Cost-effectiveness of couples’ voluntary HIV counselling and testing in six African countries: a modelling study guided by an HIV prevention cascade framework

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Abstract

Introduction: Couples’ voluntary HIV counselling and testing (CVCT) is a high-impact HIV prevention intervention in Rwanda and Zambia. Our objective was to model the cost-per-HIV infection averted by CVCT in six African countries guided by an HIV prevention cascade framework. The HIV prevention cascade as yet to be applied to evaluating CVCT effectiveness or cost-effectiveness.

Methods: We defined a priority population for CVCT in Africa as heterosexual adults in stable couples. Based on our previous experience nationalizing CVCT in Rwanda and scaling-up CVCT in 73 clinics in Zambia, we estimated HIV prevention cascade domains of motivation for use, access and effectiveness of CVCT as model parameters. Costs-per-couple tested were also estimated based on our previous studies. We used these parameters as well as country-specific inputs to model the impact of CVCT over a five-year time horizon in a previously developed and tested deterministic compartmental model. We consider six countries across Africa with varied HIV epidemics (South Africa, Zimbabwe, Kenya, Tanzania, Ivory Coast and Sierra Leone). Outcomes of interest were the proportion of HIV infections averted by CVCT, nationwide CVCT implementation costs and costs-per-HIV infection averted by CVCT. We applied 3%/year discounting to costs and outcomes. Univariate and Monte Carlo multivariate sensitivity analyses were conducted.

Results: We estimated that CVCT could avert between 54% (Sierra Leone) and 62% (South Africa) of adult HIV infections. Average costs-per-HIV infection averted were lowest in Zimbabwe ($550) and highest in South Africa ($1272). Nationwide implementations would cost between 7% (Kenya) and 21% (Ivory Coast) of a country’s President’s Emergency Plan for AIDS Relief (PEPFAR) budget over five years. In sensitivity analyses, model outputs were most sensitive to estimates of cost-per-couple tested; the proportion of adults in heterosexual couples and HIV prevention cascade domains of CVCT motivation and access.

Conclusions: Our model indicates that nationalized CVCT could prevent over half of adult HIV infections for 7% to 21% of the modelled countries’ five-year PEPFAR budgets. While other studies have indicated that CVCT motivation is high given locally relevant promotional and educational efforts, without required indicators, targets and dedicated budgets, access remains low.

Keywords: Africa; cost-effectiveness; costs and cost analysis; couples; HIV; HIV prevention cascade; prevention and control

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1 | INTRODUCTION

Incident HIV infections in sub-Saharan Africa have fallen 13% over recent years due to global prevention efforts [1]. However, this decline in new infections is slowing, gaps in the scale-up of treatment and prevention services persist, and flatlined funds are not projected to meet 2030 Sustainable Development Goals [1,2]. Now more than ever, maximizing the value of limited funding is critical, and evaluating the cost-effectiveness of HIV prevention and treatment strategies is essential for improved resource allocation [1,3]. The HIV prevention cascade, which evaluates domains of intervention motivation for use, access and effectiveness among a priority population, provides a useful framework to evaluate and advocate for prevention interventions [4] and has been used to evaluate interventions such as pre-exposure prophylaxis (PrEP), voluntary medical male circumcision (VMMC) and prevention of mother-to-child transmission (PMTCT) [5-8].

The HIV prevention cascade has yet to be described or evaluated for couples’ voluntary HIV counselling and testing.
(CVCT), an evidence-based intervention in which couples receive joint pre-test counselling, testing and post-test counselling with counsellor-facilitated serostatus disclosure [9,10]. CVCT decreases sexual and perinatal HIV incidence [11-16] by educating and placing joint responsibility on the dyad to increase uptake of condoms, VMMC, family planning, antiretroviral therapy (ART) and PMTCT [13-15,17]. The priority population for CVCT is stable couples. With the exception of South Africa, most African adults are in cohabiting sexual unions [18], and the majority of HIV transmissions in sub-Saharan Africa occur in heterosexual HIV discordant or concordant HIV-negative couples [19]. Despite World Health Organization (WHO) [9] and the US Centers for Disease Control and Prevention (CDC) [10] CVCT recommendations, only a small percentage of African adults have been tested with partners.

Building on our technical support for the nationalization of CVCT in antenatal clinics (ANC) in Rwanda, where >80% of couples are now tested [20], we recently reported the cost-effectiveness of a CVCT demonstration project serving 207,428 Zambian couples in 73 government clinics [21]. Receiving CVCT was associated with a 79% reduction in seroincidence among discordant couples using ART, 63% among discordant couples not using ART and 47% among concordant-negative couples. The cost-per-HIV infection averted (CHIA) for CVCT was $659. We then built and validated a deterministic compartmental model which incorporated key domains from the HIV prevention cascade framework and reported the CHIA for nationalizing CVCT in Zambia ($394 CHIA) [21].

