Sexual Health

HIV testing and counselling couples together for affordable HIV prevention in Africa

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Abstract

Background: The impact and cost-effectiveness of couples' voluntary HIV counselling and testing (CVCT) has not been quantified in real-world settings. We quantify cost-per-HIV-infection averted by CVCT in Zambia from the donor's perspective.

Methods: From 2010 to 2016, CVCT was established in 73 Zambian government clinics. The cost-per-HIV-infection averted (CHIA) of CVCT was calculated using observed expenditures and effectiveness over longitudinal follow-up. These observed measures parameterized hypothetical 5-year nationwide implementations of: 'CVCT'; 'treatment-as-prevention (TasP) for discordant couples' identified by CVCT; and 'population TasP' for all HIV+ cohabiting persons identified by individual testing.

Results: In all, 207 428 couples were tested (US $52/couple). Among discordant couples in which HIV+ partners self-reported antiretroviral therapy (ART), HIV incidence was 8.5/100 person-years before and 1.8/100 person-years after CVCT (79% reduction). Corresponding reductions for non-ART-using discordant and concordant negative couples were 63% and 47%, respectively. CVCT averted an estimated 58% of new infections at US $659 CHIA. In nationwide implementation models, CVCT would prevent 17 times the number of infections vs 'TasP for discordant couples' at 86% of the cost, and nine times the infections vs 'population TasP' at 28% of the cost.

Conclusions: CVCT is a cost-effective, feasible prevention strategy in Zambia. We demonstrate the novel, added effectiveness of providing CVCT to ART users, for whom ART use alone only partially mitigated transmission risk. Our results indicate a major policy shift (supporting development of CVCT indicators, budgets and targets) and have clinical implications (suggesting promotion of CVCT in ART clinics as a high-impact prevention strategy).

Key words: Couples' voluntary HIV counselling and testing, financial cost-effectiveness, cost-per-HIV-infection averted, HIV prevention, treatment-as-prevention

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Key Messages

- We present real-world data measuring and comparing the cost and prevention impact of couples' voluntary HIV counselling and testing (CVCT) and antiretroviral treatment/treatment-as-prevention (ART/TasP) in 73 Zambian government clinics from 2010 to 2016.
- CVCT reached over 200 000 couples and reduced HIV incidence by 79% for ART-using discordant couples, 63% for non-ART using discordant couples, and 47% for concordant negative couples.
- Overall, CVCT averted an estimated 58% of new infections at US $659/HIV infection averted.
- These results indicate a major policy shift, suggesting that governments and donors make CVCT a required monitoring indicator, and that budgets be allocated and targets set for CVCT implementation.
- Our results have major clinical implications, suggesting that promotion of CVCT in ART clinics could be a high-impact strategy to prevent transmission of HIV; this finding is novel and suggests that the prevention impact of treatment can be considerably bolstered by CVCT.

Introduction

Development assistance for HIV/AIDS has increased dramatically over the past 20 years, and since 2001, worldwide incidence has decreased 38%.[1] However, over 35 million people are HIV+ and over two million infections occur annually.[1] Most HIV+ people live in sub-Saharan Africa, where heterosexual transmission predominates and the majority of new infections occur in concordant HIV- or discordant (one partner HIV+, one HIV-) couples.[2] Couples' voluntary HIV counselling and testing (CVCT) is an evidence-based intervention that greatly improves knowledge that serodiscordance is possible,[3] increases accurate knowledge of partner status,[4,5] increases condom use and decreases HIV/sexually transmitted infection (STI) incidence.[6–9] Conservatively assuming a reduction in annual seroincidence among discordant couples from 15% to 7% after CVCT, we previously estimated that 45% and 53% of new HIV infections in cohabiting Zambian men and women, respectively, could be averted.[10]

WHO guidelines issued in 2012[11] and CDC trainings published in 2007[12] endorse CVCT for HIV prevention. However, outside Rwanda, where >80% of women in antenatal care have received CVCT with partners,[13] only a small percentage of Africans have been tested with partners. In Zambia, although CVCT is included in national guidelines, <10% of couples have tested together.[14]

In this study, we present CVCT expenditures, impact and cost-per-HIV-infection averted (CHIA) among heterosexual couples tested in 73 Zambian government clinics from 2010 to 2016. To inform future prevention implementation strategies and resource allocation, we then use observed data to model and compare expenditures and CHIA for hypothetical national implementation of three programmes: CVCT; ART-as-prevention (TasP) for discordant couples identified by CVCT; and population TasP for all HIV+ cohabiting men and women identified by individual testing.

