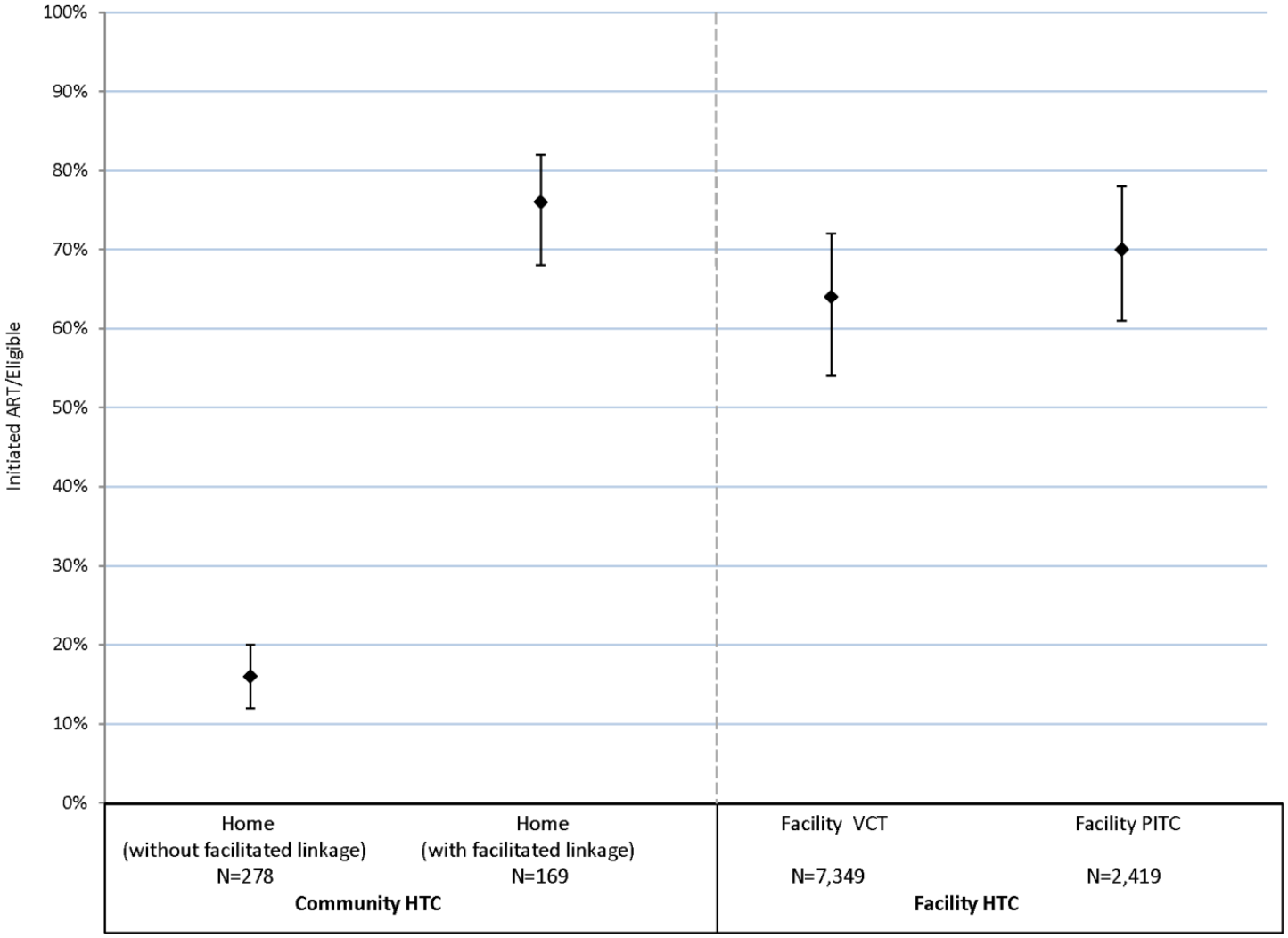
*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.i: Linkage to care after community and facility HTC*



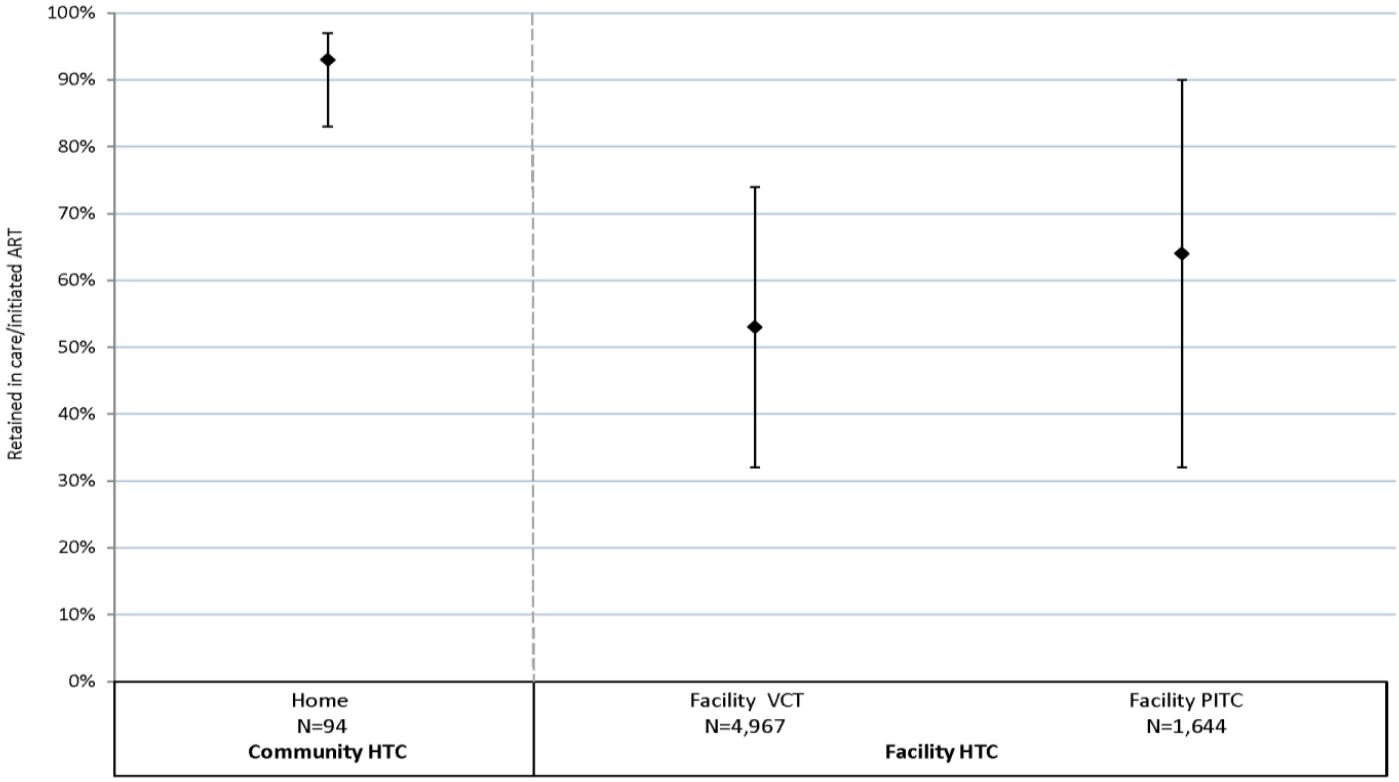
*Linkage to care defined as visiting clinic to receive CD4 results, or enrolling in pre-ART care. Bars indicate 95% confidence intervals of random effects meta-analyses

Figure S0.j: Pooled percentage initiated ART among those eligible by HTC modality*



*Bars indicate 95% confidence intervals of random effects meta-analyses.

Figure S0.k: Pooled percentage retained in care among those who initiated ART



*Bars indicate 95% confidence intervals of random effects meta-analyses. Definition of retention in care varied from 6 to 12 months.

Coverage

Figure S1: Home HTC coverage

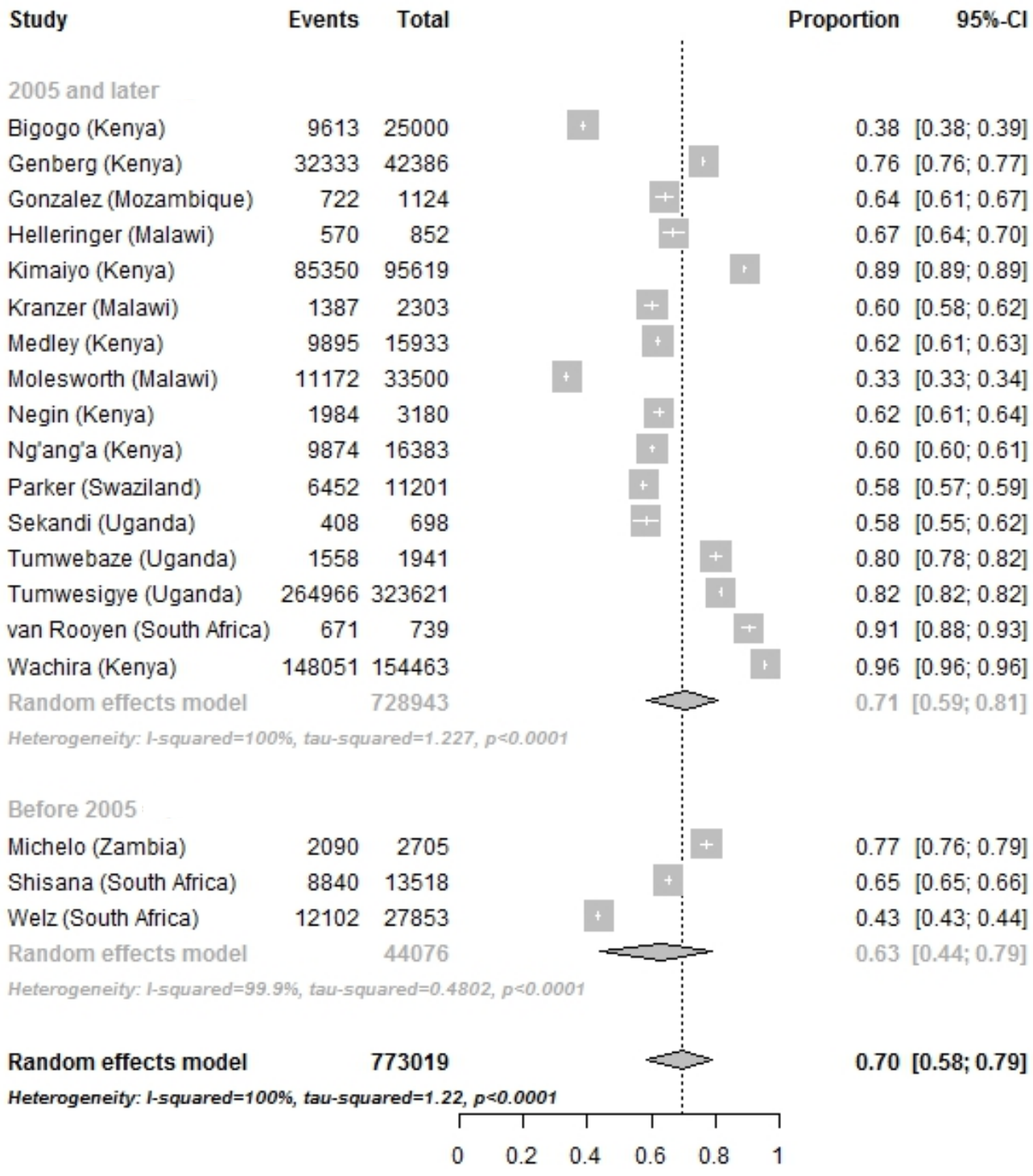


Figure S2: Mobile HTC coverage

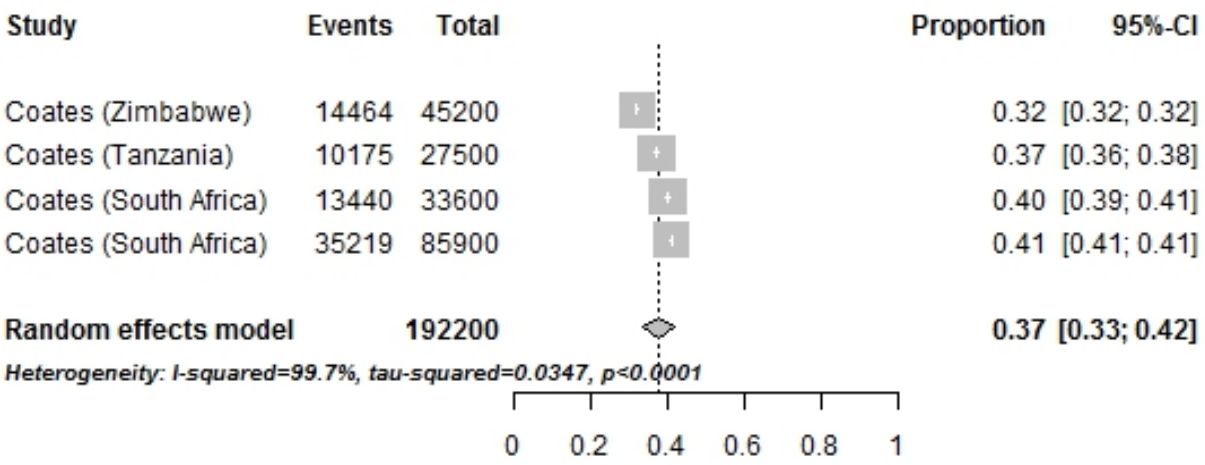


Figure S3: Campaign HTC: coverage

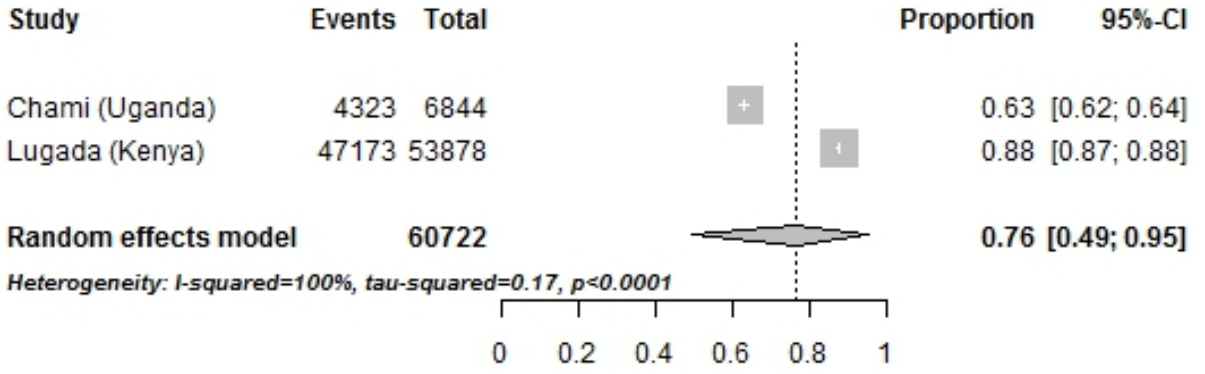


Figure S4: Index HTC: Coverage

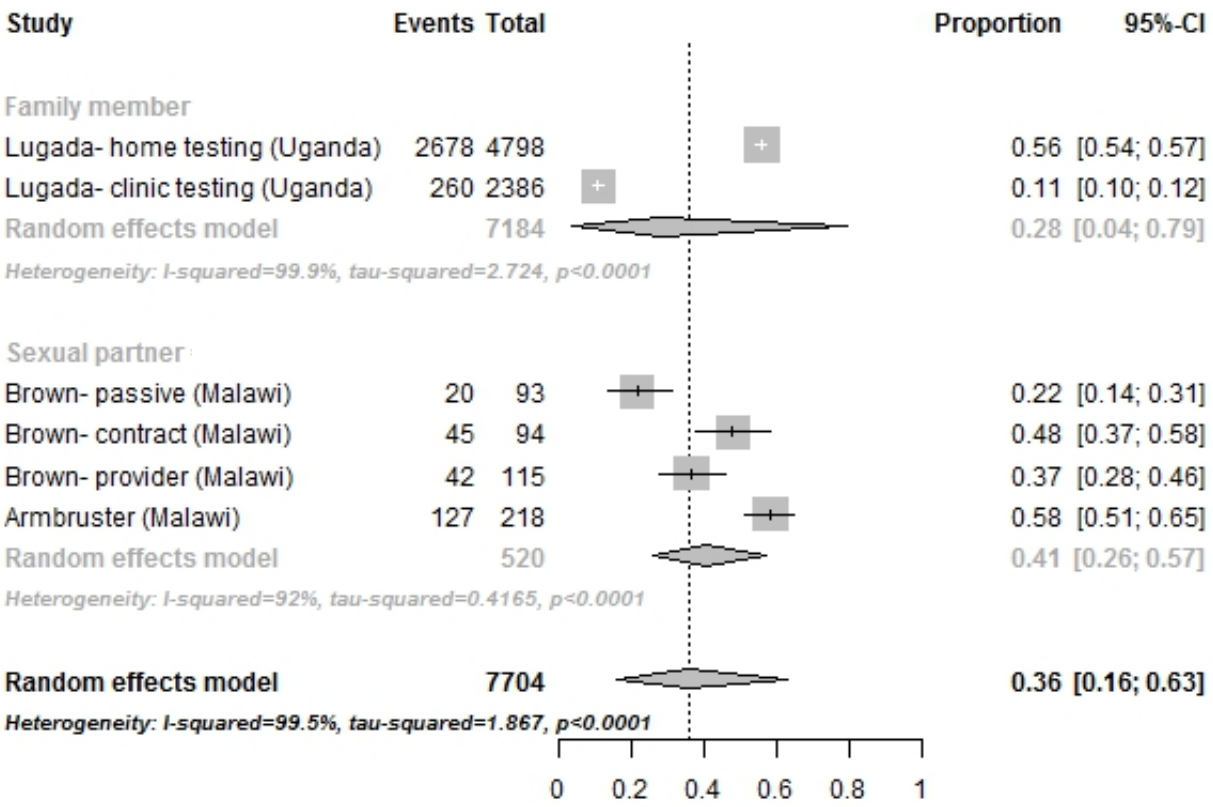


Figure S5: Facility VCT: Coverage

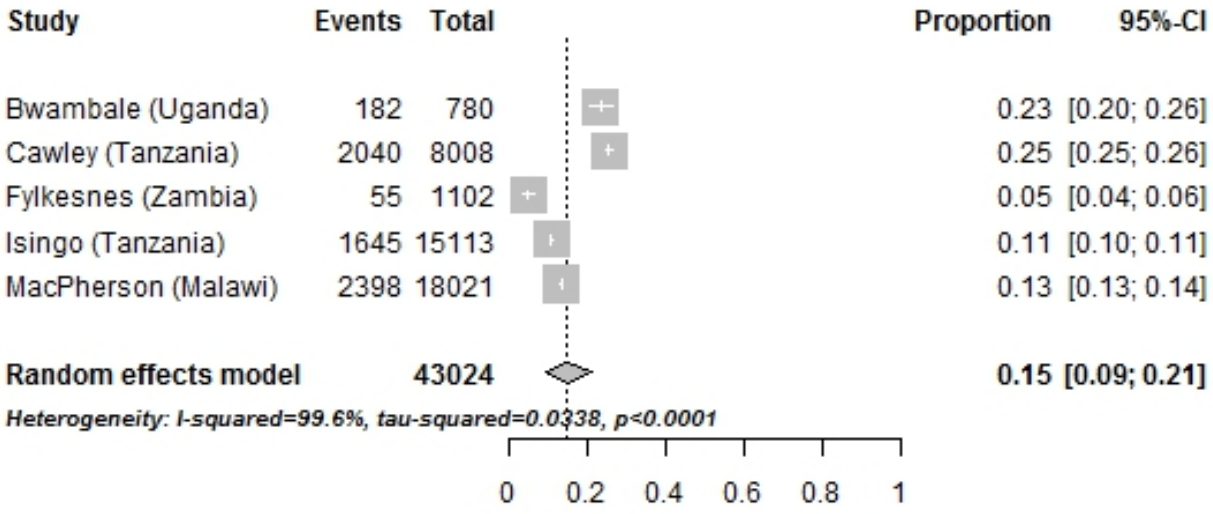
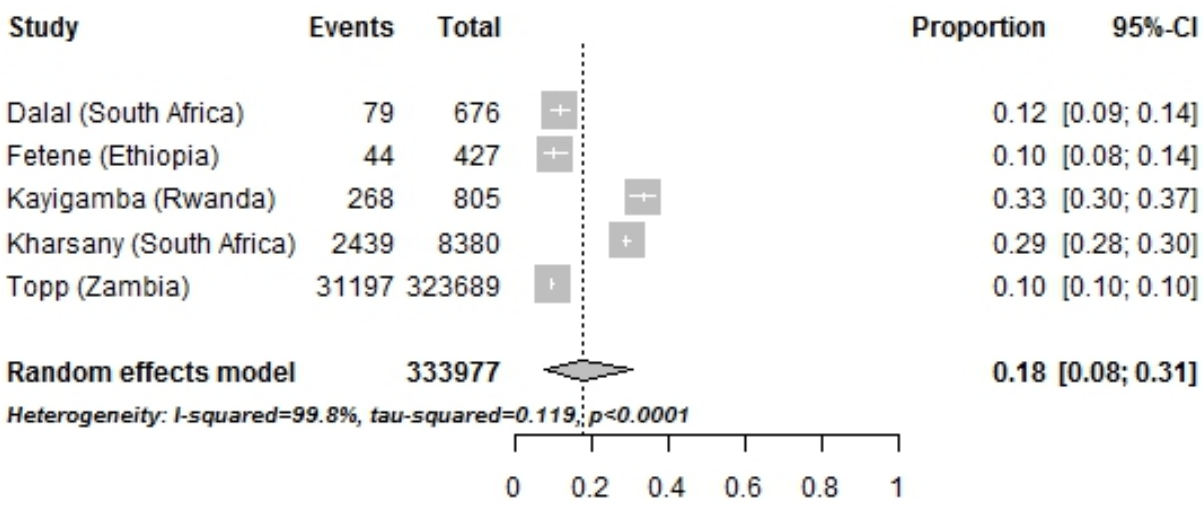


Figure S6: Facility PITC: coverage



Uptake: Figure S7: Home HTC Uptake

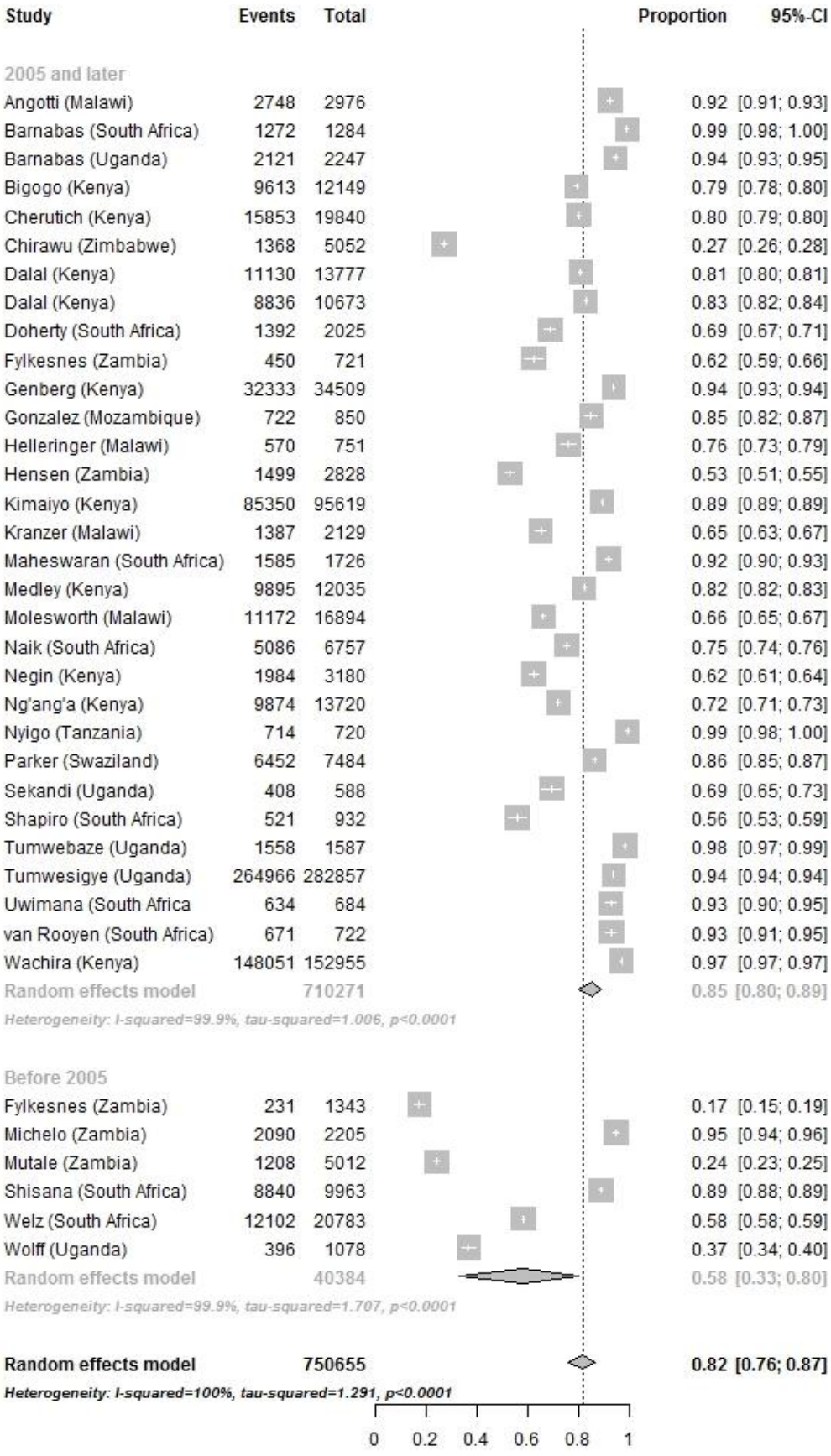


Figure S8: Home HTC with self-testing: Uptake

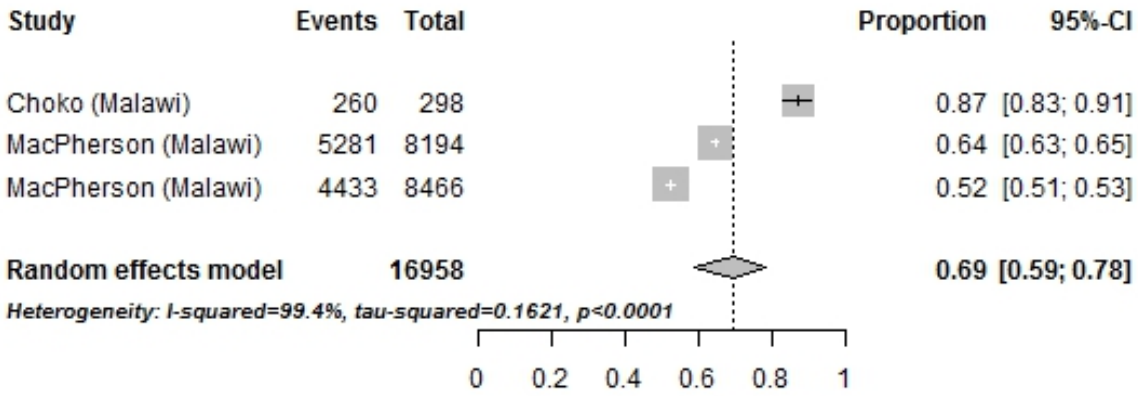


Figure S9: Mobile HTC: Uptake

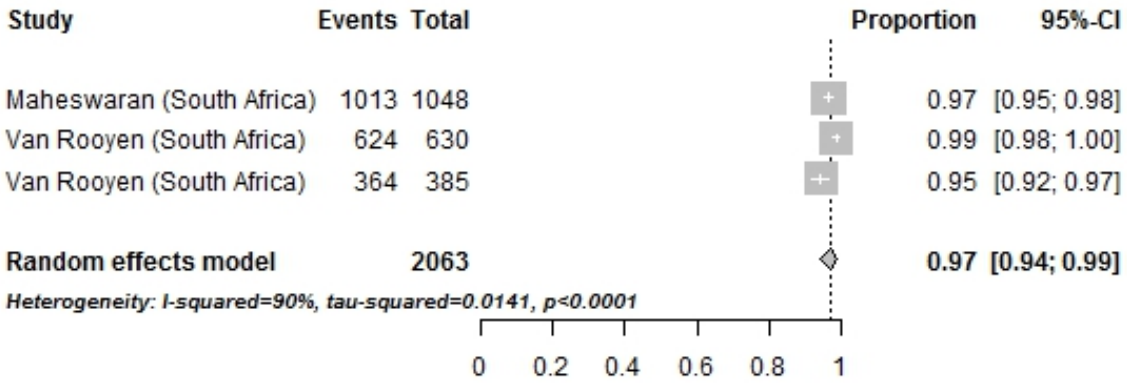


Figure S10: Index HTC: Uptake

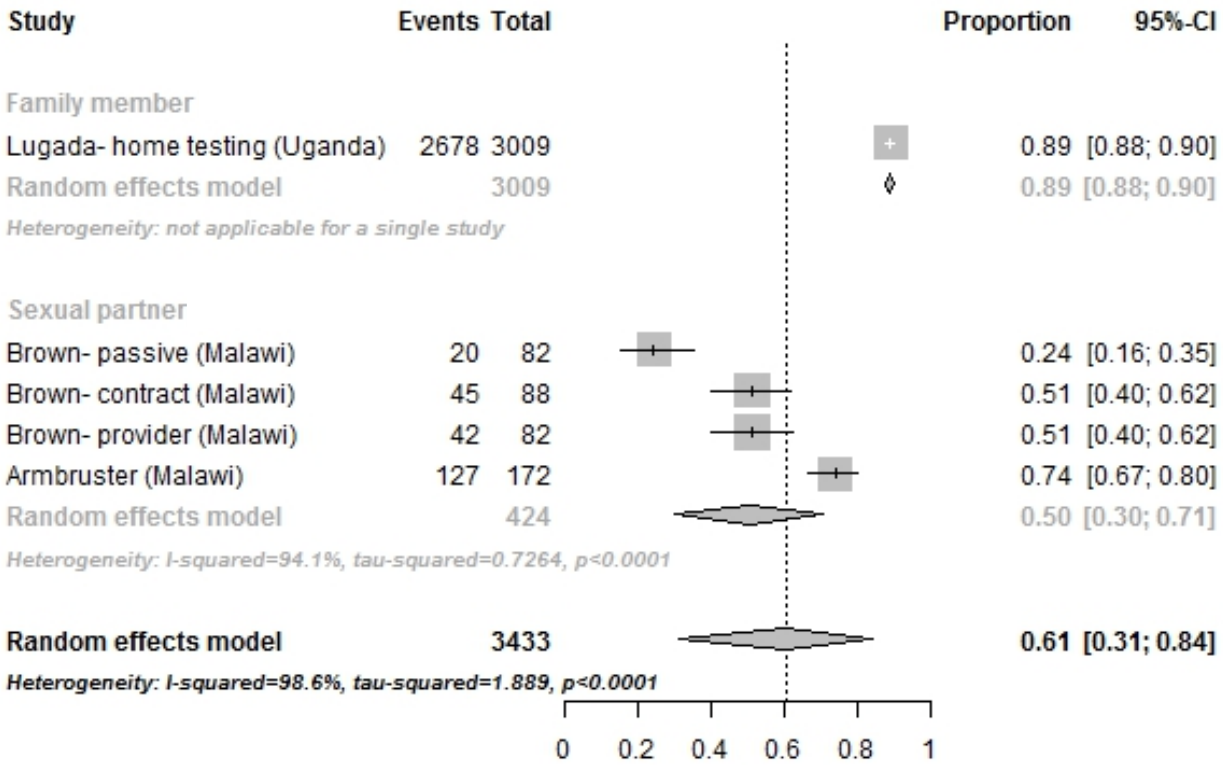


Figure S11: Campaign HTC: Uptake

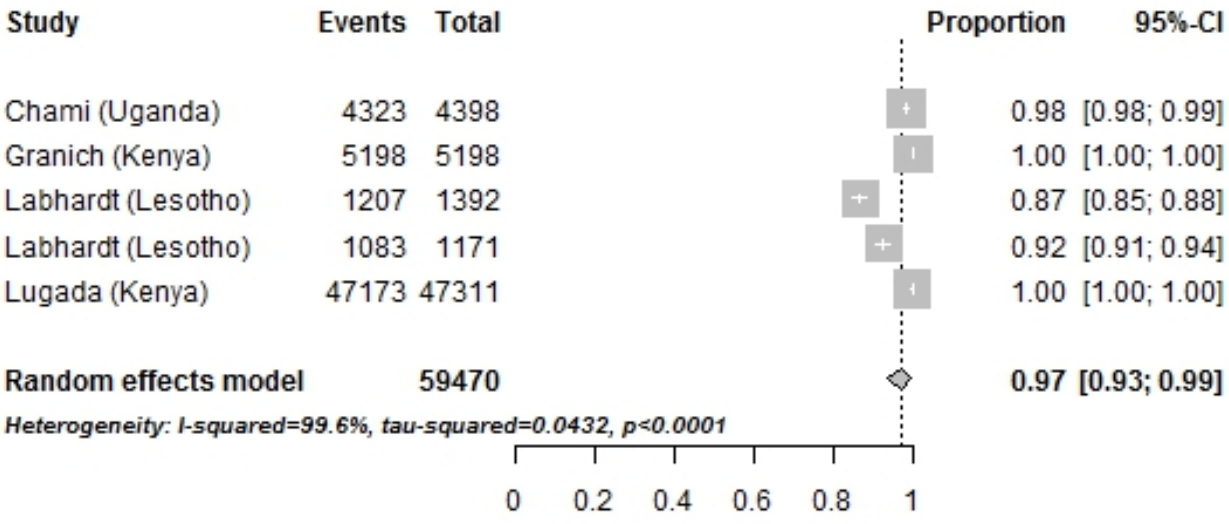
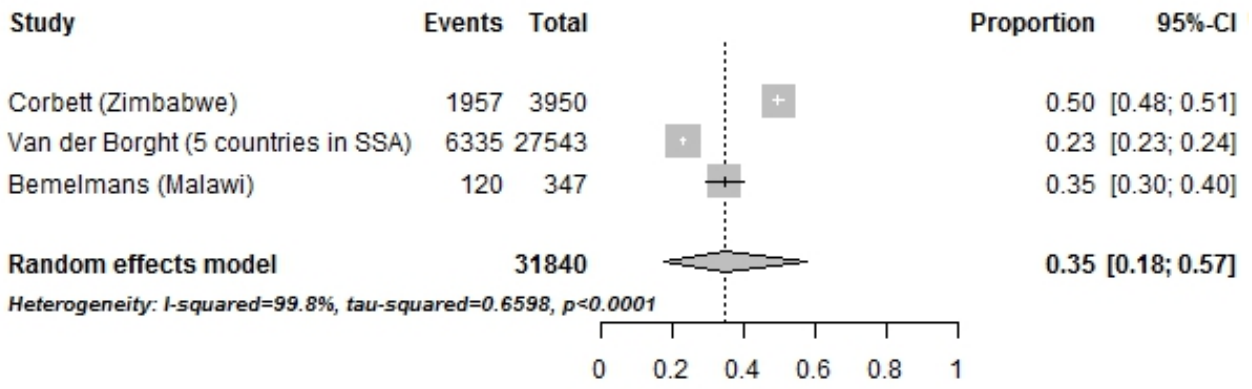


Figure S12: Workplace HTC: Uptake*



*Workplace HTC uptake and coverage are interchangeable as all workers were offered HTC.

Figure S13: Facility VCT: Uptake after referral to VCT

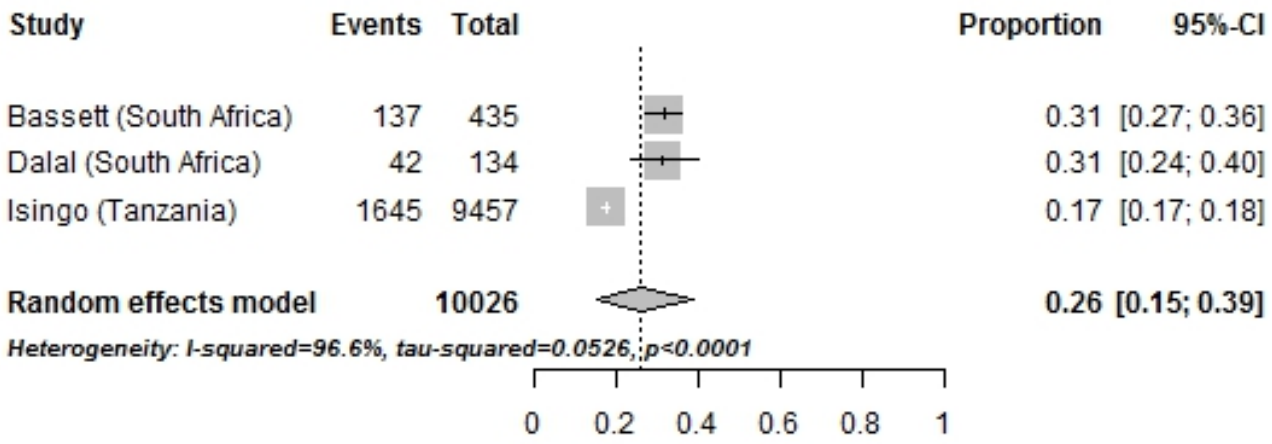
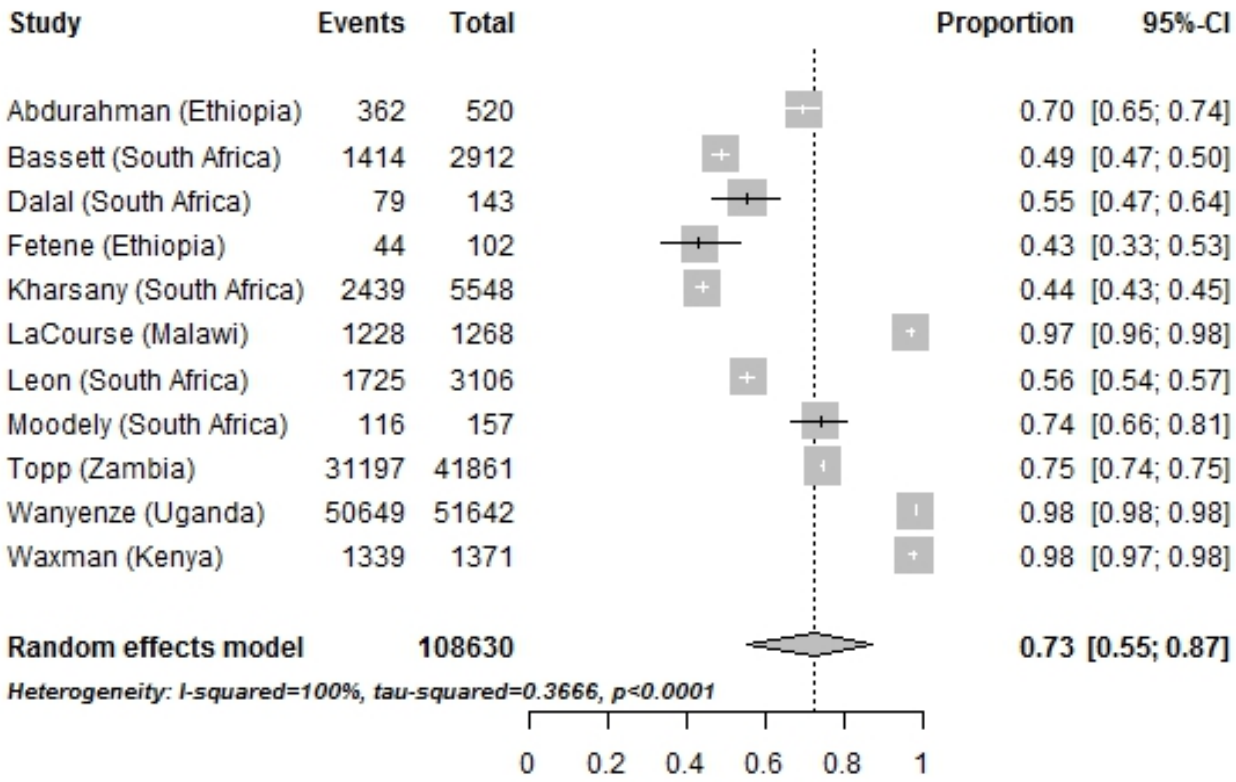