In the present analysis, we adapt this model to estimate the proportion of adult HIV infections averted, total costs and CHIA for nationalizing CVCT in six countries across sub-Saharan Africa.

2 | METHODS

2.1 | Ethics approval

This retrospective costing and modelling study used de-identified data from the publicly available sources cited. The Institutional Research Board at Emory University waived informed consent requirements.

2.2 | Deterministic compartmental model

Our CVCT CHIA model details are published [21]. In summary, a deterministic compartmental model with one-year time steps based on a series of differential equations was developed in Excel which allows heterosexual adult couples who are either concordant HIV-negative or discordant, and on ART or off ART, to transition between states of HIV status and/or ART use over time. Our previous model structure [21] has been adapted here to incorporate HIV prevention cascade domains of motivation and access, which the previous model did not include.

Our model uses HIV seroincidence rates in un counselled (“pre-CVCT”) serodiscordant and concordant-negative couples (which is assumed to be a function of all current prevention programmes taking place in country) and applies the estimated effectiveness of CVCT among couples depending on their joint HIV serostatus and ART use. These effectiveness estimates are applied each year, and couples move from concordant negative to discordant and from discordant to discordant positive accordingly. Estimated “pre-CVCT” ART use and ART initiation in the year following CVCT are also model parameters, with an additional proportion of HIV-positive individuals taking up ART each year. Estimated costs-per-couple tested are based on our programmatic experience. The model outputs HIV infections averted by CVCT (by subtracting the cumulative infections that are projected to occur post-CVCT from those occurring pre-CVCT), total incremental financial costs to implement CVCT and incremental CHIA by CVCT [21]. As evidence suggests that the HIV prevention impact of CVCT is sustainable for at least five years [22-25], we chose a five-year time horizon.

In the model, we conceptualize the expansion of CVCT in four phases: initiation, expansion, maturation and maintenance which are described in more detail below. These phases are defined by a changing set of estimated values for the HIV prevention cascade domains of motivation and access among the priority population for CVCT (Figure 1) and cost-per-couple tested.

Using this model, we previously estimated the cost-effectiveness of nationalizing CVCT in Zambia by applying the actual financial expenditures and CVCT effectiveness observed when scaling-up services in 73 government clinics in Lusaka, Copperbelt and Southern Provinces which reached 207,428 couples. We conducted sensitivity analyses to evaluate the effect of possible differential loss to follow-up, informative censoring using inverse probability of censoring weighting [26,27], and inverse probability of treatment weighting to evaluate the possibility of confounding when using observational data to estimate intervention effects. We found that our model was robust in these sensitivity analyses [21]. Additionally, to internally validate the model, we used logical testing by varying transition probabilities and setting costs and outcomes to 0 separately, which resulted in logical expected values.

2.3 | Base-case model parameters applied to all countries

Base-case estimates for CVCT HIV prevention impact were derived from our CVCT implementation in 73 Zambian government clinics [21] (Table 1). Briefly, from September 2010 to March 2016, CVCT services were implemented including joint pre-test counselling; rapid HIV testing; joint post-test counselling; provision of condoms and referrals as needed for ART, VMMC and family planning. History of prior HIV testing and self-reported ART use were documented. HIV antibody-negative individuals had repeat tests one month after CVCT. Discordant couples returned for quarterly retesting and counselling, and concordant HIV-negative couples returned for annual retesting and counselling [28]. Promotions utilized influential community health workers and mass media [28,29].

During the implementation, the impact of CVCT was assessed over longitudinal follow-up. HIV seroincidence rates for discordant and concordant HIV-negative couples were calculated as incident infections divided by HIV-negative person-years (PY) of follow-up, stratified by whether couples had (“post-CVCT”) or had not (“pre-CVCT”) received CVCT. As shown in Table 1, in discordant-negative couples, we
observed a 47% reduction in HIV seroincidence pre-CVCT (1.1/100PY) versus post-CVCT (0.6/100PY). In serodiscordant couples in which the HIV+ partner was not on ART, we observed a 63% reduction in incidence (13.0/100PY pre-CVCT versus 4.8/100PY post-CVCT). Finally, in serodiscordant couples in which the HIV+ partner was on ART, we observed a 79% reduction in incidence (8.5/100PY pre-CVCT versus 1.8/100PY post-CVCT) [21]. We also use the increase in ART uptake reported in the previously published manuscript (38% of non-users initiated ART after CVCT with 5%/year additional uptake thereafter) [21]. Self-reported ART initiation is not assumed to imply adherence-suppressive ART.