Ethical approval was not required (waiver from Emory Institutional Review Board, non-research) for this service programme.

Methods

Expenditures and infections averted by CVCT in 73 Zambian government clinics

CVCT implementation and data collection
From September 2010 to March 2016, CVCT programmes were established in 73 Zambian government clinics in the

Copperbelt, Lusaka and Southern Provinces. Promotions used community health workers and mass media.[15,16] CVCT services included: joint pre-test counselling; rapid HIV testing; joint post-test counselling and provision of condoms; and referral to combination prevention services including ART, voluntary medical male circumcision (VMMC) and family planning. Self-reported history of previous HIV testing and ART use were recorded. When possible, genetic sequencing[17] confirmed whether incident infections in discordant couples were acquired from index partners. HIV- clients underwent repeat testing 1 month after CVCT. Thereafter, discordant couples returned quarterly and concordant HIV- couples returned annually.[16]

Effects

The impact of CVCT is assessed through comparison of clinic record data collected over longitudinal follow-up from CVCT clients. HIV seroincidence rates for discordant and concordant HIV- couples are calculated as incident infections divided by HIV- person-years (PY) of follow-up, stratified by whether couples had ('after CVCT') or had not ('before CVCT') received CVCT. Seronegative partners in the 'window period' during their first CVCT visit (i.e. in Fiebig stages I-II[18] with HIV viral RNA+ at the time of counselling and/or seroconverting before first follow-up with a median 35 days and maximum of 90 days) are classified as 'before CVCT' and all others (including those self-reporting previous joint testing) are classified as 'after CVCT'. 'Before CVCT' PY are calculated as the time from first visit to first follow-up visit. Seroincidence rates are calculated as:

$$
\begin{aligned}
&\text{'Before CVCT' seroincidence rate} \\
&= \frac{(\text{no. Ab} + \text{at first follow-up visit but Ab} - \text{at baseline})}{(\text{total time to first follow-up (median} \sim 35\,\text{days}))}
\end{aligned}
$$

$$
\begin{aligned}
&\text{'After CVCT' seroincidence rate} \\
&= \frac{(\text{no. seroconverting after first follow-up visit})}{\begin{array}{c}(\text{time since first follow-up for those Ab} \\ -\text{at first follow-up (i.e., not infected 'Before CVCT'))}\end{array}}
\end{aligned}
$$

where Ab– indicates antibody negativity. Seroincidence rates in discordant couples are stratified by HIV+ partner self-reported ART use. Percent reductions [and conditional maximum likelihood rate ratios (RR) and 95% confidence intervals (CIs)] in seroincidence rates before vs after CVCT are calculated.

To evaluate the possibility of differential loss to follow-up, we descriptively compared those who returned for follow-up vs those who did not (and therefore were not included in the longitudinal analyses) with respect to characteristics collected during routine service delivery (age, cohabitation status, length of relationship, HIV testing history, current pregnancy status, contraceptive use and ART

use). To explore potential impact of any informative censoring, we then re-calculated HIV seroincidence rates using inverse probability of (loss to follow-up) censoring weighting by adapting from standard methods,[19,20] and applied weighted HIV seroincidence rates to the model. Using similar methods, we also conducted an inverse probability of treatment weighting analysis to evaluate the possibility of confounding when using observational data to estimate the effect of treatment, and applied these new weighted HIV seroincidence rates to the model.