Figure S14 Facility: Uptake after Facility PITC



Men

Figure S15: Home HTC: Percentage males tested

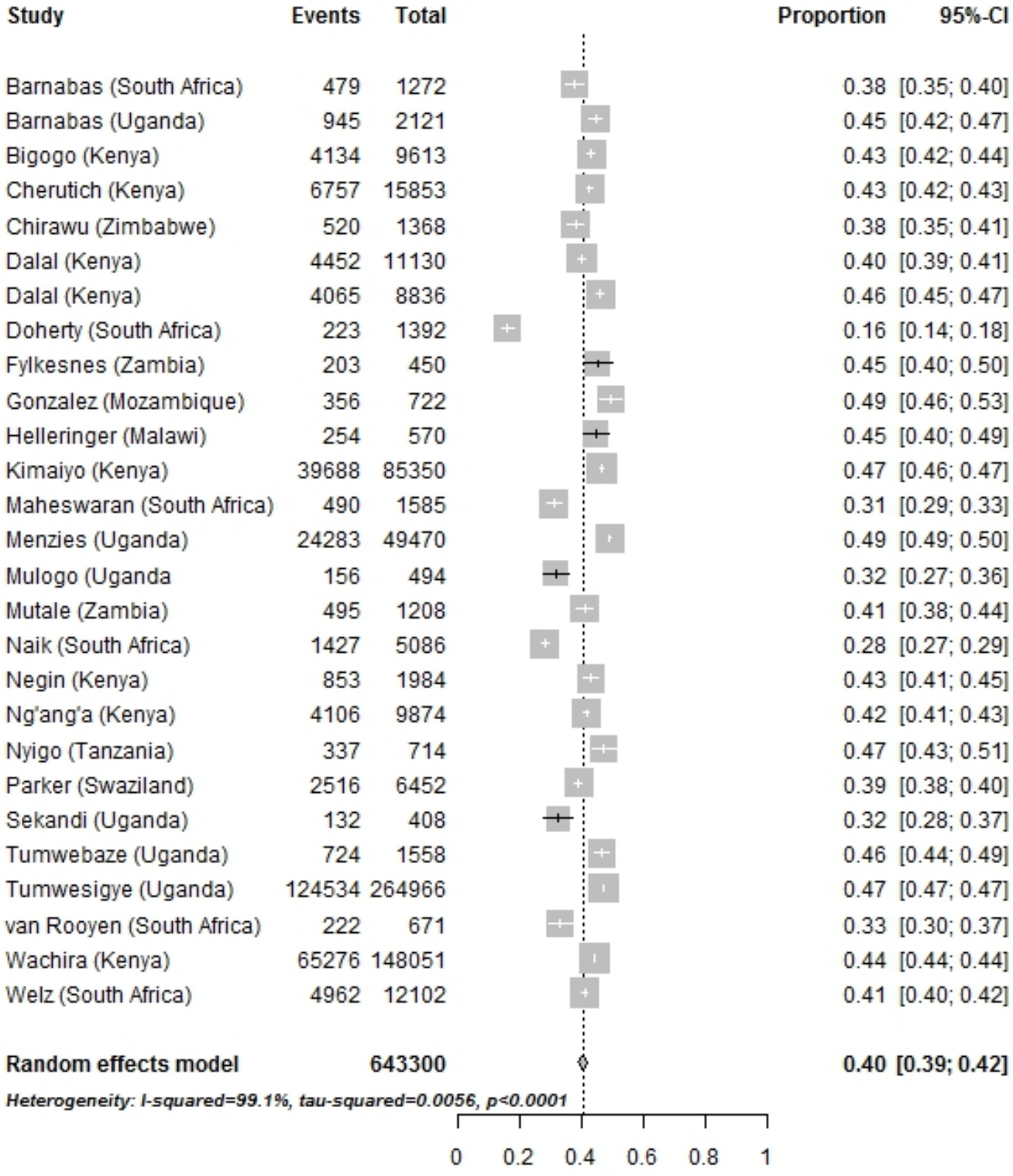


Figure S16: Home HTC with self-testing: Percentage males tested

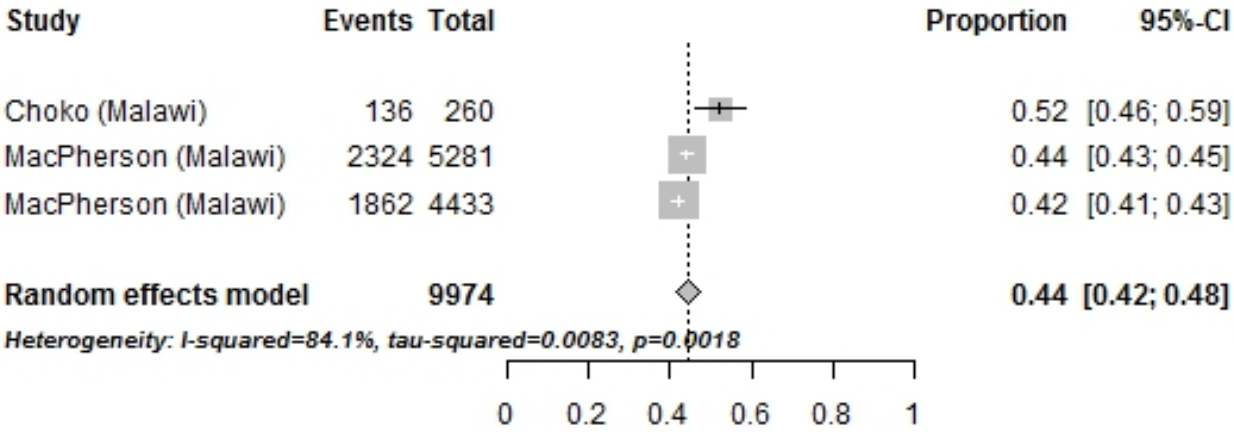


Figure S17: Mobile HTC: Percentage males tested

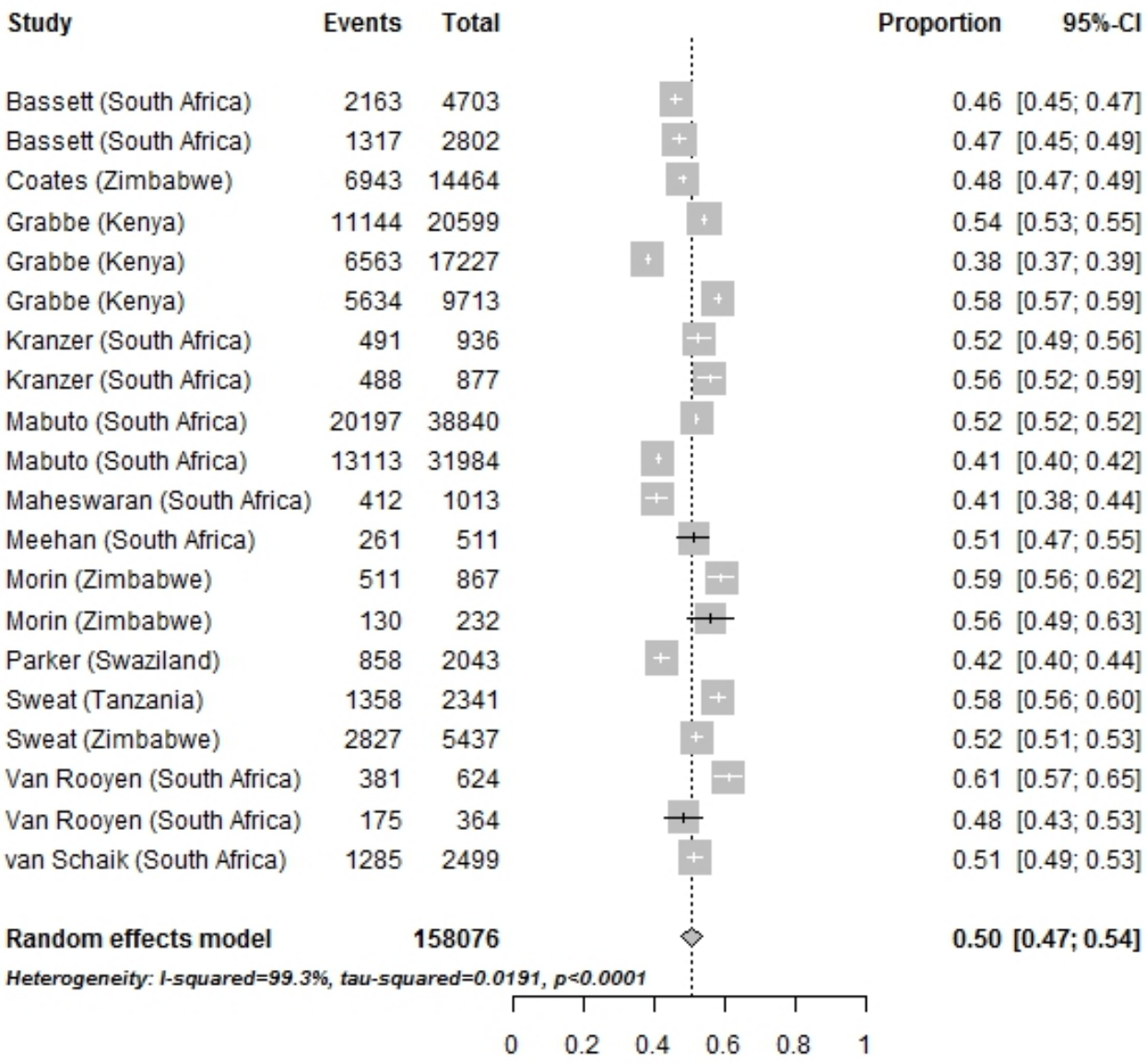


Figure S18: Index HTC: Percentage men tested

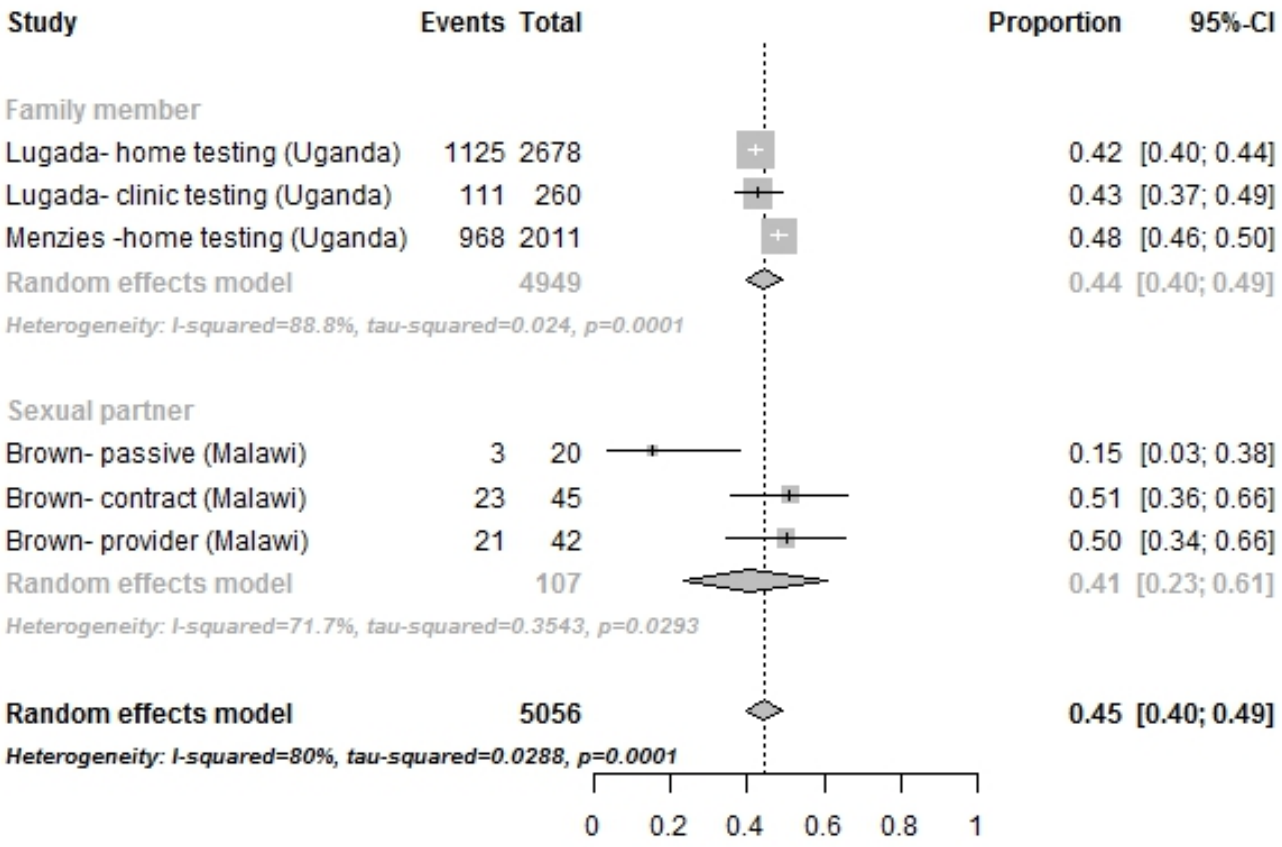


Figure S19: Campaign HTC: percentage men tested

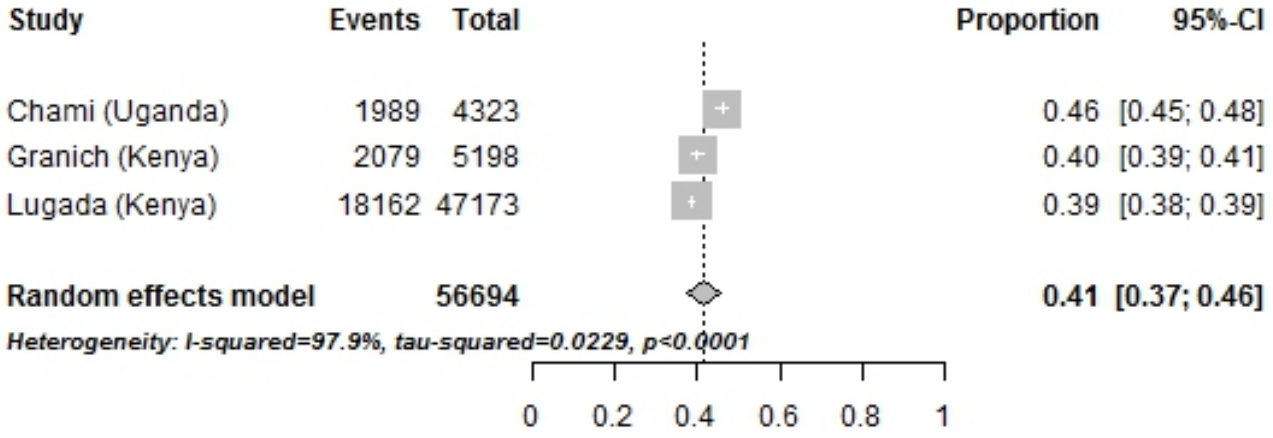


Figure S20: Workplace HTC with self-testing (healthcare workers): Percentage men tested

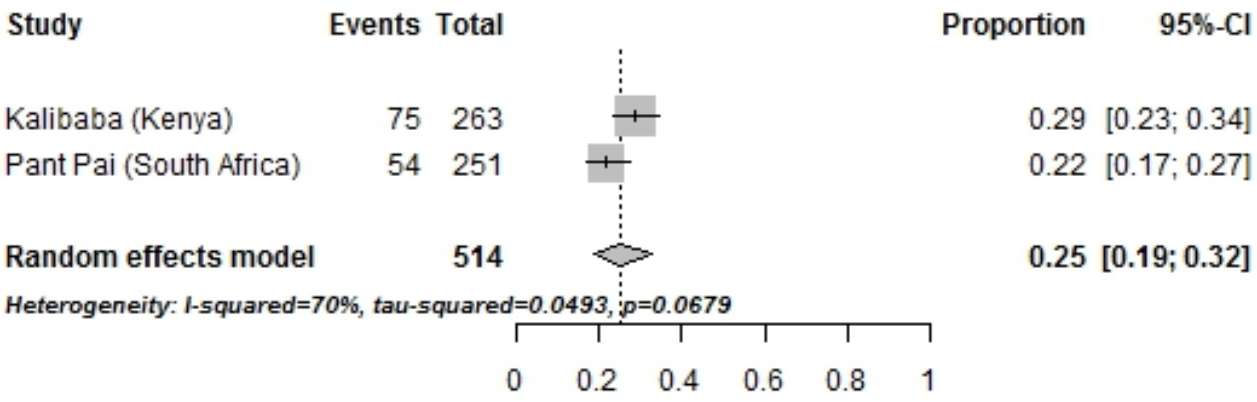


Figure S21: Facility: Percentage of males tested

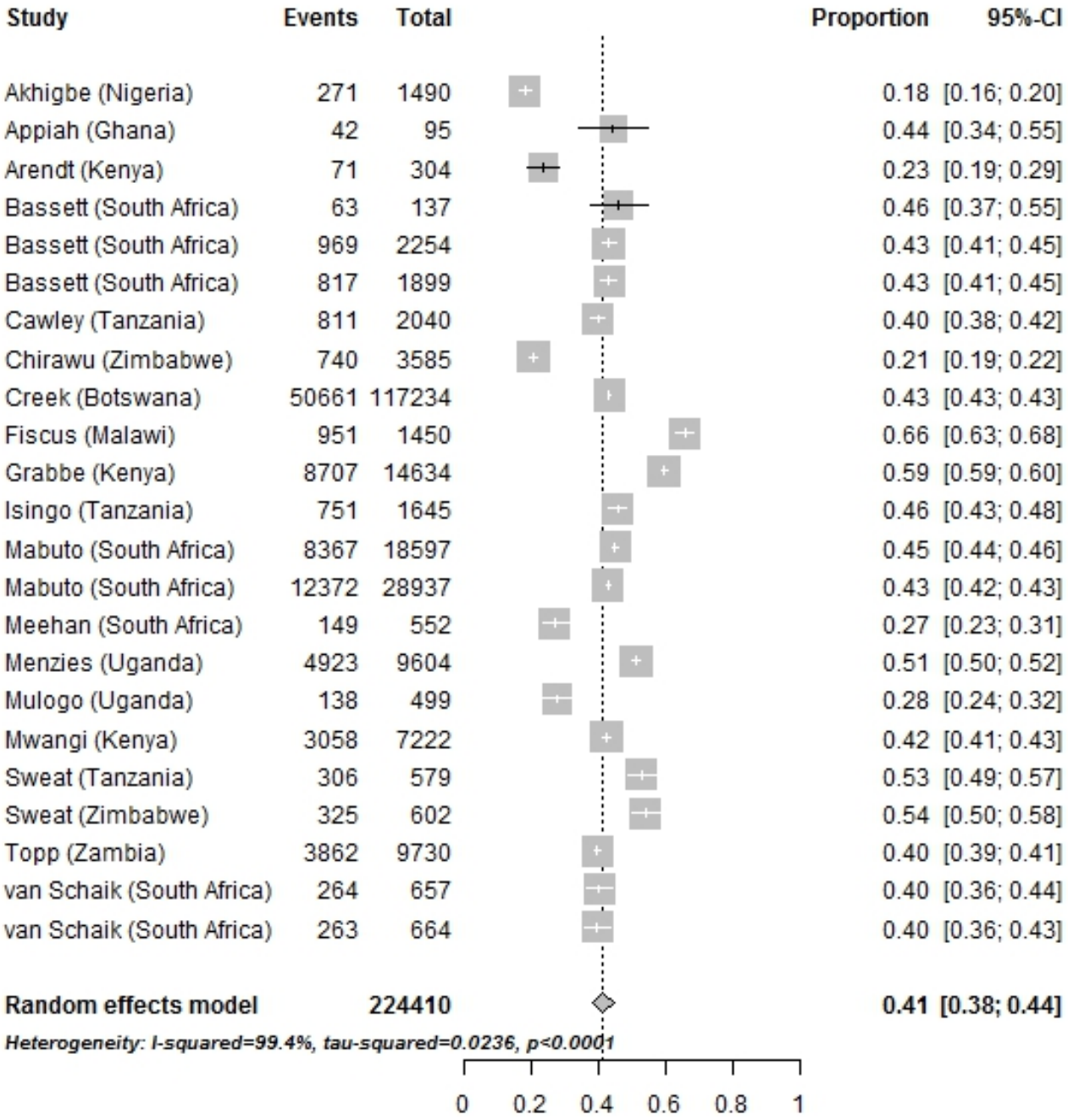
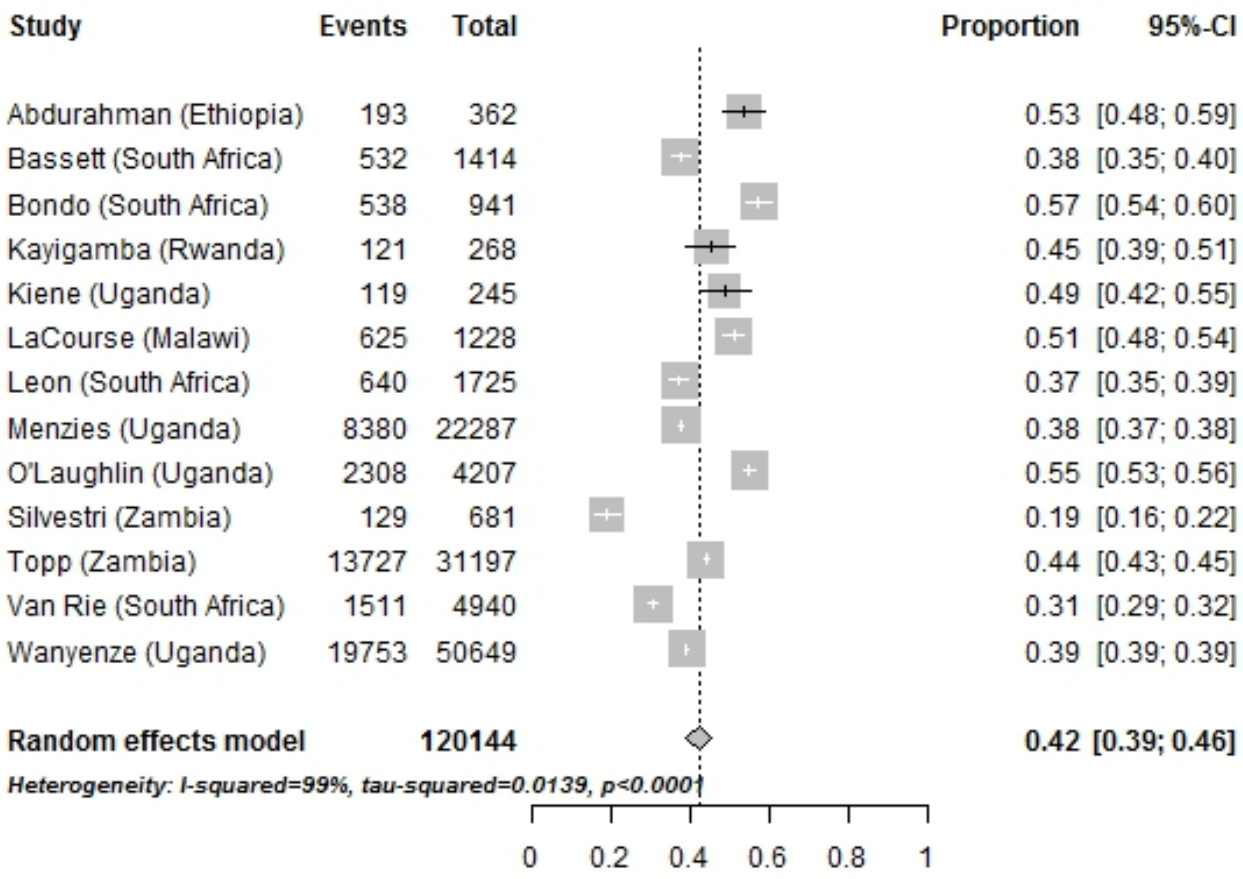


Figure S22: Provider initiated HTC: Percentage men tested



First time testers: Figure S23: Home HTC: First time testers

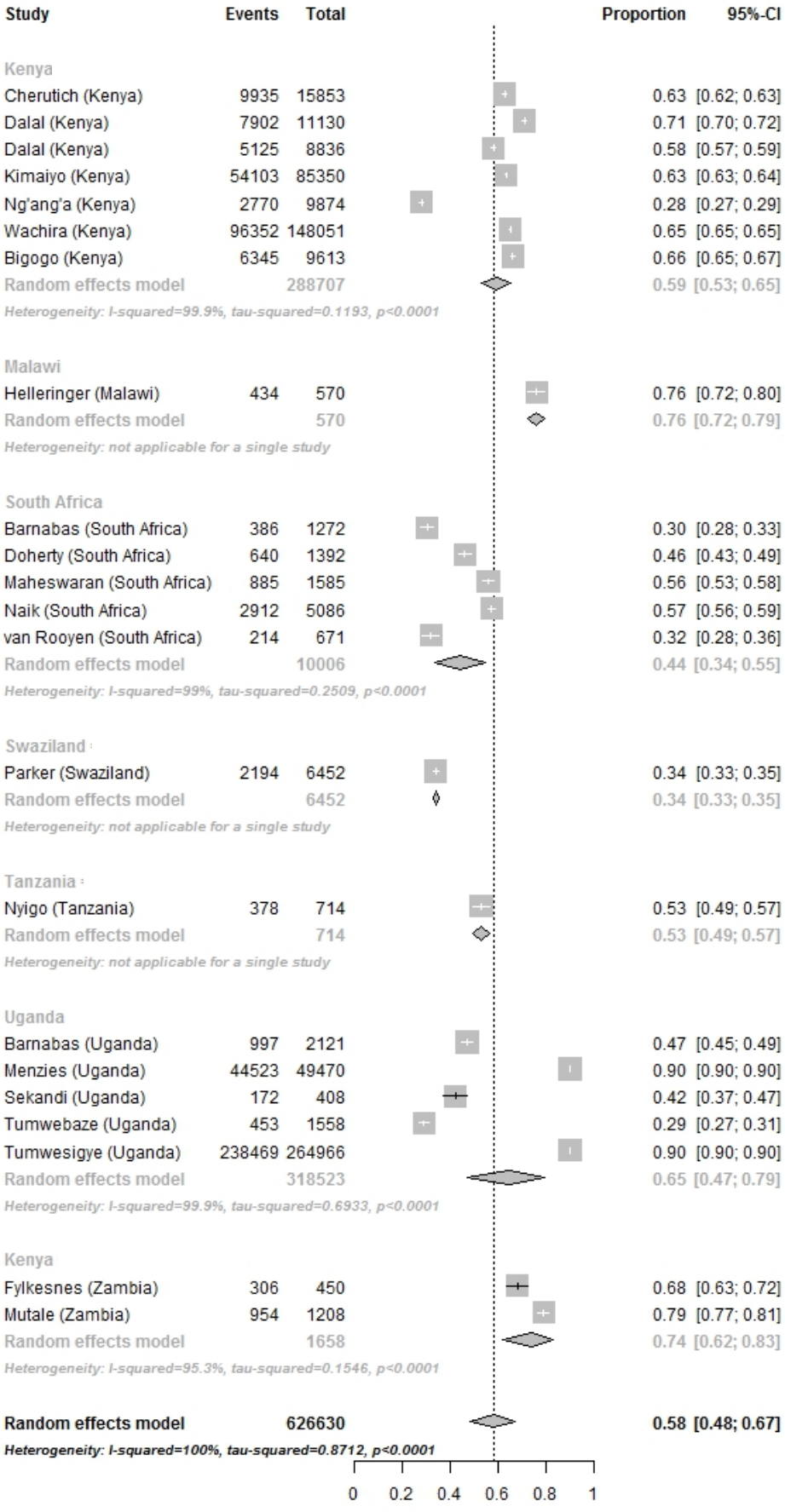


Figure S24: Mobile: First time testers

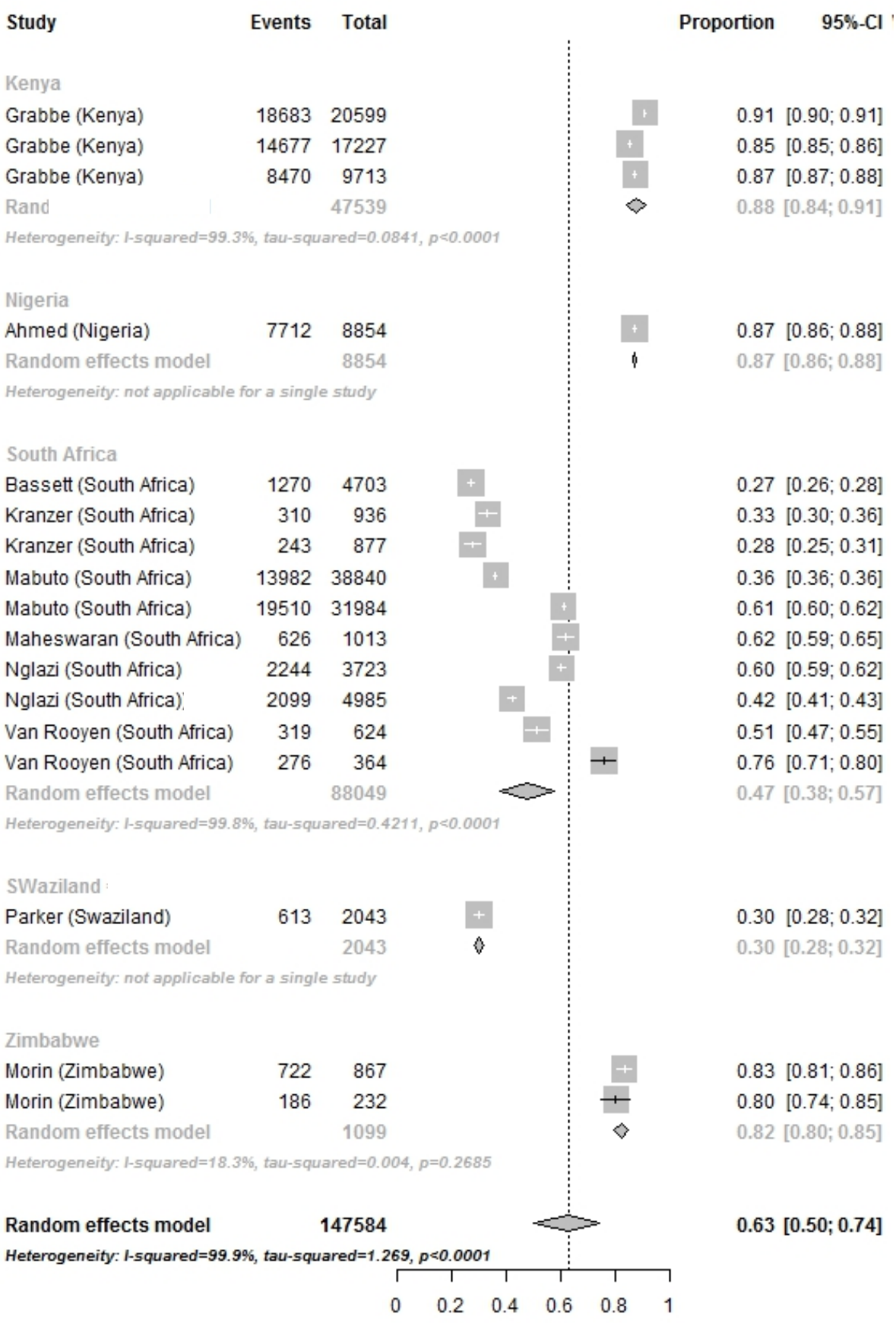


Figure S25: Campaign: First time testers

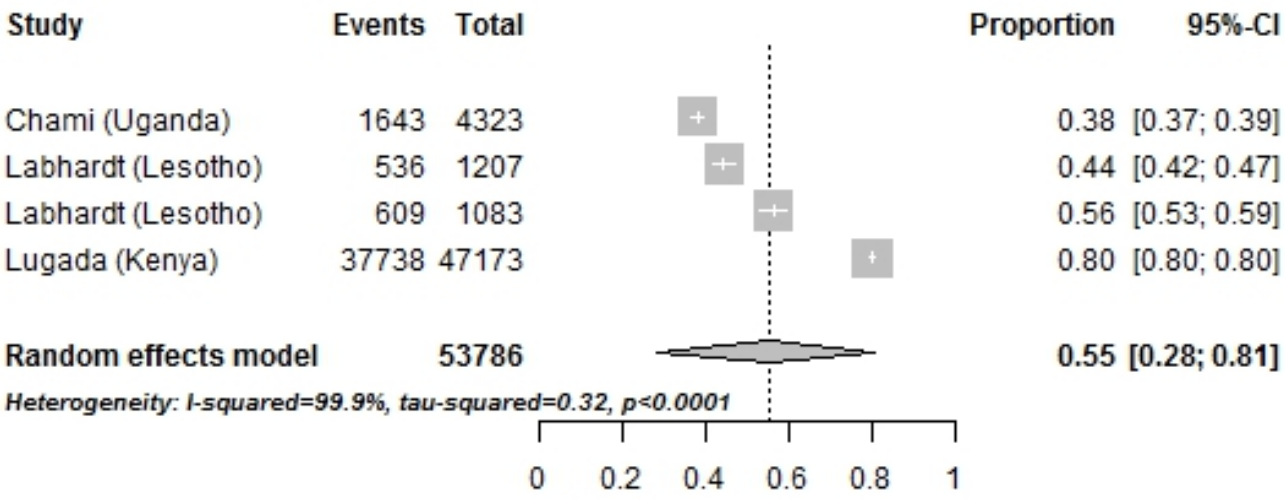


Figure S26: Key populations: First time testers

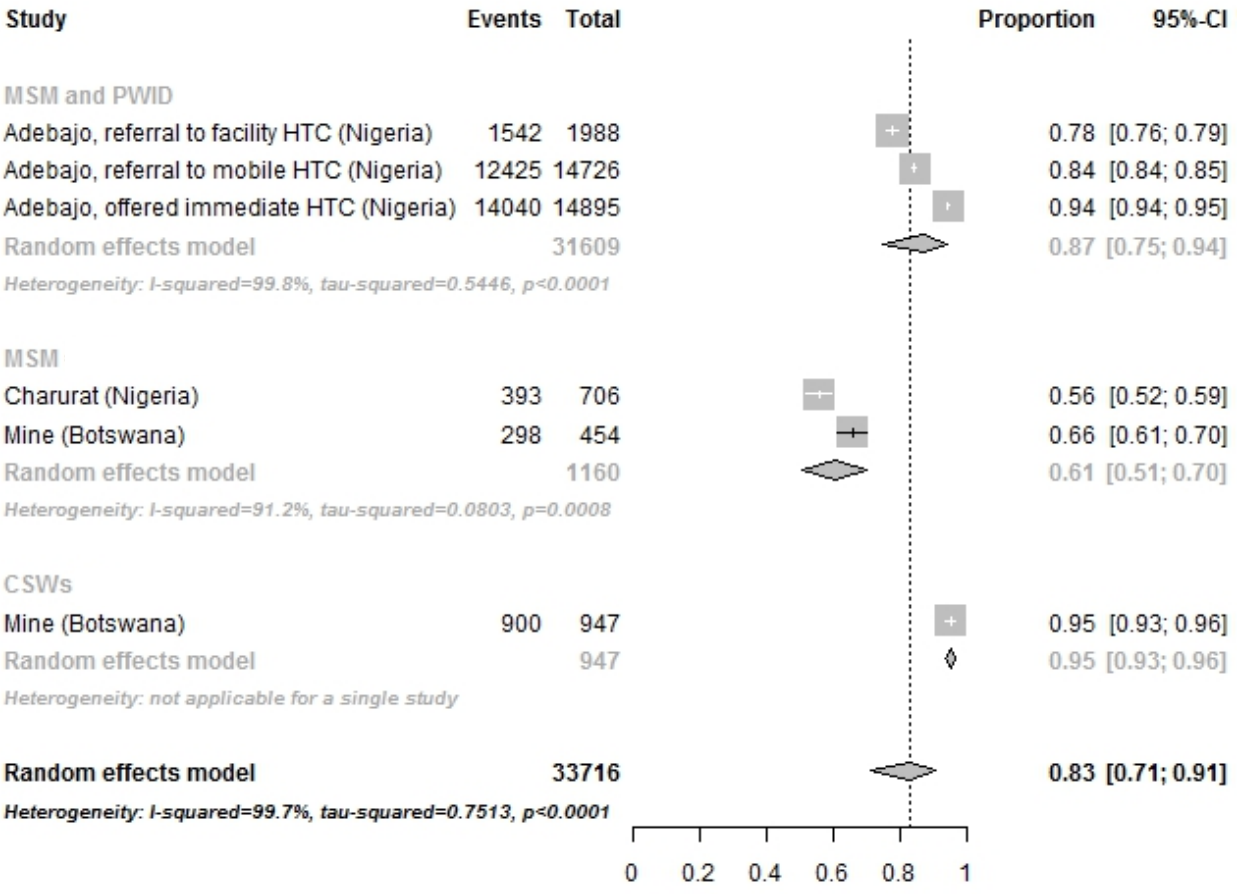


Figure S27: Facility VCT: First time testers

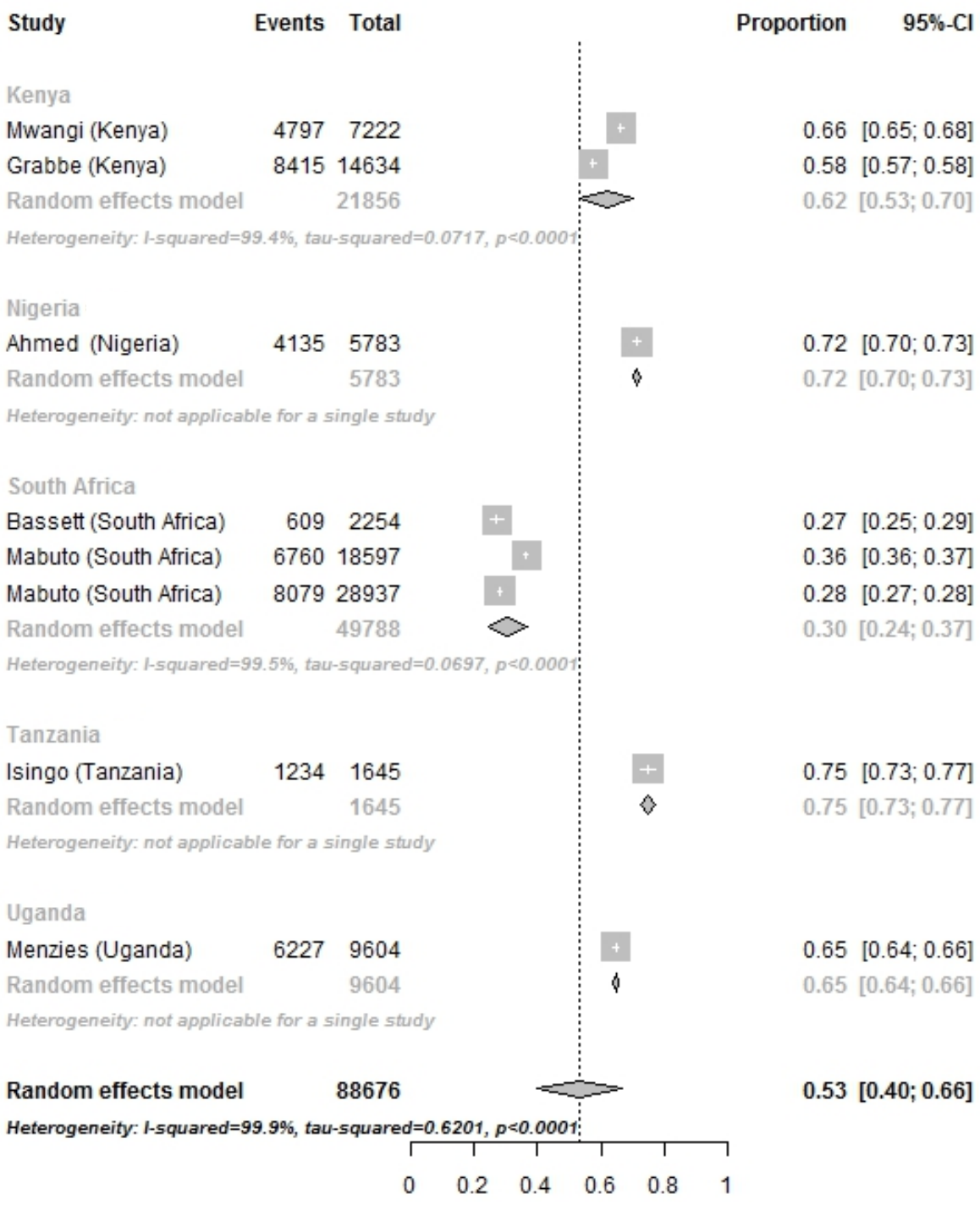
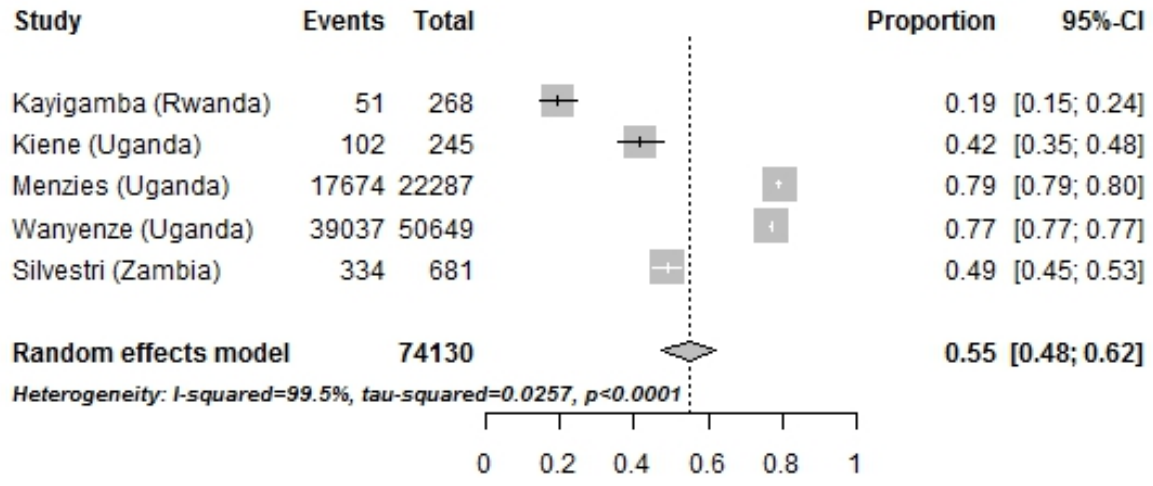


Figure S28: Facility PITC: First time testers



Young adults (age <25 or <30 years)