Base-case estimates for cost-per-couple tested, motivation for CVCT, and access to CVCT were derived from both the Zambian implementation study described and our years of experience supporting nationalization of CVCT in Rwanda [20,21]. We derived incremental financial costs from the donor’s perspective from a primary costing study of actual expenditures to implement CVCT in government clinics following Global Heath Cost Consortium guidance [30]. Cost data were reported by activity were recorded by study staff during programme implementation and entered in AccPac (Sage Group). Based on our experiences in Rwanda and Zambia [20,21], motivation for CVCT, and access to CVCT varied over time and are used to define implementation phases as shown in Table 1: initiation phase (advocacy, training and promotions to motivate 20% of couples, 50% of whom have CVCT access); expansion phase (continued advocacy and training, increased community and politico-administrative involvement, CVCT certification for a majority of providers and active promotions to motivate 38% of couples, 56% of whom have CVCT access); maturation phase (an established programme with CVCT integrated into existing services including ANC, individual HIV counselling and testing, ART, VMMC and family planning services and 66% of couples are motivated, 60% of whom have CVCT access); and finally the maintenance phase (for hard-to-reach residual and new couples where only 15% are motivated, of whom 70% have CVCT access). Thus, 80% of couples are assumed to be reached with testing, as seen in Rwandan ANC [20].

### 2.4 Country-specific parameters

South Africa, Zimbabwe, Kenya, Tanzania, Ivory Coast and Sierra Leone have diverse HIV epidemics and published data available for the model inputs (Table 2). Country-specific model parameters include: (1) proportion of adults in cohabiting heterosexual couples, (2) couple HIV serostatus distribution, (3) ART use, (4) HIV seroincidence in uncounselled (pre-CVCT) discordant-negative couples, (5) HIV seroincidence in uncounselled discordant couples not on ART, (6) HIV seroincidence in uncounselled discordant couples not on ART, (7) estimated cost-per-couple tested. Published estimates of HIV seroincidence in uncounselled discordant-negative couples [31-34] and uncounselled discordant non-ART using couples [31-35] are limited to Eastern Africa. Given limited data for Southern African countries, model inputs 4, 5 and 6 (Table 2) were estimated from Zambia data [21]. As no published data are

### Table 1. Base-case model parameters applied to all countries

| Parameter                                      | Value and source |
|------------------------------------------------|------------------|
| CVCT effective use (HIV prevention impact)     |                  |
| Among concordant HIV-negative couples          | 47% [21]         |
| Among discordant couples                       |                  |
| not on ART                                     | 63% [21]         |
| Among discordant couples on ART                 | 79% [21]         |
| ART use                                        |                  |
| Immediate increase in uptake after CVCT        | 38% [21]         |
| Additional uptake per year                     | 5% [21]          |
| CVCT motivation among the priority population  |                  |
| Initiation phase                               | 20% of couples [20,21] |
| Expansion phase                                | 38% of couples [20,21] |
| Maturation phase                               | 66% of couples [20,21] |
| Maintenance phase                              | 15% of couples [20,21] |
| CVCT access among those motivated              |                  |
| Initiation phase                               | 50% of motivated couples [20,21] |
| Expansion Phase                                | 56% of motivated couples [20,21] |
| Maturation phase                               | 60% of motivated couples [20,21] |
| Maintenance phase                              | 70% of motivated couples [20,21] |

ART, antiretroviral treatment; CVCT, couples’ voluntary HIV counselling and testing; USD, United States Dollar.
| Model input                                                                 | Southern Africa | Eastern Africa | Zimbabwe | Tanzania | Ivory Coast | Western Africa | Sierra Leone |
|---------------------------------------------------------------------------|-----------------|----------------|----------|----------|------------|----------------|-------------|
| Adult population (ages 15 to 64)                                          | 37,904,001      | 7,892,000      | 1,393,900 | 428,200  | 1,874,500  | 2,974,500      | 1,383,900   |
| Adult population in stable couples (%)                                     | 35%             | 58%            | 59%      | 57%      | 59%        | 57%            | 59%         |
| Discordant couples among all stable couples (%)                            | 16%             | 9%             | 6%       | 5%       | 6%         | 6%             | 9%          |
| Discordant-negative couples (%)                                           | 91%             | 80%            | 59%      | 59%      | 57%        | 57%            | 59%         |
| Concordant-negative couples (%)                                           | 16%             | 88%            | 84%      | 84%      | 84%        | 84%            | 84%         |
| Concordant-negative couples (%)                                           | 16%             | 88%            | 84%      | 84%      | 84%        | 84%            | 84%         |
| Adults on ART of all estimated positive adults (%)                        | 62%             | 89%            | 89%      | 89%      | 89%        | 89%            | 89%         |
| Uncounselled seroincidence among concordant-negative couples (per 100 PY) | 1/100 PY        | 1/100 PY       | 1/100 PY | 1/100 PY | 1/100 PY   | 1/100 PY       | 1/100 PY    |
| Uncounselled seroincidence among non-ART using discordant couples (per 100 PY) | 13/100 PY | 13/100 PY | 10/100 PY | 10/100 PY | 10/100 PY | 10/100 PY | 10/100 PY |
| Uncounselled seroincidence among ART using discordant couples (per 100 PY) | 8/100 PY        | 8/100 PY       | 5/100 PY | 5/100 PY | 5/100 PY   | 5/100 PY       | 5/100 PY    |
| Initiation phase cost per couple tested (2015 USD)                        | $229            | $84            | $59      | $73      | $49        | $39            | $19         |
| Expansion phase cost per couple tested (2015 USD)                         | $153            | $56            | $39      | $49      | $39        | $26            | $19         |
| Maintenance phase cost per couple tested (2015 USD)                       | $76             | $28            | $20      | $24      | $24        | $28            | $28         |