Expenditures

Expenditures were reported by both category and activity, and the distribution is presented to illustrate CVCT implementation, monitoring and evaluation outlays from the donor's perspective. We adhere to Consolidated Health Economic Evaluation Reporting Standards.[21]

CHIA

We calculate CVCT CHIA using expenditures and effects observed during the CVCT implementation in 73 government clinics in Copperbelt, Lusaka and Southern Provinces. Based on previous work,[7–9,22] we assume a duration of prevention impact of 5 years after CVCT. Observed baseline ART use and initiation in the year following CVCT are used, with an additional 5% of clients per year estimated to initiate ART in years 2–5 after CVCT (as clinically indicated). In the 'before CVCT' group, baseline ART use is also assumed to increase by 5% per year. CVCT prevention impact with and without ART is applied each year, and couples move from concordant negative to discordant and from discordant to concordant positive according to observed annual seroincidence. Subtracting the cumulative number of infections 'after CVCT' from the cumulative number of infections 'before CVCT' yields the number of infections averted over the 5-year time horizon. Neither costs nor effects were discounted, given the short time horizon.

Modelling expenditures and CHIA in hypothetical nationwide implementations of: CVCT, TasP for discordant couples identified by CVCT and population TasP for HIV+ cohabiting men and women identified by individual testing

Primary modelling analyses use estimates of CVCT impact, ART uptake and TasP impact observed during the 73-clinic implementation; sensitivity analyses assume worst-case estimates of CVCT impact combined with best-case estimates of ART uptake and TasP impact.

The hypothetical nationwide CVCT implementation occurs in four phases typical of development programmes: initiation, expansion, maturation and maintenance. Based

on previous research and implementation studies in Rwanda and Zambia, we assume that in the initiation phase, 10% of couples test at US $75 per couple; in the expansion phase, an additional 10% of couples test at US $50 per couple; in the first maturation phase, an additional 20% of couples test at US $25 per couple; in the second maturation phase, an additional 30% of couples test at US $25 per couple; and in the maintenance phase, 10% of residual and new couples test at US $30 per couple. Thus, we assume to reach 80% of couples overall, with costs increasing for the 'hard to reach' last 10% of couples.

We define TasP for discordant couples identified by CVCT as immediate ART initiation among HIV+ adults in discordant couples. Population TasP for HIV+ cohabiting men and women identified by individual testing is defined as ART initiation among HIV+ cohabiting adults, regardless of CD4 count or partner serostatus. We assume that individual testing will also only reach 80% of individuals over the time horizon. We assume no prevention impact of CVCT or TasP provided to concordant HIV+ couples. Only those who initiate ART are included in the TasP cost calculations. However, those on ART at baseline or who initiate contribute to infections-averted.

Results

Expenditures and infections averted by CVCT in 73 Zambian government clinics

Expenditure details
During the implementation of CVCT in Copperbelt Province, 68 340 couples were tested at cost of US

$3 167 934 (US $46 per couple tested). Table 1 shows the two largest categories were government clinic counselling personnel salaries (24%) and promotions (21%), followed by facilities and equipment (12%), overheads (11%), project coordinators and trainers (10%), trainings (8%) and monitoring and evaluation technical staff (7%). Overall cost-per-couple-tested during the 73-clinic implementation was US $52 per couple [a weighted average of Lusaka and Southern Province (US $70 per couple) and Copperbelt (US $46 per couple)].

Effect of CVCT on HIV incidence
From 2010 to 2016, 207 428 couples were tested in 73 clinics (Figure 1); 8% were serodiscordant and 79% were concordant HIV-. Total follow-up time for serodiscordant couples was 706 972 days, and for concordant negative couples was 3 469 154 days. Average follow-up time for serodiscordant couples was 182 days (standard deviation = 254) and for concordant negative couples was 79 days (standard deviation = 138); 20% of HIV+ partners in serodiscordant couples reported using ART before CVCT, increasing to 50.6% in the year following CVCT.

In serodiscordant couples in which the HIV+ partner was not on ART, HIV seroincidence rates were 13.00/100 PY (95% CI: 9.16–17.91) before CVCT and 4.82/100 PY (95% CI: 3.15–7.06) after CVCT (63% reduction, 98.9% power). Analogous rates for ART-using discordant couples were 8.53/100 PY (95% CI: 3.63–16.96) and 1.78/100 PY (95% CI: 1.05–2.81) (79% reduction, 98.4% power), and for concordant negative couples were 1.06/100 PY (95% CI: 0.76–1.44) and 0.57/100 PY (95% CI: 0.39–0.80) (47%

Table 1. Financial expenditures for CVCT implementation in Copperbelt Province, Zambia, August 2010-March 2013