Figure S29: Home HTC: Percentage young adults

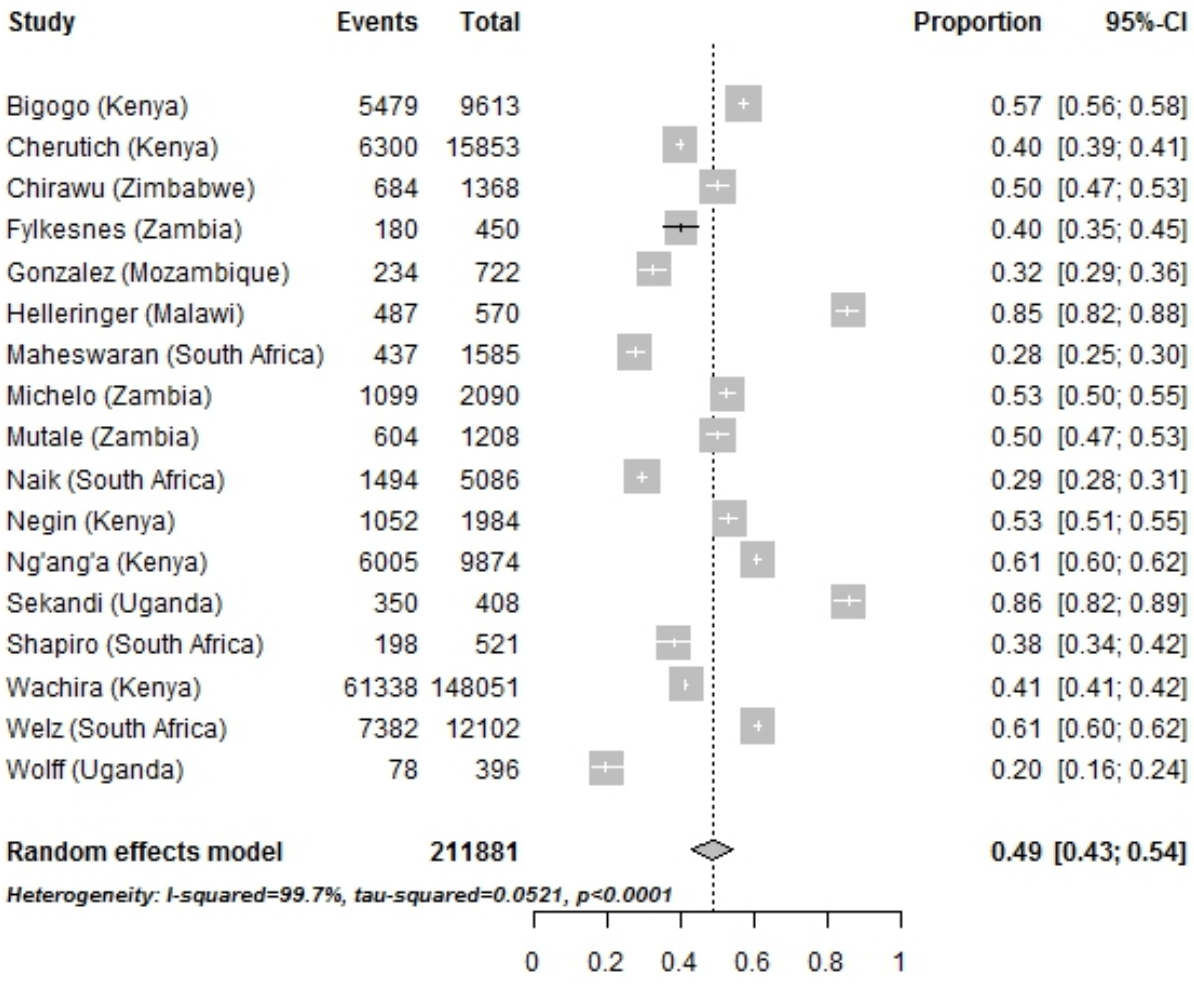


Figure S30: Home with self-testing: Percentage young adult

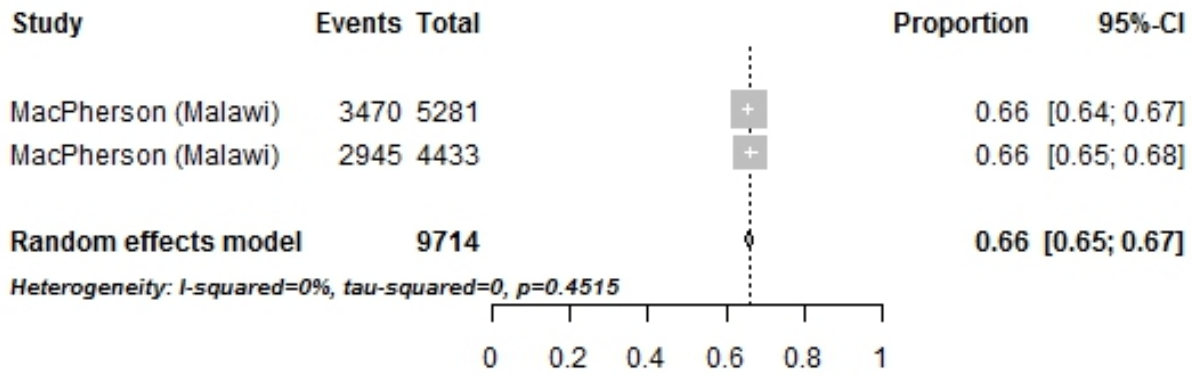


Figure S31: Index HTC: Percentage young adults

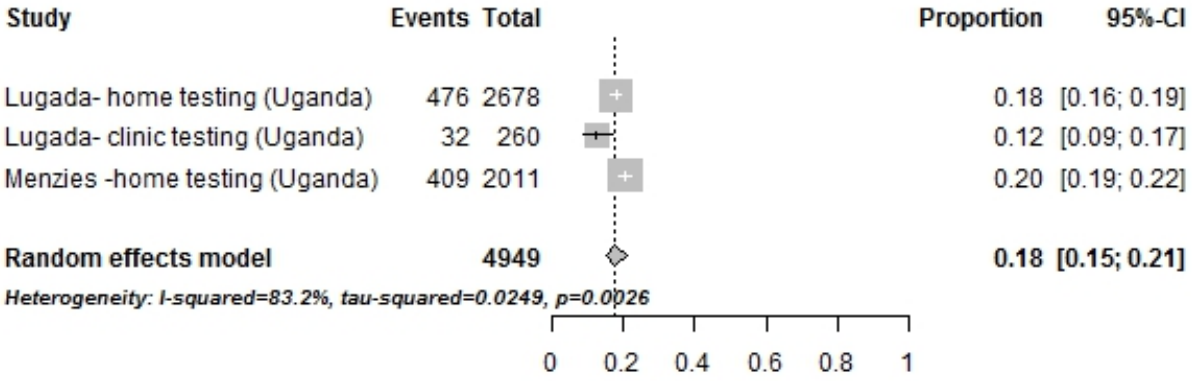


Figure S32: Campaign HTC: Percentage young adults

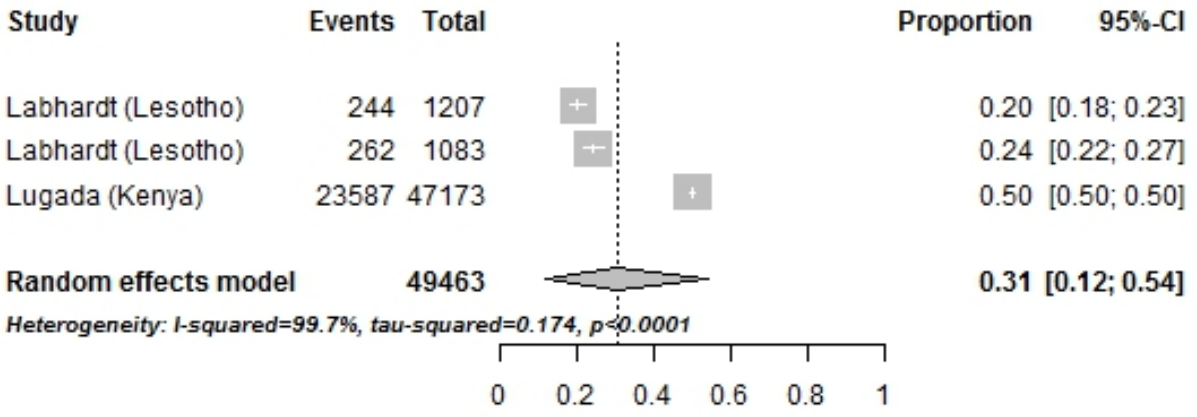


Figure S33: Mobile HTC: Percentage young adult

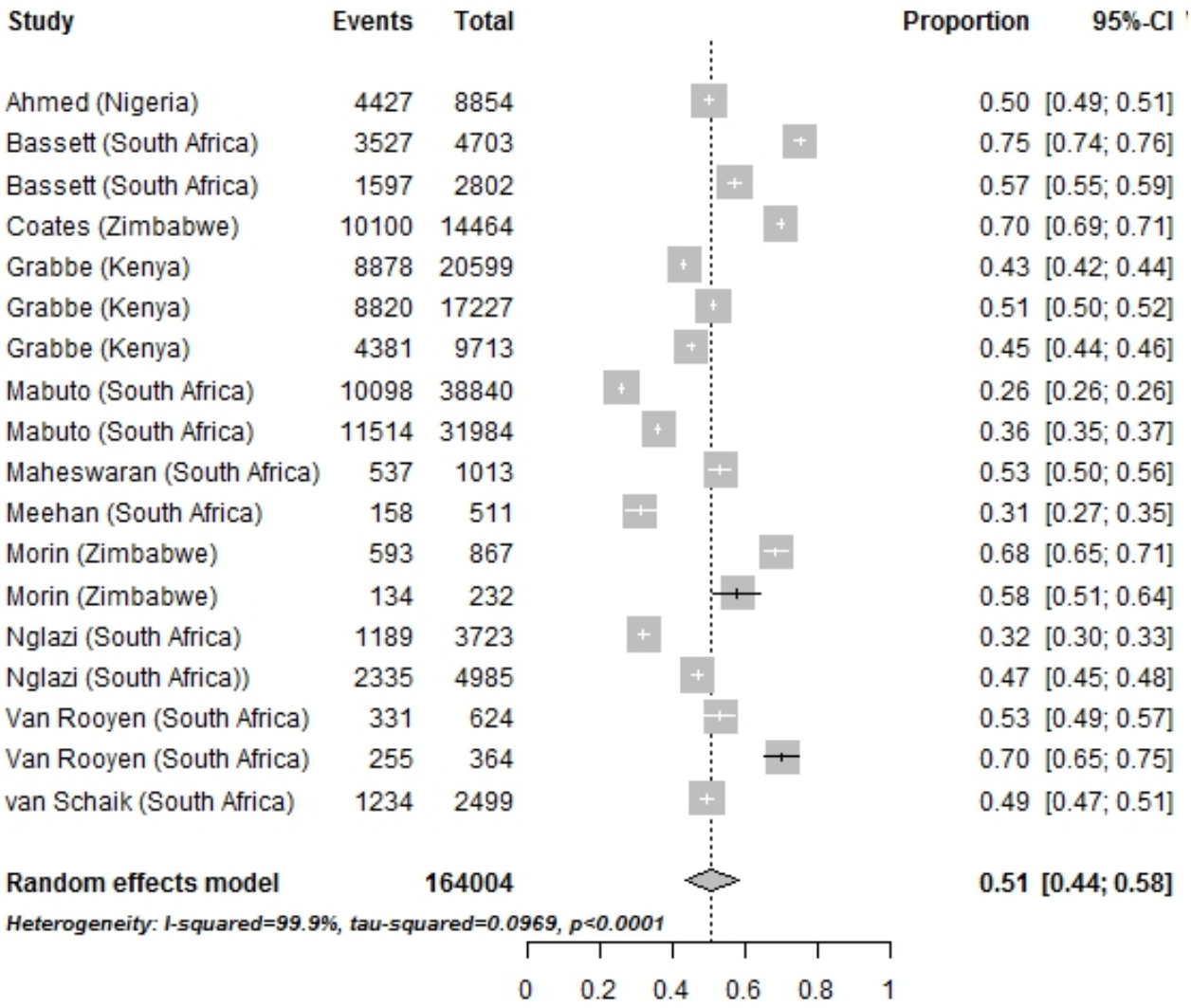


Figure S34: Facility VCT: Percentage young adults

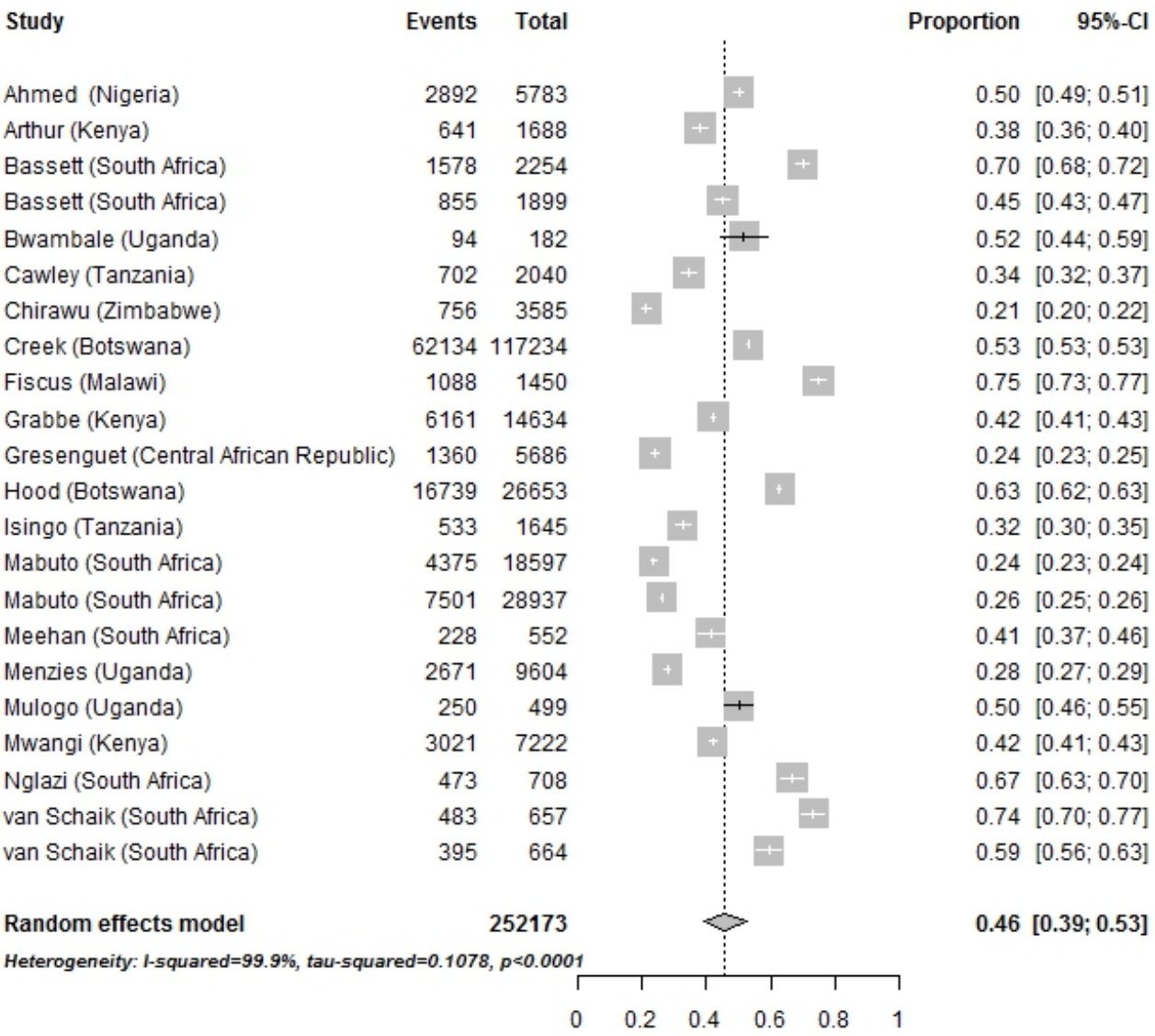
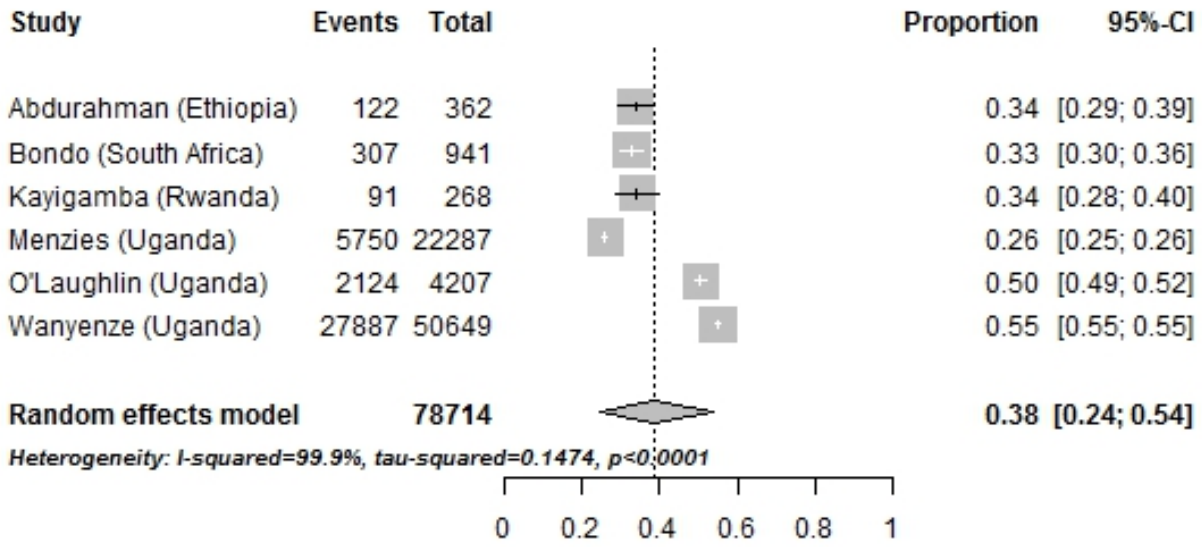


Figure S35: Facility PITC: young adults



HIV positivity

Figure S36: Home HTC: HIV positivity compared to overall HIV prevalence by country

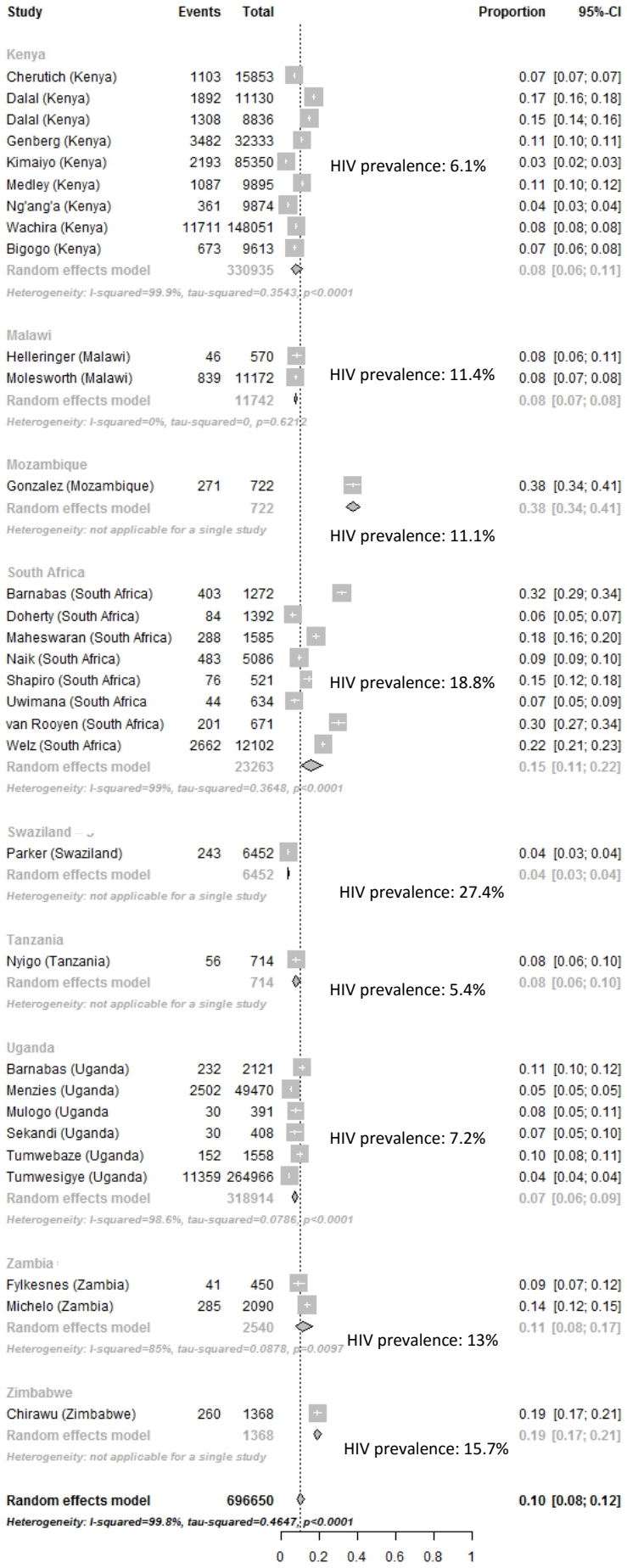


Figure S37: Home HTC with self-testing: HIV positivity compared to country-level HIV prevalence

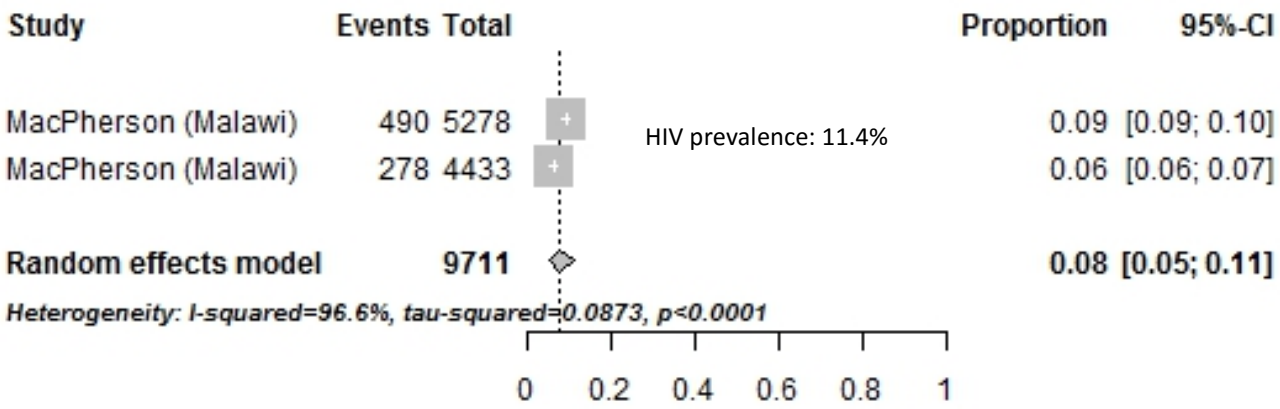


Figure S38: Mobile HTC: HIV positivity compared to overall HIV prevalence by country

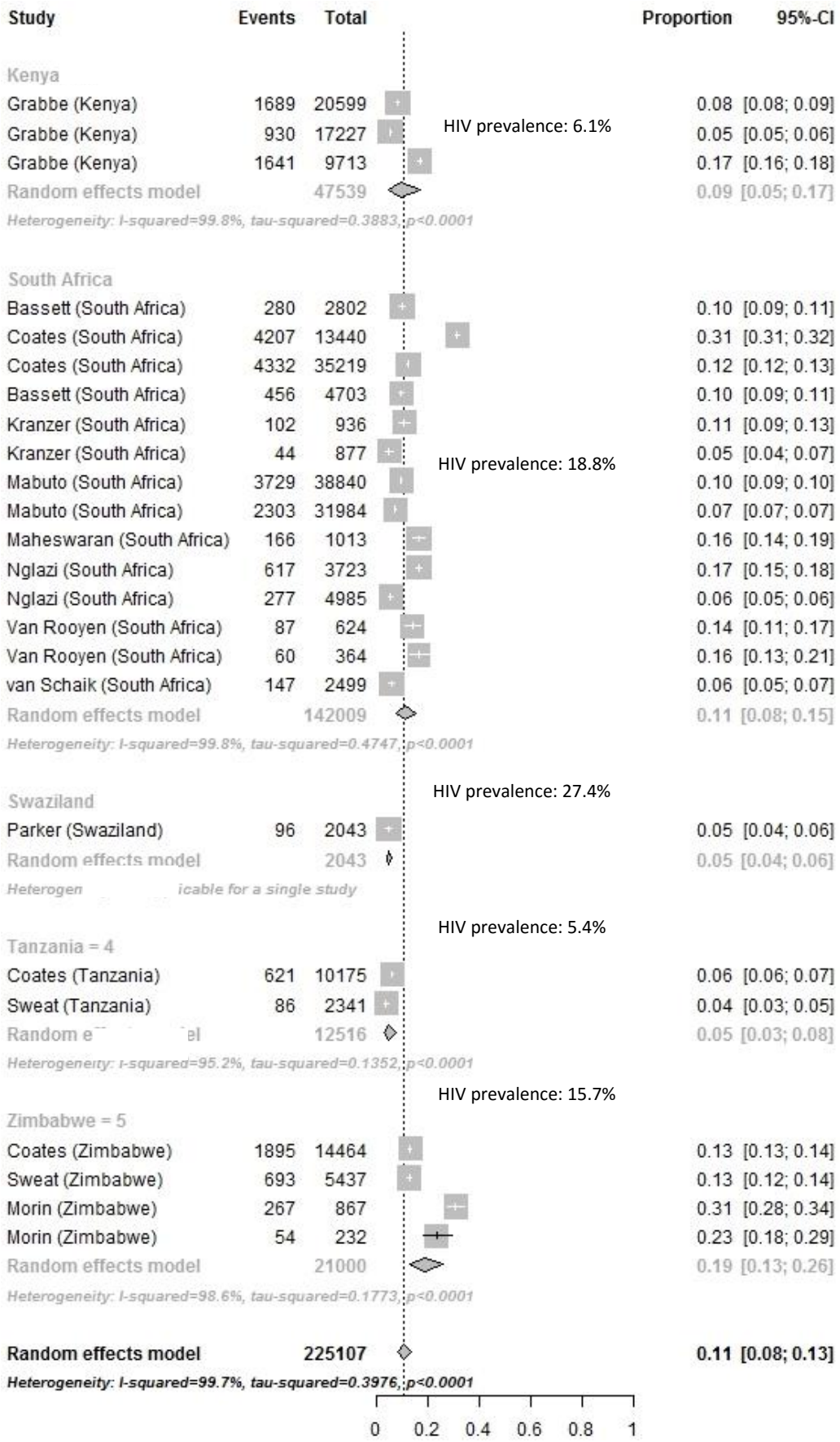


Figure S39: Campaign: HIV positivity compared to overall HIV prevalence by country

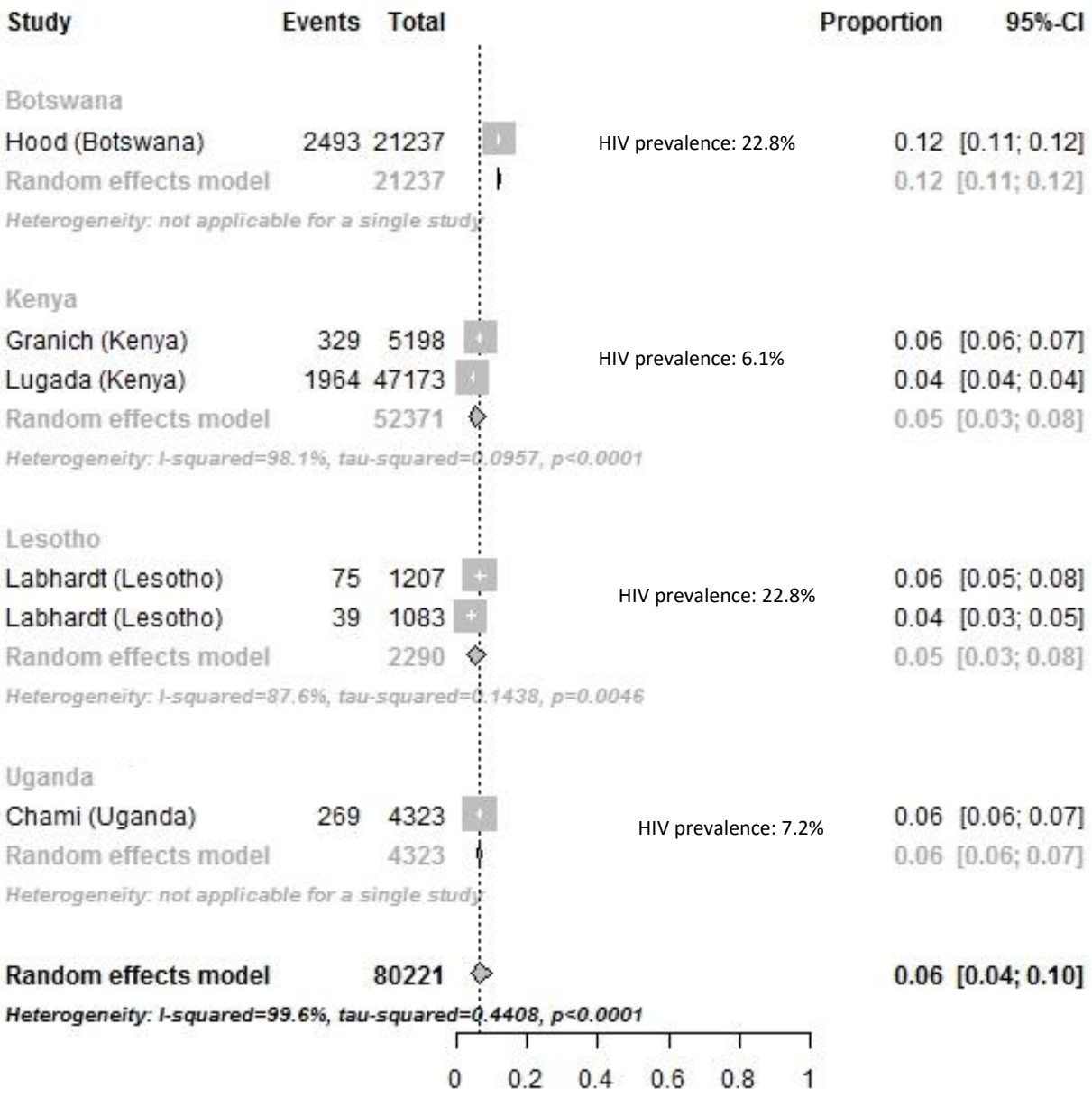


Figure S40: Workplace: HIV positivity

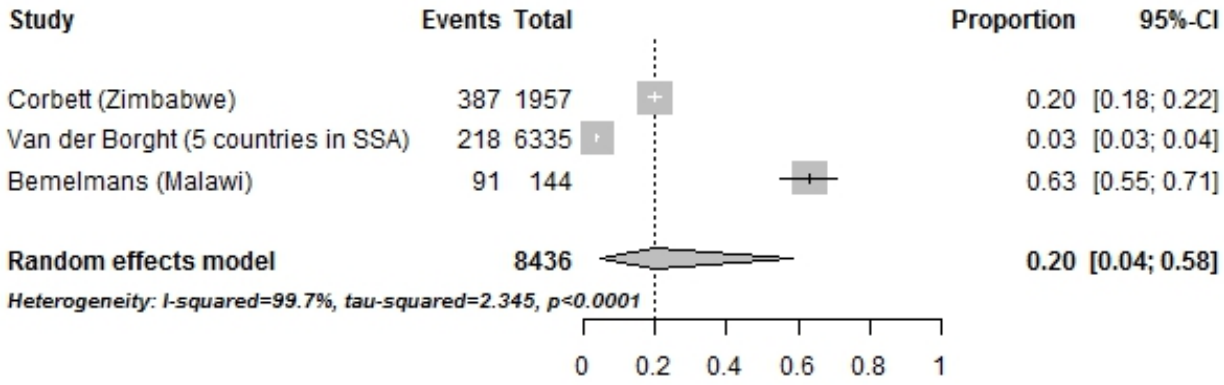


Figure S41: Key populations: HIV positivity

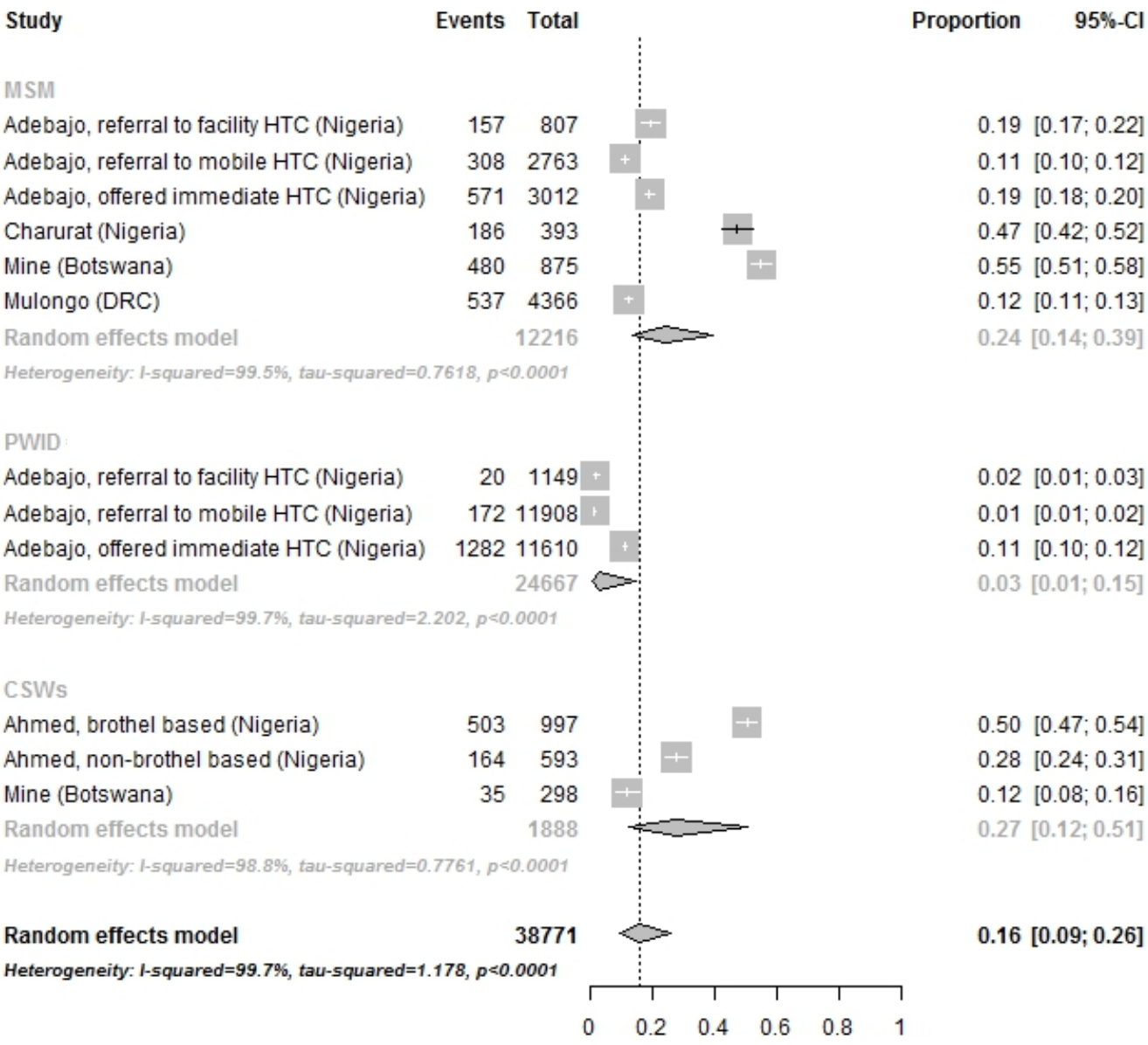


Figure S42: Index: HIV positivity

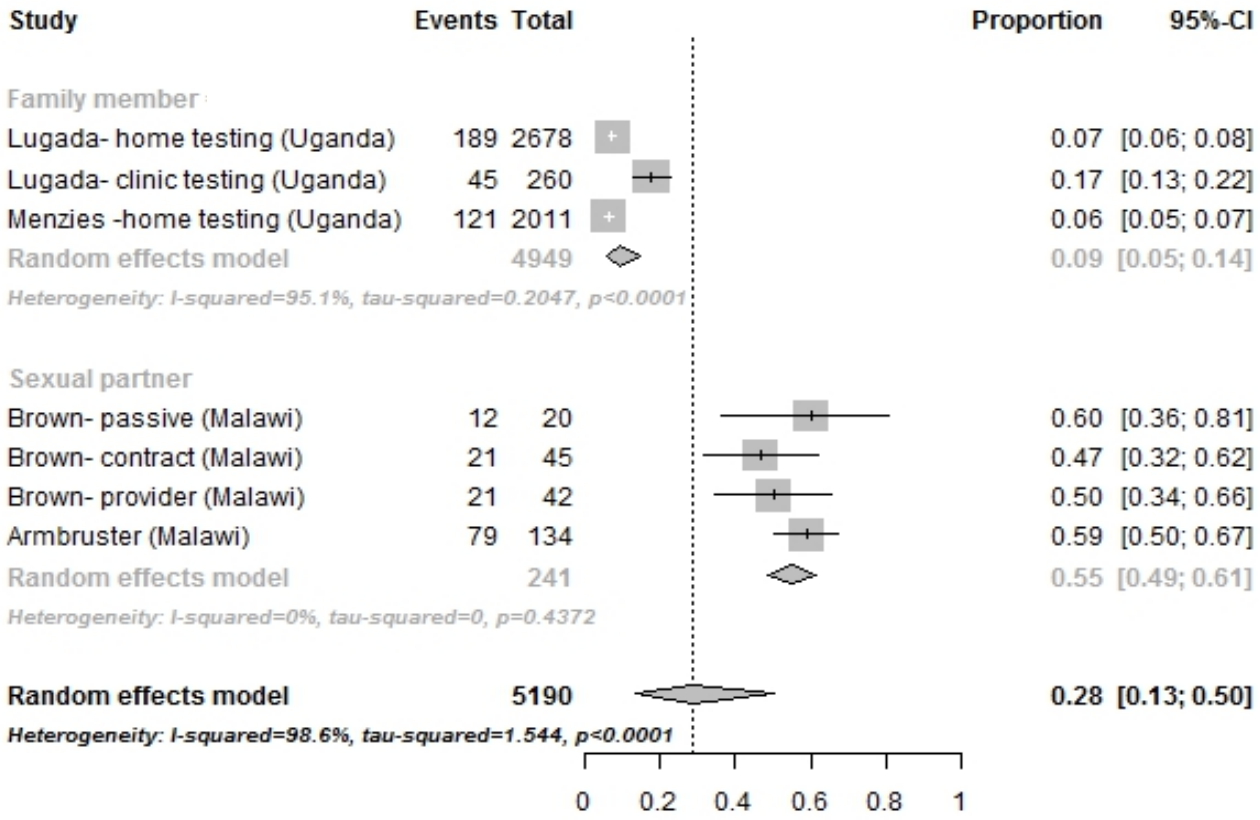


Figure S43: Facility VCT: HIV positivity compared to overall HIV prevalence by country

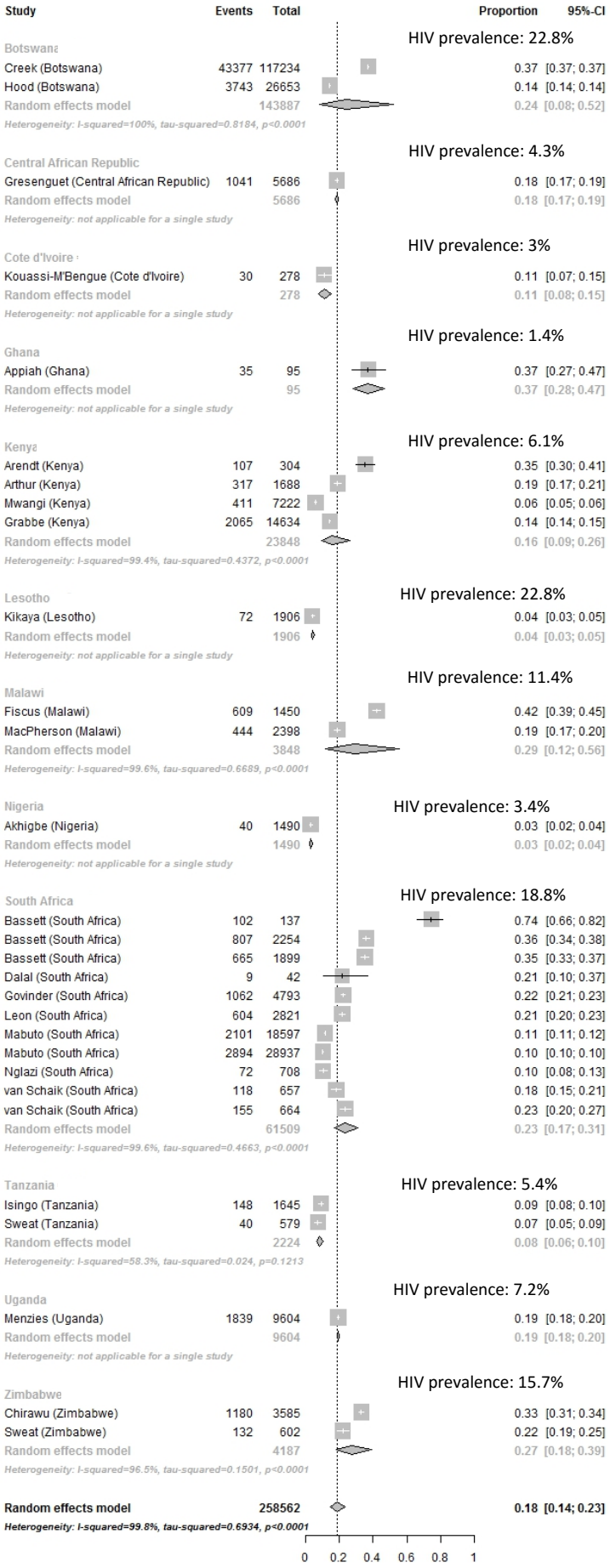


Figure S44: Facility PITC: HIV positivity compared to overall HIV prevalence by country

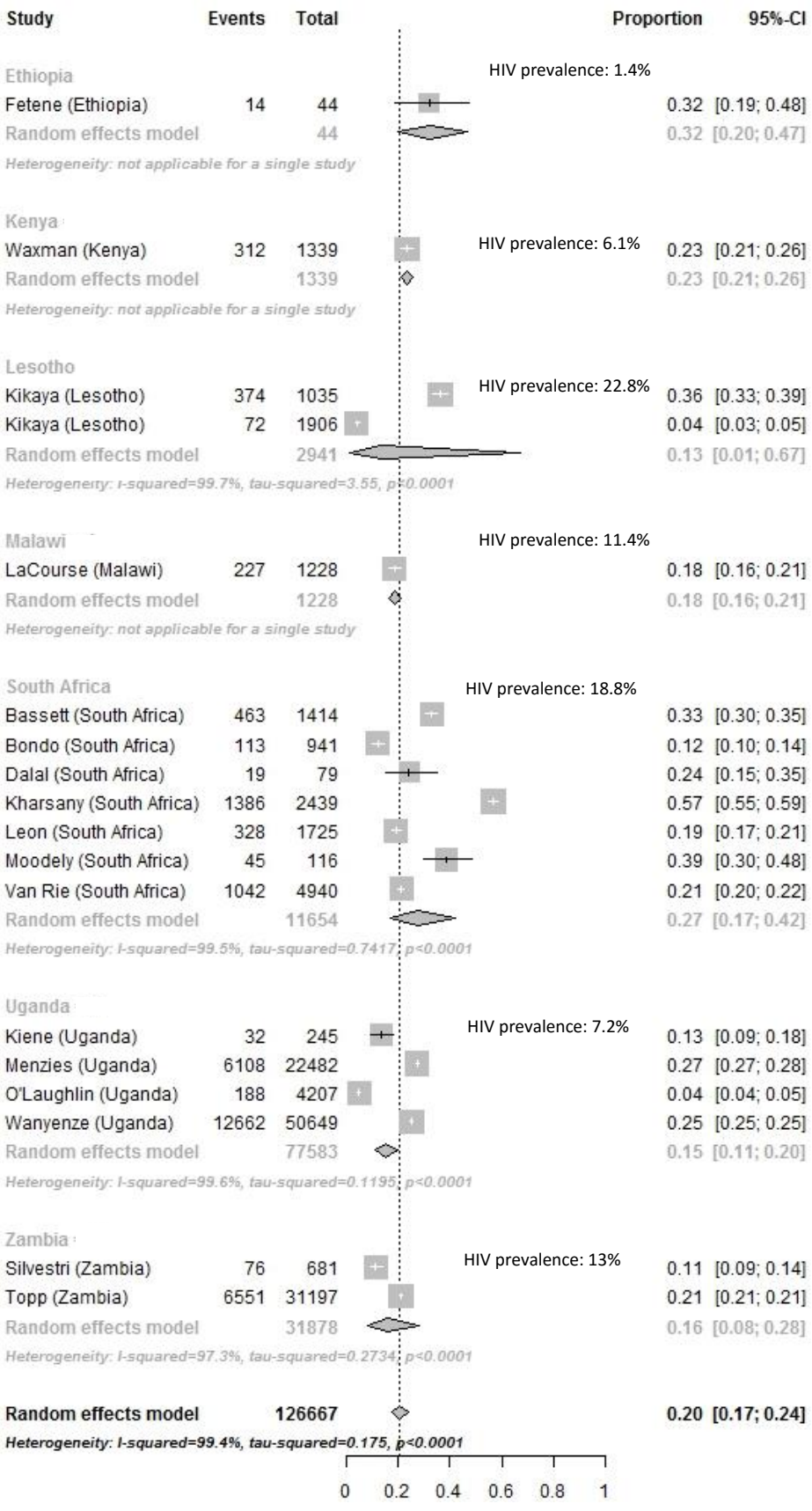


Figure S45: Home: CD4≤350 cells/μL

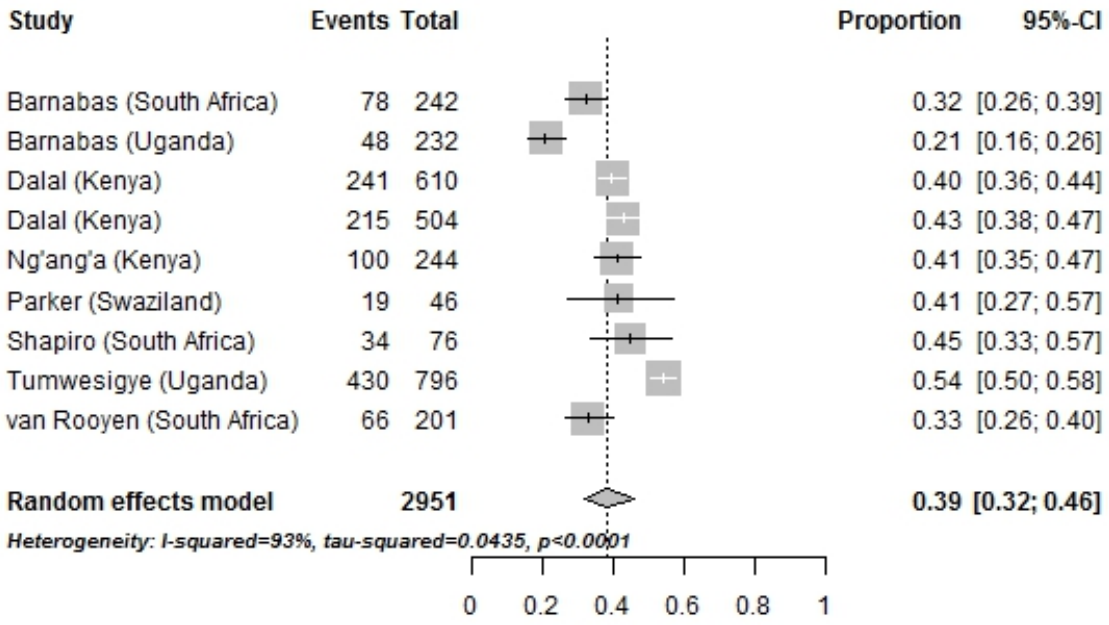


Figure S46: Mobile: CD4≤350 cells/μL

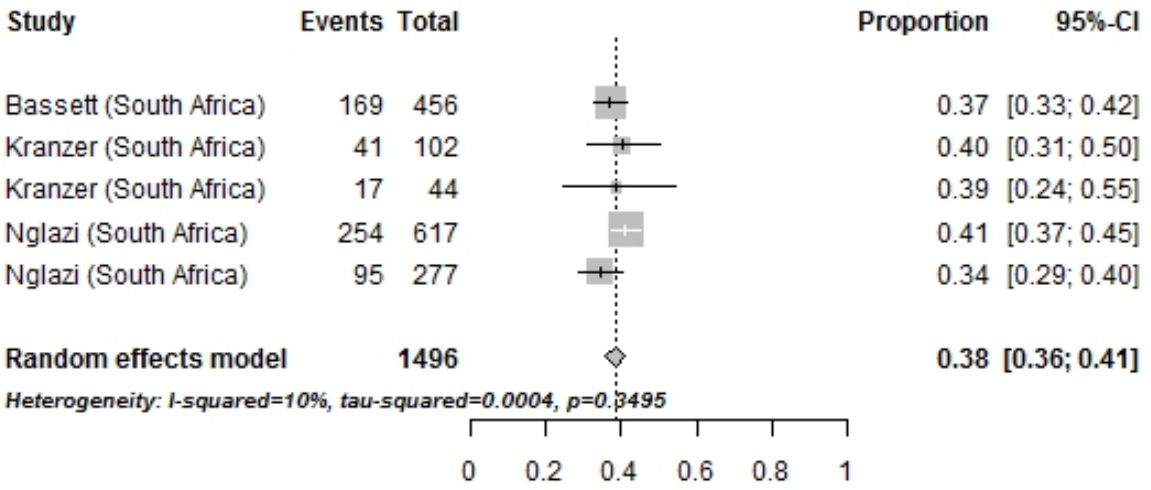


Figure S47: Campaign: CD4≤350 cells/μL

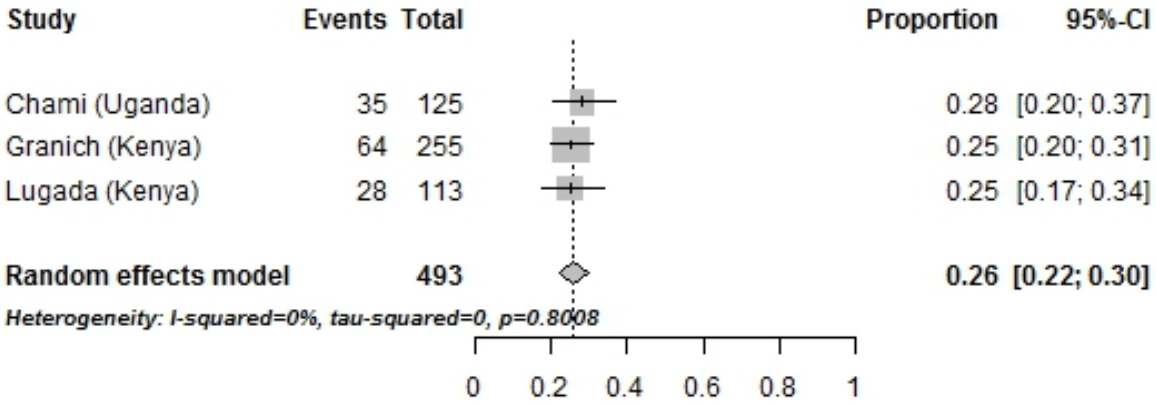


Figure S48: Facility VCT: CD4≤350 cells/μL

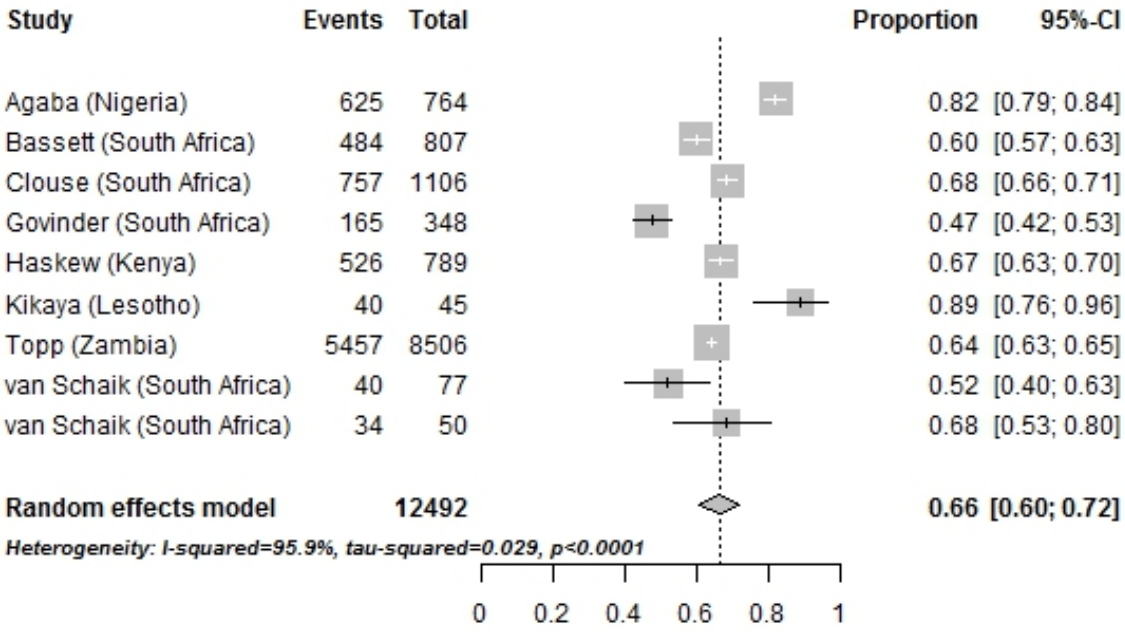
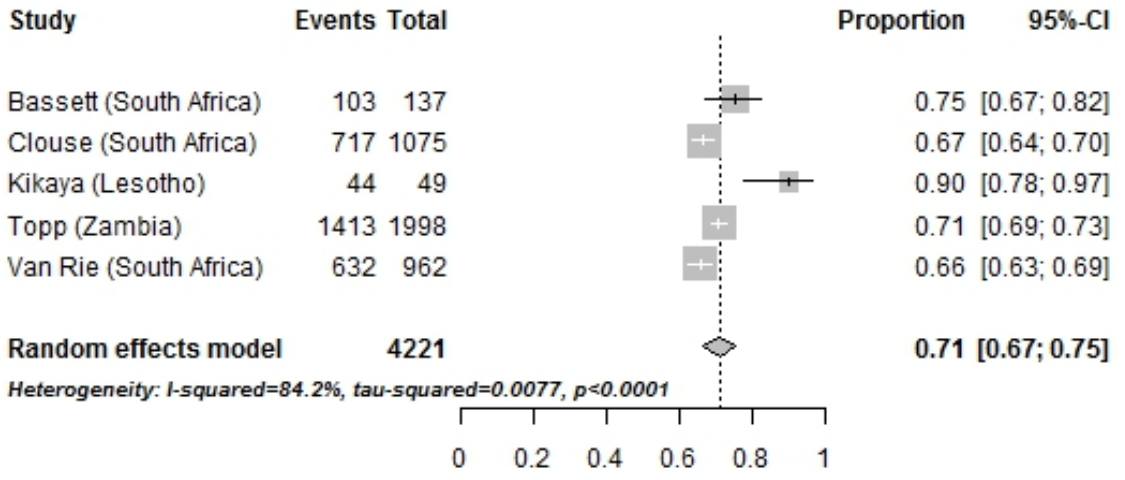
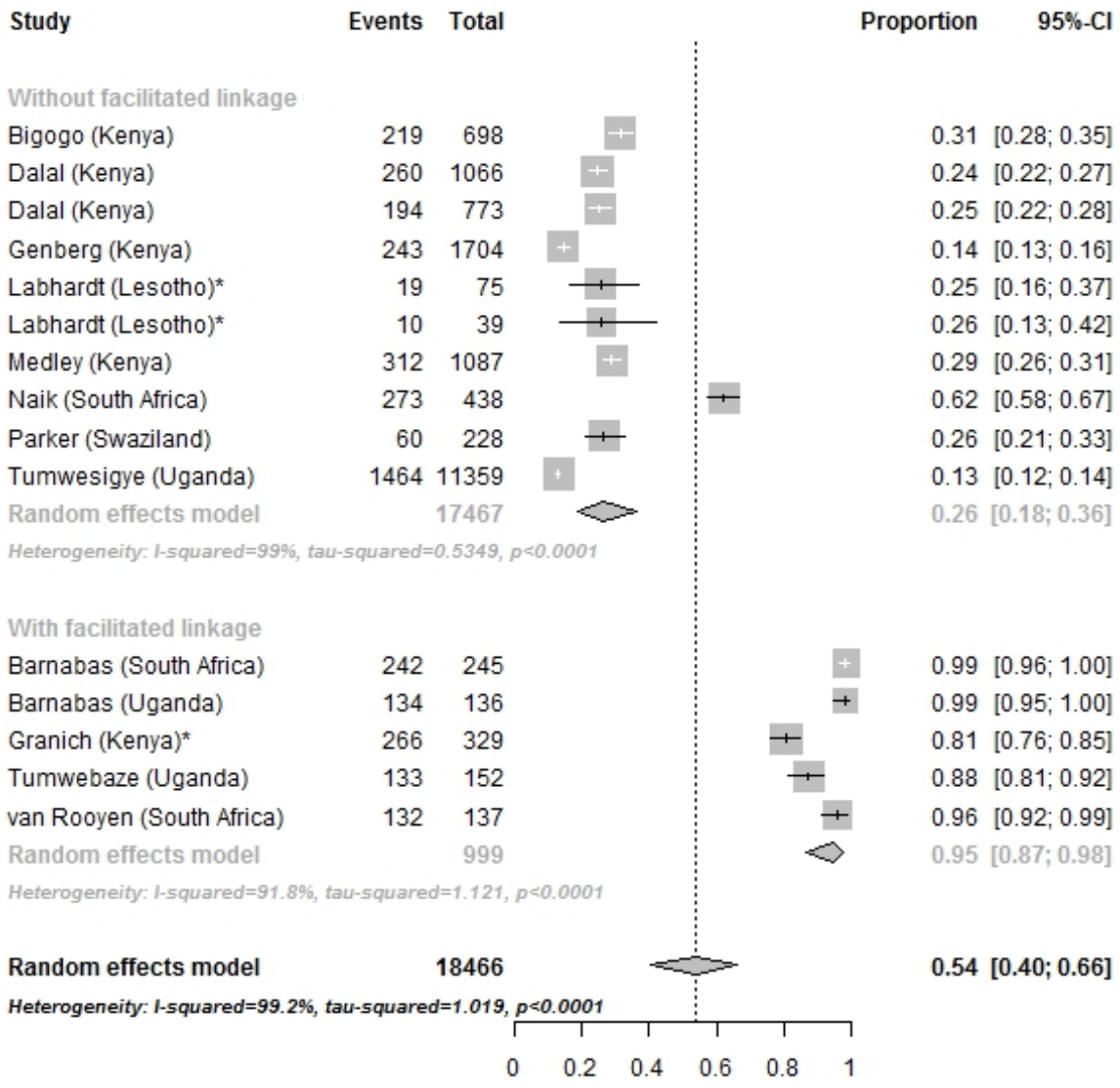


Figure S49: Facility PITC: CD4≤350 cells/μL



Linkage to care

Figure S50: Home and campaign HTC: Linkage to care



Studies with asterisk* denote Campaign HTC, all other studies are home HTC.