*Uncounselled indicates pre-couples voluntary HIV counselling and testing. Demographic Health Survey defines stable couples as partners consensually living together in a union within a household. Most recent Demographic Health Survey data used ART, antiretroviral treatment; PY, person year. *Estimated based on lower HIV incidence in Eastern and Western Africa versus Southern Africa. [34].
available for HIV seroincidence in uncounseled ART-using discordant couples in Eastern and Western Africa, we used 5/100PY reflecting the broadly lower incidence in Eastern/Western versus Southern Africa [36]. Finally, since the primary cost driver for CVCT is salaries for counselling, testing and promotions [20,21], we derived a conversion factor using country-specific nurse salaries (USD 2015) applied to cost-per-couple tested estimates calculated from our Zambian implementation ($75 initiation phase, $50 expansion phase, $25 maturation phase, $30 maintenance phase [21]) to generate cost-per-couple tested estimates for each country.

2.5 | Base-case analyses

The estimated proportion of adult HIV infections averted, total CVCT implementation costs, CHIA and proportion of President's Emergency Plan for AIDS Relief (PEPFAR) budgets required for nationwide implementation in each selected country are outcomes of interest. These are presented alongside per capita gross domestic products (GDPs) for context. All outcomes and costs were discounted at 3%/year as recommended by the US Public Health Service Task Force [41]. We adhered to Consolidated Health Economic Evaluation Reporting Standards [42] for cost-effectiveness analyses.

2.6 | One-way and probabilistic sensitivity analyses

We conducted one-way sensitivity analyses for all model inputs by varying each parameter ±20%. Inputs which most influenced model outputs are reported. Because key model parameters of cost-per-couple tested and CVCT effectiveness were derived from just two countries, we also conducted probabilistic Monte Carlo simulation multivariate sensitivity analyses for each parameter of interest (±50% of base-case estimates using a uniform distribution) with 1000 draws in Excel. Average outcomes and standard deviations from simulated results are reported. A uniform distribution was chosen to fix a functional form on the parameter estimates and to reflect a large degree of uncertainty around the selected parameters.

3 | RESULTS

The total cost for nationwide CVCT implementation and cumulative infections averted are also shown in Table 3. Estimated average CHIA ranged from $1272 in South Africa to $550 in Zimbabwe. Our model estimated that CVCT could prevent between 54% and 62% of HIV infections. The proportion of the 2018 PEPFAR budget required for CVCT nationalization over five years ranged from 7% in Kenya to 21% in Ivory Coast. For context, per capita GDP for each country is shown.

Figure 2 presents country-specific CHIA estimates by implementation phase. During the initiation phase, the CHIA ranged from $2503 in South Africa to $1080 in Zimbabwe. During the expansion phase, the CHIA ranged from $720 to $1672. During the maturation phase, the CHIA ranged from $360 to $831. Finally, during the maintenance phase, the CHIA ranged from $437 to $1005.

3.1 | Sensitivity analyses

One-way sensitivity (Table 4 presents representative findings from South Africa) analyses indicated our model was relatively robust to parameter assumptions, with resulting CHIA still relatively low compared to other HIV prevention interventions (discussed below). Our model was most sensitive to the costs-per-couple tested (varying input parameters by ±20% resulted in total CVCT costs which were ±20% different from base-case). Our model was also sensitive to varying the proportion of adults in heterosexual couples (a higher proportion of adults in heterosexual couples lead to a proportional increase in HIV infections averted and total CVCT costs). Similarly, our model was sensitive to the proportion of couples motivated for and with access to CVCT (with increasing

Table 3. Proportion of adult infections averted, overall CHIA and total cost for CVCT in six African countries (primary base-case analyses)

| Country            | Total cost of CVCT | Cumulative HIV infections averted | Average CHIA | Proportion of infections averted, % | 2018 PEPFAR Budget | Cost of CVCT as % of PEPFAR budget for five years, % | Per capita GDP |
|--------------------|-------------------|-----------------------------------|--------------|-------------------------------------|--------------------|--------------------------------------------------|--------------|
| South Africa       | $532,704,861      | 418,855                           | $1272        | 62                                  | $575,258,390       | 19                                               | $13,054      |
| Zimbabwe           | $67,053,208       | 121,984                           | $550         | 58                                  | $145,546,200       | 9                                                | $2,224       |
| East-Central Africa| $176,419,535      | 231,312                           | $763         | 57                                  | $505,480,000       | 7                                                | $3,384       |
| Kenya              | $219,582,392      | 219,486                           | $1000        | 56                                  | $512,422,250       | 9                                                | $3,094       |
| Tanzania           | $145,955,594      | 119,508                           | $1221        | 57                                  | $140,508,601       | 21                                               | $3,771       |
| Western Africa     | $33,113,126       | 34,803                            | $951         | 54                                  | Unknown            | –                                                | $1,547       |