Expenditure categories	Cost (USD) and percentage of total cost (%)
CVCT counsellors in government clinics	$760 304.16 (24%)
Promotions, advocacy, communications	$665 266.14 (21%)
Facilities and equipment	$380 152.08 (12%)
Overheads	$348 472.74 (11%)
Project coordinators and trainers	$316 793.40 (10%)
Trainings	$253 434.72 (8%)
International staff	$221 755.38 (7%)
Transport	$126 717.36 (4%)
Health commodities	$63 358.68 (2%)
Printing/duplicating/other	$31 679.34 (1%)
Total	$3 167 934.00

Expenditures for Copperbelt Province couples' voluntary HIV counselling and testing (CVCT) implementation reaching 68 340 couples: counsellors (salaries for off-duty government employees employed part-time); project coordinators and trainers (salaries for full-time project employees who provided training, supervision and monitoring and evaluation; international technical assistants; promotions, advocacy and communications (promotional materials, promoter salaries and patient transport reimbursement); training (CVCT trainer/trainee transport and accommodation); transportation (fuel, maintenance and licences); health commodities (lab supplies, pharmaceuticals, condoms, and HIV test kits purchased when government clinic stocks were low); printing/duplicating/other (printing flipcharts/logbooks and non-capital materials); facilities and equipment (rent/utilities, security, internet and phones); and overheads (indirect costs assessed at 13% of total direct costs).
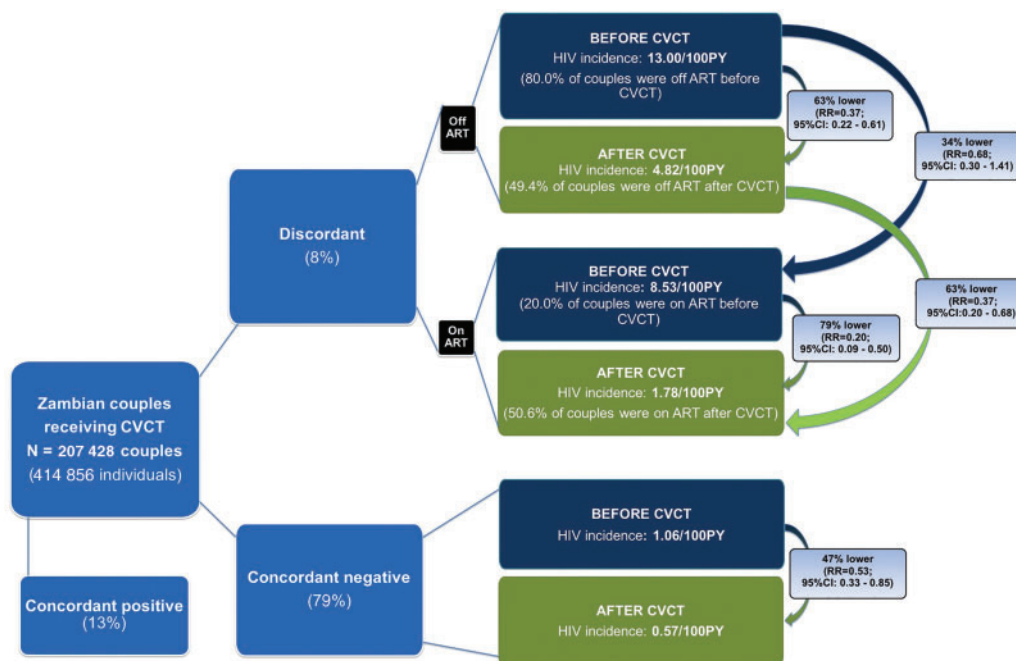
Figure 1. Observed HIV serostatus distribution, self-reported therapeutic ART use and HIV incidence before and after CVCT among discordant and concordant negative couples, Copperbelt, Lusaka and Southern Province, Zambia, September 2010-March 2016. PCR, polymerase chain reaction. Of 14 individuals seroconverting at the first follow-up visit for whom PCR results at the initial CVCT visit were available, 86% of those tested (12/14) were RNA+, antibody negative.

reduction, 82.0% power). Before CVCT, the difference in HIV seroincidence between non-ART users and ART users was 34% (20.8% power). After CVCT, the difference in HIV seroincidence between non-ART users and ART users was 63% (93.0% power).