Figure S51: Mobile HTC: Linkage to care

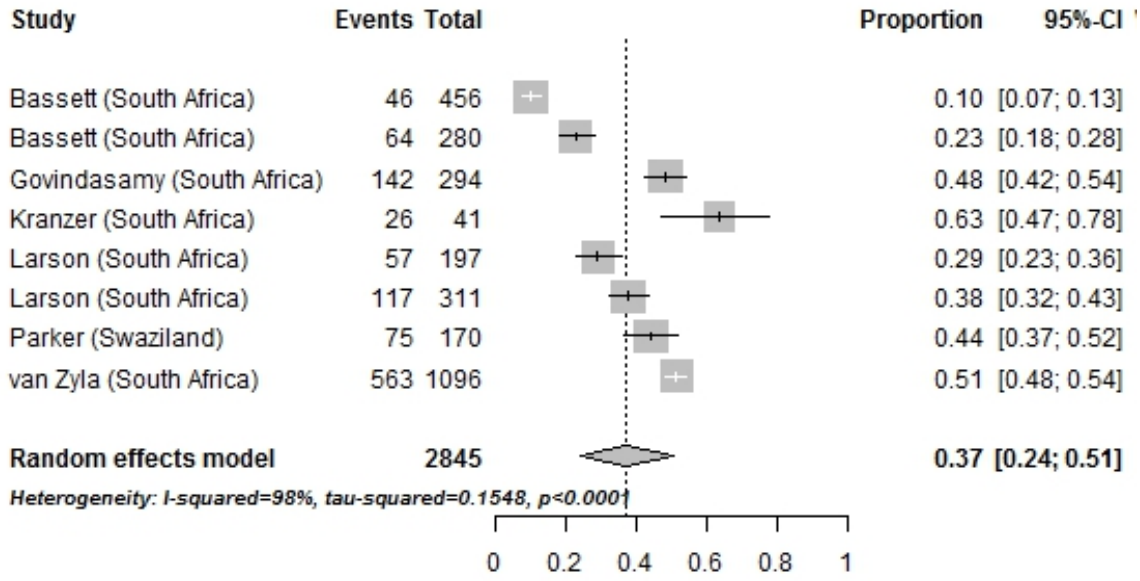
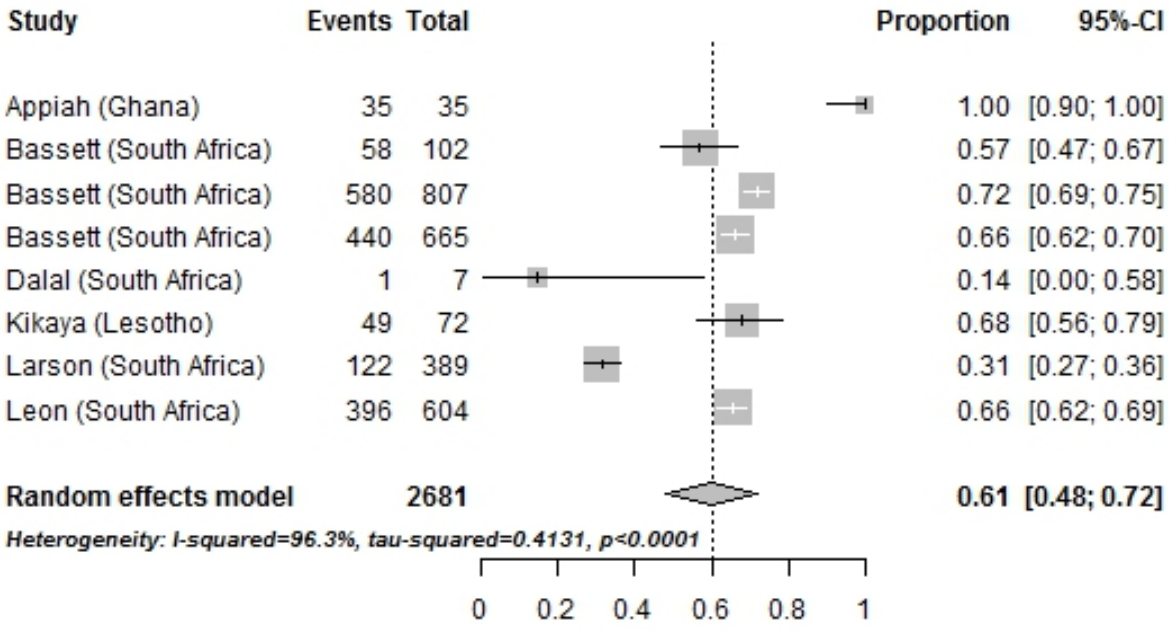
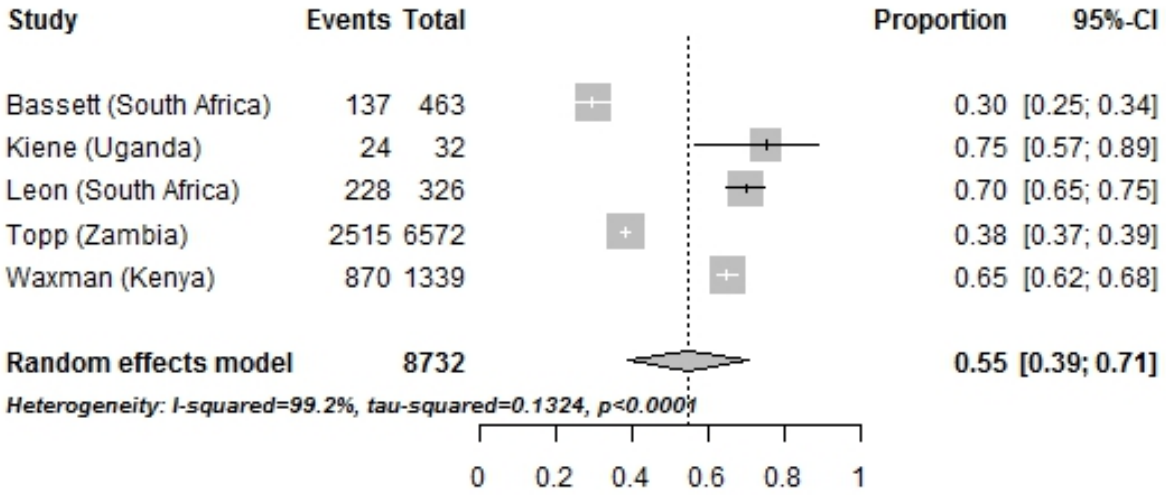


Figure S52: Facility VCT: Linkage to care*



*Defined as returning to the clinic to receive CD4 results, or enrolling in pre-ART care.

Figure S53: Facility PITC: Linkage to care*



*Defined as returning to the clinic to receive CD4 results, or enrolling in pre-ART care.

Initiated ART

Figure S54: Home HTC: ART initiation among those eligible (only included those studies with POC CD4 to determine eligibility for ART

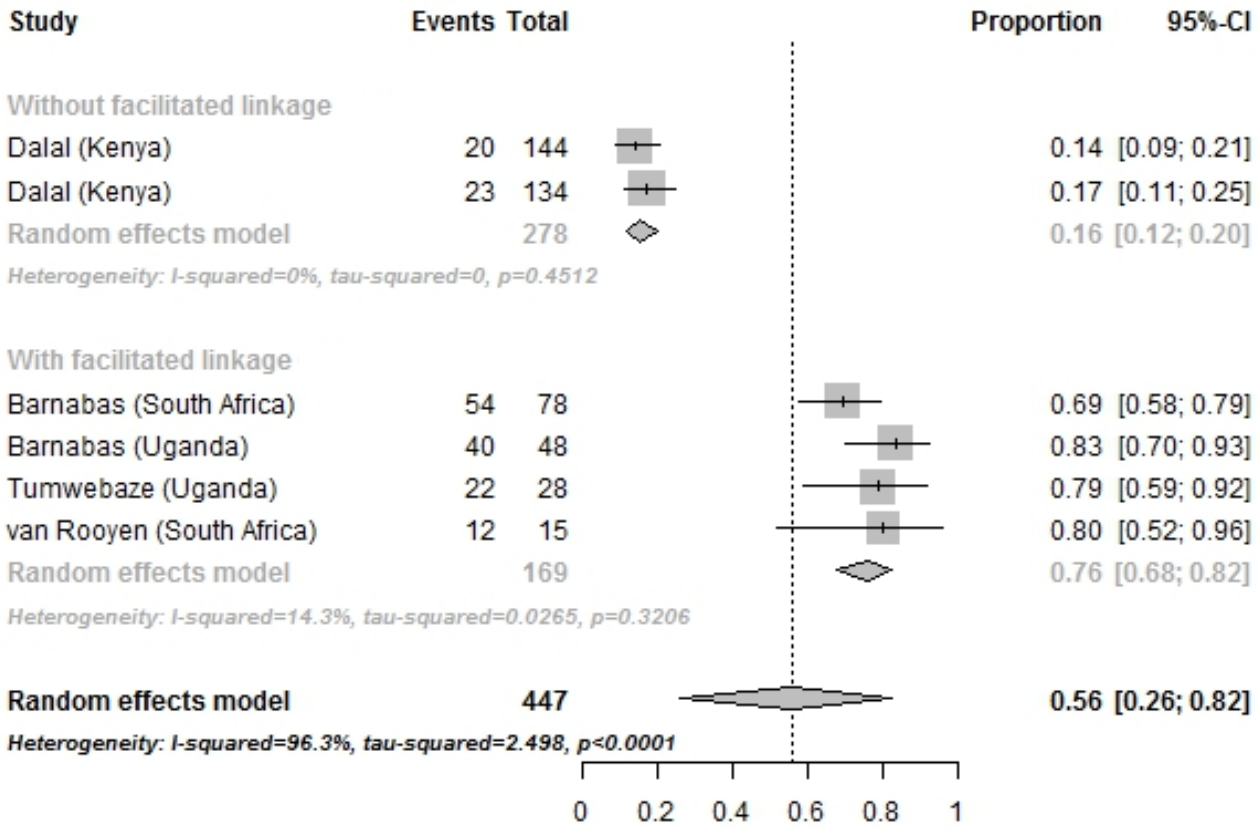


Figure S55: Home HTC with self-testing: ART initiation among all HIV positives

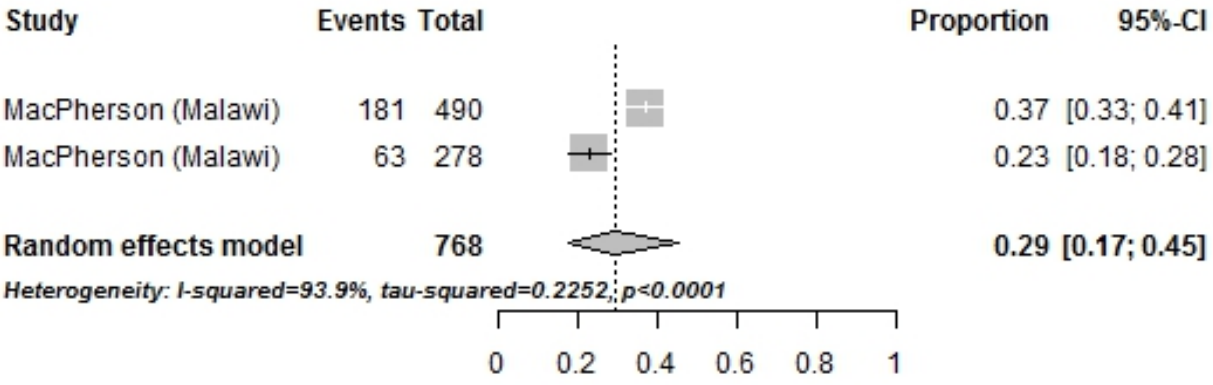


Figure S56: Facility VCT: ART initiation among those eligible

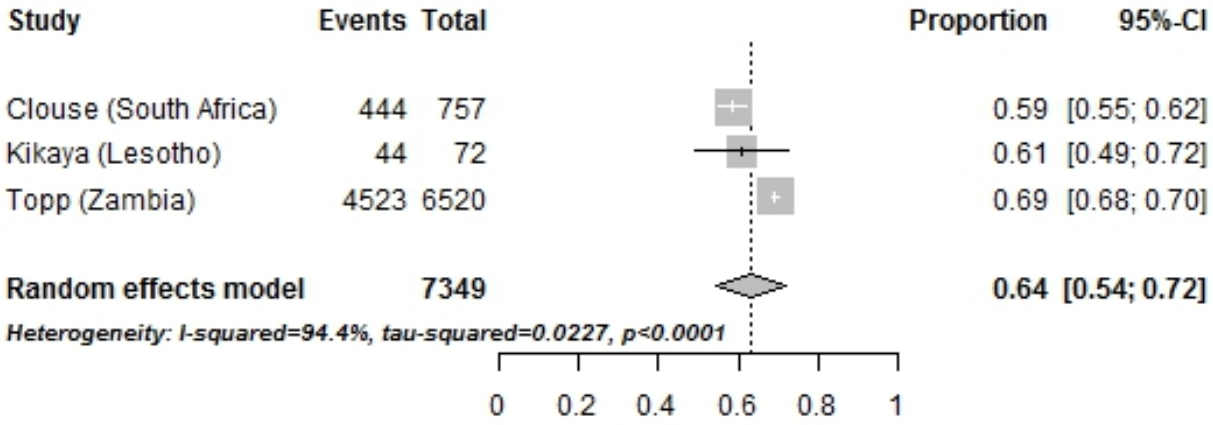
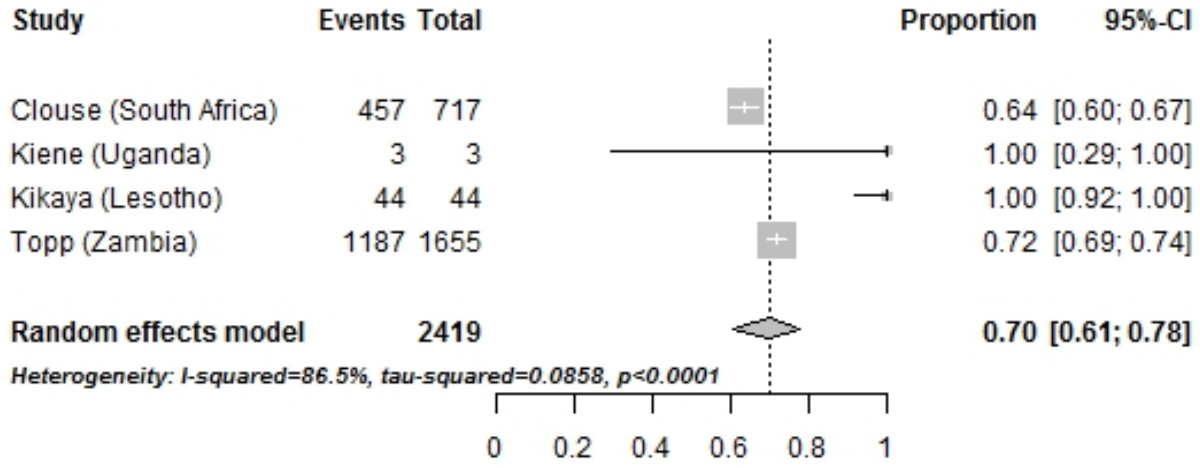


Figure S57: Facility PITC: ART initiation among those eligible



Retained in care

Figure S58: Facility VCT: Retained in care (6-12 months)

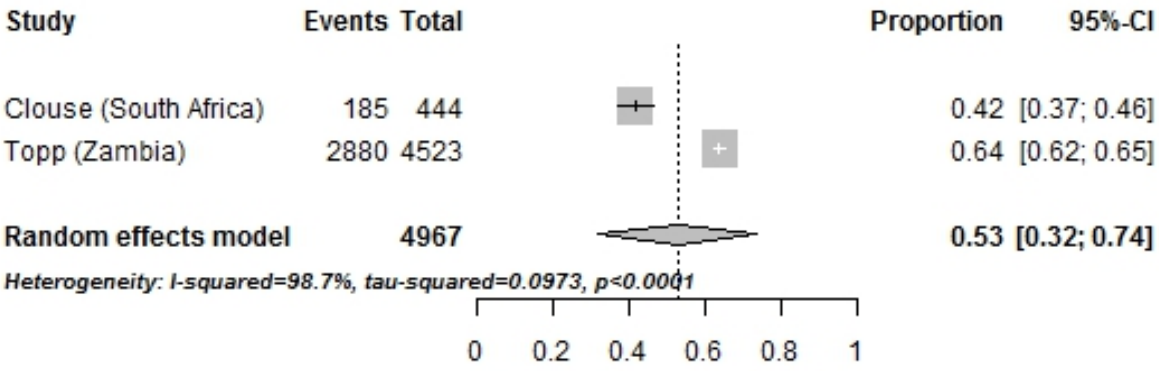


Figure S59: Facility PITC: Retained in care (6-12 months)

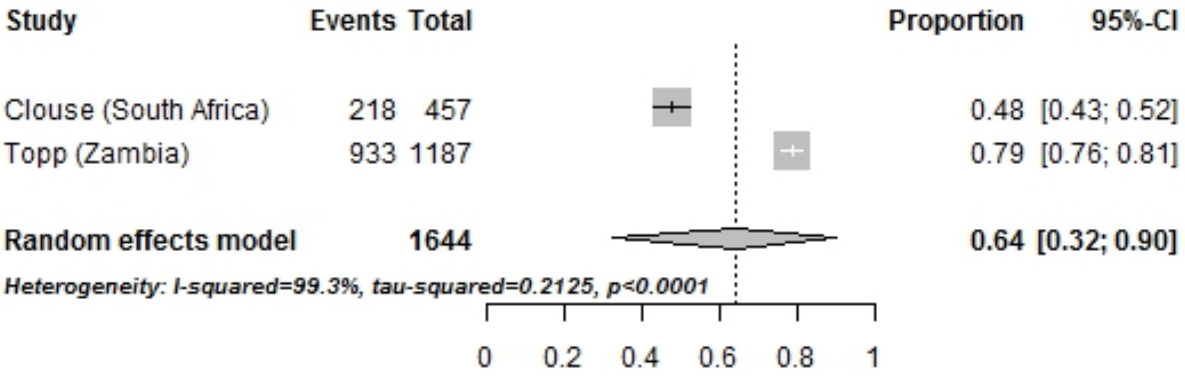
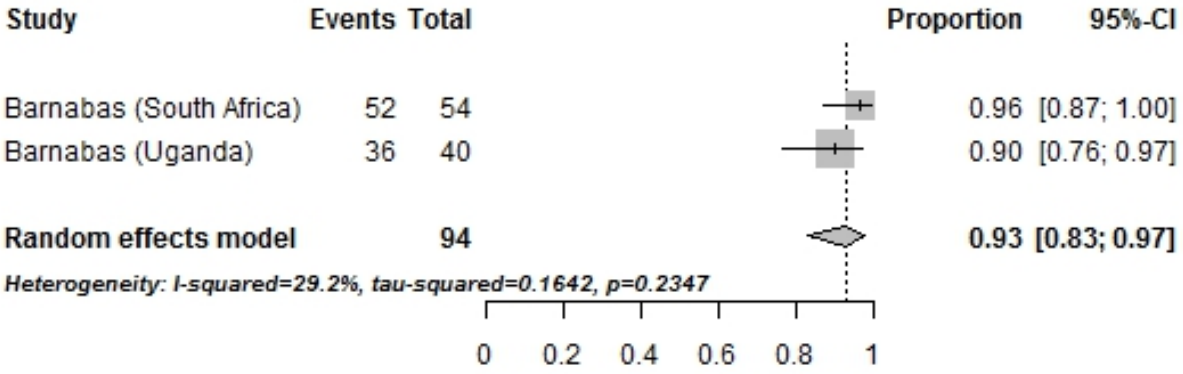


Figure S60: Home: Retained in care 12 months (viral suppression among those who initiated)



1. Dalal W. Home-Based HIV Testing and Counseling in Rural and Urban Kenyan Communities. 2013.

Table S2: Community HTC costs per person tested

AUTHOR	COUNTRY	REGION	PUB YEAR	CURRENCY (USD)	COSTING TIME	APPROACH	COST TYPE	TYPE	COST / PERSON TESTED 2012 USD	NUMBER TESTED
Terris-Prestholt	Uganda	Masaka (rural), 16 parishes	2006	2001	4 years	Step down	economic	sporadic (counselors visited community every 2 wks)	$41.24	4,425
Tumwesigye	Uganda	Bushenyi District	2007	2005	6 months	Bottom up (programmatic)	economic	home based	$11.01	264953
Bassett	South Africa	Urban	2014	2012	24 months	Top down (economic)	financial	mobile van	$29.30 (HIV neg) $31.30 (HIV pos)	18,870/2 years
Grabbe	Kenya	6 provinces in Kenya	2009	2007	12 months	Bottom up	economic	mobile van	$25.79	9,713
Grabbe	Kenya	6 provinces in Kenya	2009	2007	12 months	Bottom up	economic	mobile container	$21.80	17,227
Kahn	Kenya	Western Province (rural)	2011	2008	12 months	Bottom up (incredients based)	economic	mobile (tents)	$11.19	47,133
Menzies	Uganda		2009	2007	6-12 months	Bottom up (microcosting)	economic	household member	$16.60	2,011
Menzies	Uganda		2009	2007	6-12 months	Bottom up (microcosting)	economic	home based	$9.93	49,470
Mulogo	Uganda	rural (Mbarara)	2013	2008	5 months	Bottom up (ingredients based)	economic	home based	$7.20	494
Grabbe	Kenya	6 provinces in Kenya	2009	2007	12 months	Bottom up	economic	Community	$11.16	47,539
McConnel	South Africa	KwaZulu-Natal (urban)	2005	2003	12 months	Bottom up (economic costs)	economic	church	$87.79	662
Negin	Kenya	rural (Nyanza)	2009	2008	3 months	Bottom up (microcosting)	financial	home based	$9.99	1984
Helleringer	Malawi		2013	2007	9 months	Bottom up (microcosting)	financial	home based	$14.65	1183
Parker	Swaziland	rural (Shiselweni region)	2015	2012	12 months	Bottom up (ingredients based)	financial	home based	$11.00	7026
Parker	Swaziland	rural (Shiselweni region)	2015	2012	12 months	Bottom up (ingredients based)	financial	mobile van	$24.00	2034
Labhardt	Lesotho	rural	2014	2011		Bottom up (ingredients based)	financial	home based (campaign)	$13.48	1,433
Labhardt	Lesotho	rural	2014	2011		Bottom up (ingredients based)	financial	mobile van (campaign)	$11.06	1764

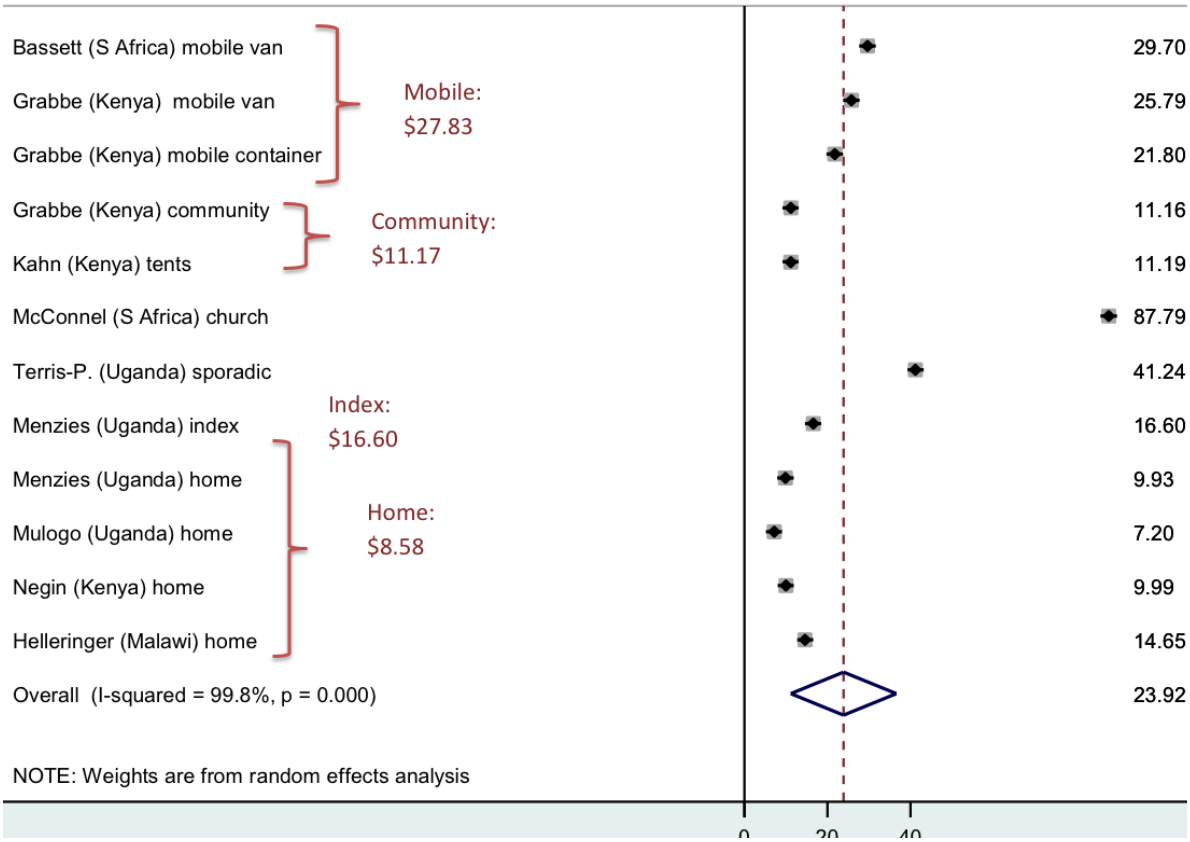
Table S3: Facility-based HTC: Cost per person tested

Author	Country	Region	Pub year	Currency (USD)	Costing time	Approach	cost type	Type	Cost per person tested 2012 USD	Number tested
Aliyu	Nigeria	urban/ rural mix	2012	2010	12 months	Top down	financial	Facility (tertiary)	$21.13	24,124
Aliyu	Nigeria	urban/ rural mix	2012	2010	12 months	Top down	financial	Facility (2ndary)	$7.22	
Aliyu	Nigeria	Urban	2012	2010	12 months	Top down	financial	Facility	$6.64	
Aliyu	Nigeria	Rural	2012	2010	12 months	Top down	financial	Facility	$11.05	
Bassett	S. Africa	Urban	2007	2005	24 months	Bottom up (microcosting)	financial	Hospital, outpatient dept	$9.30 (neg) $13.90 (pos)	1,414
Menzies	Uganda		2009	2007	6-12 months	Bottom up (microcosting)	economic	hospital	$14.00	23,238
Obure	Kenya	urban/ rural mix	2012	2009	12 months	bottom up (microcosting)	economic	hospital	$13.41	193
Obure	Swaziland	urban/ rural mix	2012	2009	12 months	bottom up (microcosting)	economic	Hospital	$21.85	1200
Forsythe	Kenya	urban/ rural mix	2002	1999		bottom up (microcosting)	economic	Health center	$18.32	1,020
Obure	Kenya	urban/ rural mix	2012	2009	12 months	bottom up (microcosting)	economic	comm health center	$5.71	73

Table S3 cont'd: Facility-based HTC: Cost per person tested

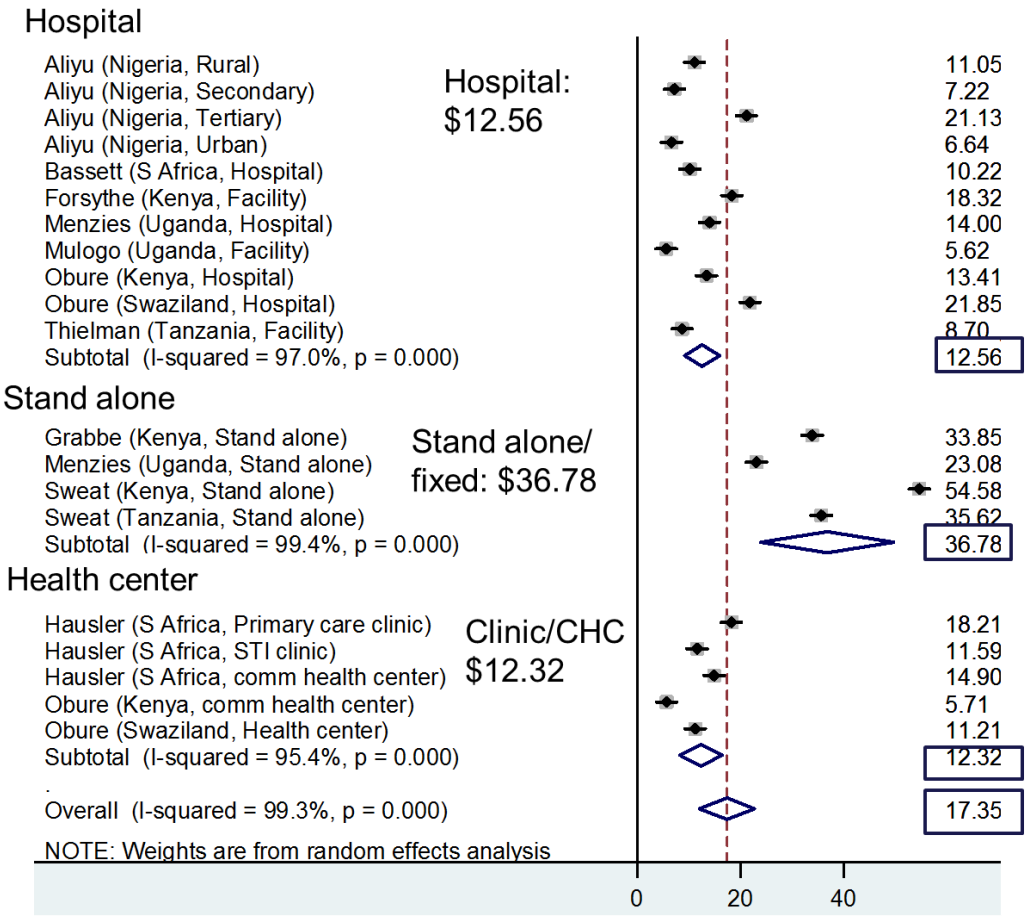
Author	Country	Region	Pub year	Currency	costing time	Approach	cost type	Type	Cost /person tested 2012 USD	Number tested
Hausler	South Africa	Cape town	2006	2003	12 months	Bottom up (ingredients based)	economic	comm health center	$14.90	
Hausler	South Africa	Cape town	2006	2003	12 months	Bottom up (ingredients based)	economic	Primary care clinic	$18.21	
Hausler	South Africa	Cape town	2006	2003	12 months	Bottom up (ingredients based)	economic	STI clinic	$11.59	
Obure	Swaziland	urban/ rural mix	2012	2009	12 months	bottom up (microcosting)	economic	Health center	$11.21	523
Thielman	Tanzania	Moshi (urban)	2006	2003	12 months	bottom up (ingredients based)	economic	comm health center	$8.70	966
Mulogo	Uganda	rural (Mbarara)	2013	2008	5 months	bottom up (ingredients based)	economic	Health center	$5.62	500
Grabbe	Kenya	6 provinces in Kenya	2010	2007	12 months	Bottom up	economic	Stand alone	$33.85	14,634
Menzies	Uganda		2009	2007	6-12 months	Bottom up (microcosting)	economic	Stand alone	$23.08	9604
Sweat	Kenya	Nairobi	2000	1998	12 months	bottom up	economic	Stand alone	$54.58	716
Sweat	Tanzania	Dar es Salaam	2000	1998	12 months	bottom up	economic	Stand alone	$35.62	601

Figure S61: Community HTC costs



Brackets are used to group together similar HTC modalities

Figure S62: Facility HTC costs



Additional information:

Authors contacted:

We contacted three authors for additional outcome information. One responded by sending the requested tester demographics. One responded to say he did not have the data and the third did not reply. We obtained CD4 count data was available by country from Barnabas as we had access to raw data from the Linkages study.

Cost conversion example:

Costs were converted from US dollars to local currency units and then inflated using the ratio of the GDP deflators. Source for currency conversions and GDP deflators was the World Bank Indicators: http://data.worldbank.org/indicator/PA.NUS.FCRF?page=1

For example, for a cost per person tested of $8.82 in 2007 USD from a Kenyan study, we used the 2011 exchange rate (67.32) to convert to local currency, then multiplied by the ratio of the 2012/2007 Kenyan GDP deflators (123.6/77.8) to account for inflation, then converted to 2012 USD using the currency conversion (84.53):

(8.82*67.32/(123.6/77.8))/84.53=11.16

CHAPTER 3: Modeling the cost-effectiveness of home-based HIV testing and education (HOPE) for pregnant women and their male partners in Nyanza Province, Kenya

Modeling the cost-effectiveness of home-based HIV testing and education (HOPE) for pregnant women and their male partners in Nyanza Province, Kenya

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Related Presentations

Sharma M, Farquhar C, Kinuthia J, Osoti A, Asila V, Parikh S, Krakowiak D, Gone A, Barnabas RV. Cost of home HIV testing and education for male partners of pregnant women in Kenya. [Poster] HIV Pathogenesis, Treatment and Prevention (IAS), Vancouver, BC, July, 2015.

Conflicts of interest: The authors declare that they have no conflicts of interest.

Abstract

Introduction: Women in sub-Saharan Africa face a two-fold higher risk of HIV acquisition during pregnancy and post-partum and the vast majority do not know the HIV status of their male partner. Home-based couples HIV testing for pregnant women can reduce HIV transmission to women and infants while increasing antiretroviral therapy (ART) coverage in men. However, the cost-effectiveness of this program has not been evaluated.

Methods: We modeled the health and economic impact of implementing a home-based partner education and HIV testing (HOPE) intervention for pregnant women and their male partners in a region of Western Kenya (Nyanza Province). We utilized data from the HOPE randomized clinical trial conducted in Kisumu, Kenya to parameterize a mathematical model of HIV transmission. We conducted an in-country micro-costing of the HOPE intervention (payer perspective) to estimate program costs and a scenario of task-shifting to community health workers.

Results: The incremental cost of adding the HOPE intervention to standard antenatal care was $31-37 and $14-16 USD per couple tested with program and task-shifting costs, respectively. At 60% coverage of male partners, HOPE was projected to avert 6,987 HIV infections and 2,603 deaths in Nyanza province over 10 years with an incremental cost-effectiveness ratio (ICER) of $886 and $615 per DALY averted for the program and task-shifting scenario, respectively. ICERs were robust to changes in intervention coverage, effectiveness, and ART initiation and dropout rates.

Conclusions: The HOPE intervention can moderately decrease HIV-associated morbidity and mortality by increasing ART coverage in male partners of pregnant women. ICERs fall below Kenya's per capita gross domestic product ($1,358) and are therefore considered cost-effective.

Task-shifting to community health workers can increase intervention affordability and feasibility.

Keywords: HIV counseling and testing, sub-Saharan Africa, cost-effectiveness, males, pregnant, PMTCT

Introduction

HIV is one of the most serious health and economic challenges facing sub-Saharan Africa (SSA) where over 70% of the world's new HIV infections occur.[1] Pregnant and post-partum women in SSA have particularly high rates of HIV-acquisition; cohort studies report HIV incidences ranging from 2.3 to 7.6 per 100 person-years during pregnancy and post-partum,[2-5] more than two fold higher than in non-pregnant women.[6] This increased risk persists after adjustment for sexual behavior, suggesting that biological factors including hormonal or immunological changes during pregnancy may play a role in heightening susceptibility.[6] With fertility rates around 5 children per woman in SSA, this can translate into 10 or more years of increased risk. HIV-infected women in East Africa also face more than 7-fold higher risk of maternal mortality compared to uninfected pregnant women[7] and approximately 17% of HIV-infected mothers in SSA transmit HIV to their infants.[8]

While pregnant women have high rates of HIV testing coverage in SSA largely due to antenatal testing, they are less likely to know the HIV status of their male partners. For example, in Kenya during 2013, 88% of pregnant women were tested for HIV, while only 4.5% of their male partners underwent testing in the prior 12 months.[8,9] This is a significant problem in generalized epidemic settings, since persons are most likely to become infected in stable partnerships. A modeling analysis using sexual behavior survey data from 18 countries in SSA suggests that HIV transmission within couples is largely transmitted from men to women, and men are more likely than women to become infected by someone other than their main partner, both of which indicate that interventions to reduce HIV in women will likely need to target men as well.[10]

As facility-based HIV testing and counseling (HTC) has not achieved high testing coverage in male partners of pregnant women in SSA, novel testing interventions are needed.[11,12] Community-based HTC is a promising alternative that achieves high uptake and identifies asymptomatic HIV-positive individuals at higher CD4 counts than facility HTC.[13,14] One form of community HTC, home-based HIV couples counseling for pregnant women and their male partners, can attain high HIV testing coverage in both pregnant women and their partners. Couples HIV testing and disclosure has been shown to increase women's adherence to both antiretroviral therapy (ART) and prevention of mother to child transmission (PMTCT) regimens, including Option B+ (lifelong ART for HIV-infected pregnant women).[15-17] Increasing HIV testing in males reduces transmission to their female partners, while also averting morbidity and mortality in men associated with late ART initiation. Men are less likely than women to undergo HIV testing, less likely to start ART, and more likely to seek care at more advanced disease stages, interrupt treatment, and die on ART.[18] Antenatal clinic attendance is high (95.4% of pregnant women in Kenya, 2012), indicating the potential to achieve high coverage of male partners.[19] However, home-based couples counseling for pregnant women is resource intensive and its cost-effectiveness (i.e. value for money) has not been well evaluated. We used a mathematical model to assess the cost-effectiveness of providing home-based partner education and HIV testing (HOPE) to couples as a part of routine antenatal care in Western Kenya. Primary cost and effectiveness data were collected from the HOPE study, a randomized controlled trial conducted in Kisumu, Kenya in which couples either received the HOPE intervention (HOPE arm) or written invitations for male partners to attend clinic (INVITE arm). In addition to HIV education and testing, couples in the HOPE arm received information on facility delivery, exclusive breastfeeding, family planning, and voluntary medical male circumcision. In this

analysis, we project the health and economic impact of implementing the HOPE intervention in Nyanza Province, a region in Western Kenya with high HIV prevalence (15.1%). From an implementation science perspective, we sought to translate the HOPE clinical trial results into projections of HIV burden averted and costs incurred under realistic program scale-up. Our analysis can be useful to policy makers charged with implementing evidence-based HIV interventions that maximize health benefits within a fixed budget.

Methods

Home-based partner education and testing (HOPE) Intervention:

Costs and effectiveness data were obtained from the HOPE intervention, a randomized controlled trial conducted from September 2013 to June 2015 in Kisumu, Kenya. Study design and outcomes are described in detail in this supplement.[20] Briefly, 601 pregnant women in stable partnerships were enrolled when they presented for antenatal care at Kisumu County Hospital and randomized to HOPE (intervention) or INVITE (control) arm. Couples in the intervention arm received a home visit where study staff (health advisors) screened male partners and offered couples HIV counseling and testing. Health advisors also administered a standardized health education intervention on the importance of facility delivery, exclusive breastfeeding, family planning, and methods to prevent HIV transmission. Women in the INVITE arm were asked *via* written invitation to bring their partners to the clinic for couple HIV testing. The study compared uptake of male partner HIV testing, condom use, facility delivery, exclusive breastfeeding, HIV transmission to infants and mothers, and contraceptive use in the two arms. Outcomes were assessed at six weeks and again at six months after delivery. The HOPE intervention was found to increase male partner testing by more than two-fold (RR 2.1, 95% CI: 1.81-2.42) and

identified more HIV serodiscordant couples (13%) compared to the INVITE arm (4%). The HOPE intervention was not associated with an increase in intimate partner violence or other adverse events.