No PEPFAR budget reported for Sierra Leone. Per capita GDP (2017 estimates in 2015 USD): https://www.cia.gov/library/publications/the-worldfactbook/rankorder/2004rank.html. CHIA, cost per HIV infection averted; CVCT, Couples’ HIV voluntary counselling and testing; PEPFAR: President’s Emergency Plan for AIDS Relief.

Weighted average across all implementation phases.
motivation and access was associated with proportional changes in increased infections averted and costs).

Additionally, our model was relatively sensitive (with results varying roughly ±10% relative to base-case) to the proportion of concordant negative and discordant couples in the population (with higher proportions of at-risk couples leading to increased infections averted and therefore lower CHIAs).

A higher pre-CVCT seroincidence rate in concordant-negative couples and higher CVCT effectiveness in concordant-negative couples both increased HIV infections averted. Finally, increasing CVCT effectiveness in ART using discordant couples by ±20% varied total infections averted by roughly ±10% (with higher prevention impact leading to increased infections averted and improved cost-effectiveness).

Examining the country-specific parameters specifically, differences in model outcomes across countries are influenced by differences in seroincidence rates pre-CVCT (with higher uncounseled seroincidence rates being associated with higher numbers of infections averted and improved cost-effectiveness) and the proportion of couples who were discordant (with higher discordancy associated with higher numbers of infections averted and improved cost-effectiveness).

Probabilistic multivariate sensitivity analyses (Table 5) also highlighted that total CVCT costs were sensitive to cost-per-couple tested, with coefficients of variation of 15% to 16%. Our model was less susceptible to variation in CVCT impact, with coefficients of variation of 10% to 12%.

4 | DISCUSSION

Our model estimated that CVCT could prevent over half of adult HIV infections for 7% to 21% of selected countries’ five-year PEPFAR budgets. Applying an HIV prevention cascade framework [5] is helpful to evaluate CVCT. In the countries under study, the priority population for CVCT, stable couples, comprises 35% to 62% of the adult population. Key barriers and solutions related to this priority population’s motivation to use CVCT, CVCT access and effective use are summarized in Table 6 and discussed in detail below.

4.1 | Motivation

Sensitivity analyses indicated countries with a higher proportion of heterosexual couples motivated to uptake CVCT prevented more infections. Motivation for CVCT has been high across studies in diverse populations including heterosexual couples in Mozambique [44,45], Tanzania [46,47], South Africa [48,49], Uganda [50], Thailand [51], Iran [52] and men who have sex with men (MSM) in South Africa [53] and the US [54,55]. Although promising, these are relatively small-scale efforts; knowledge of CVCT remains low in many settings and education and demand creation are essential to increase broad motivation [28-29,56]. Key barriers to motivation include lack of community knowledge of HIV serodiscordance and HIV risk. For example we found that only 30% of couples seeking CVCT in Durban knew about serodiscordance [49]. Other barriers to motivation include opportunity costs, men’s inability to attend regular clinic hours, limited knowledge that CVCT services exist, and concerns about consequences like relationship dissolution [28-29,56,57].

Reports highlight successful strategies to overcome these barriers and increase motivation including use transport reimbursement [57]; nonmonetary incentives in Zambia [58] and rural Zimbabwe [59]; invitations plus facilitated contact tracing to support partner attendance in Malawi [60]; male-focused interactive sessions with testimonies from ‘expert couples’
Table 4. Parameters and results of one-way sensitivity analyses: Illustrative example of South Africa