CHIA

Over 5 years without CVCT, 9991 infections would have occurred in discordant couples and 13 790 in concordant negative couples, compared with 2578 in discordant and 7484 in concordant negative couples after CVCT. Overall, 58% of HIV infections were averted by CVCT at US $659 CHIA (46% in concordant HIV negative, 74% in discordant couples).

Inverse probability weighting analyses to assess potential biased retention and treatment

We found that couples with no follow-up data who were not retained were less likely to have had a previous HIV test (58% vs 63%), were younger (29.7 vs 32.8) and had been with their current partner for fewer years (5.7 vs 7.6). These differences suggest that those not retained may have been at higher risk for HIV. Giving more weight to individuals with profiles similar to those with no follow-up increased estimated seroincidence rates minimally (<3% increase), with the exception of ART-using couples before CVCT (9% increase) and non-ART-using discordant couples after

CVCT (1.5% decrease) (Supplementary Table 1, available as Supplementary data at *IJE* online). Findings from the inverse probability of treatment weighted analysis showed similar changes in seroincidence.

In concordant negative and non-ART-using discordant couples, prevention impacts of CVCT were similar in the unweighted primary analyses compared with the inverse probability weighting for both censoring and treatment. In general, prevention impacts remained stable in weighted analyses. The most notable effect of weighting was on the impact of ART use in discordant couples before CVCT: 34% in unweighted primary analysis, 29% with weighting for censoring and 25% with weighting for treatment.

Expenditures and infections averted in hypothetical nationwide implementation scenarios

Model parameters are shown in Table 2. In primary analyses (Table 3 and Figure 2A), we estimate that during a nationwide expansion of CVCT, 166 153 cumulative infections would be averted by CVCT with a CHIA of US $394. In comparison, TasP would avert 9656 cumulative infections for discordant couples identified by CVCT with a CHIA of US $7930 per year. Population TasP for HIV+ cohabiting adults identified by individual testing would avert 17 872 cumulative infections with a CHIA of US

Table 2. Parameter values used in hypothetical nationwide implementation models

Model Parameters	Value and source	
	Primary analyses	Sensitivity analyses
HIV seroincidence rates (before CVCT), cases per 100 PY	Observed[a]	
Among concordant HIV-negative couples	1.06	
Among non-ART using HIV discordant couples	13.00	
Among ART using HIV discordant couples	8.53	
CVCT prevention impact	Observed[a]	Worst-case
Among concordant HIV-negative couples	47%	30%[10]
Among discordant couples not on ART	63%	50%[10]
Among discordant couples on ART	79%	50%[10]
ART use	Observed[a]	Best-case
Among HIV-positive adults before CVCT	20.0%[b]	55.0%[23]
Among HIV-positive adults 12 months after CVCT	50.6%[b]	80.0%[24]
TasP impact	Observed[a]	Best-case
Among discordant couples identified by CVCT	63%	96%[25]
Among HIV-positive cohabiting men and women identified by individual testing	34%	96%[25]
Population values (Zambia)		
Adult population (ages 15-64)	7 931 000[26,27]	
Adult population in couples	59%[28]	
HIV discordant couples among all couples	11%[28]	
Concordant HIV negative couples among all couples	81%[28]	
Proportion of adults who have received results of an individual HIV test in the past year	26%[29]	
Annual ART costs per person (2014 average costs incurred by PEPFAR, low- and lower-middle income countries)	US $442[30]	

[a]Observed: estimates observed during the 73 Zambian government clinic implementation.
[b]With 5% additional uptake per year.

$12 891 per year. Comparatively, CVCT would prevent 17.2 times the infections vs TasP for discordant couples identified by CVCT at 86% of the cost and 9.3 times the infections vs population TasP for all HIV+ cohabiting men and women identified by individual testing at 28% of the cost. Finally, population TasP for HIV+ cohabiting men and women identified by individual testing would avert twice the infections vs TasP for discordant couples identified by CVCT, but would cost 301% more. Sensitivity analyses (Table 3 and Figure 2B) confirm that even with worst-case CVCT and best-case ART/TasP assumptions, CVCT prevents more infections at lower cost vs either TasP implementation scenario.