Mathematical model:

We adapted a previously published dynamic HIV transmission model to include pregnancy states.[21] The model was parameterized with epidemiologic data from Nyanza Province and calibrated to fit HIV incidence and prevalence from that region. The model simulates the natural history of HIV/AIDS using 3 month time steps. Men and women are stratified by 5-year age group (0-59 years), sexual activity (low, medium, and high), circumcision status, viral load (six stages), and CD4 count (six stages). Sexual behavior is assumed to change over time as individuals age. Susceptible individuals can acquire HIV and transition to acute infection. CD4 count declines over time based on clinical estimates from a prospective cohort.[21] Persons on ART have a 96% reduction in transmission risk.[22] Disability weights are assigned to each HIV state.[23] In addition to background mortality, HIV-positive individuals face a disease-specific mortality that varies by age and CD4 count.[24] Persons on ART are assumed to have the same mortality rates as those who are uninfected.[25] Dropout of ART occurs yearly and individuals are assumed to return to the CD4 count and viral load status they had prior to initiating ART. The model estimates the force of HIV infection as a function of sexual mixing (by age and sexual activity), proportion of HIV infected individuals, circumcision, and HIV transmission probability. HIV-positive women who are not on ART have a probability of transmitting HIV to their infants. Changes in the population over time are estimated using a system of ordinary differential equations (ODEs) that are solved in MATLAB version 2015a

using 4th-order Runge-Kutta methods.[26] Before projecting the impact of the HOPE intervention, the model was calibrated to reflect the age-specific and overall HIV prevalence from Nyanza province and CD4 distribution and ART coverage from Kenya. Additional details about the model, parameters, and calibration results are available in the **Supplemental Appendix**.

Status quo and intervention scenarios:

For the status quo (no intervention) scenario, we modeled the impact of continued facility HIV testing and ART expansion at current scale-up rates.[27] In the intervention scenario, HOPE is added to the status quo scenario with 60% coverage of male partners of pregnant women, based on coverage from the trial. However, as coverage could either be higher or lower if implemented as a government program, we conducted sensitivity analyses varying coverage from 40-80%. We assumed that the HOPE intervention increased ART initiation rate for HIV-positive male partners by 2.1 fold (the increase in male partner HIV testing found in the clinical trial).

Micro-costing:

A detailed micro-costing was conducted following established guidelines for costing HIV interventions.[28,29] Primary cost data were collected from budgets, expense reports staff and local expert interviews. Costs were divided into mutually exclusive categories of: personnel, transportation, equipment, supplies, buildings and overhead, start up, and phones and data monitoring. Time and motion studies were conducted over three weeks (June 10-30th 2014) to record staff time spent on intervention activities (e.g. conducting HTC, tracing male partners, traveling to couples' homes). Research time (administering informed consent, reimbursements, etc.) and other research cost were removed from the programmatic costs. The time and motion

studies and interviews with staff were used to inform efficiency assumptions about the mean number of couples that could be tested per day. Capital costs, software development, and start-up cost (staff hiring, training, and community mobilization) were annualized assuming a 5-year useful life expectancy discounted annually at 3%. Costs were inflated to 2014 US dollars (USD) using the Kenya consumer price index. Total program costs were divided by the number of couples tested by HIV status under each scenario to determine the cost per person tested. Other costs including facility HIV testing, ART, and HIV/AIDS related hospitalizations were estimated from the literature;[30-32] additional information is available in the **Supplementary Appendix**.

Cost-effectiveness analysis:

We calculated the incremental cost-effectiveness ratio (ICER) of adding the HOPE intervention to standard antenatal care for DALYs averted over 10 years. The ICER is measured as the additional cost divided by the additional health benefit of the intervention strategy compared to the next less costly strategy (the status quo). Consistent with health economic conventions, we considered the intervention to be very cost-effective if the ICER is less than Kenya's 2014 GDP per capita (1,358 USD).[33] We employed a 10-year time horizon as is common in cost-effectiveness analyses of HIV prevention.[34,35]

Sensitivity analyses:

To explore the impact of key assumptions on our findings, we conducted sensitivity analyses varying coverage, costs, intervention effectiveness, projected ART expansion, and task shifting from health advisors to community health workers. We also evaluated a scenario in

which the HOPE intervention increased adherence to Option B+ as studies found couples HIV testing and disclosure increases women's adherence.[15]

Results

Micro-costing:

Costs were estimated for two scenarios: 1) a higher cost program model, reflecting the staff cadre of the research study—nurses enrolling pregnant women into the intervention, highly trained health advisors administering the intervention, and higher cost supplies including research compatible mobile phones, and 2) a lower cost task shifting model in which nurses and health advisors are replaced with community health workers, the field coordinator is replaced with a community health worker manager, the data manager is reduced to a half-time position, and lower cost supplies are used **(Figure 1)**. Results of the time and motion observations showed that the HOPE educational component and couples HIV testing and counseling together take approximately 1 hour per couple (15-30 minutes longer for couples with discordant HIV-status who require additional counseling). After accounting for travel time to participant's home, follow-ups, paperwork, and other staff responsibilities, we estimated that health advisors could test 3 couples per day. Staff were assumed to work 7 hours per day for 215 days per year (after accounting for holidays, vacation, and sick time). Supply costs per person tested included gloves, HIV screening test kit, and alcohol swabs. Additional supplies for HIV-positive persons included confirmatory test, and tie breaker test (assumed to be used in 5% of all HIV-positive cases). Supply wastage was assumed to be 5%. Transport costs included motorcycles used to travel to participants homes to conduct the intervention. Economic costs were estimated for donated goods, including hospital space. Incremental costs per couple tested were estimated separately for HIV-positive and HIV-negative persons as the former required more staff time for counseling

and additional diagnostics supplies. Costs per couple tested ranged from $31-37 for the program model and $14-16 for the task shifting model. Staff salaries represented the bulk of the costs (65-70%) **(Table 1)**.

Model estimated health and economic impact of the HOPE intervention

In the base-case scenario, assuming the HOPE intervention increased male partner ART initiation by 2.1 fold and achieved 60% coverage of male partners, the model estimated that 6,987 incident HIV infections and 2,603 deaths would be averted over a 10 year time horizon **(Table 2)**. Discounted incremental costs of adding the HOPE intervention to standard of care (ART expansion) were $14.3 million USD over 10 years with program model costs and $9.9 million USD with the task-shifting model. The ICER for adding HOPE to standard of care was $886 and $615 USD per DALY averted for the program and task-shifting model respectively. ICERs were similar with changing intervention coverage (40-80%), although health benefits varied, as expected. At 40% coverage of male partners, HIV infections and deaths averted were reduced to 4,659 and 1,734 respectively while 80% coverage was estimated to avert 9,134 HIV infections and 3,594 deaths. Lower intervention linkage to ART increased the ICER to $1,076 and $730 for the program and task-shifting model respectively, although ICERs were still below the threshold of Kenya's GDP per capita. Lower intervention linkage to ART at 60% coverage achieved greater reductions in HIV infections and deaths than higher intervention ART linkage at lower (40%) coverage. Similarly, higher HOPE coverage (80%) averted more HIV infections and deaths compared to 60% coverage with higher ART linkage. The ICERs were robust to changes in ART dropout although intervention health benefits were lower at increased dropout rates. Since ART expansion in the next 10 years is uncertain, we assessed a scenario in which

ART was rolled out at a lower rate (lower baseline ART initiation); this decreased intervention health benefits and resulted in higher ICERs—although they remained below the threshold of Kenya's GDP per capita. We also assessed a scenario in which undergoing couples HIV testing through the HOPE intervention increased women's initiation of Option B+. Results showed that increasing Option B+ initiation by just 5% yielded the highest benefits and lowest ICERs of all strategies at 60% coverage; ICERs were $749 and $533 for the program and task shifting model respectively. Overall, the HOPE intervention was projected to achieve 8% population coverage per year, as 14% of women are pregnant annually and 60% of couples would receive the HOPE intervention.

Figure 1 displays tornado diagrams of the sensitivity of ICERs for the program (1a) and task-shifting cost model (1b) to changes in the cost of HOPE, ART, and HIV/AIDs related hospitalization. ICERs for both cost models were most sensitive to HOPE intervention costs, with the ICER exceeding the GDP for the program model at twice the intervention costs. ICERs were less sensitive to ART costs, with higher ART costs resulted in less attractive (higher) ICERs while lower ART costs resulted in lower ICERs. The ICERs were least sensitive to hospitalization costs, which were inversely related to ICERs.

Discussion

Women in Kenya attend antenatal care at rates over 90% and the vast majority are tested for HIV.[19] However, they continue to experience disproportionately high HIV incidence, partially due to the lack of HIV testing and linkage for their male partners.[9] Scaling up the HOPE intervention in Nyanza Province, Kenya can cost-effectively reduce HIV infections in pregnant women and their partners while averting morbidity and mortality associated with late initiation

of ART in both sexes. Since men present to healthcare facilities at later HIV stages, have lower ART linkage and poorer clinical outcomes, they are more likely to transmit HIV to their female partners.[36] Additionally, morbidity and mortality in men has a negative economic impact on women and their children. The HOPE intervention can identify HIV-positive men earlier in the course of their illness and link them to care before they infect their pregnant partners.

The projected health benefits of the HOPE intervention varied depending on the coverage achieved, the intervention's ability to link male partners to ART, and the baseline levels of ART initiation and dropout. However, the ICERs were robust to changes in these parameters and remained very cost-effective **(Table 2)**. ICERs were most sensitive to increases in intervention costs, with the program model exceeding the cost-effectiveness threshold of Kenya's GDP per capita at double intervention costs **(Figure 1)**. However, the detailed micro-costing completed as part of the analysis increases our confidence in the estimated costs. Further, the task-shifting model remained cost-effective despite increased intervention costs. In addition, if the HOPE intervention increases women's adherence to ART, as found in prior studies, the health benefits increase substantially and the ICERs become more attractive.[16]

Scaling up the HOPE intervention will likely be more affordable if implemented under a task-shifting model as staff salaries account for the majority of program costs. Training community health workers to conduct health interventions is an increasingly utilized strategy in sub-Saharan Africa; community health workers can fill in service gaps caused by the shortage of healthcare professionals and deliver health care to rural areas more efficiently.[37] Integrating health interventions is another way to reduce program costs. For example, community health workers can deliver the HOPE intervention along with diabetes and hypertension screening. Integrating services can also reduce the stigma associated with an HIV testing intervention.[38]

Additionally, a tiered program can be implemented where women are given a few weeks to bring their partner into the clinic for testing. Those who do not present to the clinic can be followed up at home. Further, a risk score could be developed to identify male partners that are less likely to come to the clinic so they can be traced at home. Such a score has been developed for HIV intimate partner notification in Malawi and has been shown to have good sensitivity and specificity. [39] Additionally, the HOPE intervention can be utilized to identify serodiscordant couples to target PrEP, further integrating HIV services and decreasing costs. Finally, the HOPE intervention can be implemented within the context of home or mobile HTC for the general population. Although HOPE is cost-effective, it has a limited population-level impact on HIV burden as it is targeted to a specific portion of the population. Overall, it is projected to reach 8% population coverage annually and reduce approximately 2.5% of HIV infections in Nyanza over 10 years. Therefore it should be combined with community-based HIV interventions which have been found to be cost-effective in other settings.[35]

The strengths of our analysis include obtaining primary cost and effectiveness data from a randomized controlled trial in Nyanza, Kenya. Our results should be interpreted within the context of our limitations. We assume male partners testing HIV-positive through the HOPE intervention have the same rate of linkage to ART as facility testing. Community-based testing can result in lower linkage rates since is conducted outside of the healthcare system.[40] If implemented, the HOPE intervention should be monitored for linkage and community health workers may need to conduct follow-up visits to encourage reluctant partners to link to care. However, if the HOPE intervention increases adherence to ART and PMTCT, health benefits could be greater than projected. The effectiveness estimates were obtained from a randomized controlled trial that utilized highly trained and closely monitored health advisors. If the HOPE

intervention is scaled up through a government program, effectiveness may decrease if counselors were less able to persuade reluctant male partners to undergo testing, or were less efficient in delivering the intervention. However, we explored a scenario of lower linkage and still found the intervention to be cost-effective. Additionally, implementing standardized training and monitoring for community health workers would be essential to maintaining intervention fidelity. Currently community health workers in Kenya are currently not trained to conduct HIV testing and counseling. Therefore efficiency may be lower than expected during the first few years of the intervention as community health workers solidify their HIV testing skills. Indeed, the translation of a clinical trial to real world implementation poses significant challenges and the HOPE intervention would be most successful if it is integrated into other health interventions and employs community health workers instead of higher cadre staff.

In conclusion, we find the HOPE intervention to be a cost-effective method to reduce HIV disease burden in Nyanza, Kenya. Our results are similar to previous analyses that have found community-based HIV counseling and testing in sub-Saharan Africa to be cost-effective.[35,41] Although absolute costs will vary, our results are likely generalizable to other regions of sub-Saharan Africa with a similar HIV epidemic profile.

References

1. UNAIDS 2013 Report on the Global AIDS Epidemic . Available from: http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport. Accessed on 22/5/15.
2. Leroy V, Van de Perre P, Lepage P, et al. Seroincidence of HIV-1 infection in African women of reproductive age: a prospective cohort study in Kigali, Rwanda, 1988-1992. AIDS (London, England) 1994;8:983-6.
3. Taha TE, Dallabetta GA, Hoover DR, et al. Trends of HIV-1 and sexually transmitted diseases among pregnant and postpartum women in urban Malawi. AIDS (London, England) 1998;12:197-203.
4. Humphrey JH, Hargrove JW, Malaba LC, et al. HIV incidence among post-partum women in Zimbabwe: risk factors and the effect of vitamin A supplementation. AIDS (London, England) 2006;20:1437-46.
5. Kinuthia J, Kiarie JN, Farquhar C, et al. Cofactors for HIV-1 incidence during pregnancy and postpartum period. Curr HIV Res 2010;8:510-4.
6. Gray RH, Li X, Kigozi G, et al. Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study. Lancet 2005;366:1182-8.
7. Calvert C, Ronsmans C. The contribution of HIV to pregnancy-related mortality: a systematic review and meta-analysis. AIDS (London, England) 2013;27:1631-9.
8. WHO. Global Update on the health sector response to HIV, 2014 Accessed from: http://apps.who.int/iris/bitstream/10665/128494/1/9789241507585_eng.pdf?ua=1 on 10/16/2015.
9. UNAIDs. Kenya AIDS Response Progress Report, 2014. Accessed on 1/20/2016 from http://www.unaids.org/sites/default/files/country/documents/KEN_narrative_report_2014.pdf.
10. Bellan SE, Fiorella KJ, Melesse DY, Getz WM, Williams BG, Dushoff J. Extra-couple HIV transmission in sub-Saharan Africa: a mathematical modelling study of survey data. Lancet 2013;381:1561-9.
11. Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society 2012;15:17383.
12. UNAIDS World AIDS Day Report 2012. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2434_WorldAIDSday_results_en_1.pdf. Accessed on 25/5/15.
13. Paulin HN, Blevins M, Koethe JR, et al. HIV testing service awareness and service uptake among female heads of household in rural Mozambique: results from a province-wide survey. BMC public health 2015;15:1388.
14. Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. PLoS medicine 2013;10:e1001496.
15. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis 2015;33:123-9.
16. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. AIDS and behavior 2010;14:558-66.
17. Rosenberg NE, Mtande TK, Saidi F, et al. Recruiting male partners for couple HIV testing and counselling in Malawi's option B+ programme: an unblinded randomised controlled trial. The lancet HIV 2015;2:e483-91.
18. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Tropical medicine & international health : TM & IH 2011;16:828-9.
19. Kenya AIDS indicator Survey 2012. Accessed on 1/1/2016 from: http://www.nacc.or.ke/images/documents/KAIS-2012.pdf.

20. Krakowiak D. Home-based HIV testing among pregnant couples increases partner testing and identification of serodiscordant partnerships. JAIDS Supplement.
21. Ying R, Sharma M, Heffron R, et al. Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda. Journal of the International AIDS Society 2015;18:20013.
22. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet 2010;375:2092-8.
23. Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 2012;380:2129-43.
24. Mills EJ, Bakanda C, Birungi J, et al. Mortality by baseline CD4 cell count among HIV patients initiating antiretroviral therapy: evidence from a large cohort in Uganda. AIDS (London, England) 2011;25:851-5.
25. Jahn A, Floyd S, Crampin AC, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. Lancet 2008;371:1603-11.
26. MATLAB and Statistics Toolbox Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States.
27. World Bank Development Indicators: Antiretroviral therapy coverage (% of people living with HIV). Accessed on 11/9/2015 from: http://data.worldbank.org/indicator/SH.HIV.ARTC.ZS?page=1.
28. Drummond M, Drummond M. Methods for the economic evaluation of health care programmes. 3rd ed. Oxford ; New York: Oxford University Press; 2005.
29. UNAIDS. Costing guidelines for HIV prevention strategies. Geneva: UNAIDS; 2000. Accessed on 10/1/2015 from: http://data.unaids.org/Publications/IRC-pub05/jc412-costguidel_en.pdf.
30. Obure CD, Vassall A, Michaels C, et al. Optimising the cost and delivery of HIV counselling and testing services in Kenya and Swaziland. Sex Transm Infect 2012;88:498-503.
31. Tagar E, Sundaram M, Condliffe K, et al. Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia. PloS one 2014;9:e108304.
32. Meyer-Rath G, Brennan AT, Fox MP, et al. Rates and cost of hospitalization before and after initiation of antiretroviral therapy in urban and rural settings in South Africa. Journal of acquired immune deficiency syndromes (1999) 2013;62:322-8.
33. Gold MR. Cost-effectiveness in health and medicine. New York: Oxford University Press. 1996.
34. Fasawe O, Avila C, Shaffer N, et al. Cost-effectiveness analysis of Option B+ for HIV prevention and treatment of mothers and children in Malawi. PloS one 2013;8:e57778.
35. Smith JA, Sharma M, Levin C, et al. Cost-effectiveness of community-based strategies to strengthen the continuum of HIV care in rural South Africa: a health economic modelling analysis. The lancet HIV 2015;2:e159-e68.
36. Cornell M, Myer L. Men and mortality: sex inequality in health outcomes. AIDS (London, England) 2013;27:849-50.
37. One million community health workers. Technical task force report. Accessed on 1/24/2016 from: http://frontlinehealthworkers.org/wp-content/uploads/2014/09/CHW-Report.pdf.
38. Chamie G, Clark TD, Kabami J, et al. A hybrid mobile approach for population-wide HIV testing in rural east Africa: an observational study. The lancet HIV 2016;3:e111-9.
39. Brown LB, Miller WC, Kamanga G, et al. Predicting partner HIV testing and counseling following a partner notification intervention. AIDS and behavior 2012;16:1148-55.
40. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. Nature 2015;528:S77-85.

41. Bassett IV, Govindasamy D, Erlwanger AS, et al. Mobile HIV screening in Cape Town, South Africa: clinical impact, cost and cost-effectiveness. PloS one 2014;9:e85197.

Table 1: Unit costs for the HOPE intervention per couple tested (2014 USD).

	Program model			Task shifting model		
	concordant HIV-	**concordant HIV+**	**Discordant**	**concordant HIV-**	**concordant HIV+**	**Discordant**
Personnel	22.90	22.90	25.45	9.27	9.27	10.30
Transportation	2.16	2.16	2.40	2.16	2.16	2.40
Equipment	0.17	0.17	0.18	0.17	0.17	0.19
Supplies	3.63	7.65	6.27	0.53	0.89	0.79
Buildings & overhead	0.96	0.96	1.07	0.96	0.96	1.07
Startup	0.44	0.44	0.49	0.27	0.27	0.30
Data capture and use	0.52	0.52	0.57	0.44	0.44	0.49
TOTAL (per couple tested)	30.78	34.80	36.43	13.81	14.17	15.55

The task shifting model replaces professional counselors with community health workers (CHWs), lower cost mobile phones.

Table 2: Health and economic impact of the HOPE intervention under base-case assumptions and sensitivity analyses

	Current ART scale up	**HOPE intervention§**								
		Base-case	Lower intervention coverage (40%)	Higher intervention coverage (80%)	30% lower intervention linkage to ART	30% higher intervention linkage to ART	50% lower ART dropout	50% higher ART dropout	Lower baseline ART initiation	5% increased uptake of Option B+
Total HIV infections	301,870									
Total deaths¥	275,469									
Total DALYs	2,514,475									
HIV infections averted*	--	6,987	4,659	9,314	5,480	8,289	7,293	6,385	6,398	8,445
Deaths averted*	--	2,603	1,734	3,474	2,040	3,090	2,614	2,539	2,502	3,304
DALYs averted	--	16,192	10,788	21,601	12,651	19,270	16,282	15,769	15,268	20,419
Incremental costs program model (millions)	--	14.3	9.6	19.1	13.6	15	14.5	14.1	13.9	15.3
Incremental costs task shifting model (millions)	--	9.9	6.6	13.3	9.2	10.6	10.0	9.7	9.5	10.9
ICER program model ($/DALY averted)	$240	$886	$886	$885	$1,076	$778	$888	$892	$911	$749
ICER task shifting model ($/DALY averted)	$240	$615	$614	$614	$730	$549	$616	$616	$621	$533

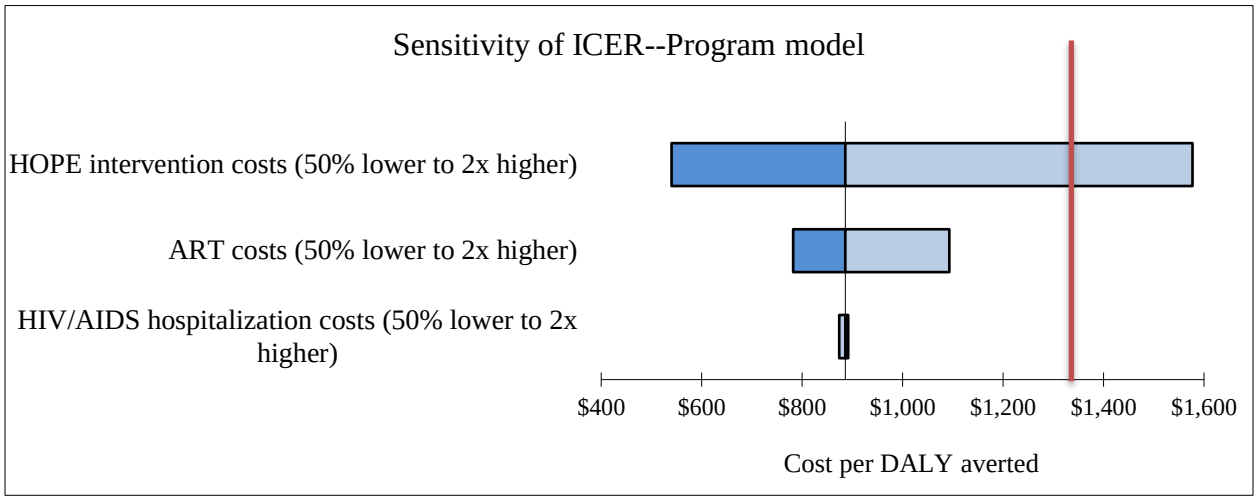
§ICER: incremental cost-effectiveness ratio; DALY: disability-adjusted life year. Costs and infections are over 10 year time horizon. Incremental costs and DALYS associated with each strategy are discounted. HOPE intervention is added to current ART expansion. Percent coverage refers to coverage of male partners of pregnant women. Costs are in 2014 USD.

¥All deaths, not only those related to HIV/AIDS.

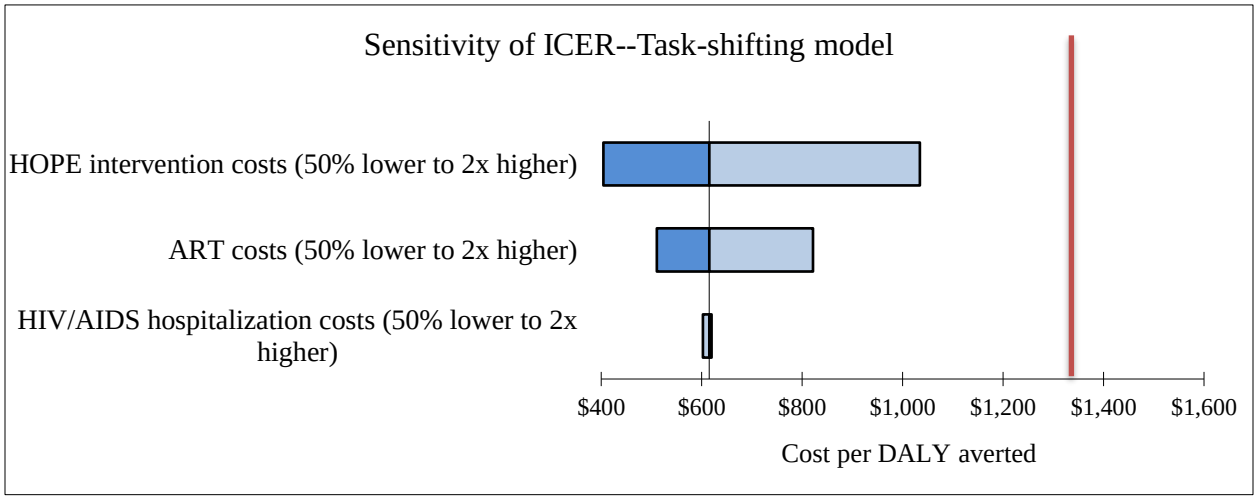
*Discounted health benefits

Figure 1: Tornado diagram of ICERs with varying costs*

a)



b)



*Red line represents Kenya's GDP per capita, the threshold utilized for cost-effectiveness.

Supplementary appendix
to:

Cost-effectiveness of home HIV testing and education for male partners of pregnant women in Kenya: A mathematical modeling analysis of the HOPE intervention

I. Technical Specifications

Model Overview:

The mathematical model simulates heterosexual HIV transmission and is parameterized to Kenya. The model reproduces population-level dynamics and stratifies the population by age, gender, and sexual risk. The model begins with an entirely HIV-negative population at time $t = 0$ with a size and distribution reflecting Nyanza in 1979. The population dynamics are governed by a system of ordinary differential equations (ODEs) that are solved in MATLAB 2014a[1]. The model iterates in three-month intervals. The natural history of HIV infection is modeled in stages defined by CD4 count and viral load as shown in Figure S1. When a person becomes HIV-infected, s/he enters the acute stage characterized by a short duration and high probability of HIV transmission. The person then progresses through stages of CD4 count and viral load. Pregnancy was incorporated into the model by the addition of health states for pregnancy stratified by CD4 count and viral load. Women transition into pregnancy states at a fertility rate determined by their age and CD4 count status (if HIV-positive). New births enter the population as a function of the fertility rate. Women have a 40% higher HIV susceptibility compared to men based on the UNAIDS Spectrum model will uses a ratio of female-to-male incidence of 1.4.[2]

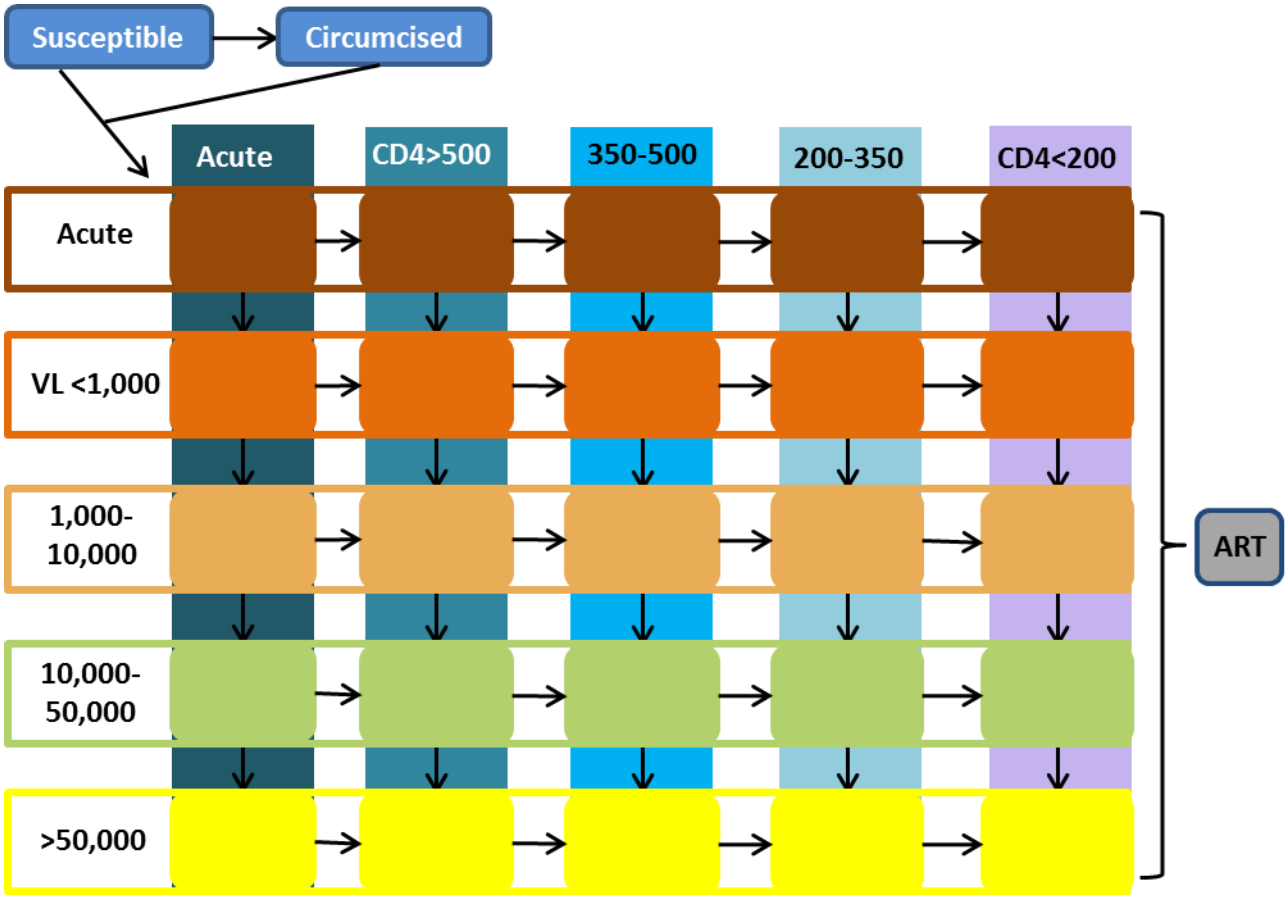


Figure S1. Model transition diagram. A diagram of the natural history of HIV infection. All movement is in one direction except for enrollment in and dropout from interventions from ART.

II. Interventions

ART Treatment Enrollment:

ART treatment is assumed to reduce the likelihood of HIV transmission by 96% and persons on ART are expected to have the same life expectancy as HIV-negative persons of similar age and sex, and thus, are assumed not to be subject to HIV-associated mortality [3-7]. The annual drop-out rate is 6%, which is equally likely for all individuals regardless of their HIV state prior to treatment. Individuals who drop out of ART return to the infected stages at the same proportion with which they enrolled. This model includes a background level of

circumcision of 66% as observed in Nyanza. We assume a 60% lower risk of acquiring HIV based on prior studies. [8-10]

III. Cost Parameters

Cost estimates:

Costs were collected onsite in June 2014 in Kisumu, Kenya from the HOPE study, a randomized control trial of home testing of male partners of pregnant women. Time and motion observation of the HOPE intervention was conducted to determine staff time and resource utilization per home visit and also to facilitate removal of research time and costs for the operational cost estimate. We observed that the HOPE educational component and couples HIV testing and counseling take approximately 1 hour per couple (slightly longer for couples with discordant HIV-status who require additional counseling). After accounting for travel time to participant's home, follow-ups, paperwork, and other staff responsibilities, we estimated that a community care worker could test 3 couples per day. We assumed a program of 20 community care workers and 4 supervisory nurses. Staff were assumed to work 7 hours per day, 215 days per year after accounting for national holidays, sick days, and paid vacations. Total program costs were divided by the number of persons tested by HIV status under each scenario to determine the cost per person tested. Supply costs per person tested included gloves, HIV screening test kit, lancet, cotton balls, and alcohol swabs. Additional supplies for HIV+ persons tested included confirmatory test, and tie breaker test (assumed to be used in 5% of all HIV+ cases).

Costs of a facility-based HIV test was obtained from a costing exercise conducted in Kenya and inflated to 2014 USD (Obure).[11] ART costs were estimated by using a multi-country analysis of treatment costs in five countries in sub-Saharan Africa.[12] Since costs for Kenya were

not evaluated, we generated a linear regression to describe the relationship between each country's GDP per capita and ART costs (R2=98%) (shown below). We then put the GDP per capita into the equation described below to estimate yearly ART costs: 150.47 + 0.0586*1,167.50 = $218.96 per year.

```
      Source |       SS       df       MS              Number of obs =       5
-------------+------------------------------           F(  1,     3) =  233.51
       Model |  132256.083     1  132256.083           Prob > F      =  0.0006
    Residual |    1699.117     3  566.372334           R-squared     =  0.9873
-------------+------------------------------           Adj R-squared =  0.9831

       Total |    133955.2     4     33488.8           Root MSE      =  23.799

------------------------------------------------------------------------------
        cost |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         GDP |    .058662   .0038388    15.28   0.001     .0464451    .0708789
       _cons |   150.4761    13.4603    11.18   0.002     107.6394    193.3128
------------------------------------------------------------------------------
```

We estimated the HIV-related hospitalization costs using primary cost data from South Africa (Meyer-Rath)[13] and adjusting it by multiplying by the ratio of ART costs in Kenya/South Africa from the model above.

IV. Epidemiological Parameters

Table S1. Initial population size. Nyanza total population 1979 size scaled with Kenya national data for age and sex distribution.

Age Cohort	Initial Population Size		Reference
	Male	Female	
0 – 4	293,191	287,674	Kenya Bureau of Statistics, UN population data [14,15]
5 – 9	221,895	218,405	
10 – 14	184,334	182,359	
15 – 19	149,528	151,279	
20 – 24	114,647	120,244	
25 – 29	89,629	95,951	
30 – 39	68,154	72,704	
35 – 39	54,083	57,338	
40 – 44	45,403	47,338	
45 – 49	37,906	38,974	
50 – 54	30,905	31,547	
55 – 59	25,188	25,279	
TOTAL	1,329,093	1,314,863	

Table S2. Total population size. Nyanza total population over time for model calibration

Year	Total population size	
1979	2,643,956	Kenya Bureau of Statistics[14]
1989	3,507,162	
2009	4,392,196	

Table S3. Sexual risk distribution by age and sex. Values are calibrated to fit age-specific HIV incidence and prevalence data.

Age Cohort	Male Risk Distribution			Female Risk Distribution			Reference
	Low-Risk	Moderate-Risk	High-Risk	Low-Risk	Moderate-Risk	High-Risk	
0 – 4	0.999	0.0005	0.0005	0.998	0.001	0.001	
5 – 9	0.999	0.0005	0.0005	0.998	0.001	0.001	
10 – 14	0.98	0.015	0.005	0.975	0.015	0.01	
15 – 19	0.80	0.17	0.03	0.80	0.17	0.03	
20 – 24	0.78	0.20	0.02	0.62	0.31	0.05	
25 – 29	0.65	0.29	0.06	0.60	0.35	0.05	Calibrated
30 – 34	0.66	0.28	0.05	0.65	0.30	0.05	to fit data
35 – 39	0.68	0.27	0.05	0.65	0.30	0.05	
40 – 44	0.75	0.20	0.05	0.78	0.17	0.05	
45 – 49	0.78	0.17	0.05	0.80	0.16	0.04	
50 – 54	0.88	0.08	0.04	0.85	0.13	0.02	
55 – 59	0.96	0.035	0.005	0.95	0.045	0.005	

Table S4. Annual number of sexual partnerships by age, gender, and sexual risk. Values are based on a previous study and calibrated to fit age-specific HIV incidence and prevalence data.

Age Cohort	Male Partnerships per Year			Female Partnerships per Year			Reference
	Low-Risk	Moderate-Risk	High-Risk	Low-Risk	Moderate-Risk	High-Risk	
0 – 4	0.00006	0.00006	0.00006	0.00006	0.00012	0.00012	Adapted from Barnabas *et al.* [13]
5 – 9	0.0006	0.006	0.06	0.0007	0.007	0.12	
10 – 14	0.006	0.06	0.6	0.006	0.06	0.9	
15 – 19	0.1	1.8	41.0	0.1	0.6	32.2	
20 – 24	0.3	2.3	41.0	0.4	3.5	61.4	
25 – 29	0.6	4.7	52.7	0.4	2.9	58.5	
30 – 34	0.6	5.3	52.7	0.4	4.1	59.7	
35 – 39	0.5	4.1	52.7	0.4	3.5	54.4	
40 – 44	0.5	2.3	46.8	0.3	2.9	49.7	
45 – 49	0.5	2.3	43.9	0.3	2.9	43.9	
50 – 54	0.5	2.9	46.8	0.3	2.3	30.4	
55 – 59	0.4	1.8	35.1	0.1	0.3	5.9	

Table S5. Background mortality. Values for age 5-59 years are Kenya's age-specific mortality in 1990, prior to the generalized HIV epidemic. Values for under 5 mortality are 2012 mortality estimates adjusted for the contribution of HIV/AIDS to mortality using UNAIDS World Mortality Report[16].

Age Cohort	Background Mortality		Reference
	Male	Female	
0 – 4	0.01502	0.01304	UNICEF [17]
5 – 9	0.00405	0.00345	WHO [18]
10 – 14	0.00216	0.00195	
15 – 19	0.00295	0.00245	
20 – 24	0.00457	0.00338	
25 – 29	0.00511	0.00395	
30 – 34	0.00551	0.00428	
35 – 39	0.00610	0.00475	
40 – 44	0.00709	0.00573	
45 – 49	0.00842	0.00680	
50 – 54	0.01176	0.00874	
55 – 59	0.01575	0.01157	

Table S6. Fertility rate by age and HIV status. Females on ART are assumed to have equal fertility to HIV-negative females. Source: DHS 2008 Kenya rural estimates. [19]

Age Cohort	Fertility Rate (per year)					Reference
	Uninfected RR=1	**Acute** RR=1	**>350** RR=0.59	**200-350** RR=0.42	**<200** RR=0.42	
0 – 4	0	0	0	0	0	Anderson *et al.*, Ross *et al.* [20,21]
5 – 9	0	0	0	0	0	
10 – 14	0	0	0	0	0	
15 – 19	0.108	0.064	0.046	0.108	0.064	
20 – 24	0.289	0.171	0.122	0.289	0.171	
25 – 29	0.262	0.155	0.110	0.262	0.155	
30 – 34	0.209	0.123	0.088	0.209	0.123	
35 – 39	0.141	0.083	0.059	0.141	0.083	
40 – 44	0.061	0.036	0.025	0.061	0.036	
45 – 49	0.013	0.008	0.006	0.013	0.008	
50 – 54	0	0	0	0	0	
55 – 59	0	0	0	0	0	

Table S7. HIV-associated mortality. Values are estimates are from observational studies of untreated HIV-positive persons.

Age Cohort	HIV Mortality				Reference
	Acute	**CD4>350**	**CD4 200 to 350**	**CD4<200**	
0 – 4	0.47	0.47	0.47	0.47	Newell *et al.* [22]
5 – 49	0.01	0.05	0.08	0.27	Badri *et al.* [23]
50 – 59	0.02	0.10	0.16	0.54	Adler *et al.* [24]

Table S8. Probability of HIV transmission by viral load.

Baseline Transmission Probability	Increase in transmission probability by HIV stage						Reference
	Acute	VL≤1,000	VL 1,000-10,000	VL 10,000-50,000	VL>50,000	ART	
0.00053	26	1	5.8	6.9	11.9	0.04	Quinn *et al.*, Boily *et al.* [25,26]

Table S9. The duration of time in each CD4 and viral load stage by sex (Ying et al. [27])

CD4 Transition	Acute	CD4>500	500-350	350-200
Time for Males (years)	0.25	1.71	1.05	4.71
Time for Females (years)	0.25	1.94	1.35	6.71
Viral Load Transition	**Acute**	**VL≤1,000**	**1,000-10,000**	**10,000-50,000**
Time for Males (years)	0.25	3.44	1.45	3.04
Time for Females (years)	0.25	3.06	2.27	5.45

Table S10. Proportion of births from HIV-positive females that result in mother-to-child transmission

Year	MTCT rate	Reference
Overall	0.151	Sirgeno *et al.* [28]
Without PMTCT	0.25	Connor et al[29]
With PMTCT	0.05	Thomas et al[30]

Table S11. Coverage treatment for prevention of mother to child transmission (PMTCT)*

Kenya estimate		
Year	**PMTCT coverage**	**Reference**
2012	0.901	Kenya AIDS Indicator Survey[31]

*Among women who were tested at the clinic or aware of HIV infection

Table S12. Proportion of pregnant women attending antenatal care during last pregnancy

Nyanza estimates		
Year	**ANC coverage**	**Reference**
2012	0.968	Kenya AIDS Indicator Survey[31]

Table S13. The number of coital acts per partnership by gender and sexual risk group. Values are calibrated to fit age-specific HIV incidence and prevalence data.

Gender	**Coital Acts per Partnership**			**Reference**
	Low-Risk	**Moderate-Risk**	**High-Risk**	
Male	99	33	3.3	Calibrated to fit data
Female	77	22	3.3	

Table S14. Sexual mixing by age and sexual risk group. The mixing parameter varies from random ($\boldsymbol{\epsilon = 1}$) to assortative ($\boldsymbol{\epsilon = 0}$), calibrated to fit age-specific HIV incidence and prevalence data.

Year	**Force of Infection Mixing**		**Reference**
	$\boldsymbol{\epsilon_a}$ **(age)**	$\boldsymbol{\epsilon_r}$ **(sexual risk)**	
Before 1998	0.7	0.7	Calibrated to fit data
2003	0.5	0.5	
After 2010	0.1	0.1	

Table S15. HIV prevalence for model calibration

Kenya national data		**Reference**
Year	**Prevalence**	
1995	0.105	Kenya AIDS Indicator Surveys[31,32]
2003	0.067	
2007	0.071	
2008	0.063	
2010	0.062	
2012	0.056	
Nyanza data		
Year	**Prevalence**	
2003	0.151	Kenya AIDS Indicator Surveys[31,32]
2007	0.149	
2008	0.139	
2012	0.151	

Table S16. Age-specific HIV prevalence: Nyanza estimates*

Age	2012 HIV prevalence		Reference
	Male	Female	
15 – 19	0.028	0.026	
20 – 24	0.041	0.107	
25 – 29	0.136	0.184	
30 – 34	0.209	0.154	Kenya AIDS
35 – 39	0.158	0.287	Indicator
40 – 44	0.256	0.247	Survey [31]
45 – 49	0.281	0.250	
50 – 54	0.212	0.238	
55 – 59	0.117	0.119	

*Estimates were calculated by using Kenya national prevalence data scaled up to reflect the overall HIV prevalence of Nyanza.

Table S17. Utility weights for estimating disability-adjusted life-years averted

Health State	**DALY Weight** Salomon *et al.* [33]
HIV-negative	0
HIV-positive CD4>350	0.053
HIV-positive CD4 200-350	0.221
HIV-positive CD4<200	0.547
HIV-positive on ART	0.053
Dead	1

Table S18. Coverage of adult voluntary medical male circumcision:

Nyanza estimates		Reference
Year	**Male circumcision coverage**	
2012	0.66	Kenya AIDS Indicator Survey[31]

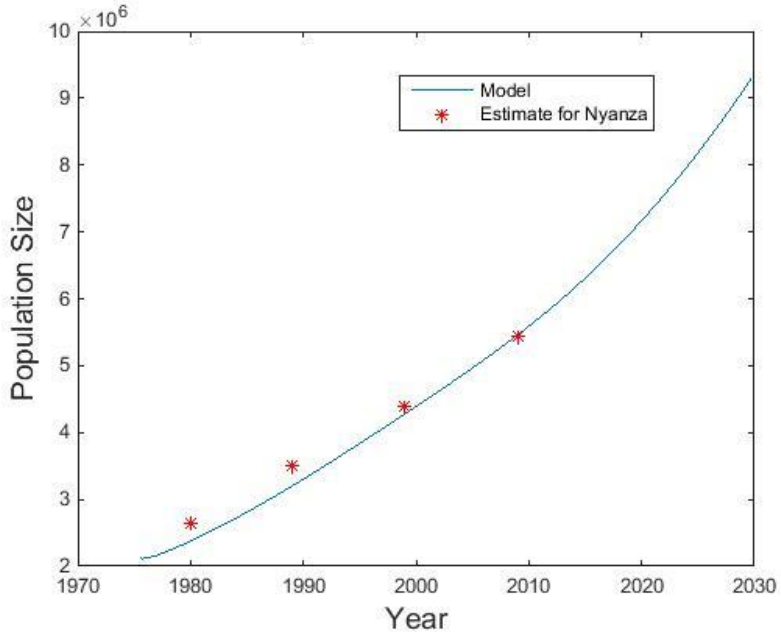
Table S19. Proportion of HIV-positive persons receiving ART

Kenya estimates		Reference
Year	**ART coverage**	
2006	0.10	World Bank Development Indicators[34]
2007	0.14	
2008	0.19	
2009	0.27	
2010	0.33	
2011	0.41	
2012	0.46	
2013	0.49	
2014	0.55	

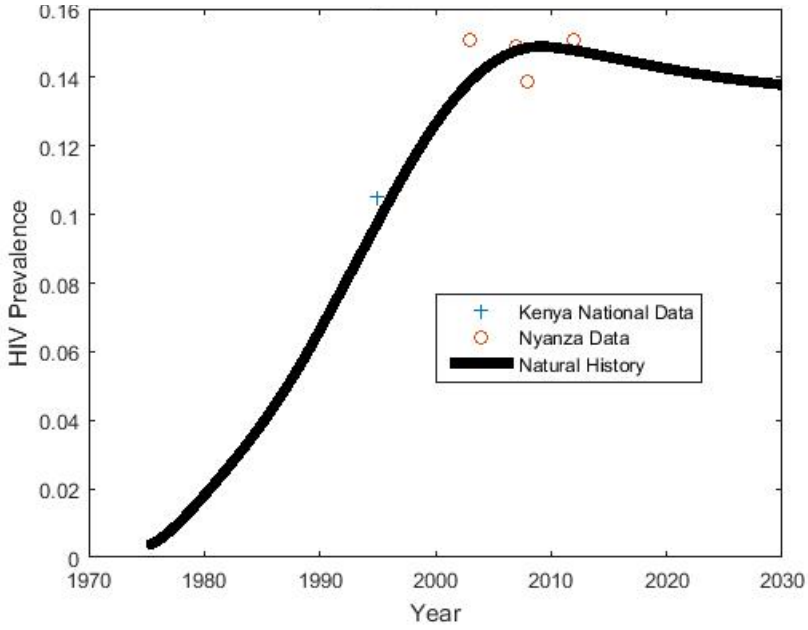
V. Calibration results

The following figures display model outputs and primary data from Kenya and Nyanza listed in the tables in the previous section of this supplemental appendix.