| Sensitivity analysis parameters                                      | Infections averted % change<sup>a</sup> | Total cost of CVCT % change<sup>a</sup> | CHIA % change<sup>a</sup> |
|---------------------------------------------------------------------|----------------------------------------|----------------------------------------|--------------------------|
| Discount rate                                                       |                                        |                                        |                          |
| 2%                                                                  | 3%                                     | 5%                                     | 2%                       |
| 4%                                                                  | −3%                                    | −5%                                    | −2%                      |
| Cost/couple tested (by implementation phase)                        |                                        |                                        |                          |
| $183; $122; $61; $74                                               | 0%                                     | −20%                                   | −20%                     |
| $274; $184; $91; $110                                              | 0%                                     | 20%                                    | 20%                      |
| Proportion adults in heterosexual couples                           |                                        |                                        |                          |
| 28%                                                                | −20%                                   | −20%                                   | 0%                       |
| 42%                                                                | 20%                                    | 20%                                    | 0%                       |
| Proportion couples motivated for CVCT (by implementation phase)    |                                        |                                        |                          |
| 40%; 40%; 53%; 12%                                                 | −20%                                   | −20%                                   | 0%                       |
| 60%; 60%; 79%; 18%                                                 | 20%                                    | 20%                                    | 0%                       |
| Proportion couples with access to CVCT (by implementation phase)   |                                        |                                        |                          |
| 16%; 32%; 48%; 56%                                                 | −20%                                   | −20%                                   | 0%                       |
| 24%; 48%; 72%; 84%                                                 | 20%                                    | 20%                                    | 0%                       |
| Proportion concordant negative                                      |                                        |                                        |                          |
| 56%                                                                | −9%                                    | 0%                                     | 10%                      |
| 84%                                                                | 10%                                    | 0%                                     | −9%                      |
| Proportion discordant                                               |                                        |                                        |                          |
| 13%                                                                | −9%                                    | 0%                                     | 10%                      |
| 19%                                                                | 11%                                    | 0%                                     | −10%                     |
| HIV seroincidence rates before CVCT (per 100 PY)                    |                                        |                                        |                          |
| Among concordant HIV-negative couples                               |                                        |                                        |                          |
| 0.80                                                               | −9%                                    | 0%                                     | 10%                      |
| 1.20                                                               | 9%                                     | 0%                                     | −8%                      |
| Among ART using HIV discordant couples                              |                                        |                                        |                          |
| 6.40                                                               | −6%                                    | 0%                                     | 6%                       |
| 9.60                                                               | 6%                                     | 0%                                     | −6%                      |
| Among non-ART using HIV discordant couples                          |                                        |                                        |                          |
| 10.40                                                              | −4%                                    | 0%                                     | 4%                       |
| 15.60                                                              | 4%                                     | 0%                                     | −4%                      |
| CVCT prevention impact                                              |                                        |                                        |                          |
| Among concordant HIV-negative couples                               |                                        |                                        |                          |
| 38%                                                                | −7%                                    | 0%                                     | 8%                       |
| 56%                                                                | 7%                                     | 0%                                     | −7%                      |
| Among ART using HIV discordant couples                              |                                        |                                        |                          |
| 63%                                                                | −10%                                   | 0%                                     | 11%                      |
| 95%                                                                | 11%                                    | 0%                                     | −10%                     |
| Among non-ART using HIV discordant couples                          |                                        |                                        |                          |
| 50%                                                                | −2%                                    | 0%                                     | 2%                       |
| 76%                                                                | 2%                                     | 0%                                     | −2%                      |
| ART use                                                             |                                        |                                        |                          |
| Among HIV-positive adults before CVCT                               |                                        |                                        |                          |
| 50%                                                                | 2%                                     | 0%                                     | −2%                      |
| 74%                                                                | −3%                                    | 0%                                     | 3%                       |
| Among HIV-positive adults after CVCT                                |                                        |                                        |                          |
| 61%                                                                | −1%                                    | 0%                                     | 1%                       |
| 92%                                                                | 1%                                     | 0%                                     | −1%                      |
| Proportion initiating ART each year after CVCT                      |                                        |                                        |                          |
| 4%                                                                  | 0%                                     | 0%                                     | 0%                       |
| 6%                                                                  | 0%                                     | 0%                                     | 0%                       |

ART, antiretroviral treatment; CHIA, cost-per-HIV infection averted; CVCT, couples’ voluntary HIV counselling and testing; PY, person-years. % Change relative to base-case primary analyses.
who received CVCT in rural Uganda [50]; and CVCT invitations and promotions delivered by influential community leaders and via mass media in Zambia and Rwanda [28-29,56]. Additionally, the desire to keep one’s partners safe from transmission is a motivating factor for ART and PrEP use [61,62], and “undetectable = untransmittable” messaging may reduce stigma and motivate couples to uptake CVCT and ART to achieve viral suppression [63]. Finally, messaging should emphasize that outcomes of intimate partner violence (IPV), relationship dissolution or emotional distress are rare and CVCT typically strengthens relationships [16-17,54,60,64,65].

To broadly increase CVCT motivation, budgets for training, demand creation and incentives (all included in our modelled CVCT costs) will be required.

### 4.2 Access

Sensitivity analyses indicated that countries with a higher proportion of heterosexual couples with CVCT access will prevent more infections at a higher cost. The PEPFAR 2020 Country Operation Plan [43] highlights family HIV testing and emphasizes that HIV prevention among pregnant, postpartum and breastfeeding women should include “couples-based services to promote scaled-up testing and treatment of male partners.” However, as CVCT is not broadly offered as standard of care in the selected countries, nor it is a required indicator for reporting [66], access remains low across Africa. As with most interventions, a main barrier to access is the cost of wide-spread implementation. As expected, higher costs-per-couple tested increase total CVCT costs. Economies of scale are incorporated into estimated cost-per-couple tested (over time, costs to test couples decrease, with the exception of the final “hard-to-reach” couples).