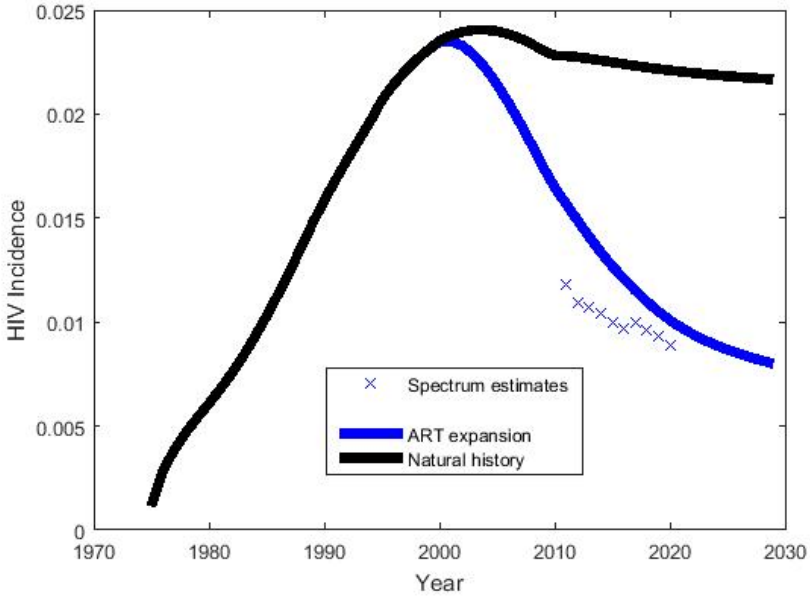
Population size



HIV prevalence over time



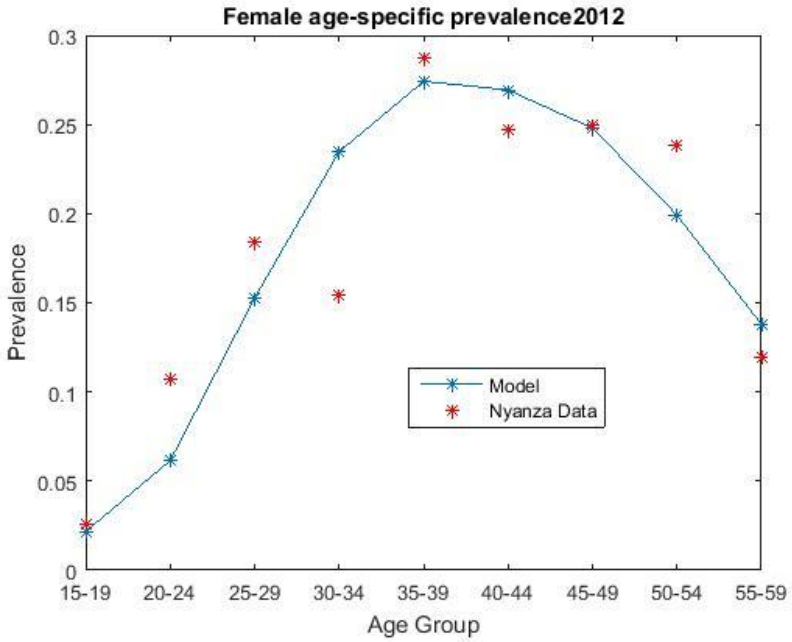
HIV incidence over time*



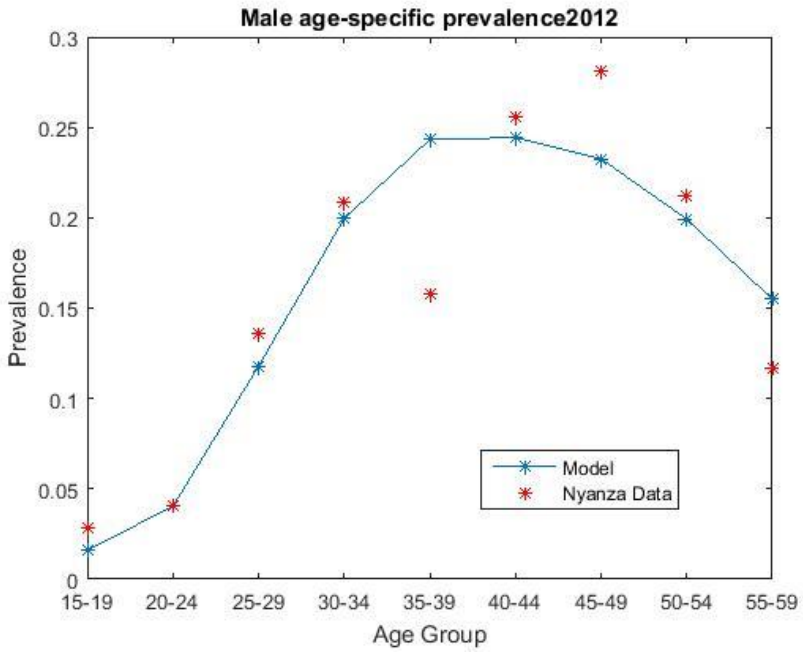
*HIV incidence estimates were obtained from the UNAIDS Spectrum model[2]

Age-specific HIV prevalence

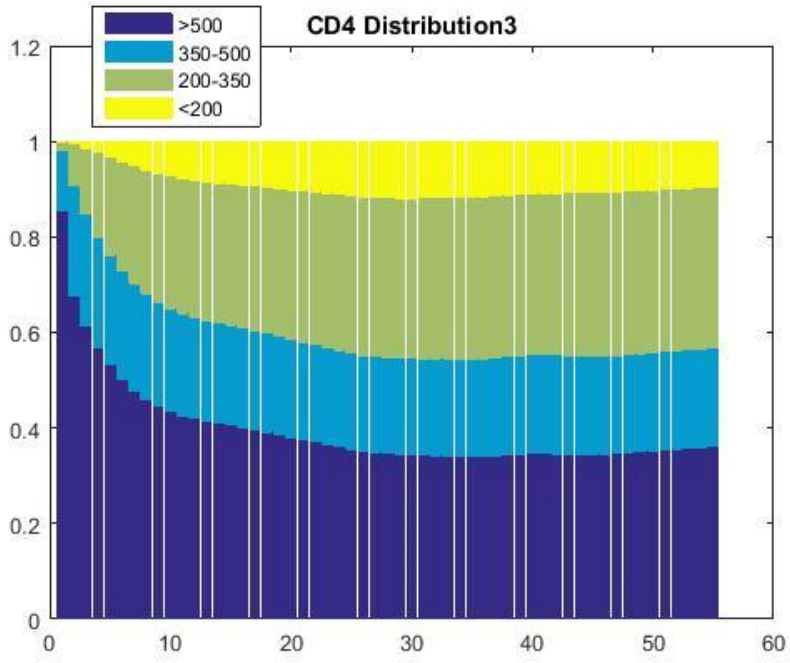
Females:



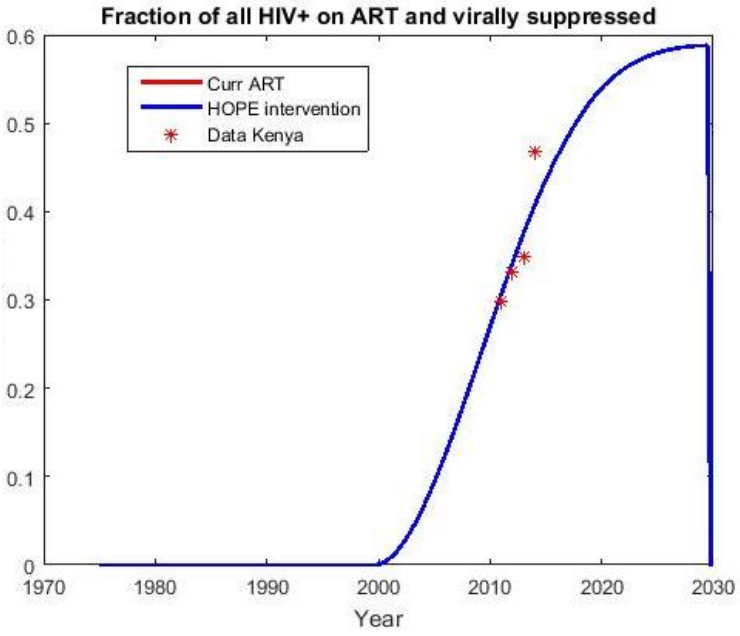
Males:



CD4 Distribution over time



ART Coverage



Primary data on ART coverage reduced by 15% assuming not all persons are virally suppressed.

VI. Additional Results

Cost-effectiveness of the HOPE intervention at lower efficacy (i.e. just 30% increase in likelihood of linking to ART)*

	Current ART scale up	**HOPE intervention with 30% increased probability of ART linkage**
HIV infections averted	--	1,213
DALYs averted	--	5,410
Incremental costs study model (millions)	--	12.2
Incremental costs task shifting model (millions)		6.0
ICER program model ($/DALY averted)	$240	$2,251
ICER task shifting model ($/DALY averted)	$240	$1,105

*Costs and health benefits discounted at 3% annually.

VII. References

1. MATLAB and Statistics Toolbox Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States.
2. Spectrum UNAIDS HIV Model. Available at: http://www.unaids.org/en/dataanalysis/datatools/spectrumepp.
3. Mills EJ, Bakanda C, Birungi J, et al. Mortality by baseline CD4 cell count among HIV patients initiating antiretroviral therapy: evidence from a large cohort in Uganda. AIDS (London, England) 2011;25:851-5.
4. Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS (London, England) 2009;23:1397-404.
5. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.
6. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet 2010;375:2092-8.
7. Jahn A, Floyd S, Crampin AC, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. Lancet 2008;371:1603-11.
8. 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 medicine 2005;2:e298.
9. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet 2007;369:657-66.
10. Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. AIDS (London, England) 2000;14:2361-70.
11. Obure CD, Vassall A, Michaels C, et al. Optimising the cost and delivery of HIV counselling and testing services in Kenya and Swaziland. Sex Transm Infect 2012;88:498-503.
12. Tagar E, Sundaram M, Condliffe K, et al. Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia. PloS one 2014;9:e108304.
13. Meyer-Rath G, Brennan AT, Fox MP, et al. Rates and cost of hospitalization before and after initiation of antiretroviral therapy in urban and rural settings in South Africa. Journal of acquired immune deficiency syndromes (1999) 2013;62:322-8.
14. Kenya National Bureau of Statistics. Accessed on 11/10/2015 from: http://www.prb.org/pdf11/kenya-population-data-sheet-2011.pdf.
15. UN Population data. Accessed from: http://data.un.org/Data.aspx?d=POP&f=tableCode%3A22 on 11/9/2015.
16. World Mortality Report 2011. United Nations. Accessed on 10/27/2015 from http://www.un.org/en/development/desa/population/publications/pdf/mortality/worldMortalityReport2011.pdf.
17. South Africa Basic Indicators. United Nations Children's Education Fund. at http://www.unicef.org/infobycountry/southafrica_statistics.html.)
18. Life Tables for WHO Member States: Kenya. Accessed on 10/28/2015 from: http://www.who.int/gho/countries/ken/en/. Geneva: World Health Organization.
19. UNAIDS Demographic Health Survey: Kenya 2008. Accessed from http://pdf.usaid.gov/pdf_docs/Pnadq650.pdf on 10/15/2015.
20. Anderson R, May R, Ng T, Rowley J. Age-Dependent Choice of Sexual Partners and the Transmission Dynamics of HIV in Sub-Saharan Africa. Phil Trans R Soc London B 1992;336:135 - 55.

21. Ross A, Van der Paal L, Lubega R, Mayanja BN, Shafer LA, Whitworth J. HIV-1 disease progression and fertility: the incidence of recognized pregnancy and pregnancy outcome in Uganda. AIDS (London, England) 2004;18:799-804.
22. Newell ML, Coovadia H, Cortina-Borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. Lancet 2004;364:1236-43.
23. Badri M, Lawn SD, Wood R. Short-term risk of AIDS or death in people infected with HIV-1 before antiretroviral therapy in South Africa: a longitudinal study. Lancet 2006;368:1254-9.
24. Adler WH, Baskar PV, Chrest FJ, Dorsey-Cooper B, Winchurch RA, Nagel JE. HIV infection and aging: mechanisms to explain the accelerated rate of progression in the older patient. Mech Ageing Dev 1997;96:137-55.
25. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med 2000;342:921-9.
26. Boily MC, Baggaley RF, Wang L, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. The Lancet infectious diseases 2009;9:118-29.
27. Ying R, Sharma M, Heffron R, et al. Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda. Journal of the International AIDS Society 2015;18:20013.
28. Sirengo M, Muthoni L, Kellogg TA, et al. Mother-to-child transmission of HIV in Kenya: results from a nationally representative study. Journal of acquired immune deficiency syndromes (1999) 2014;66 Suppl 1:S66-74.
29. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med 1994;331:1173-80.
30. Thomas TK, Masaba R, Borkowf CB, et al. Triple-antiretroviral prophylaxis to prevent mother-to-child HIV transmission through breastfeeding--the Kisumu Breastfeeding Study, Kenya: a clinical trial. PLoS medicine 2011;8:e1001015.
31. Kenya AIDS indicator Survey 2012. Accessed on 1/1/2016 from: http://www.nacc.or.ke/images/documents/KAIS-2012.pdf.
32. Kenya AIDS indicator Survey 2007. Accessed on 10/1/2015 from: http://www.wofak.or.ke/Publications/kais__preliminary_report_july_29.pdf.
33. Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 2012;380:2129-43.
34. World Bank Development Indicators: Antiretroviral therapy coverage (% of people living with HIV). Accessed on 11/9/2015 from: http://data.worldbank.org/indicator/SH.HIV.ARTC.ZS?page=1.

CHAPTER 4: Cost-effectiveness of implementing assisted partner notification for HIV in Kenya: A mathematical modeling analysis

Cost-effectiveness of implementing assisted partner notification for HIV in Kenya: A mathematical modeling analysis

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Conflicts of interest: None

Key words: HIV counseling and testing, sub-Saharan Africa, partner notification, mathematical modeling, cost-effectiveness

Abstract

Background: Assisted partner services (aPS) or provider notification for sexual partners of persons diagnosed HIV-positive can increase HIV testing and linkage to care in sub-Saharan Africa. Additionally, aPS is a high yield strategy to identify persons with HIV. However, aPS is resource intensive and its cost-effectiveness is not well-evaluated.

Methods: Using primary cost and effectiveness data from a randomized clinical trial of aPS in Kenya, we parameterized an individual-based, stochastic, dynamic mathematical model of HIV transmission. The model incorporates partner concurrency, migration, coinfection with sexually transmitted infections, household structure, and health seeking behavior. We simulated 200 cohorts of 500,000 individuals and calculated the incremental cost-effectiveness of scaling up aPS in a region of western Kenya (formerly Nyanza Province) under different thresholds of ART initiation (CD4≤350, CD4≤500, and all HIV+ persons), with CD4≤500 as the base-case.

Findings: Over a 10 year time horizon, adding aPS to standard of care in western Kenya is projected achieve 12% population coverage and reduce HIV infections by 2.8% and HIV-related deaths by 1.5%. The incremental cost-effectiveness ratio (ICER) of implementing aPS is $1,703 USD (range $1,198-2,887) per disability-adjusted life year (DALY) averted. Task-shifting intervention activities from healthcare professionals to community health workers decreases the ICER to $1,302 (range $955-2,789) per DALY averted. The task-shifting scenario falls below Kenya's per capita gross domestic product (GDP) and is therefore considered very cost-effective while the full program cost scenario is considered cost-effective under the higher threshold of 3-times Kenya's per capita GDP. Intervention cost-effectiveness and HIV-related deaths averted among aPS partners increased with expanded ART initiation criteria.

Interpretation: APS is a cost-effective strategy to reduce HIV associated morbidity in western Kenya and other similar settings. Task-shifting to community health workers will likely be necessary to increase program affordability.

Introduction

Over 70% of HIV-positive persons live in Sub-Saharan Africa (SSA), a region disproportionately affected by the epidemic. In 2013, there were 1.5 million new HIV infections and 1.1 million AIDs-related deaths in SSA.[1] Despite high burden, only 50% of HIV-positive individuals are aware of their status.[2,3] Knowledge of one's serostatus is vital for accessing lifesaving antiretroviral therapy (ART) and preventing onward transmission. A substantial proportion of HIV transmission is estimated to occur from individuals who are unaware that they are infected.[4] HIV-positive individuals in SSA are generally identified through facility-based HIV testing. However testing coverage is low in SSA and will likely be insufficient to curb the epidemic.[5] Barriers to facility testing include distance from clinic, long wait times, costs, and concerns about confidentiality.[6,7] In addition, HIV-positive individuals often present for care when they are symptomatic, late in the course of their illness.[8]

To address HIV burden, UNAIDS has created ambitious 90-90-90 targets—90% of HIV-positive persons knowing their status, 90% of HIV-positive persons who are aware of their status on ART, and 90% of persons on ART virally suppressed.[9] Identifying and evaluating innovating HIV testing interventions can assist in reaching these targets. One promising strategy is partner notification services.[10] Partner services (PS), refers to efforts to identify sex partners of persons diagnosed with a sexually transmitted disease, notify them of their potential exposure, provide counseling, testing, and referral to treatment and prevention. Types of partner services include: 1) passive referral—the newly diagnosed individual (index case) is asked to notify their sexual partners of potential exposure and encourage them to seek HIV testing, 2) provider notification or assisted partner services (aPS)— healthcare providers contact sexual partners directly and provide counseling and testing, and 3) contract referral—the index patient is given a certain

amount of time to contact their partners, after which the healthcare provider conducts notification.[11] Partner services are widely implemented in high income countries and growing evidence from sub-Saharan Africa shows PS is feasible and acceptable.[12] APS was recently scaled up by the Ministry of Health in Cameroon and achieved 66% coverage of reported sexual partners. HIV positivity in sexual partners was high (50%) and 86% of those found positive were enrolled in care.[12] Index cases were identified through facility testing and given a choice of passive, provider, or contract referral, but the majority index cases chose provider referral. Most sexual partners preferred to test outside the healthcare facility, highlighting the importance of having community-based testing options. A recent PS randomized control trial with three arms in Malawi attained 51% coverage of partners in both the provider and contract referral arms compared to only 24% in the passive referral arm; overall 64% of partners tested HIV-positive and most had high CD4 counts (median 344 cells/uL) including one acutely infected partner.[13] The high HIV positivity found through APS interventions are similar to those reported in the literature of 45-50% prevalence in cohabitating partners of HIV-positive adults, the vast majority of whom are unaware of their status.[14] In addition, the high CD4 counts of HIV-positive partners reflect the ability of PS to reach individuals early in earlier in their course of infection, which can allow a shorter time to linkage to care. Early ART initiation improves patient survival, preserves the immune system, and delays HIV progression.[15]Additionally, ART averts future infections by reducing HIV transmission from virally suppressed individuals by up to 96%.[16,17] PS can also be used as a prevention tool to target Pre-Exposure Prophylaxis (PrEP) to HIV-negative persons in a serodiscordant partnership who are at high risk of acquiring HIV.[18] In light of the recently released WHO guidelines which recommend immediate treatment for individuals diagnosed with

HIV and PrEP for those at substantial risk of infection, HIV testing interventions that identify persons in need of both treatment and prevention will likely be needed.[19]

Although aPS has been shown to be effective in sub-Saharan Africa, its cost-effectiveness is not well evaluated. Implementing aPS requires significant economic investment so determining its efficiency is crucial, particularly in settings with limited resources. We utilize mathematical modeling to assess the cost-effectiveness of implementing assisted provider notification for sexual partners of newly diagnosed index cases in Kenya. Primary cost and effectiveness data were collected from the aPS study, a cluster randomized controlled trial conducted in Kenya in which communities were randomized to either provider notification (intervention arm) or passive referral (standard of care) followed by aPS after a 6-week delay (delayed arm). In this analysis, we project the health and economic impact of implementing aPS throughout the former Nyanza province, a region of Western Kenya with high HIV prevalence (15.1%).[20] Our analysis can be useful to policy makers in SSA charged with deciding which HIV interventions to implement to maximize health benefits within a fixed budget.

Methods

Assisted Partner Services (aPS) intervention

The aPS study was a large-scale cluster randomized clinical trial conducted in 18 communities across Kenya (9 intervention and 9 control (delayed intervention) sites) from May 2013-May 2015.[21] Study staff were based in health care facilities in each community and provided HIV testing and counseling to individuals presenting at the facility through both voluntary counseling and testing (VCT) and provider initiated testing and counseling (PITC). Sixty individuals testing HIV-positive per community (index cases) were enrolled into the trial

(inclusion criteria: ≥18 years, positive HIV test at study site, willing to disclose sexual partners, and never enrolled for HIV care; exclusion criteria: pregnancy or high risk of intimate partner violence). Index cases provided names and contact information for all sexual partners in the past 3 years. At intervention sites, study staff immediately contacted sexual partners to notify them of exposure, offer HIV testing, and encourage linkage to care for those found HIV-positive. At control sites, passive partner referral was conducted according to national guidelines and assisted partner notification was performed after a 6 week delay. The study approached 1,776 index partners, of whom enrolled 1,119 enrolled (63% acceptance rate) and listed 1,872 sexual partners. Overall 69% of the sexual partners were located and enrolled (620 in the intervention arm and 672 in the control arm). Partner enrollment rates were slightly higher in Nyanza province, 72% (258/339) the immediate arm. The intervention was found to be effective; HIV testing in sexual partner during the 6 weeks following index partner diagnosis was higher in the intervention compared to delayed arm (41% vs. 9%). The majority of sexual partners chose to test outside healthcare facilities HIV testing (most often at their homes). Study staff also facilitated couples HIV testing and counseling and disclosure when appropriate.

Mathematical model:

We adapted a previously published individual-based dynamic HIV transmission model to epidemiologic, clinical, and economic data from Nyanza, Kenya.[22] **(Figure 1)** Full model specifications have been published previously, and model details are available in the **Supplemental Appendix.**[22] Briefly, the model simulates the natural history of HIV/AIDS using monthly transitions probabilities and incorporating stochastic variability. For HIV-positive persons, CD4 count declines over time based on clinical estimates. Men and women are characterized by age (18 years and older), sexual activity (low, medium, and high), circumcision

status, condom use, herpes simplex virus (HSV) infection status and CD4 count (if HIV-positive). Individuals can form partnerships with an adult of the opposite sex (with a tendency for the male partner to be slightly older than the female). Persons can form either long-term or short-term partnerships, and can have up to two concurrent partnerships (with only one being long-term). The model accounts for migration patterns by allowing a proportion of individuals to be absent from the community for 3 months each year, during which time they can form external partnerships (i.e. outside of the community). Community residents can also form external short-term partnerships. Nyanza-specific demographics, household structure, migration patterns, HIV prevalence, sexual behavior, and condom use by relationship type and HIV-status were obtained by analyzing the UNAIDS Kenya AIDs Indicator Survey (KAIS) 2012 dataset.[23] The model was calibrated to age-specific and overall HIV prevalence in Nyanza. Model data and calibration results are available in the **Supplemental Appendix**.

The model estimates the force of HIV infection as a function of sex, condom use, HSV infection, CD4 count and ART status of partner, and male circumcision status. Disability weights are assigned to each HIV state.[24] In addition to background mortality (estimated from Kenya mortality rates prior to the HIV-epidemic), HIV-positive individuals face a disease-specific mortality that varies by age and CD4 count. Persons on ART are assumed to have the same mortality rates as those who are uninfected.[25] The model simulates HIV testing, clinic visits, and ART initiation. Dropout of ART occurs yearly and individuals are assumed to return to the CD4 count and viral load status they had prior to initiating ART. We simulated a community of 231,850 households with a mean population of 500,000 adults. We ran the model 200 times and summarized results over 10 years and use the 5^{th} and 95^{th} percentile outcomes to represent 90% stochastic model variability.

Status quo and intervention scenarios:

For the status quo (no intervention), scenario, we modeled the impact of current rates of facility HIV testing and ART initiation.[26] Individuals have a monthly probability of undergoing HIV testing and counseling that depends on their sex, HIV status, and CD4 count (if infected). For HIV-negative individuals, repeat testing can occur as early as one year after initial test, with the same testing probability. Individuals testing HIV-positive have a monthly probability of linking to care and subsequently initiating ART which depends on their CD4 count. Health-care seeking behavior (including probabilities of undergoing an HIV test and linking to ART) were estimated using KAIS 2012 data for Nyanza.[23] Additional assumptions are detailed in the **Supplemental Appendix**.

In the intervention scenario, newly diagnosed HIV-positive index cases have a probability of consenting to aPS and providing names of sexual partners that is based on the RCT (71%). Similarly, sexual partners of index cases have a sex-dependent probability of being located and consenting to the intervention based on the aPS trial (68% and 57% for women and men respectively who are not aware of their HIV-status 6% for all persons aware of their HIV-positive status). Only partner who are present in the community (i.e. not currently migrating) and not currently on ART can consent to aPS, although the intervention can re-test unlinked HIV-positive individuals. Additionally, we assumed that individuals testing HIV-positive through aPS would link to ART at the same CD4-dependent background rate as those testing at the facility, as was found in the aPS trial.

Micro-costing:

A detailed micro-costing was conducted following established guidelines for costing HIV interventions in three aPS study clinics in Nyanza, Kenya.[27,28] Primary cost data were collected from budgets, expense reports staff, expert interviews, and travel logs. Costs were divided into mutually exclusive categories of: personnel, transportation, equipment, supplies, buildings and overhead, start-up, and phones and data monitoring. Time and motion studies were conducted over three weeks (June 10-30th 2014) to record staff time spent on intervention activities (e.g. tracing sexual partners, traveling to partners' homes, conducting HIV testing). Research time (administering informed consent, reimbursements, etc.) and other research costs were removed from the programmatic costs. The time and motion observations and interviews with staff were used to inform efficiency assumptions about the average number of partners that can be tested per day. Capital costs (e.g. motorcycles, office furniture), software development, and start-up cost (e.g. staff hiring, training, and community mobilization) were annualized assuming a 5-year useful life expectancy and discounted annually at 3%. Costs were inflated to 2014 US dollars using the Kenya consumer price index.[29] Supply costs per person tested included gloves, HIV screening test kit, and alcohol swabs.[29] Additional supplies for HIV-positive persons included confirmatory test, and tie breaker test (assumed to be used in 5% of all HIV-positive cases). Supply wastage was assumed to be 5%. Transport costs included motorcycles fuel as well as public transportation. Economic costs were estimated for donated goods, including hospital space.

Costs were estimated for two scenarios: 1) a higher cost program model, similar to the staff structure of the research study— with health advisors conducting aPS, a highly trained project supervisor, and research compatible mobile phones, and 2) a lower cost task-shifting

model in which health advisors are replaced with community health workers, the project supervisor is replaced with a community health worker manager, the data manager is reduced to a half-time position, and the program tests partners with 25% lower efficiency. Total program costs were divided by the number of partners tested by HIV status under each scenario to determine the cost per person tested. Costs per partner tested was estimated separately for HIV-positive and HIV-negative persons as the former required more staff time for counseling and additional diagnostics supplies. Other costs including HIV testing, ART, and HIV/AIDS related hospitalizations were estimated from the literature;[30-32] additional information is available in the **Supplementary Appendix**. All other healthcare-related costs were adapted from the literature (**Table 1**).[31,33]

Cost-effectiveness analysis:

We calculated the incremental cost-effectiveness ratio (ICER) of adding the aPS intervention to standard antenatal care per disability adjusted life year (DALY) averted over a 10-year time horizon. The ICER is measured as the additional cost divided by the additional health benefit of the intervention strategy compared to the next less costly strategy (in this case, the status quo). Consistent with health economic conventions, we considered an intervention to be very cost-effective if the ICER was less than Kenya's 2014 GDP per capita (1,358 USD) and cost-effective if the ICER was less than 3-times Kenya's per capita GDP.[34]

Sensitivity analyses

As HIV treatment initiation guidelines are a moving target—Kenya has recently expanded ART eligibility all HIV-positive persons, which is not yet fully implemented—we

assessed the health and economic impact of aPS under different ART initiation thresholds: ≤350 cells/uL, ≤500 cells/uL, and universal ART initiation. In addition, we evaluate two scenarios of intervention costs. We considered the ART initiation threshold of CD4≤500 cells/uL to be the base case, as the guidelines have just recently expanded to all HIV-positive persons.

Results

Micro-costing:

The time and motion observations showed that the aPS intervention takes approximately 40 minutes once a partner is successfully traced. After accounting for time needed for index case screening, partner tracing (including phone calls with partners to set meeting time, travel time to partners' home), unsuccessful tracings, paperwork, and other staff responsibilities, we estimated that health advisors could test approximately 2 partners per day with 25% lower efficiency for community health workers. Staff were estimated to work 7 hours per day for 215 days per year (after accounting for holidays, vacation, and sick time). Costs per partner tested ranged from $48-55 for the program model and $27-32 for the task-shifting model. Staff salaries represented the bulk of the costs (65-70%) **(Table 2)**.

Model estimated health and economic impact of aPS

The aPS intervention was estimated to achieve 12% population coverage over a 10 year time horizon with an HIV-positivity of 24% in sexual partners tested. Under the base-case scenario (ART initiation at CD4≤500 cells/uL), aPS was estimated to avert 2.8% of HIV infections and 1.5% of HIV-related deaths, and 0.8% of DALYs compared to status-quo (standard of care) **(Table 3)**. Intervention health impact for the total population and HIV

infections averted in aPS partners remained stable under all three ART initiation criteria. However, HIV-related deaths averted in aPS partners increased with expanding ART initiation criteria. With the base-case ART initiation of CD4≤500 cells/uL, 6.7% deaths were averted among APS partners. Assuming universal ART initiation, HIV-related deaths averted among aPS increased to 7.6% deaths averted while lower CD4 initiation of 350 cells/uL was associated with 5.5% deaths averted.

Similar to HIV-related deaths, aPS cost-effectiveness increased with expanding ART initation criteria, as did the percentage of ICERs that fell under the threshold of Kenya's per capita GDP. In the base-case scenario, the incremental cost-effectiveness ratio of implementing aPS was $1,703 per DALY averted (90% model variability $1,119-2,887) using higher cost program scenario and $1,302 per DALY averted (90% model variability $955-2,789) under the task-shifting scenario. The ICER associated with the task-shifting scenario fell below Kenya's per capita GDP ($1,358) and were therefore considered very cost-effective while the ICER for the full program costs was only cost-effective under the expanded criteria of 3-times Kenya's per capita GDP. With task-shifting costs, 54% of model simulations fell below Kenya's per capita GDP, and 100% fell below 3-times the GDP. Using full program costs, 22% and 100% of model simulations fell below Kenya's per capita GDP and 3-times GDP, respectively. **Figure 2** displays the model estimated health benefits and costs associate with the three health outcomes assessed (DALYs, HIV infections, and HIV-related deaths averted). Health benefits varied by model run as a result of stochastic variability, but all runs projected positive health gains.

Discussion

APS can cost-effectively reduce HIV-related morbidity and mortality in western Kenya by reaching HIV positive persons earlier in the course of their disease, before they would have

presented at a facility for HIV testing. In SSA, where the primary driver of the HIV-epidemic is heterosexual transmission and 50% of HIV-positive persons do not know they are infected, aPS is a promising strategy to fill in testing gaps. The high HIV positivity found in the modeled results as well as several clinical trials demonstrates that aPS is an efficient and high yield method to target resources towards those at highest risk of HIV infection. Although aPS is only projected to achieve 12% population coverage over 10 years, the intervention has a considerable impact on HIV burden (reducing infections by 2.8% in the base-case scenario). In contrast, passive notification (standard of care) has had low success in SSA, with few partners coming to the clinic for HIV testing. The 7% projected deaths averted in aPS partners indicate that the intervention reaches persons who may otherwise have not accessed care. Intervention impact among aPS partners is projected to increase with expanding ART eligibility thresholds; this can be partially attributed to the high CD4 counts of partners identified who would not be eligible for ART at lower thresholds.

We conservatively assumed that aPS would only provide benefits to sexual partners who are newly diagnosed HIV-positive through the intervention and would not impact HIV-negative or unlinked HIV-positive partners. Therefore the largest projected intervention impact was on HIV-related deaths in aPS partners. However, aPS likely reduces transmission by notifying HIV-negative persons that they are at high-risk of HIV acquisition and facilitating couples HIV-testing and disclosure. Indeed, the aPS clinical trial did conduct couples testing of the index case with their sexual partner when appropriate. Couples testing has been shown to increase adherence to ART and decrease high risk sexual behavior.[35] Couples testing for HIV-positive pregnant women has been found to increase adherence to both ART and prevention of mother to child transmission (PMTCT) regimens which reduce HIV incidence to their infants.[36-39]

Additionally, aPS can be a useful vehicle to provide PrEP to HIV-negative persons in serodiscordant partnerships. PrEP demonstration projects in Kenya and Uganda found high adherence in HIV-negative partners given short-term PrEP (for use before their HIV-positive partner initiated ART and for 6 months afterwards to allow for viral suppression).[40] Finally, unlinked HIV-positive person may be motivated to link to care after aPS. As more data becomes available on additional benefits from aPS, this analysis should be revisited.

Scaling up the aPS intervention would likely be more affordable under a task-shifting model that uses community health workers to conduct HIV testing and counseling; this is also a more realistic scenario in SSA given the shortage of healthcare professionals.[41] Further, conducting aPS within the context of antenatal care and community-based strategies (e.g. home, campaign, and mobile testing), in addition to clinic VCT would increase intervention coverage and efficiency. APS can be used in these settings to facilitate couples testing and disclosure. Implementing a tiered approach in which HIV-positive index cases are first encouraged to bring their partners in for testing (contract referral) and then staff actively trace only those partners who have not been located, can also increase efficiency. Studies of aPS in Cameroon and Malawi have found that contract referral is as effective as provider notification in locating and testing sexual partners, likely because index cases are given a certain amount of time to contact partners and provider referral is implemental for those who are not successful.[12,13] Additionally, index case involvement in contacting sexual partners can improve successful tracing and testing. Community-based HTC interventions often result in lower linkage to HIV care since is conducted outside of the healthcare system.[5] If implemented, aPS should be monitored for linkage and staff may need to conduct follow up visits to encourage partners to access care. Finally, although aPS is effective, its population impact is not sufficient to curb the HIV

epidemic. Therefore it should be scaled up alongside a combination of community-based prevention strategies including home, campaign and mobile HIV testing, PrEP rollout, and promotion of voluntary medical male circumcision. This package of strategies will likely vary by setting.

The strengths of this analysis include the use of an individual-based model parameterized to sexual and health seeking behavior (HIV testing and ART initiation by CD4 count) from a representative survey in western Kenya. The model incorporates concurrency, migration, HSV coinfection, household structure, and health seeking behaviors that vary by sex and CD4 count. We simulate the health and economic impact of aPS based on primary cost and effectiveness data from a clinical trial conducted in the same region of Kenya. However, as with all model-based analyses, our results are subject to certain limitations. Data on age-specific HIV incidence in Nyanza, Kenya were not available so we calibrated the model to plausible ranges adapted from other settings in SSA. Intervention effectiveness was obtained from a randomized clinical trial that utilized well-trained health advisors to conduct HIV testing and may not fully translate to real world scale up. To account for this, we utilized time and motion studies to estimate realistic testing volume and reduced efficiency under the task shifting scenario. The modeling analysis does not account for parameter uncertainty; however, we do incorporate stochastic variability and report the results with 90% ranges of model outputs. Since conducting an aPS randomized clinical trial for a sufficiently long time frame to collect clinical endpoints is not feasible, mathematical modeling is the best available option to synthesize epidemiologic and economic data and project the long-term health and economic benefits of implementing aPS over a 10 year time horizon.

Our results are likely generalizable to other settings in SSA. Although we focused on a high HIV prevalence region of Kenya (15.1%), aPS studies have found consistently high HIV positivity (50-60%) in sexual partners regardless of background HIV prevalence.[12,13] This is likely because sexual partners of HIV-positive persons have high exposure to the virus or may have been the source of infection. Additionally, since aPS is event-driven, cost-effectiveness should remain fairly stable, as areas with low HIV prevalence will have fewer newly diagnosed index cases that require contact tracing, thus fewer HIV-positive partners will be tested but costs will also be lower. APS may be even more cost-effective in settings where general population testing (through facility or community-based interventions) is not implemented due to low HIV prevalence. Indeed, aPS is an efficient strategy used in many developed countries with low HIV prevalence. Further, acceptability and uptake of aPS is high and shown to be similar across settings. The three largest aPS trials conducted in Malawi, Cameroon, and Kenya (the current study) report uptake rates ranging from 51% to 63%.[12,13,21] Further we evaluate aPS under three different ART initiation criteria so results can likely generalize to countries with different or changing ART guidelines. Overall, we find that aPS is a cost-effective strategy for reducing HIV burden. Results of this analysis can inform policy makers in sub-Saharan Africa.

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References

1. UNAIDS. The Gap Report. Accessed on 10/3/2015 from: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf.
2. Kranzer K, Govindasamy D, Ford N, Johnston V, Lawn SD. Quantifying and addressing losses along the continuum of care for people living with HIV infection in sub-Saharan Africa: a systematic review. Journal of the International AIDS Society 2012;15:17383.
3. UNAIDS World AIDS Day Report 2012. Available from: http://www.unaids.org/sites/default/files/media_asset/JC2434_WorldAIDSday_results_en_1.pdf. Accessed on 25/5/15.
4. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS (London, England) 2006;20:1447-50.
5. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. Nature 2015;528:S77-85.
6. Musheke M, Ntalasha H, Gari S, et al. A systematic review of qualitative findings on factors enabling and deterring uptake of HIV testing in Sub-Saharan Africa. BMC public health 2013;13:220.
7. Bwambale FM, Ssali SN, Byaruhanga S, Kalyango JN, Karamagi CA. Voluntary HIV counselling and testing among men in rural western Uganda: implications for HIV prevention. BMC public health 2008;8:263.
8. Suthar AB, Ford N, Bachanas PJ, et al. Towards universal voluntary HIV testing and counselling: a systematic review and meta-analysis of community-based approaches. PLoS medicine 2013;10:e1001496.
9. Fast-Track: Ending the AIDS Epidemic by 2030. Joint United Nations Programme on HIV/AIDS, 2014. at http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf.)
10. Hogben M, McNally T, McPheeters M, Hutchinson AB. The effectiveness of HIV partner counseling and referral services in increasing identification of HIV-positive individuals a systematic review. Am J Prev Med 2007;33:S89-100.
11. Rutstein SE, Brown LB, Biddle AK, et al. Cost-effectiveness of provider-based HIV partner notification in urban Malawi. Health policy and planning 2014;29:115-26.
12. Henley C, Forgwei G, Welty T, et al. Scale-up and case-finding effectiveness of an HIV partner services program in Cameroon: an innovative HIV prevention intervention for developing countries. Sexually transmitted diseases 2013;40:909-14.
13. Brown LB, Miller WC, Kamanga G, et al. HIV partner notification is effective and feasible in sub-Saharan Africa: opportunities for HIV treatment and prevention. Journal of acquired immune deficiency syndromes (1999) 2011;56:437-42.
14. Lugada E, Levin J, Abang B, et al. Comparison of home and clinic-based HIV testing among household members of persons taking antiretroviral therapy in Uganda: results from a randomized trial. Journal of acquired immune deficiency syndromes (1999) 2010;55:245-52.
15. Group TAS, Danel C, Moh R, et al. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. N Engl J Med 2015;373:808-22.
16. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet 2010;375:2092-8.
17. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.
18. Brown LB, Miller WC, Kamanga G, et al. Predicting partner HIV testing and counseling following a partner notification intervention. AIDS and behavior 2012;16:1148-55.

19. Pandie S, Peter JG, Kerbelker ZS, et al. Diagnostic accuracy of quantitative PCR (Xpert MTB/RIF) for tuberculous pericarditis compared to adenosine deaminase and unstimulated interferon-gamma in a high burden setting: a prospective study. BMC Med 2014;12:101.
20. Kenya AIDS indicator Survey 2012. Accessed on 1/1/2016 from: http://www.nacc.or.ke/images/documents/KAIS-2012.pdf.
21. Wamuti BM, Erdman LK, Cherutich P, et al. Assisted partner notification services to augment HIV testing and linkage to care in Kenya: study protocol for a cluster randomized trial. Implement Sci 2015;10:23.
22. Smith JA, Sharma M, Levin C, et al. Cost-effectiveness of community-based strategies to strengthen the continuum of HIV care in rural South Africa: a health economic modelling analysis. The lancet HIV 2015;2:e159-e68.
23. UNAIDS Kenya AIDS Indicator Survey Dataset 2012. Accessed from: http://statistics.knbs.or.ke/nada/index.php/auth/login/?destination=access_licensed/track/453 on 6/14/2016.
24. Salomon JA, Vos T, Hogan DR, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. Lancet 2012;380:2129-43.
25. Jahn A, Floyd S, Crampin AC, et al. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. Lancet 2008;371:1603-11.
26. World Bank Development Indicators: Antiretroviral therapy coverage (% of people living with HIV). Accessed on 11/9/2015 from: http://data.worldbank.org/indicator/SH.HIV.ARTC.ZS?page=1.
27. Tynan A, Vallely A, Kelly A, et al. Building social currency with foreskin cuts: a coping mechanism of Papua New Guinea health workers and the implications for new programmes. Health Policy Plan 2014;29:902-11.
28. Drummond M. Methods for the economic evaluation of health care programmes. Second edition. ed.
29. World Bank: Consumer Price Index. Accessed from: http://data.worldbank.org/indicator/FP.CPI.TOTL on 6/15/2016.
30. Obure CD, Vassall A, Michaels C, et al. Optimising the cost and delivery of HIV counselling and testing services in Kenya and Swaziland. Sex Transm Infect 2012;88:498-503.
31. Tagar E, Sundaram M, Condliffe K, et al. Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia. PloS one 2014;9:e108304.
32. Meyer-Rath G, Brennan AT, Fox MP, et al. Rates and cost of hospitalization before and after initiation of antiretroviral therapy in urban and rural settings in South Africa. Journal of acquired immune deficiency syndromes (1999) 2013;62:322-8.
33. Eaton JW, Menzies NA, Stover J, et al. Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models. The Lancet Global health 2014;2:e23-34.
34. Gold MR. Cost-effectiveness in health and medicine. New York: Oxford University Press. 1996.
35. Jiwatram-Negron T, El-Bassel N. Systematic review of couple-based HIV intervention and prevention studies: advantages, gaps, and future directions. AIDS and behavior 2014;18:1864-87.
36. Crepaz N, Tungol-Ashmon MV, Vosburgh HW, Baack BN, Mullins MM. Are couple-based interventions more effective than interventions delivered to individuals in promoting HIV protective behaviors? A meta-analysis. AIDS care 2015;27:1361-6.
37. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis 2015;33:123-9.

38. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. AIDS and behavior 2010;14:558-66.
39. Rosenberg NE, Mtande TK, Saidi F, et al. Recruiting male partners for couple HIV testing and counselling in Malawi's option B+ programme: an unblinded randomised controlled trial. The lancet HIV 2015;2:e483-91.
40. Baeten J, Heffron R, Kidoguchi L, et al. Near Elimination of HIV Transmission in a Demonstration Project of PrEP and ART. 2015 Conference on Retroviruses and Opportunistic Infections. Seattle, February 23-24, 2015. Abstract 24.
41. One million community health workers. Technical task force report. Accessed on 1/24/2016 from: http://frontlinehealthworkers.org/wp-content/uploads/2014/09/CHW-Report.pdf.

Table 1: Unit costs for the APS intervention per couple tested (2014 USD)*

	Program model		Task shifting model	
	HIV-negative	**HIV-positive**	**HIV-negative**	**HIV-positive**
Personnel	28.91	31.25	15.31	16.64
Transportation	2.57	2.78	3.43	3.72
Equipment	0.23	0.25	0.31	0.34
Supplies	2.02	4.42	2.13	4.54
Buildings & overhead	1.51	1.63	2.02	2.19
Startup	0.78	0.84	0.61	0.66
Phones and data monitoring	0.58	0.63	0.66	0.72
TOTAL (per partner tested)	36.61	41.81	24.46	28.81

*The task shifting intervention replaces professional counseling with community health workers (CHWs), and has lower cost mobile phones, and 25% lower efficiency.

Table 2: HIV-related healthcare costs (2014 USD)

Health care provision	Unit cost
HIV testing (cost per diagnostic test)	14.60
Pre-antiretroviral therapy care (per-person year)	106
Initiation of antiretroviral therapy (cost per initiation)	
Patients in pre-antiretroviral therapy care	37
Patients not in pre-antiretroviral therapy care	50
Antiretroviral drug provision (per person-year)	219
Health-care use for HIV-positive people not linked to care (per person-year)	
CD4 count >350 cells/μL, not in HIV care	4
CD4 count >200–350 cells/μL, not in HIV care	13
CD4 count ≤200 cells/μL, not in HIV care	48
End-of-life care (per death)	38
Supply-chain management and programmatic support	
Supply-chain management	20% mark-up on all ART costs
Programmatic support†	50% mark-up on all non-ART costs

Costs from Zambia (Eaton et al) were adapted to Kenya using the ratio of two country's gross domestic product per capita and inflated from Kenyan Schillings to 2014 US dollars. ART costs were adapted from the MATCH study.

†The mark-up for programmatic support applies to non-intervention costs only.

Table 3: Health and economic impact of the aPS intervention*

	CD4<350	CD4<500	CD4 all
Percent of population receiving APS	11.9%	11.7%	11.2%
Health impacts (total population)			
HIV infections averted	2.8% (1.3-4.3%)	2.8% (1.4-4.2%)	2.7% (1.0-4.1)
HIV-related deaths averted	1.5% (0.7-2.1)	1.5% (0.9-2.2%)	1.5% (1-2.3%)
DALYs averted	0.8% (0.3-1.2%)	0.7% (0.4-1.3%)	0.8% (0.2-1.3)
Health impacts (among aPS partners only)			
HIV infections averted	1.7% (-1.0-3.7%)	1.7% (-1.0-5%)	1.7% (-1.0-4.7%)
HIV-related deaths averted	5.5% (3.4-7.6%)	6.7% (4.6-8.9%)	7.6% (5.7-9.9%)
DALYs averted	3.0% (1.8-4.4%)	3.8% (2.2-5.3%)	4.5% (3.1-5.8%)
Cost-effectiveness			
ICER program model ($/DALY averted)	$1,734 ($1,291-3,326)	$1,703 ($1,198-2,887)	$1,568 ($1,162-4,477)
Percent of program ICERS under Kenya's per capita GDP	15%	22%	35%
ICER task shifting model ($/DALY averted)	$1,350 ($1,003-2,605)	$1,302 ($955-2,789)	$1,156 ($762-2,050)
Percent of task-shifting ICERS under Kenya's per capita GDP	49%	54%	64%

*Values in parentheses represent 90% model variability. Costs and DALYs are discounted at 3% annually. Results shown for 3 different ART initiation thresholds: <350 cells/uL, <500 cells/uL, and all HIV-positive persons.

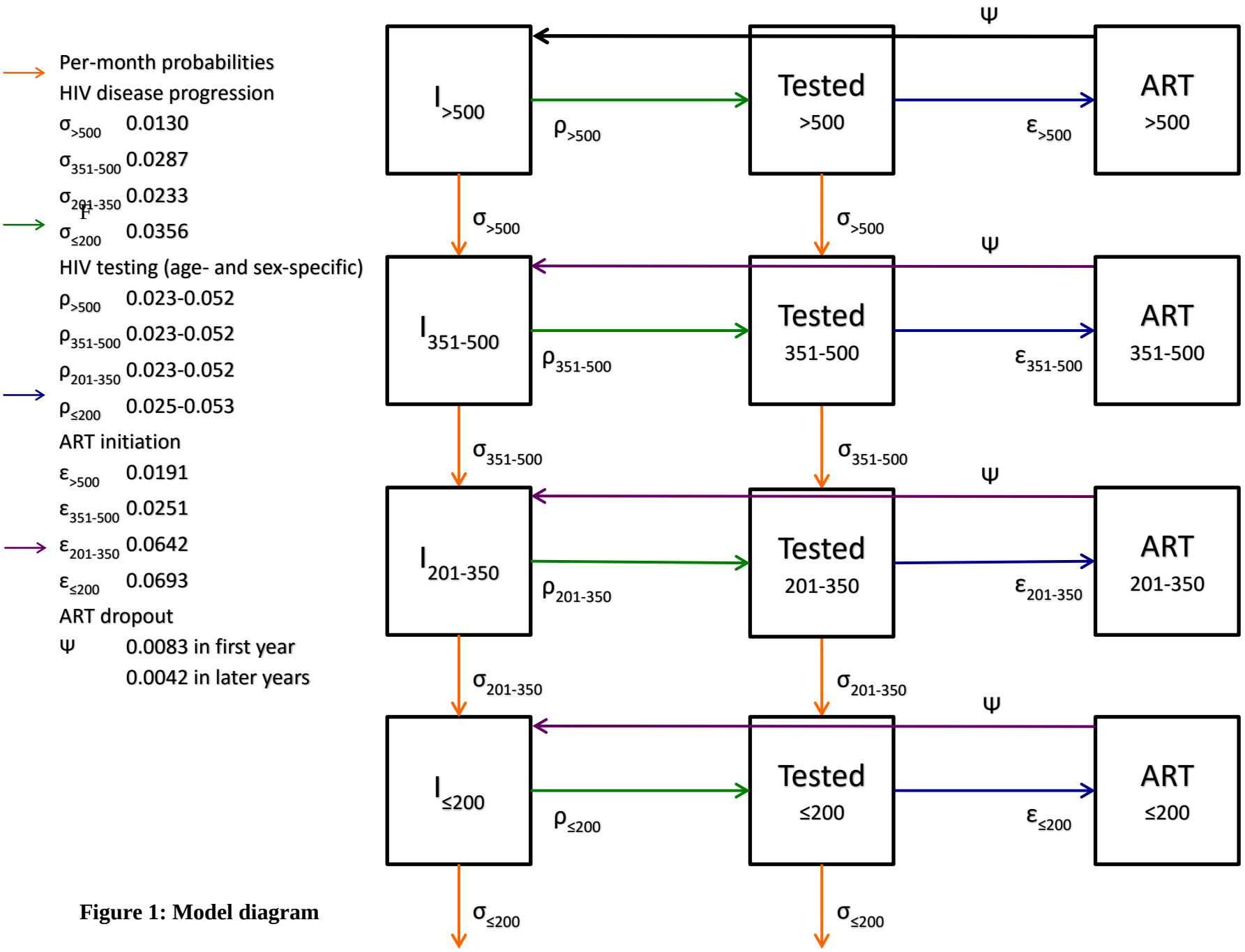

Figure 1: Model diagram

Note. HIV infection, HIV testing by uninfected individuals, natural mortality and mortality on ART are not shown.

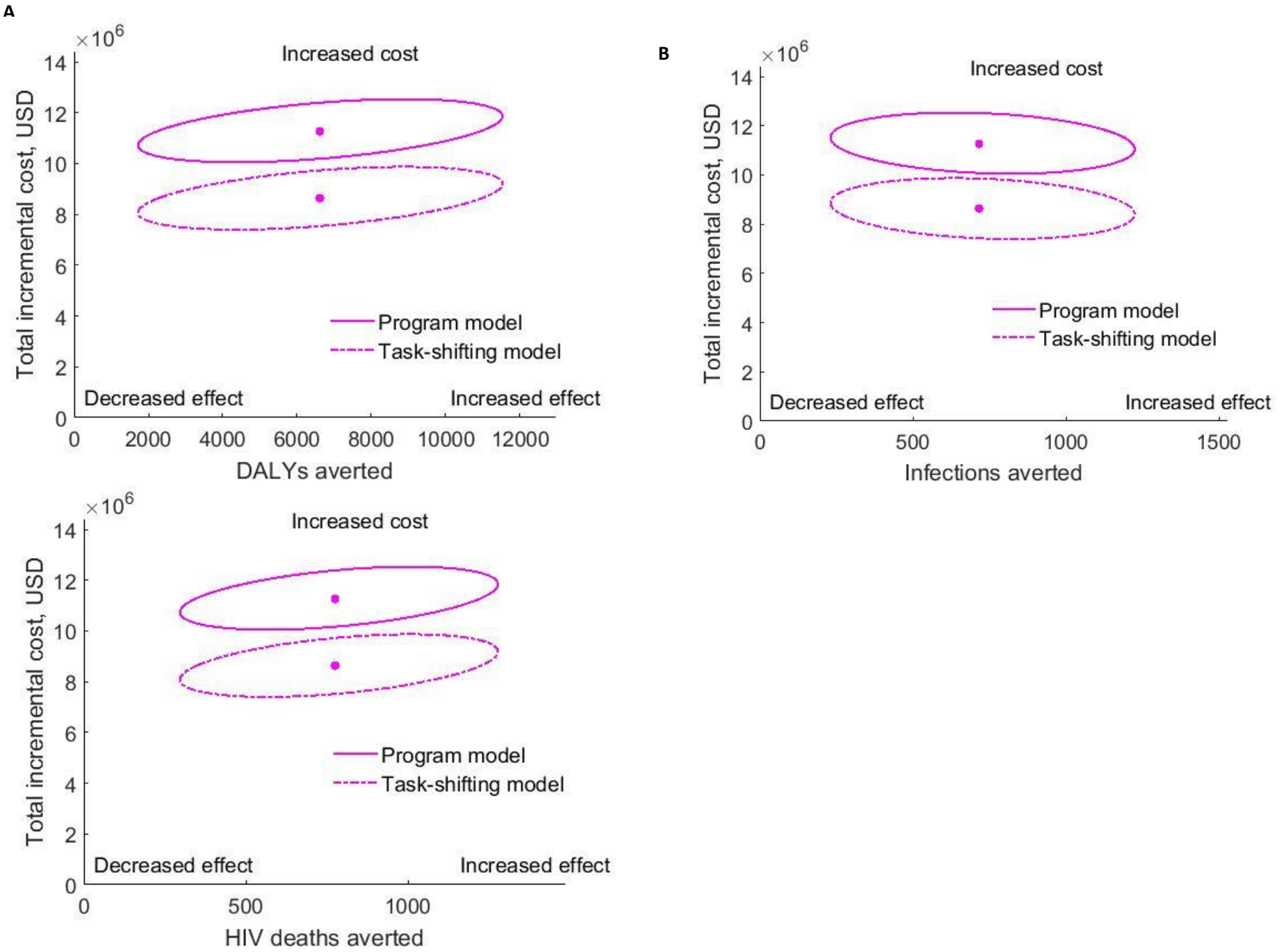

Figure 2: Model estimated health outcomes averted and 90% model variability. Costs and (A) DALYs, (B) infections, and (C) deaths averted are per 500,000 persons.

Supplemental Appendix

Accompanying the manuscript:

Cost-effectiveness of implementing active partner notification for HIV in Kenya: A mathematical modeling analysis

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1. Model definition

1.1 Overview

We adapted an individual-based microsimulation model of adults (ages 18 and over) to reflect the former Nyanza Province of Kenya. The aim of the analysis was to evaluate the health impact and cost-effectiveness of implementing assisted partner notification services (aPS) compared to a 'status quo' scenario with ongoing current levels of facility-based HIV testing and ART uptake (SQ; Box 1). The analysis was conducted with three ART eligibility criteria: 1) ≤350 CD4 cells/mm^3, 2) ≤500 CD4 cells/mm^3 and 3) all HIV-positive (universal ART initiation). The model is run with a one-month time step from a standing start at year 2012 for 13 years (the first 3 years are considered a burn-in period. Costs and effectiveness estimates are taken from the aPS randomized clinical trial conducted in Kenya. The model is coded in MATLAB (v2015b, The MathWorks, Natick, Massachusetts) and run for ten years with one-month timesteps.

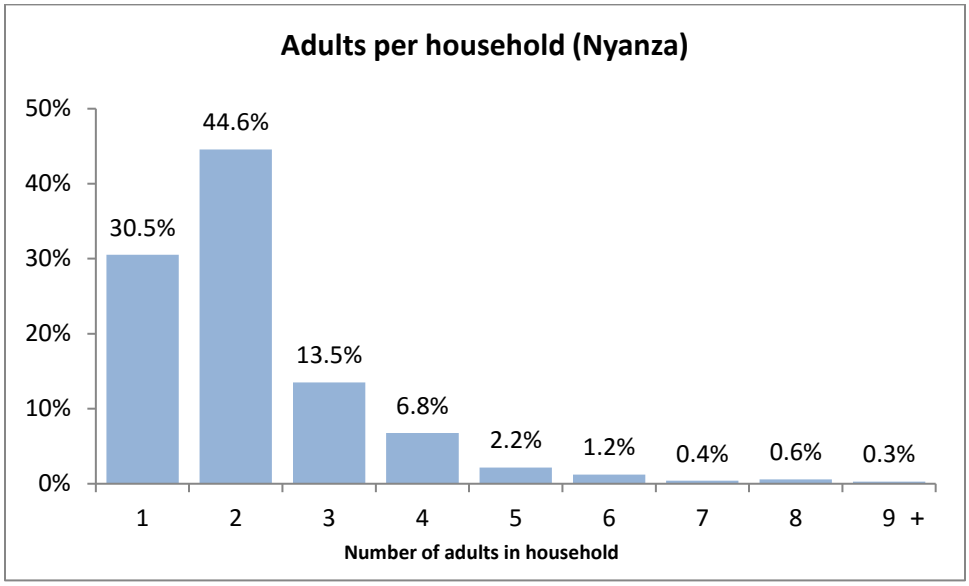
Box S1. Analysis summary.

Scenario one (baseline, SQ): Background HIV treatment cascade only, encompassing existing facility-based testing. **Scenario two (home HTC):** Assisted partner notification services (aPS) plus background treatment cascade. **Both scenarios repeated for ART eligibility at CD4≤350, ≤500 and all HIV-positive with CD4 ≤500 being the base-case scenario.**

1.2 Population and behavior

The model simulates all adults in the community irrespective of eligibility. Individuals are grouped into households with cohabiting and non-cohabiting couples explicitly defined. Household size is randomly allocated according to the distribution observed in KAIS (Figure S1).

Figure S1. KAIS data for Nyanza.



The model replicates the sex and age distribution of the community recorded in KAIS 2012 (Table S1) stratified according to position in the household: household head, cohabiting partner of household head or other members of the household. First, each household is assigned a household head, 76.3% of whom are assumed to be male (KAIS 2012). Each household head is randomly assigned an age category from the observed distribution and their specific age is generated from a uniform distribution across the whole category.

Table S1. Distribution of age and sex (KAIS 2012 Nyanza data).

	All eligible adults		Household heads only	
Age group (years)	**Men** N=662	**Women** N=947	**Men** N=463	**Women** N=318
18-19	0.09	0.06	0.00	0.02
20-24	0.15	0.21	0.08	0.11
25-29	0.14	0.18	0.12	0.15
30-34	0.13	0.11	0.16	0.11
35-39	0.10	0.11	0.13	0.13
40-44	0.08	0.08	0.10	0.11
45-49	0.08	0.08	0.11	0.13
50-54	0.10	0.07	0.13	0.10
55-59	0.06	0.05	0.09	0.08
60-64	0.05	0.05	0.08	0.08

Table S2. Age difference between household heads and their cohabiting partners or other household members (KAIS 2012 Nyanza data).

	Age difference (years)									
	Household head is younger		**Same age**	**Household head is older**						
	(-11)-(-49)	**(-10)-(-1)**	**0**	**1-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-80**
Cohabiting partners (proportion) (N=378)										
	0.0046	0.088	0.035	0.65	0.17	0.048	0.0063	0.0014	0	0
Other household members (proportion) (N=471)										
	0.0044	0.0093	0.0032	0.064	0.1326	0.377	0.3195	0.09	0.045	0

KAIS does not have data for age difference for between head of household and other members over 50, so we linearly interpolated assuming 0 age difference for age 61-80 years.

Overall, 84.7% of household respondents in Nyanza were in a union. Of these, 83.12% are cohabitating (total 70.4% cohabitating). Of head of households, 78.9% were in a union and of these 74.2% were cohabitating (total 58.5% cohabitating). The remaining individuals in each household are modeled as other household members. The ages of cohabiting partners and other household members are randomly assigned from a discrete distribution relative to the age of the household head (Table S2).

Migration, partnerships, coital frequency and condom use

The model simulates heterosexual HIV transmission only, and sexual partnerships can be formed between any two adults of the opposite sex with a preference for the male partner to be slightly older than the female (modal age difference = 0-4). Stable, or long-term, partnerships are assumed to have a mean duration of 12 years and can only be formed within the modelled community (either within the same household or with an adult in a different household). New long-term partnerships are formed dynamically by matching the number of stable partnerships within the community to KAIS partnership data (Figure S2). Short-term partnerships have a mean duration of three months and are preferentially formed with other adults within the community. Short-term partnership formation is demand-driven by either men or women (usually men who report higher numbers of partners, Table S4). If no adults are available within the community, short-term partners outside the community may be sought. These external adults are not explicitly modelled but have a probability of HIV infection based on the age and sex distribution of HIV prevalence within the study community (Table S3).

Individuals may have a maximum of two concurrent partners at any time, only one of which may be long-term. The monthly probability of an existing partnership dissolving is calculated from the mean partnership duration using a negative exponential distribution. We assume that there is a minimum two-month lag period between cessation of a partnership and formation of the next of the same type. Migrant workers are considered to be present in the community for nine months in every twelve where they form partnerships and contribute to transmission within the community (Table S4). For the remainder of the time they do not engage in sex acts with any long-term partner within the simulated community, but both they and any long-term partner are subject to an elevated risk of short-term partnership formation. Short-term partners who are external to the community are not explicitly modeled but are assumed to share the same age- and sex-specific HIV prevalence as that observed in KAIS 2012 (Table S3).

Table S3. HIV Prevalence estimates from Nyanza (KAIS 2012 data)

Age	HIV prevalence	
	Male	**Female**
18 – 19	0.0222	0.0659
20 – 24	0.0293	0.1414
25 – 34	0.2201	0.2309
35 – 44	0.2458	0.2309
45 –54	0.1895	0.1771
55 – 64	0.1203	0.0478
65-74	0.0511	0.001
75-84	0.0165	0.00
85+	0.00	0.00

Due to lack of data for ages greater than 65, we linearly interpolated age 55-64 data assuming zero prevalence at 85+.

Table S4. Migration: Proportion of persons who have stayed away from home for at least one month in the last 12 months (KAIS 2012 Nyanza data)

	Away from residence for at least one month
Men	0.29
Women	0.14

Figure S2. Distribution of partner numbers at model initiation.

We fit a quadratic equation of the form $y = ax^2 + bx + c$ to the proportion of men reporting more than one partner (where x is age and y is the proportion of the age group with more than one partner): a=-1.0x10^{-4}, b=9.9x10^{-3} and c=4.3x10^{-3}. Point estimates were taken at the mid-point of each age category. The proportion of women with more than one partner and the proportion of both sexes with only one partner were obtained from KAIS and not transformed. The point estimates for zero and >1 partners for each age group were subtracted from one to estimate the proportion of individuals with one partner (Figure S2). Men in a within-household relationship are constrained to have at least one partner.

Table S5. Age- and sex-specific distributions of the number of partners in the last 12 months (KAIS 2012).

	Age group (years)														
	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75-	80-	≥85
Proportion with no partners															
M	0.66	0.19	0.1	0.08	0.07	0.09	0.11	0.03	0.09	0.35	0.44	0.52	0.61	1	1
F	0.58	0.16	0.1	0.1	0.14	0.27	0.28	0.34	0.56	0.58	0.43	0.29	0.14	0	0
Proportion with more than one partner															
M	0.15	0.18	0.20	0.22	0.23	0.24	0.25	0.25	0.22	0.11	0	0	0	0	0
F	0.02	0.05	0.02	0.02	0.02	0.02	0.02	0.07	0.02	0	0	0	0	0	0

M: male, F: female. KAIS 2012 Nyanza data. Primary data was only available up to age category 60-64 so we linearly interpolated at older ages assuming no individuals had no partners after age 80. We also assumed no concurrency after age 65 years.

Coital frequency with stable partners can vary month-to-month with a range based on the distribution of data from the South African sites of the Partners in Prevention HSV/HIV Transmission Study: http://depts.washington.edu/uwicrc/research/studies/pip_transmission.html. We assume that coital frequency in Kenya is similar to that observed in the South Africa data. Individuals are randomly allocated into quartiles at the start of the simulation and the number of sex acts each month is sampled randomly from within that category under a uniform distribution (Table S5). All individuals are evaluated in a random order that is re-randomised every time-step, and the coital frequency used that month is the number assigned to whichever partner is evaluated first. We assume all short-term partnerships involve three sex acts per month, also based on the Partners HSV/HIV data and following the assumption made by Hallett *et al*.[1] We assume that one-quarter of women and men aged more than 65 years are sexually active with a maximum of two sex acts per month. All numbers are rounded to the nearest integer.

Table S6. Coital frequency for long-term partnership (from serodiscordant couples in HSV2/HIV data).

Age	Men				Women			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
<25	1-3	3-6	6-8	8-14	0-3	3-5	5-10	10-28
25-34	0-3	3-7	7-12	12-20	0-3	3-5	5-8	8-16
35-44	0-3	3-6	6-12	12-15	0-2	2-4	4-8	8-29
45-54	0-1	1-2	2-3	3-8	0-2	2-3	3-4	4-9
55-64	1-2	2-3	3-4	4-5	1-2	2-3	3	3
65+	0	0	0	0-2	0	0	0	0-2

Table S7. Proportion of individuals who used a condom at last sex by HIV and relationship status.

	In a long-term relationship (married or living with partner)	Not in a long-term relationship (single, divorced or widowed)
HIV-negative	0.092	0.333
HIV-positive	0.416	0.559

KAIS 2012: Condom use data are national because of small numbers in Nyanza-specific estimates.

We assume a 'take' pattern of condom use, where individuals either use condoms consistently or not at all. We replicate this joint distribution at model initialization (Table S6) and individuals are reassigned when they test HIV-positive, form or dissolve a long-term partnership.

Population turnover

The number of new 18 year olds entering the population was estimated using the crude birth rate from 18 prior (in 1998): 37.5/per 1,000 persons per year (Kenya DHS).[2] This gave a mean rate of 0.003125 per adult per month; new adults entered the population using Poisson random generation. Background (non-HIV) mortality rates for men and women are the result of fitting an exponential function ($y = \alpha e^{\beta x}$) to Kenya's age-specific mortality in 1990, prior to the generalized HIV epidemic,[3] similar to analysis performed for South Africa by Hallett *et al.*[1,4] Parameters are (α=0.0006, β=0.0643) for men and (α =0.0005, β =0.066) for women (where *y* is the mortality rate and *x* is age). Survival probabilities for each member in a partnership are modeled independently.

1.3 HIV infection & transmission

Biological parameters

The baseline transmission probability per sex act, β_0, is set at 0.1%[5], and different HIV-related cofactors are applied according to each individual's attributes and behavior. Condom use and male circumcision reduce HIV transmission by 78% and 65% per sex act, respectively.[5,6] Coinfections representing HSV2 and other STIs are assumed to increase HIV acquisition by a factor of 3.4 for women and 2.8 for men[7] and transmission by a factor of two (HSV2 is associated with an 0.18 increase in log VL[8] which equates to approximately 50% increase in infectiousness using [5]). STIs are initially distributed by age and sex according to the observed HSV2 prevalence in sub-Saharan Africa and all individuals are subject to an STI incidence rate, which is evaluated every six months (Table S8).

Table S8. Age-specific STI prevalence and incidence.[9,10]

Age (years)	Prevalence (%)		Incidence (per 100py)	
	Men	Women	Men	Women
15-19	9.4	20.7	1.83	3.39
20-24	18.5	34.8	1.68	2.25
25-29	27.0	44.7	1.56	1.50
30-34	34.8	52.0	1.44	1.01
35-39	42.0	56.0	1.32	0.66
40-44	48.6	58.4	1.20	0.43
≥45	53.3	59.3	1.08	0.28

HIV natural history

Once infected with HIV, individuals progress to one of four CD4 cell categories with the probabilities given in Table S9. The CD4 count then progresses through each subsequent category until death. The mean years spent in each CD4 cell count category were derived from Lodi et al 2011[11] and a pooled-analysis of African observational cohort studies[12] by Cori *et al.* (2014).[13] For individuals with CD4 cell counts below 200, the mean years in the category can be interpreted as mean survival time. The infectiousness rate ratio is given relative to an individual with CD4 cell count above 350[14] (in Donnell *et al.*, there is no substantial difference between transmission of those with CD4 cell counts 350-500 or 500+ so these categories were combined here). The baseline CD4 count distribution for HIV+ persons is taken from KAIS 2012 (Table S10)

Table S9. Progression, relative infectivity and duration of CD4 categories.

		Probability of immediate progression on infection*	Infectiousness rate ratio	Mean years in category	Monthly probability of progression
CD4 cell count if not treated					
	500+	0.58	1	6.37	0.0130
	350-500	0.23	1	2.86	0.0287
	200-350	0.16	1.59	3.54	0.0233
	≤200	0.03	4.99	2.30	0.0356
On ART	N/A	N/A	0.08	Life expectancy same as uninfected	Age-related, as for uninfected

*Fitted to data in Lodi *et al.* (2011) by Cori *et al.* (2014).[11,13]

Table S10: CD4 distribution at baseline (excluding those on ART) KAIS 2012, Nyanza

CD4	Proportion
<200	0.1132
200-350	0.2963
350-500	0.2258
>500	0.3647

Male circumcision

As male circumcision coverage is rapidly expanding in Kenya, we estimated an increase in coverage from the 2012 KAIS estimates to 75% (Table S10). We assumed this coverage to be constant over the intervention time period.

Table S11: Coverage of adult voluntary medical male circumcision (Nyanza estimate)

Year	Male circumcision coverage	Reference
2012	0.66	Kenya AIDS Indicator Survey[15]
2016	0.75	Estimate

Model fitting

Age- and sex-specific prevalence in the model was manually fitted to the pattern of prevalence observed in Nyanza (KAIS 2012) (Table S3).[16,17] For each sex and age group, the baseline transmission probability per sex act β_0 was multiplied by a fitting cofactor, F. This cofactor is intended to represent all age- and sex-related differences in incidence as well as accounting for any misreporting of behavioural factors in the study data.

Table S12. Age-specific HIV fitting cofactor.[16,17]

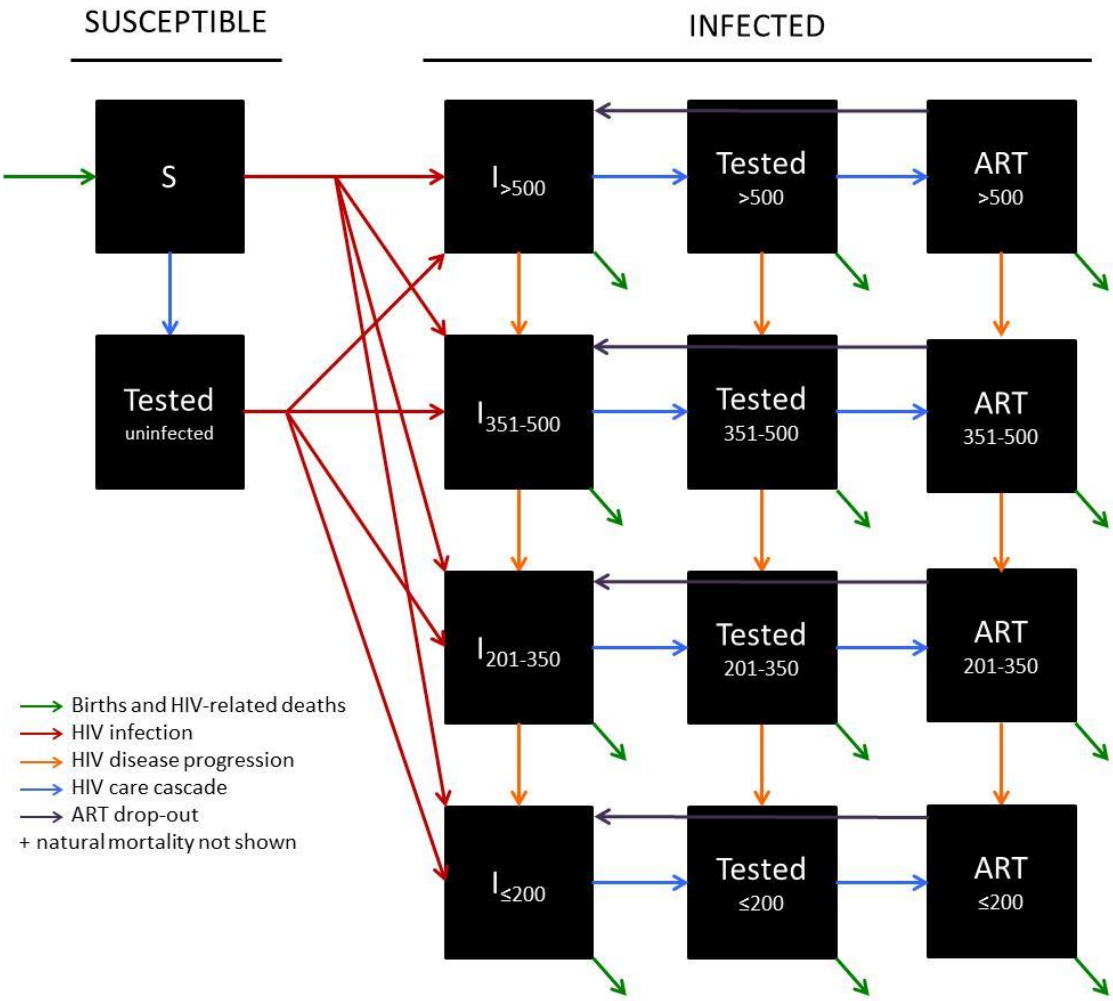
Age (years)	Fitting cofactor, F	
	Females	Males
18-19	0.08	0.08
20-24	0.72	0.09
25-29	0.65	0.4
30-34	0.47	1.15
35-39	0.16	0.3
40-44	0.05	0.15
45-49	0.12	0.16
50-55	0.12	0.19
≥55	0.10	0.12

1.4 Background: HIV testing, linkage to care and ART initiation

Background care cascade overview

All individuals may progress through a background care cascade comprising facility-based HIV testing, linkage to care and ART initiation regardless of whether or not they have been exposed to the aPS intervention (Figure S3). Progression rates between these stages are given in the form of a monthly probability of progression from one state to another. These are based KAIS Nyanza data on the coverage of HIV testing, pre-ART clinic visit and ART (Tables S13-14).

Figure S3. Treatment cascade in status quo scenario.



HIV testing

The background coverage of HIV testing is specific to sex, age and infection status and is derived from KAIS (Table S13). This is used in the 'status quo' scenario, as well as during non-intervention years and for individuals who have not received the intervention in the aPS scenario. The observed coverage of having ever tested for HIV at baseline is multiplied by the proportion of those tested whose test was in the preceding year to estimate the proportion of individuals who test in one year. The monthly probability of HIV testing is then estimated using equation (eq.) 1. This method assumes that background HIV testing rates do not change over time and that all infected individuals will eventually get tested, unless they die first. Proportion ever tested was estimated from KAIS (Nyanza Province). However, KAIS data for tested in the last year was estimated from national KAIS data due to small numbers for HIV-positive individuals in Nyanza Province. We assumed testing coverage in HIV positive

persons with CD4 count>200 cells/uL was the same as uninfected persons as there was no difference in testing rates in KAIS. There was a small increase (1.2-1.5%) in probability of HIV testing in HIV-positive persons who were not linked to ART in KAIS. This is reflected in the increased probability in testing in the last year for HIV-positive individuals with CD4 count <200 cells/uL.

$$ProbHIVTest_{i,j,k} = HIVTestInLastYear_k * EverTestedForHIV_{i,j,k} * \left(1 - e^{-\frac{1}{12}}\right) \quad \text{(eq. 1)}$$

Table S13. HIV testing parameters by age, sex and HIV status.

Age group (*j*)	Women (*i*=1)			Men (*i*=2)		
	Uninfected (*k*=1)	CD4 >200 (*k*=2)	CD4 ≤200 (*k*=3)	Uninfected (*k*=1)	CD4 >200 (*k*=2)	CD4 ≤200 (*k*=3)
	KAIS data: HIV testing coverage (prop. ever tested)					
18-19	0.806	0.806	0.816	0.653	0.653	0.694
20-24	0.980	0.980	0.990	0.887	0.887	0.928
25-29	0.935	0.935	0.945	0.839	0.839	0.880
30-34	0.932	0.932	0.942	0.803	0.803	0.844
35-39	0.882	0.882	0.892	0.747	0.747	0.788
40-44	0.748	0.748	0.758	0.613	0.613	0.654
45+	0.821	0.821	0.831	0.703	0.703	0.744
	KAIS data: HIV testing coverage (prop. tested in the last 11 months) of those who ever tested					
18-19	0.694	0.694	0.706	0.555	0.555	0.570
20-24	0.661	0.661	0.673	0.622	0.622	0.637
25-29	0.562	0.562	0.574	0.619	0.619	0.634
30-34	0.500	0.500	0.512	0.535	0.535	0.550
35-39	0.532	0.532	0.544	0.521	0.521	0.536
40-44	0.469	0.469	0.481	0.464	0.464	0.479
45+	0.459	0.459	0.471	0.474	0.474	0.489
	Model: per month probability of HIV test					
18-19	0.045	0.045	0.046	0.029	0.029	0.032
20-24	0.052	0.052	0.053	0.044	0.044	0.047
25-29	0.042	0.042	0.043	0.041	0.041	0.045
30-34	0.037	0.037	0.039	0.034	0.034	0.037
35-39	0.037	0.037	0.039	0.031	0.031	0.034
40-44	0.028	0.028	0.029	0.023	0.023	0.025
45+	0.030	0.030	0.031	0.027	0.027	0.029

Clinic visit and ART initiation

Since KAIS data reports number of persons who have visited a clinic and linked to ART by CD4 count at the time of the survey and not CD4 count at the time of linkage, we assumed that those who were on

ART for less than one year had started treatment at their current CD4 counts. For persons with current CD4 counts of >500 cells/uL or 351-500 cells/uL who had been on ART for more than one year, we assumed that they linked while in the next lowest CD4 count category (351-500 and 201-350, respectively). We also assume that individuals must visit the clinic and incur pre-ART costs before ART initiation can take place.

After initiation, ART takes three months to reach full efficacy and infectiousness decays exponentially over this period to reach an overall reduction in infectivity of 96%.[18] Mortality on ART varies by the CD4 cell count at initiation and by the time since initiation (Table S12).[19-21]

Table S14. Combined probability of clinic visit ART initiation for HIV-positive individuals by CD4 count, after HIV test

	CD4 category			
	>500	351-500	201-350	≤200
ART initiation	0.24	0.31	0.80	0.87
Model: per-month probability of ART initiation for HIV-positive individual				
	0.0191	0.0251	0.0642	0.0693

Drop-out from an ART program is fixed at 10% per year in the first year of treatment and 5% per year thereafter for individuals who initiate ART through the background care cascade or after aPS intervention. Following ART drop-out, we assume that an individual's CD4 count reverts to its category prior to initiation..

1.5 Intervention: Partner Notification Services

The assisted partner services (aPS) intervention acts to strengthen the HIV care cascade via an immediate HIV test for all eligible and consenting adults. Probabilities pf linkage to care and ART uptake remain the same as the background rates after HIV testing, as seen in the aPS randomized clinical trial. It is implemented continuously over the ten-year model run. All eligible and consenting adults receive an immediate HIV test unless they are already on ART.

We obtained the probabilities of an index case consenting to the APS intervention from the aPS randomized trial (Nyanza region). We assumed expanded eligibility criteria (e.g. pregnancy status and

distance from clinic were no longer reasons for exclusion from aPS). The probability of index partner acceptance of the intervention did not differ by sex, but the probability of sexual partner acceptance of aPS did vary by sex and knowledge of HIV status, so the probabilities were stratified accordingly (Table S16-18).

Table S16. Probability of newly diagnosed index case consenting to APS intervention

	Probability
Index case	0.71

Table S17. Combined probability of consent to HIV testing and knowledge of HIV test result of those who do not already know that they are HIV-positive.

Sexual partner listed by index	Probability
Women	0.68
Men	0.57

Uptake is increased to account for proportion migrating.

Table S18. Combined probability of consent to HIV testing and knowledge of HIV test result of those who already know that they are HIV-positive

Sexual partner listed by index	Probability
Men and women	0.06

Linkage to care following APS intervention

Following the intervention, 60.3% of HIV-positive individuals who were not previously linked to care had visited a clinic within 6 weeks after APS compared to 66.7% background linkage (the numbers are small so there may be no difference between background and intervention linkage rates after testing. Clinic attendance following aPS was not associated with sex or age (although numbers are small).

1.6 Quantifying health states

Disability-adjusted life years (DALYs) are attached to each HIV-related health state and these are summed over all individuals for the duration of the model runtime.

Table S19. Disability weights for health states in the model.

Status	Disability weight
Uninfected	0
HIV infected: CD4 cell count 500+	0.078
HIV infected: CD4 cell count 350-500	0.078
HIV infected: CD4 cell count 200-350	0.274
HIV infected: CD4 cell count ≤200	0.582
On ART: First year, CD4 at initiation >200	0.078
On ART: First year, CD4 at initiation ≤200	0.078
On ART: Subsequent years	0.078
Deceased	1

DALYs: AIDS cases, receiving ARV treatment, from Salomon *et al.* (2015).[22] No category in GBD classification for infected with CD4 >350, assumed the same as HIV-positive on ART.[23]

1.7 Cost estimates

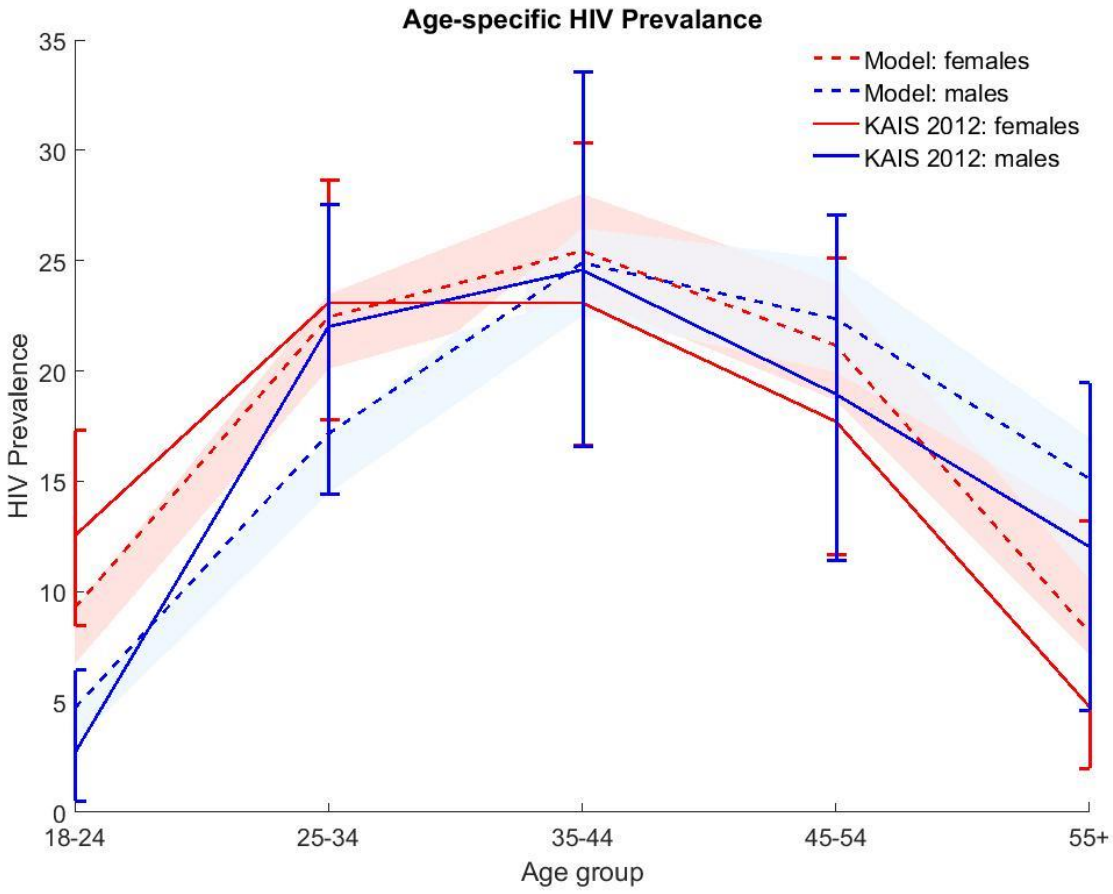
Costs were collected onsite in June 2014 in Nyanza Province, Kenya from the Assisted Partner Services study, a community randomized trial of community-based partner notification and HIV counseling and testing. Time and motion observation of the intervention was conducted to determine staff time and resource utilization per partner tested and also to facilitate removal of research time and costs to estimate program costs. We observed that partner notification and HIV counseling and testing takes approximately 40 minutes per HIV- partner and 60 minutes per HIV-positive partner tested. After accounting for travel time, follow-ups, unsuccessful attempts to track partners, paperwork, and other staff responsibilities, we estimated that a health advisor would test 2 HIV- persons per day or 1.85 HIV-positive persons per day (with the average number tested changing depending on HIV prevalence). For the task shifting scenario, we assumed 25% lower efficiency. We assumed a program of 12 health advisors (or community care workers in the task shifting scenario). Staff were assumed to work 7 hours per day, 215 days per year after accounting for national holidays, sick days, and paid vacations. Total program costs were divided by the number of persons tested by HIV status under each scenario to determine the cost per person tested. Supply costs per person tested included gloves, HIV screening test kit, lancet, cotton balls, and alcohol swabs. Additional supplies for HIV+ persons tested included confirmatory test, and tie breaker test (assumed to be used in 5% of all HIV+ cases). Supply wastage was assumed to be 5%. We assumed that 20% of sexual partners underwent couples HIV testing and incurred additional HIV test supply costs.

2. Model calibration and validation

Figure S4 compares the mean HIV prevalence over projected by the model in 2012 to KAIS 2012 survey data from Nyanza Province.[16] The predicted age-specific pattern in the model closely matches the observed data.

Figure S4. Model HIV prevalence

Age-specific prevalence over ten years with ART initiation at ≤500 CD4 cells mm^{-3}. Solid lines and error bars show the prevalence with 95% confidence interval (CI) reported in KAIS 2012. Dashed lines and block colors show the median and 90% variability in model outputs.



Model validation.

Figure S5. Age and sex distribution at model initiation.

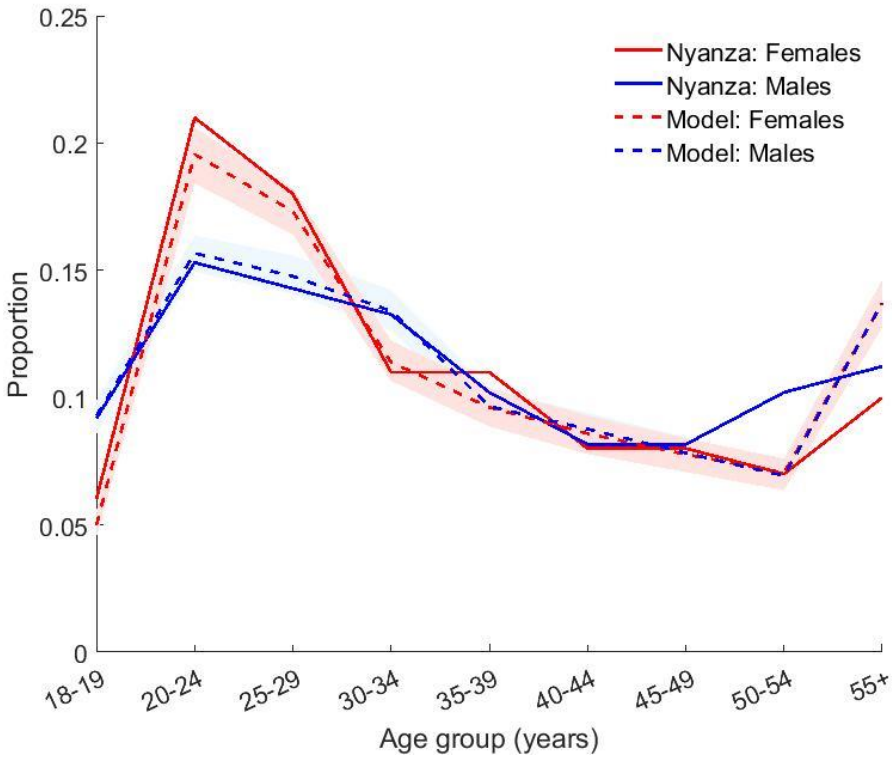


Figure S6. Model age specific incidence

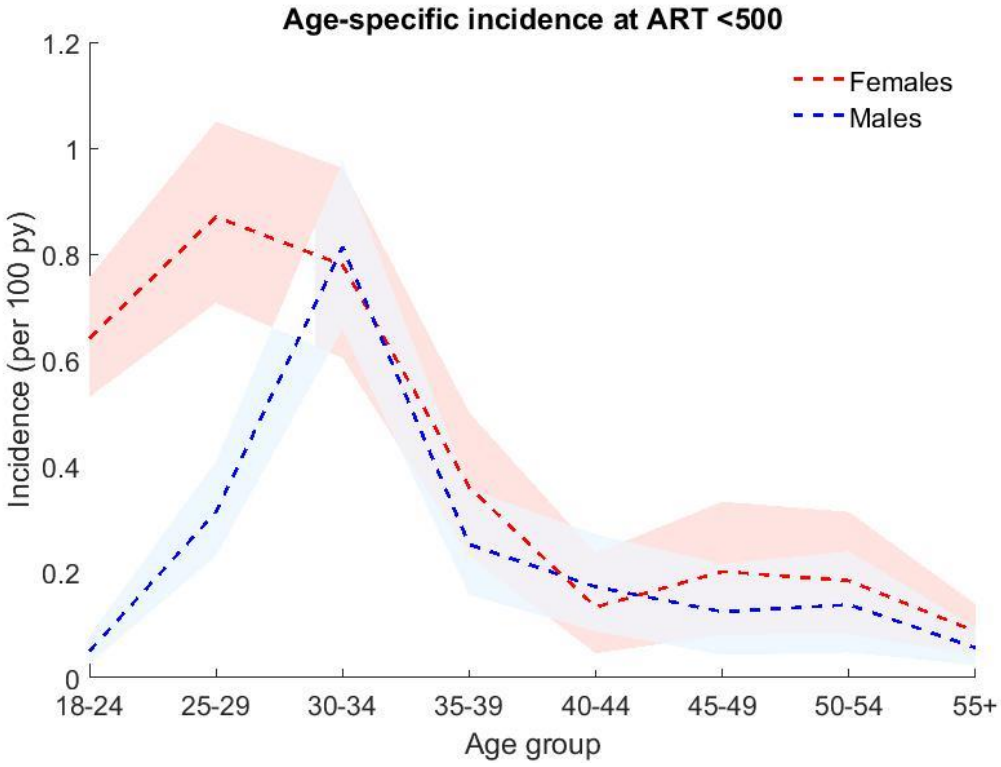


Figure S7. Model incidence over ten years.