Our experience in Zambia reflected the initiation and expansion phases [21]. Government clinic staff were paid during their off-duty hours. Unfortunately, the amount of funding available was insufficient to maintain momentum. In contrast, Rwanda succeeded in increasing access and nationalizing CVCT in ANC between 2008 and 2013 (after which CVCT became a social norm and demand creation was no longer needed) [20]. Based on the estimated impact of CVCT in Rwanda from observational epidemiological studies [11,23,24], the Rwandan government health insurance and performance-based financing plans now reimburse the costs of CVCT, and additional funding for off-duty staff is no longer required. Reaching Rwanda’s success will require investment. As many demonstration projects correspond to the more expensive initiation phase, implementers may fail to see that continuous investment is necessary to achieve social diffusion, incorporate CVCT into daily clinical practice and adapt data recording and reporting tools to achieve sustained access [57].

In addition to clinic-based CVCT, mobile testing in Rwanda [29]; home-based couples’ testing in Tanzania [67], Kenya [68] and Malawi [69]; and self-testing to increase CVCT in Kenya

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### Table 5. Probabilistic sensitivity analysis results

| **Southern Africa** | **Total cost of CVCT** | **SD** | **CV** | **Average CHIA** | **SD** | **CV** |
|---------------------|------------------------|--------|--------|-----------------|--------|--------|
| South Africa        | 527,493,591            | 80,271,276 | 15%    | $1280          | $198   | 15%    |
| Zimbabwe            | 67,478,299             | 9,792,498  | 15%    | $466          | $73    | 16%    |
| East-Central Africa |                       |        |        |                |        |        |
| Kenya               | 175,560,051            | 28,074,065 | 16%    | $765          | $116   | 15%    |
| Tanzania            | 219,184,615            | 33,759,017 | 15%    | $997          | $158   | 16%    |
| Western Africa      |                       |        |        |                |        |        |
| Ivory Coast         | 145,820,457            | 22,312,561 | 15%    | $1217         | $191   | 16%    |
| Sierra Leone        | 33,384,147             | 4,850,786  | 15%    | $953          | $145   | 15%    |

| **Southern Africa** | **Cumulative HIV infections averted** | **SD** | **CV** | **Average CHIA** | **SD** | **CV** |
|---------------------|--------------------------------------|--------|--------|-----------------|--------|--------|
| South Africa        | 420,653                              | 45,818 | 11%    | $1304          | $146   | 11%    |
| Zimbabwe            | 116,862                              | 14,257 | 12%    | $570           | $68    | 12%    |
| East-Central Africa |                                      |        |        |                |        |        |
| Kenya               | 232,821                              | 25,860 | 11%    | $788           | $86    | 11%    |
| Tanzania            | 220,013                              | 25,895 | 12%    | $1043          | $120   | 12%    |
| Western Africa      |                                      |        |        |                |        |        |
| Ivory Coast         | 118,752                              | 12,769 | 11%    | $1269          | $131   | 10%    |
| Sierra Leone        | 34,876                               | 4091   | 12%    | $998           | $120   | 12%    |

CHIA, cost per HIV infection averted; CV, coefficient of variation is the standard deviation divided by the mean estimate; CVCT, couples voluntary HIV counselling and testing; SD, standard deviation.

*a* No impact on cumulative HIV infections averted; *b* no impact on total cost of CVCT.

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have been studied. An improved understanding of differences in CVCT access and costs (as well as motivation) for different modalities is warranted.

4.3 | Effective use

CVCT decreases sexual and perinatal HIV incidence [11-16] by educating and placing joint responsibility on the dyad to increase uptake of condoms, VMMC, family planning, ART and PMTCT [13-15,17]. CVCT effectiveness must be monitored to understand facilitators and barriers to achieving reductions in HIV incidence. Our previous analyses found factors associated with inconsistent condom use, non-ART initiation or continued outside partner risk in discordant couples post-CVCT included alcohol use and fertility intentions [71]. To improve effective use of CVCT for all couples, targeted safe conception and alcohol counselling may be warranted. Importantly, as seen in sensitivity analyses, a higher prevention impact in concordant-negative couples increased CVCT cost-effectiveness. It has been argued that CVCT may have a sizable impact on the epidemic through HIV prevention in concordant-negative couples (via reduction in outside relationship risk) since they comprise the majority of the population [72,73].