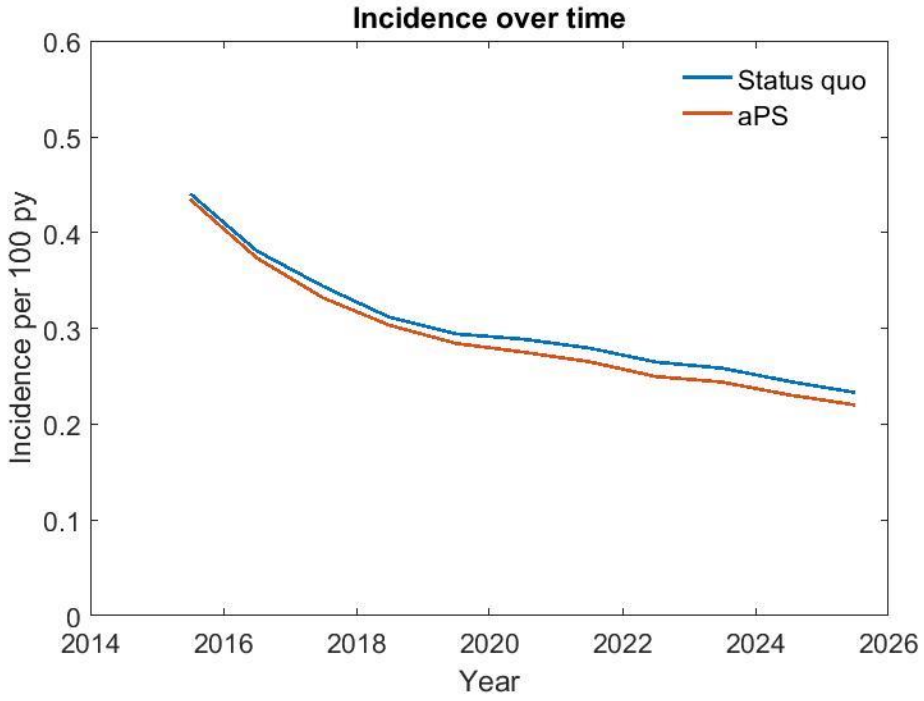


Figure S8. CD4 category distribution over ten years with no intervention and ART eligibility at CD4 ≤500 cells/mm^3.

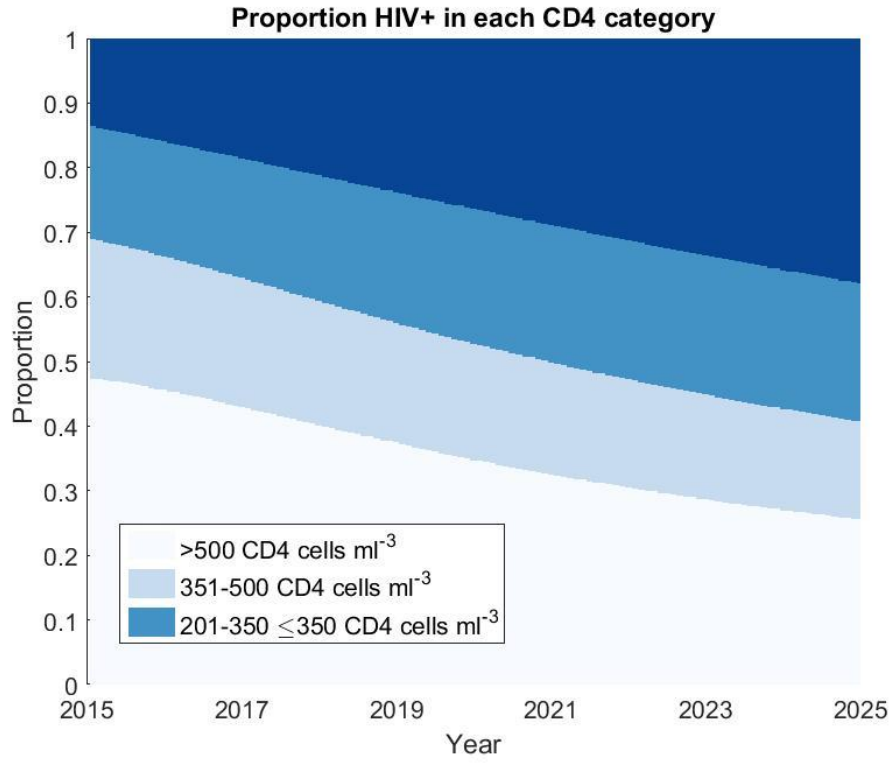


Figure S9. Source of HIV transmissions over ten years by CD4 category with ART eligibility at CD4 ≤500 cells/mm^3.

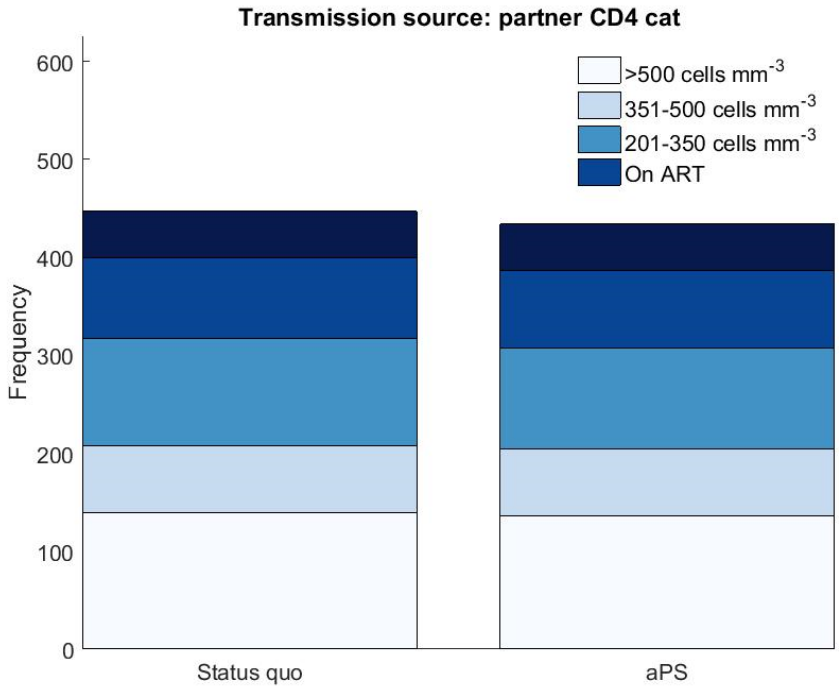
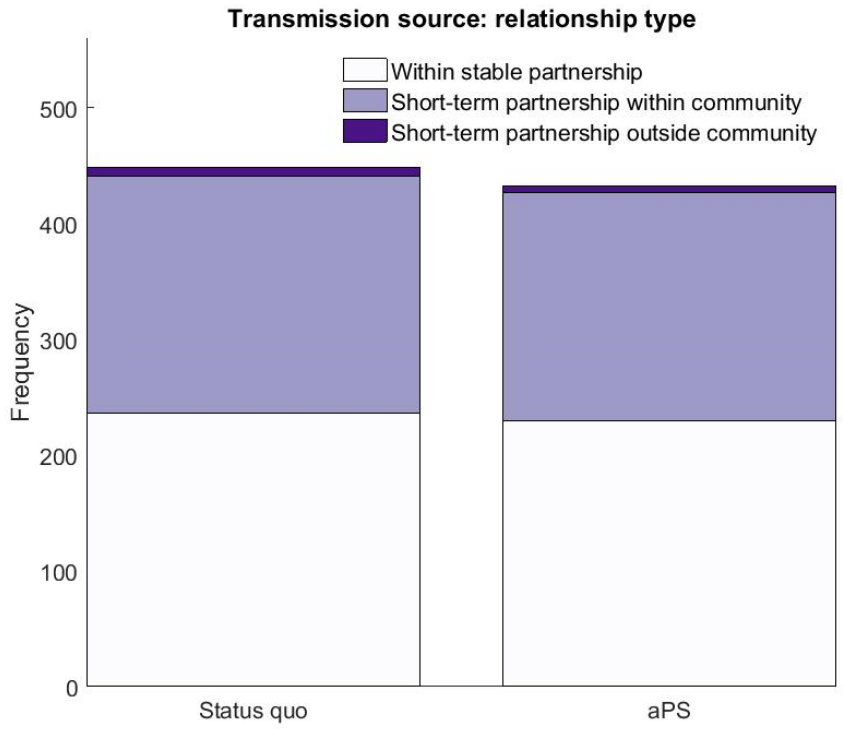


Figure S10. Source of HIV transmissions over ten years by partnership type with ART eligibility at CD4 ≤500 cells/mm^3.



References

1. Hallett TB, Baeten JM, Heffron R, et al. Optimal Uses of Antiretrovirals for Prevention in HIV-1 Serodiscordant Heterosexual Couples in South Africa: A Modelling Study. *PLoS Medicine* 2011; **8**(11): e1001123.
2. USAID. Kenya Demographic Health Survey 1998. Accessed on 6/1/2016 from: http://dhsprogram.com/publications/publication-FR102-DHS-Final-Reports.cfm.
3. World Mortality Report 2011. United Nations. Accessed on 10/27/2015 from http://www.un.org/en/development/desa/population/publications/pdf/mortality/worldMortalityReport2011.pdf.
4. Dorrington R, Bradshaw D, Wegner T. Estimates of the Level and Shape of Mortality Rates in South Africa Around 1985 and 1990 Derived by Applying Indirect Demographic Techniques to Reported Deaths. 1999. http://www.mrc.ac.za/bod/1999report.pdf (accessed 20th May 2013).
5. Hughes JP, Baeten JM, Lingappa JR, et al. Determinants of Per-Coital-Act HIV-1 Infectivity Among African HIV-1–Serodiscordant Couples. *Journal of Infectious Diseases* 2012; **205**(3): 358-65.
6. Weiss HA, Halperin D, Bailey RC, Hayes RJ, Schmid G, Hankins CA. Male circumcision for HIV prevention: from evidence to action? *AIDS* 2008; **22**(5): 567-74.
7. Glynn J, Biraro S, Weiss H. Herpes simplex virus type 2: a key role in HIV incidence. *AIDS* 2009; **23**(12): 1595-8.
8. Barnabas RV, Webb EL, Weiss H, Wasserheit JN. The role of coinfections in HIV epidemic trajectory and positive prevention: a systematic review and meta-analysis. *AIDS* 2011; **25**(13): 1559-73.
9. Looker KJ, Magaret AS, May MT, et al. Global and Regional Estimates of Prevalent and Incident Herpes Simplex Virus Type 1 Infections in 2012. *PloS one* 2015; **10**(10): e0140765.
10. Programme C. Global & Regional Population Pyramids. http://collen.ageing.ox.ac.uk/data/international/global-population-trends/ (accessed May 1 2016).

11. Lodi S, Phillips A, Touloumi G, et al. Time From Human Immunodeficiency Virus Seroconversion to Reaching CD4+ Cell Count Thresholds <200, <350, and <500 Cells/mm3: Assessment of Need Following Changes in Treatment Guidelines. *Clinical Infectious Diseases* 2011; **53**(8): 817-25.
12. Duration from seroconversion to eligibility for antiretroviral therapy and from ART eligibility to death in adult HIV-infected patients from low and middle-income countries: collaborative analysis of prospective studies. *Sexually Transmitted Infections* 2008; **84**(Suppl 1): i31-i6.
13. Cori A, Ayles H, Beyers N, et al. HPTN 071 (PopART): A Cluster-Randomized Trial of the Population Impact of an HIV Combination Prevention Intervention Including Universal Testing and Treatment: Mathematical Model. *PLoS ONE* 2014; **9**(1): e84511.
14. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *The Lancet* 2010; **375**(9731): 2092-8.
15. Kenya AIDS indicator Survey 2012. Accessed on 1/1/2016 from: http://www.nacc.or.ke/images/documents/KAIS-2012.pdf.
16. Tanser F, Bärnighausen T, Grapsa E, Zaidi J, Newell M-L. High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa. *Science* 2013; **339**(6122): 966-71.
17. Wallrauch C, Barnighausen T, Newell ML. HIV prevalence and incidence in people 50 years and older in rural South Africa. *South African Medical Journal* 2010; **100**(12): 812-4.
18. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**(6): 493-505.
19. Kitahata MM, Gange SJ, Abraham AG, et al. Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival. *New England Journal of Medicine* 2009; **360**(18): 1815-26.
20. Etard JF, Ndiaye I, Thierry-Mieg M, et al. Mortality and causes of death in adults receiving highly active antiretroviral therapy in Senegal: a 7-year cohort study. *AIDS* 2006; **20**(8): 1181-9.
21. Mahy M, Lewden C, Brinkhof MWG, et al. Derivation of parameters used in Spectrum for eligibility for antiretroviral therapy and survival on antiretroviral therapy. *Sexually Transmitted Infections* 2010; **86**(Suppl 2): ii28-ii34.
22. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *The Lancet Global health* 2015; **3**(11): e712-23.
23. Eaton JW, Menzies NA, Stover J, et al. Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models. *The Lancet Global Health* 2014; **2**(1): e23-e34.

CHAPTER 5: Conclusion

Conclusions and future research:

This dissertation as a whole seeks to synthesize available data on HTC in sub-Saharan Africa. Chapter 2, a meta-analysis, characterizes diverse HTC modalities and provides a head-to-head comparison of how each strategy performs in population coverage, uptake, risk groups reached, and persons linked to care. Chapter 3 and 4 combine clinical, epidemiologic, and cost data on two specific HTC modalities using a mathematical model and projects their long-term impact on HIV burden.

Chapter 2: A systematic review and meta-analysis of community and facility-based approaches to address gaps in HIV testing and linkage in sub-Saharan Africa

Chapter 2 yielded a number of important findings. Community HTC modalities were found to have high acceptability across settings in SSA. Additionally, they reached a large proportion of first-time testers, indicating scale up would result in more persons tested who would otherwise not have undergone HTC at a healthcare facility. The low coverage of facility HTC suggests that many persons in SSA still do not have access to healthcare. Community-based methods are essential to achieving widespread HTC coverage. In addition to sub-population reached, we also estimated cost (per person tested) associated with various HTC modalities. Together, the costs and coverage can be used as parameters in mathematical models to determine the optimal combination of HTC strategies. As this analysis provides a broad overview of HTC in sub-Saharan Africa, future research should focus on specific countries/regions and assess the costs and effectiveness of HTC scale-up in those regions.

This chapter also highlights gaps in the published literature. While we found many studies that evaluated facility, home, and mobile HTC, the data were sparse for other modalities.

Additionally the majority of studies were conducted in South Africa, Kenya, and Uganda. Data are needed from other countries in sub-Saharan Africa.

Data were also limited for key populations. Despite having an HIV prevalence up to eight times higher than the general population, interventions for key populations are scarce and scale up is urgently needed.[1,2] Currently, numerous policy barriers exist that restrict the availability and access of HIV-related services for MSM and CSWs, including police harassment and criminal laws.[3] Most key population HTC studies were from Nigeria, so data are needed from other parts of sub-Saharan Africa. We report a high HIV positivity combined with a high proportion of first-time testers in MSM and CSWs, highlighting the need for service expansion. Successful HTC programmes for key populations are community-based (particularly mobile), as many high-risk groups are marginalized and do not have access to conventional health systems.[4] In addition, self-testing is a potential strategy to reach key populations, as it demonstrates high acceptability and is considered convenient and private.[5] It is also a useful strategy for groups that benefit from frequent re-testing.

Another underserved group that requires additional research is men. Men in SSA are less likely than women to undergo HIV testing;[6,7] they are more likely to start ART at advanced disease stages, interrupt or drop out of ART, and die on ART.[8] These disparities have resulted in a life expectancy gap of up to 10 years between HIV-positive men and women.[9-11] However, most HTC interventions have been focused on women and children so more research is needed on men.[12] Our review found only a few HTC interventions that specifically targeted men.[78] We found that mobile HTC is a particularly promising strategy to achieve high testing coverage in men and is considered more private than home HTC. A large community randomized trial in Tanzania and Zimbabwe (Project Accept) reported male testing coverage of 44-53% in sites

randomized to mobile testing compared to just 4-9% coverage of facility testing in control sites.[13] Further, integrating HTC into mobile multi-disease campaigns has also had success in reaching men.[14] Community health campaigns have been shown to achieve rapid HTC coverage in short time frames (approximately two weeks).[15,16] The SEARCH campaign conducted in Uganda and Kenya included HTC, a men's health station, information on VMMC, and home HTC for persons who did not participate in the campaign. This hybrid approach tested 86% of male residents in the communities, with the vast majority testing at the campaigns.[14] Combining HTC with other health interventions can reduce HIV-related stigma and also improve transport and waiting times. Studies have found that men prefer HIV services that are not separate from other healthcare services.[17] Future studies could assess the effectiveness HTC interventions that are tailored to the needs of men.

Although we found many studies evaluating coverage and population reached by community HTC, far fewer studies assessed linkage to care. As community HTC is conducted outside the healthcare system, particular attention should be given to linkage, as the success of an intervention depends on its ability to link and retain HIV-positive persons on ART. Future studies are needed to assess long-term outcomes (linkage to the clinic, initiating ART, and retention in care). One novel linkage strategy that can benefit from additional research is community-based ART initiation. As individuals in SSA face barriers to visiting healthcare facilities for HTC (distance from clinic, inconvenient operating hours, long wait times), they are likely to face the same barriers when visiting the clinic for ART. Community ART initiation can provide convenient and private access to treatment. A randomized control trial in Malawi found significantly higher ART uptake with optional home initiation compared to facility initiation

with no difference in retention in care at 6 months.[18] Future studies can incorporate community ART initiation into various community HTC modalities.

Similar to ART initiation, retention in care can be improved with more streamlined and convenient services. Distance from clinic has been found to be negatively associated with ART retention.[19] Community-based ART delivery (i.e. dispensing ART outside of healthcare systems) may be useful in promoting retention; it can also reduce burden on facilities as ART eligibility criteria expand and more people attempt to access treatment. Home, workplace, or mobile ART pickup sites would be particularly convenient. To our knowledge, only one study is investigating the effectiveness of community ART delivery.

Chapter 3: Modeling the cost-effectiveness of home-based HIV testing and education (HOPE) for pregnant women and their male partners in Nyanza Province, Kenya

In Chapter 3, we evaluate the health and economic impact of scaling up the HOPE intervention, which provided home HTC to pregnant women and their male partners in western Kenya. This intervention has multiple benefits: 1) it reaches pregnant women with couples HTC, as pregnant and post-partum women in SSA have high rates of HIV acquisition, 2) it reaches men who did attend ANC with their partners with home HTC; as mentioned in the prior section, men are an underserved group with low access to healthcare, and 3) it can identify serodiscordant couples and target PrEP, which can avert HIV infections in mothers and infants.

We found that the HOPE intervention is cost-effective for averting HIV-related morbidity and mortality. Our results were robust to a number of sensitivity analyses including intervention coverage, proportion linked to care, and cost of ART and HIV/AIDS related hospitalizations. Not surprisingly, task shifting from healthcare professionals to community health workers made the program more affordable, particularly because the bulk of the program costs were associated with staff salaries. Overall, HOPE was projected to reach 8% population coverage annually and

reduce approximately 2.5% of HIV infections in Nyanza over 10 years. Because of the limited population-level impact, it should be combined with community-based HIV interventions which have been found to be cost-effective.[20]

This research has a number of limitations which provide opportunities for future research. We assume male partners testing HIV-positive through the HOPE intervention have the same rate of linkage to ART as facility testing. Community-based testing can result in lower linkage rates since is conducted outside of the healthcare system.[21] The effectiveness estimate was obtained from a randomized controlled trial that utilized highly trained and closely monitored health advisors. If the HOPE intervention is scaled up through a government program, effectiveness may decrease if counselors were less able to persuade reluctant male partners to undergo testing, or were less efficient in delivering the intervention. In fact, due to the shortage of healthcare professionals in SSA, HOPE would likely be implemented using lower cadre community health workers, making this effectiveness estimate particularly relevant to scale up.

Further research is needed to evaluate the effectiveness of HOPE outside of a clinical trial and also track linkage outcomes. A potential future study is a HOPE demonstration project conducted in several healthcare facilities with real-world supervision. The project could employ community health workers and gauge any losses in intervention effectiveness without healthcare professionals. Community health workers could conduct follow-up visits to encourage partners to link to care. HIV-positive partners could be given study cards to present at the clinic when they enroll in ART so that linkage outcomes could be tracked. Additionally, the HOPE intervention could be used to identify serodiscordant couples to target PrEP, which increase the health benefits.

Chapter 4: Cost-effectiveness of implementing active partner notification for HIV in Kenya: A mathematical modeling analysis

In Chapter 4, we evaluate the efficiency of active partner notification using primary cost and effectiveness data from the aPS randomized control trial. We find that aPS can cost-effectively reduce HIV-related morbidity and mortality in western Kenya. In SSA, where the primary driver of the HIV-epidemic is heterosexual transmission and 50% of HIV-positive persons do not know they are infected, aPS is a promising strategy to fill in testing gaps. The high HIV positivity found in the modeled results as well as several clinical trials demonstrates that aPS is an efficient and high yield method to target resources towards those at highest risk of HIV infection. Although aPS is only projected to achieve 12% population coverage over 10 years, the intervention has a considerable impact on HIV burden, particularly in HIV-related deaths averted. In contrast, passive notification (standard of care) has had low success in SSA, with few partners coming to the clinic for HIV testing. Additionally, aPS is effective at testing both men and women. In a study of partner notification in Malawi, men represented only 15% of those presenting to the clinic for testing through passive referral compared to 50% of those tested through active tracing.[22]

Unlike HOPE, aPS has been evaluated in real world demonstration projects scenarios and found to have high uptake and effectiveness (similar to that of aPS clinical trials).[23] Future studies can investigate the effectiveness of implementing aPS through other testing modalities. For example aPS can be integrated into home, mobile, and ANC testing. Couples testing for HIV-positive pregnant women has been found to increase adherence to both ART and prevention of mother to child transmission (PMTCT) regimens which reduce HIV incidence to their infants.[24-27] Similar to HOPE, aPS can be utilized as a vehicle to target PrEP to serodiscordant couples. PrEP demonstration projects in Kenya and Uganda found high adherence in HIV-

negative partners given short-term PrEP (for use before their HIV-positive partner initiated ART and for 6 months afterwards to allow for viral suppression).[28] Finally, integrating health interventions is another way to reduce program costs. For example, the aPS intervention could be delivered along with diabetes and hypertension screening. Integrating services can also reduce the stigma associated with an HIV testing intervention.[14]

References

1. Wheeler T, Wolf RC, Kapesa L, Cheng Surdo A, Dallabetta G. Scaling-up HIV responses with key populations in West Africa. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S69-73.
2. Adebajo S, Eluwa G, Njab J, et al. Evaluating the effect of HIV prevention strategies on uptake of HIV counselling and testing among male most-at-risk-populations in Nigeria; a cross-sectional analysis. Sex Transm Infect 2015.
3. Duvall S, Irani L, Compaore C, et al. Assessment of policy and access to HIV prevention, care, and treatment services for men who have sex with men and for sex workers in Burkina Faso and Togo. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S189-97.
4. Mulongo S, Kapila G, Hatton T, et al. Applying innovative approaches for reaching men who have sex with men and female sex workers in the Democratic Republic of Congo. Journal of acquired immune deficiency syndromes (1999) 2015;68 Suppl 2:S248-51.
5. Figueroa C, Johnson C, Verster A, Baggaley R. Attitudes and Acceptability on HIV Self-testing Among Key Populations: A Literature Review. AIDS and behavior 2015;19:1949-65.
6. Tsai AC, Siedner MJ. The Missing Men: HIV Treatment Scale-Up and Life Expectancy in Sub-Saharan Africa. PLoS medicine 2015;12:e1001906.
7. Hensen B, Taoka S, Lewis JJ, Weiss HA, Hargreaves J. Systematic review of strategies to increase men's HIV-testing in sub-Saharan Africa. AIDS (London, England) 2014;28:2133-45.
8. Cornell M, McIntyre J, Myer L. Men and antiretroviral therapy in Africa: our blind spot. Tropical medicine & international health : TM & IH 2011;16:828-9.
9. Nsanzimana S, Remera E, Kanters S, et al. Life expectancy among HIV-positive patients in Rwanda: a retrospective observational cohort study. The Lancet Global health 2015;3:e169-77.
10. Geng EH, Bwana MB, Muyindike W, et al. Failure to initiate antiretroviral therapy, loss to follow-up and mortality among HIV-infected patients during the pre-ART period in Uganda. Journal of acquired immune deficiency syndromes (1999) 2013;63:e64-71.
11. Johnson LF, Mossong J, Dorrington RE, et al. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. PLoS medicine 2013;10:e1001418.
12. Mills EJ, Beyrer C, Birungi J, Dybul MR. Engaging men in prevention and care for HIV/AIDS in Africa. PLoS medicine 2012;9:e1001167.
13. Sweat M, Morin S, Celentano D, et al. Community-based intervention to increase HIV testing and case detection in people aged 16-32 years in Tanzania, Zimbabwe, and Thailand (NIMH Project Accept, HPTN 043): a randomised study. The Lancet infectious diseases 2011;11:525-32.
14. Chamie G, Clark TD, Kabami J, et al. A hybrid mobile approach for population-wide HIV testing in rural east Africa: an observational study. The lancet HIV 2016;3:e111-9.
15. Chamie G, Kwarisiima D, Clark TD, et al. Uptake of community-based HIV testing during a multi-disease health campaign in rural Uganda. PloS one 2014;9:e84317.
16. Lugada E, Millar D, Haskew J, et al. Rapid implementation of an integrated large-scale HIV counseling and testing, malaria, and diarrhea prevention campaign in rural Kenya. PloS one 2010;5:e12435.
17. Mak J, Mayhew SH, von Maercker A, Colombini M. Men. Sex Health 2016.
18. MacPherson P, Lalloo DG, Webb EL, et al. Effect of optional home initiation of HIV care following HIV self-testing on antiretroviral therapy initiation among adults in Malawi: A randomized clinical trial. JAMA - Journal of the American Medical Association 2014;312:372-9.

19. Geng EH, Glidden DV, Bwana MB, et al. Retention in care and connection to care among HIV-infected patients on antiretroviral therapy in Africa: estimation via a sampling-based approach. PloS one 2011;6:e21797.
20. Smith JA, Sharma M, Levin C, et al. Cost-effectiveness of community-based strategies to strengthen the continuum of HIV care in rural South Africa: a health economic modelling analysis. The lancet HIV 2015;2:e159-e68.
21. Sharma M, Ying R, Tarr G, Barnabas R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. Nature 2015;528:S77-85.
22. Brown LB, Miller WC, Kamanga G, et al. HIV partner notification is effective and feasible in sub-Saharan Africa: opportunities for HIV treatment and prevention. Journal of acquired immune deficiency syndromes (1999) 2011;56:437-42.
23. Henley C, Forgwei G, Welty T, et al. Scale-up and case-finding effectiveness of an HIV partner services program in Cameroon: an innovative HIV prevention intervention for developing countries. Sexually transmitted diseases 2013;40:909-14.
24. Crepaz N, Tungol-Ashmon MV, Vosburgh HW, Baack BN, Mullins MM. Are couple-based interventions more effective than interventions delivered to individuals in promoting HIV protective behaviors? A meta-analysis. AIDS care 2015;27:1361-6.
25. Ebuy H, Yebyo H, Alemayehu M. Level of adherence and predictors of adherence to the Option B+ PMTCT programme in Tigray, northern Ethiopia. Int J Infect Dis 2015;33:123-9.
26. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. AIDS and behavior 2010;14:558-66.
27. Rosenberg NE, Mtande TK, Saidi F, et al. Recruiting male partners for couple HIV testing and counselling in Malawi's option B+ programme: an unblinded randomised controlled trial. The lancet HIV 2015;2:e483-91.
28. Baeten J, Heffron R, Kidoguchi L, et al. Near Elimination of HIV Transmission in a Demonstration Project of PrEP and ART. 2015 Conference on Retroviruses and Opportunistic Infections. Seattle, February 23-24, 2015. Abstract 24.

Curriculum Vitae

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EDUCATION

University of Washington School of Public Health, Seattle, WA 8/2012-present
PhD student, **Epidemiology**
Dissertation: Evaluating the efficiency of HIV prevention and linkage to care strategies in sub-Saharan Africa

Johns Hopkins Bloomberg School of Public Health**,** Baltimore, MD 5/2009
Master of Science in Public Health (ScM), **Infectious Disease Epidemiology**
Thesis: Correlates of Consistent Condom Use with Clients among Female Sex Workers in Andhra Pradesh, India: Implications for Interventions

Tufts University**,** Medford, MA 5/2004
Bachelor of Science, *Cum Laude*, Major: **Biology**, Minor: **English**

WORK EXPERIENCE

University of Washington School of Public Health, Seattle, WA 6/2013-present
Department of Epidemiology
Research Assistant (20 hr/week) for Drs. Ruanne Barnabas and Carey Farquhar

- Travel to South Africa, Uganda, and Kenya to collect primary data on costs and conduct time-motion studies to estimate costs of HIV testing interventions.
- Parameterize dynamic HIV simulation model to South Africa, Uganda, and Kenya to analyze cost-effectiveness of HIV counseling and testing strategies.
- Serve on CFAR Health Economics Impact Study Team, present talk entitled "Data sources and resources for modeling cost-effectiveness of HIV interventions" at cost-effectiveness methods for HIV research workshop at Bill and Melinda Gates Foundation for UW students and faculty.
- Co-led day-long health economics workshop in Kisumu, Kenya entitled "Cost-effectiveness methods for HIV research."
- Served as part of WHO diagnostics and modeling consortium to characterize the costs and effectiveness of community-based counseling and testing in sub-Saharan Africa for WHO testing guidelines.

University of Washington School of Public Health, Seattle, WA 1/2013-6/2013
Department of Epidemiology
Research Assistant (20 hr/week) for Dr. Annette Fitzpatrick

- Analyzed association between biomarkers of inflammation and cognitive decline in the Ginkgo Evaluation of Memory (GEM) cohort using generalized-estimating equations and mixed effects models.

University of Washington School of Public Health, Seattle, WA 9-12/2012
Department of Global Health
Research Assistant (20 hr/week) for Dr. Dilys Walker

- Evaluated PRONTO maternal and neonatal health intervention in Guatemala by analyzing changes in clinic staff knowledge and self-efficacy via pre and post intervention surveys. Create database for pre and post surveys, clean and analyze dataset with codebook in Spanish. Collaborate with in-country investigators to obtain data.
- Evaluated the completeness and accuracy of WHO Near Miss forms in recording maternal and neonatal complications and active management of labor in Guatemala.
- Mentored an undergraduate in data analysis for student project.

Harvard School of Public Health, Boston, MA 8/2009-8/2012
Department of Health Policy and Management, Center for Health Decision Science
Research Analyst/Data Manager

- Conduct extensive literature reviews and extract and synthesize epidemiologic data into format used by individual-based Monte-Carlo cervical cancer (CC) simulation model.
- Calibrated Monte-Carlo and dynamic simulation models to epidemiologic data to analyze the cost-effectiveness of CC prevention strategies.
- Analyzed large databases such as Medical Health Expenditure Survey (MEPS), Behavioral Risk Factor Surveillance System (BRFSS), and National Health and Nutrition Examination Survey (NHANES)

MA Department of Public Health, Boston, MA 3/2006-6/2007
Occupational Health Surveillance Program

Research Analyst

- Managed and analyzed work-related asthma (WRA) databases.
- Reviewed medical records to identify WRA cases.
- Conducted phone interviews with individuals with WRA.
- Wrote quarterly Occupational Asthma Bulletin distributed to 1,600 physicians.

LIFT, Cambridge, MA 7/2004-8/2005
Site Coordinator/Americorps VISTA (Volunteers in Service to America)

- Assisted low-income clients in accessing employment, housing, public benefits, etc.
- Recruited, trained, and managed 30 undergraduate volunteers from Harvard University.

TEACHING EXPERIENCE

The University of Washington, Seattle, WA 4/2013-6/2013
Teaching Assistant

- Introduction to Epidemiology (EPI 420)

Taught weekly discussion sections and gave class lecture on disease screening.
Harvard School of Public Health, Boston, MA 11/2011-12/2012
Teaching Assistant

- Research in Decision Science (RDS 280)

The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 8/2008-3/2009
Teaching Assistant

- Principles of Epidemiology†
- Epidemiologic Methods II
- Epidemiologic Methods III

Co-led weekly laboratory sessions of 40 graduate students in addition to regular TA duties.
† Nominated for TA of the year

INTERNSHIP/RESEARCH EXPERIENCE

Harvard School of Public Health, Boston, MA 1/2011-5/2011
Department of Epidemiology
Independent Study (with Drs. Marc Lipsitch and Ted Cohen)

- Created an Excel-based dynamic transmission model and accompanying training module with real world scenarios to serve as an introduction to infectious disease outbreaks. Module used in CDC training and HSPH introductory class.

YRG Centre for AIDS Research and Education (YRG CARE), Nellore, India 6/2009-8/2009
Research Assistant

- Conducted a survey of demographics, risk behavior, and HIV knowledge in female sex workers in rural India.
- Co-wrote research proposal for IRB approval.
- Designed questionnaire and trained staff on interview implementation.
- Supervised survey language translation and created documentation and tracking for project.
- Met with local NGOs to recruit study participants.
- Piloted survey, analyzed initial results, and modified survey.

Public Health Applications for Student Experience (PHASE) Internship, Baltimore, MD
Intern with the Baltimore City Health Department 11/2008-5/2009

- Created a strategic plan for the Baltimore City Health Department to implement Internet-based HIV and STD prevention and intimate partner notification (IPN).
- Created staff training module on use of the Internet for intimate partner searches and notification, analyzed results.

Tufts University, Research Experience for Undergraduates Program, Medford, MA 5/2002-8/2003
Research Assistant

- Conducted plant biology research for Dr. Colin Orians with NSF-REU summer sponsorship.

Boston University Medical Center, Boston, MA 6/2002-8/2002
Research Assistant

- Performed Western Blots, PCR Analysis, and cell culture to study impact of stress on Gulf War Disease.

PUBLICATIONS

Sharma M, Ying R, Farquhar C, Krakowiak D, Kinuthia J, Osoti A, Asila V, Gone A, Mark J, Barnabas R. Modeling the Cost-Effectiveness of Home-Based HIV Testing and Education (HOPE) for Pregnant Women and Their Male Partners in Nyanza Province, Kenya. *J Acquir Immune Defic Syndr. 2016 Aug 1;72 Suppl 2:S174-80*

Krakowiak D, Kinuthia J, Osoti A, Asila V, Gone A, Mark J, Betz B, Parikh S, **Sharma M**, Barnabas R, Farquhar C Home-based HIV testing among pregnant couples increases partner testing and identification of serodiscordant partnerships in a randomized clinical trial. *J Acquir Immune Defic Syndr. 2016 Aug 1;72 Suppl 2:S167-73.*

Ying R, **Sharma M**, Celum C, Baeten JM, Murnane P, Hong T, Krows M, van Rooyen H, Humphries H, Hughes JP, Barnabas RV. The cost-effectiveness of periodic home-based HIV testing and counseling campaigns in a generalized epidemic setting: a mathematical modelling analysis. *Lancet HIV. 2016 Jun;3(6):e275-82.*

Sharma M, Fitzpatrick AL, Chi GC, Lopez OL, Jenny NS, DeKosky S. Inflammatory biomarkers and global cognition: The Ginkgo Evaluation of Memory (GEM) Study. *Journal of the American Geriatrics Society*

Sharma, M, Ying, R, Tarr, G, and Barnabas, R. Systematic review and meta-analysis of community and facility-based HIV testing to address linkage to care gaps in sub-Saharan Africa. *Nature. 2015; 528: S77–S85*

Sharma M, Sy S, Kim JJ. The value of male HPV vaccination in preventing cervical cancer in South Vietnam. *BJOG. 2015 Jul 14.*

Ying R, **Sharma M**, Heffron R, Celum C, Baeten JM, Katabira, Bulya N, Barnabas RV. 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.*

Smith JA, **Sharma M**, Levin C, Baeten JM, van Rooyen H, Celum C, Hallett TB, Barnabas RV. Community-based strategies to strengthen the continuum of HIV care are cost-effective in rural South Africa: a health economic modelling analysis. *Lancet HIV*. 2015 Apr 1;2(4):e159-e168.

Levin C, **Sharma M**, Olson Z, Verguet S, Jamison D, Kim JJ. An extended cost-effectiveness analysis of publicly financed HPV vaccination to prevent cervical cancer in China. *Vaccine.* 2015 Mar 12. pii: S0264-410X(15)00241-8.

Campos N, Burger E, Sy S, **Sharma M**, Schiffman M, Rodriguez AC, Hildesheim A, Herrero R, Kim JJ. An enhanced natural history model of cervical cancer: Derivation of model parameters. *American Journal of Epidemiology*. 07/2014

Holme F, Kestler E, Raney J, **Sharma M**, Walker D. Adaptation and validation at the primary level of health of the format "Almost-dead" by WHO to detect maternal and perinatal morbidity in indigenous population of Guatemala. *REVCOG* Vol.18 núm. 3 julio-septiembre Artículo Original, 2013.

Kim JJ, **Sharma M**, O'Shea M, Sweet S, Diaz M, Sancho-Garnier H, Seoud M. Model-Based Impact and Cost-Effectiveness of Cervical Cancer Prevention in the Extended Middle East and North Africa (EMENA). *Vaccine*. 2013 Dec 30;31 Suppl 6:G65-77. doi: 10.1016/j.vaccine.2012.06.096.

Berkhof J, Bogaards JA, Demirel E, Diaz M, **Sharma M**, Kim JJ. Cost-effectiveness of cervical cancer prevention in Central and Eastern Europe and central Asia. Vaccine. 2013 Dec 31;31 Suppl 7:H71-9. doi: 10.1016/j.*Vaccine*.2013.04.086.

Kim JJ, **Sharma M,** Ortendahl J. Optimal interval for routine cytology screening in the United States. *JAMA Intern Med.* 2013;173(3):241-242. doi:10.1001/2013.jamainternmed.1034.

Sharma M, Bruni L, Diaz Sanchis M, Bosch FX, Kim JJ. Using HPV Prevalence to predict cervical cancer incidence. *Int J Cancer*. 2012 Sep 11. doi: 10.1002/ijc.27835.

Sharma M, Ortendahl J, van der Ham E, Sy S, Kim JJ. Cost-effectiveness of human papillomavirus vaccination and cervical cancer screening in Thailand. *BJOG* 2012;119:166–176.

Zanne AE, Sweeney K, **Sharma M**, Orians CM (2006) Patterns and consequences of differential vascular sectoriality in 18 temperate tree and shrub species. *Functional Ecology*, 20, 200-206.

BOOK CHAPTERS

Levin C, **Sharma M**, Olson Z, Verguet S, Jamison D, Kim JJ. Chapter 16: The equity and financial risk protection benefits from a publicly financed HPV vaccination policy in China: An extended cost-effectiveness analysis. *Disease Control Priorities3*, 2013.

RESEARCH IN PROGRESS

Campos NG, **Sharma M**, Clark A, Kim JJ, Resch SC. The Cost of Action: A Research Initiative to Determine the Global Price of Comprehensive Global Cervical Cancer Prevention. *Revise and resubmit: PLOS One*

Chi GC, Fitzpatrick AL, **Sharma M**, Lopez OL, Jenny NS, DeKosky S. Inflammatory Biomarkers Predict Low Domain-Specific Cognitive Function in Older Adults. *Under review: Preventing Chronic Disease*

Kim JJ, **Sharma M**, Sy S Ortendahl J, The tradeoff of harms and benefits of early cervical cancer screening in the US.

Sharma M, Kim JJ, Seoud M. Cost-effectiveness of increasing cervical cancer screening coverage and efficiency in Lebanon.

Kim JJ, Sy S, **Sharma M**. Health and Economic Consequences of Male HPV Vaccination on Cervical Cancer Burden in Thailand.

Sharma M, Sivaram S, Srikrishnan AK, Vasudevan CK, Hari R, Solomon S, Celentano DD. Correlates of Consistent Condom Use with Clients Among Female Sex Workers in Andhra Pradesh, India: Implications for Interventions.

PRESENTATIONS/ABSTRACTS

Krakowiak D, Kinuthia J, Osoti A, Asila V, Gone MA, Mark J, **Sharma M**, Barnabas RV. Male partner home HIV testing vs clinic invitation in pregnancy: A randomized trial. [Oral] Conference on Retroviruses and Opportunistic Infections (CROI), Boston, MA, February, 2016.

Sharma M, Ying R, Tarr G, Barnabas RV. Community-based approaches address gaps in HIV testing and linkage in sub-Saharan Africa: A systematic review and meta-analysis. [Poster] HIV Pathogenesis, Treatment and Prevention (IAS), Vancouver, BC, July, 2015.

Sharma M, Farquhar C, Kinuthia J, Osoti A, Asila V, Parikh S, Krakowiak D, Gone A, Barnabas RV. Cost of home HIV testing and education for male partners of pregnant women in Kenya. [Poster] HIV Pathogenesis, Treatment and Prevention (IAS), Vancouver, BC, July, 2015.

Sharma M, Van Rooyen H, Celum C, Baeten J, Levin C, Barnabas R. The Cost of Community Based HIV Counseling and Testing and Linkage to Care in Rural South Africa: Estimates from the Linkages Randomized Control Trial. [Poster] Research for Prevention (R4P), Capetown, SA, November, 2014.

Sharma M, Fitzpatrick AL, Chi GC, Lopez OL, Jenny NS, DeKosky S. Inflammatory biomarkers and global cognition: The Ginkgo Evaluation of Memory (GEM) Study. [Poster] The Society for Epidemiologic Research (SER), Boston, MA, June 2013.

Chi GC, Jenny NS, Lopez OL, **Sharma M**, Fitzpatrick AL. Inflammation is associated with separate domains of cognitive decline in the elderly. [Poster] The Society for Epidemiologic Research (SER), Boston, MA, June 2013.

Holme, F, Walker D, Kestler E, Dettinger J, **Sharma M**, Fritz J, Olvera M, Fahey J, Cohen S. Catalyzing change in rural Guatemalan childbirth care: Evidence for a low-tech, low-cost obstetric and neonatal emergency simulation training program, PRONTO. (Oral APHA, Boston, MA, October 2013).

Walker D, Holme F, Kestler E, **Sharma M**, Raney J, Dettinger J. Detecting severe maternal and neonatal morbidity in rural Guatemala: Validating the WHO's near miss approach in a primary care clinic setting. [Oral] Global Maternal Health Conference Arusha, Tanzania, January 2013.

Sharma M, Kim JJ, Seoud M. Cost-effectiveness of increasing cervical cancer screening coverage and efficiency in Lebanon. [Oral] Society for Medical Decision Making, Phoenix, AZ, October 2012.
Lee Lusted Presentation Award Finalist

Sharma M, Sy S, Kim JJ. The value of male HPV vaccination in preventing cervical cancer in South Vietnam [Poster] Society for Medical Decision Making, Chicago, IL, October 2011.
Lee Lusted Presentation Award Finalist

Sharma M, Bruni L, Diaz Sanchis M, Bosch FX, Kim JJ. Predicting Country-Level Cervical Cancer Incidence: Development and Validation of a Prognostic Model Based on HPV Prevalence, Geographical Region and Screening Coverage. [Poster] Infectious Disease Society of America, Boston, MA, October 2011.

Sharma M, Ortendahl J, van der Ham E, Sy S, Kim JJ. Cost-Effectiveness of HPV Vaccination and Cervical Cancer Screening in Thailand. [Poster] International Papillomavirus Conference, Montreal, Canada, July 2010.

Kim JJ, Sy S, **Sharma M**. Cost-Effectiveness of Targeted HPV-16,-18 Vaccination of Men Who Have Sex With Men in the U.S. [Poster] International Papillomavirus Conference, Montreal, Canada, July 2010.

Kim JJ, Sy S, Ortendahl J, van der Ham E, **Sharma M**. Health and Economic Consequences of Male HPV Vaccination on Cervical Cancer Burden in Thailand. [Poster] International Papillomavirus Conference, Montreal, Canada, July 2010.

Sharma M, Sivaram S, Srikrishnan AK, Vasudevan CK, Hari R, Solomon S, Celentano DD. Correlates of Consistent Condom Use with Clients Among Female Sex Workers in Andhra Pradesh, India: Implications for Interventions. [Poster] Infectious Disease Society of America, Philadelphia, PA, October 2009.

Sharma M, Burnett P. Utilizing the Internet for Intimate Partner Services. [Oral presentation] Public Health Applications for Student Experience (PHASE) Symposium, Baltimore, MD, May 2009.

GRANTS & HONORS

HIV Research for Prevention (R4P) Travel Scholarship (2016)
Center for AIDS and STD Training Grant, NIAID T32 AI07140, funding for pre-doctoral research (2015-present)
SPH Endowed Fellow (2015)
IAS Young Investigator Award (2015)

PEER REVIEW ACTIVITIES

Journal Reviewer for *American Journal of Epidemiology* (2012-Present)
Journal Reviewer for *International Journal of Cancer* (2012-Present)
Journal Reviewer for *Vaccine* (2014-Present) (Outstanding reviewer status)

COMMUNITY SERVICE AND LEADERSHIP EXPERIENCE

- Tufts Alumni (Seattle Chapter) President (2013-present)
- Epidemiology curriculum committee (2015-2016)
- President of Seattle Chapter of Tufts Alumni Association (2012-present)
- Founding member and Membership Chair of Active Citizens of Tufts Alumni (ACT) Boston (12/2009-2012)
- Membership Chair of Alumni Executive Board for LIFT (2/2006-2/2007)
- Board Member of Leonard Carmichael Society (LCS), Tufts University volunteer organization (2002-2004)

COMPUTER AND LANGUAGE SKILLS

Proficient in MSWord, PowerPoint, Excel, Access, EndNote, Stata, SAS, TreeAge, Matlab. Proficient in Spanish and Hindi.