For the smaller though higher-risk population of discordant couples, “Test-and-Treat” will continue to expand. Unfortunately, many country’s HIV incidence rates have not decreased as substantially as predicted in the test-and-treat era, and several large cluster-randomized trials have failed to clearly demonstrate the population-level prevention impact of universal test-and-treat policies [74]. Where CVCT increases ART uptake and adherence in serodiscordant couples, it may bolster the effectiveness of test-and-treat. Additionally, to achieve the PEPFAR 2020 priority of PrEP for discordant couples [43], CVCT can effectively identify discordant couple candidates. Although PrEP is not currently available in most countries outside of relatively small demonstration and research projects, CVCT counselling can be updated to include PrEP as it becomes available.

Finally, an improved understanding of the effectiveness of CVCT in home-based settings, mobile-testing and via self-testing is needed with regular monitoring and evaluation of these delivery platforms. With self-testing in particular, how well couples disclose, understand their respective results and adopt appropriate risk reduction without facilitated joint post-test counselling merits further investigation [75-78].

4.4 | Comparative cost-effectiveness

We found CVCT CHIA estimates to be similar to interventions largely considered cost-effective including individual voluntary HIV counselling and testing (estimated in a previous systematic review of studies in sub-Saharan Africa at $1315 [79] and $483

Table 6. CVCT HIV prevention cascade domains with key barriers and solutions

| Motivation | Access | Effective use |
|------------|--------|---------------|
| Lacking knowledge and low risk perception | Lack of availability or easy access in government facilities | Inconsistent condom use, continued outside partner risk |
| Lacking men’s ability to attend regular clinic hours, opportunity costs | Lack of trained government providers | Lack of ART uptake |
| Concerns about CVCT consequences | Perceived cost/affordability | Non-linkage to ART programmes |
| Evidence-based ways to close the gap | Convenient service delivery hours and platforms | Ongoing condom and behavioural counselling, targeted safe conception and alcohol counselling |
| Interventions | Provider training and reimbursement (possibly during off-hours) | Integration with ART (for treatment and prevention) programmes |
| Platforms to deliver interventions | Clinic-based services, mobile testing, home-based testing, self-testing | Clinic-based services, mobile testing, home-based testing, self-testing |
| Clinics, community health workers, influential peers and mass media | Budgets, required reporting indicators and targets for CVCT | Budgets for integrated services, ongoing M&E |
| Policies to support interventions | Training and reimbursement of providers | |

ART, antiretroviral treatment; CVCT, couples voluntary HIV counselling and testing; M&E, monitoring and evaluation.
for an individual and couples testing intervention in Kenya [79,80] and family planning for PMTCT via prevention of unintended pregnancy ($663) [79]. A recent systematic review of 60 studies from African countries reported median CHIA estimates for VMMC ($2965), ART for PMTCT ($1144), treatment-as-prevention interventions ($7903) and PrEP ($13,267) [81].

4.5 | Limitations

As in all models, we attempt to simplify a complex reality, and outputs are dependent on assumptions. Extensive sensitivity analyses quantify the impact of these assumptions. Our model seeks to isolate the impact of CVCT on HIV infections averted given constant pre-CVCT and post-CVCT HIV incidence. We do not attempt to predict the course of the epidemic in the selected countries over time by considering myriad other prevention or treatment interventions. More detailed models isolating the prevention impact of CVCT attributable to condom use, VMMC uptake, improved ART uptake and adherence, and/or reductions in concurrent relationships are warranted. While deterministic compartmental models are well-suited to examine average characteristics in a population and are thus appropriate for our goal, they do not evaluate individual-level effects as do agent-based models. Finally, while some studies of HIV prevention interventions translate infections averted into disability-adjusted life-years averted or quality-adjusted life-years gained, a recent systematic review did not find standard conversions applicable across country settings [81]. While such cost-utility estimates are often applied to determine if an intervention is cost-effective [82], this threshold is often questioned by experts since it does not consider intervention affordability [83,84]. While cost-utility analyses are useful for comparing interventions with different natural units, given dedicated HIV prevention budgets and the common use of CHIA estimates in other studies [81], we feel that CHIA is a more useful comparative measure.

5 | CONCLUSIONS

Our model indicated that nationalized CVCT could prevent over half of adult HIV infections for 7% to 21% of the modelled countries’ five-year PEPFAR budgets. Unfortunately, WHO CVCT guidelines have yet to be broadly implemented. While studies indicate that CVCT motivation is high given locally relevant promotional and educational efforts, access remains low without dedicated budgets or required indicators.

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COMPETING INTEREST

The authors have no conflicts of interest.

AUTHORS’ CONTRIBUTIONS

KMW contributed to the analysis and interpretation of data; drafted the article and revised it critically for important intellectual content; and gave final approval of the version to be published. MI contributed to the conception and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. WK contributed to the conception and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. EK contributed to the conception and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. EC contributed to the conception and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. BV contributed to the conception and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. TS contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. RP contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. TS contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. BS contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. RJ contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. HR contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. PC contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. SA contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. JM contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. BV contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published. EC contributed to the analysis and interpretation of data; revised the article critically for important intellectual content and gave final approval of the version to be published.

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