Discussion

Our results demonstrate the high impact, relative cost-effectiveness and feasibility of CVCT implemented in 73 government clinics in three Zambian Provinces. This couple-centred approach reduced HIV transmission by 47–79% and prevented an estimated 58% of infections at US $659 per infection averted. The prevention impact is not surprising, since the risk reduction plan and the motivation to act on it depends on the combination of test results. This

prevention impact likely reflects increased condom use and reduction in concurrent partnerships and sexually transmitted infections (STIs),[9] as well as improved ART uptake and adherence and increased voluntary medical male circumcision (VMMC) uptake among HIV- men with HIV+ partners.

To our knowledge, the finding that CVCT increases HIV prevention among discordant couples in which the HIV+ partner is already on ART has not been reported and indicates a critically important, novel venue for CVCT scale-up within ART clinics. Weighted models modestly strengthened the case for CVCT by reducing the prevention impact of ART-absent CVCT. The finding that ART use alone only partially mitigates transmission among uncounselled discordant couples is likely due to low condom use and treatment access, adherence and retention challenges.[31–33] Additionally, the effect of CVCT among concordant HIV- couples is important: this group, comprising over four-fifths of all couples tested and 47% of infections averted, benefits from CVCT by reducing concurrent partner exposures.

Our findings confirm the feasibility of measuring the real-world impact of CVCT irrespective of ART/TasP in a low-resource setting. These findings lend perspective to

Table 3. Comparisons of cumulative HIV infections averted and expenditures for hypothetical nationwide implementations of CVCT, TasP for discordant couples identified by CVCT and population TasP for HIV+ cohabiting men and women identified by individual testing

Hypothetical nationwide implementation outcomes	Primary analyses	Sensitivity analyses
Nationwide CVCT		
Cumulative infections averted	166 153	110 044
Cumulative expenditures	$65 510 060[a]	$65 510 060
CHIA	$394	$595
TasP for discordant couples identified by nationwide CVCT		
Cumulative infections averted	9656	30 272
Cumulative expenditures	$76 578 898[b]	$62 564 459
CHIA (per year)	$7930	$2066
Population TasP for all HIV+ cohabiting men and women identified by individual testing		
Cumulative infections averted	17 872	76 121
Cumulative expenditures	$230 384 424[c]	$188 468 933
CHIA (per year)	$12 891	$2476
Comparison: nationwide CVCT vs TasP for discordant couples identified by nationwide CVCT		
Ratio of infections averted	17.2:1	3.6:1
Relative percent of cumulative expenditures	86%	105%
Comparison: nationwide CVCT vs population TasP for all HIV+ cohabiting men and women identified by individual testing		
Ratio of infections averted	9.3:1	1.4:1
Relative percentage of cumulative expenditures	28%	35%
Comparison: population TasP for all HIV+ cohabiting men and women identified by individual testing vs TasP for discordant couples identified by nationwide CVCT		
Ratio of infections averted	1.9:1	2.5:1
Relative percent of cumulative expenditures	301%	301%

Model assumptions: we assume a 5-year impact of CVCT with movement of seroconvertors from concordant negative to discordant and from discordant to concordant positive each year. In both CVCT and in the comparison group with individual VCT ('without CVCT'), uptake of ART is as described below.

Primary analyses (using observed data during the 73 Zambian government clinic implementation, see Table 2): the prevention impact of CVCT among couples is 79% reduction in seroconversion for discordant couples on ART, 63% for discordant couples not on ART and 47% for concordant negative couples. A total of 20.0% of HIV+ partners in discordant couples are ART users before CVCT, increasing to 50.6% after CVCT (with 5% per year additional ART uptake thereafter). In the comparison group without CVCT, 20% are ART users at baseline, increasing by 5% per year thereafter. The reduction in seroconversion due to ART/TasP before CVCT is 34%, and 63% after CVCT.

Sensitivity analyses (using worst-case estimates of CVCT impact and best-case estimates of ART/TasP uptake and impact, see Table 2): the prevention impact of CVCT among discordant couples is 50% and among concordant negative couples is 30%. A total of 55% of HIV+ partners in discordant couples are ART users before CVCT, increasing to 80% after CVCT (with 5% per year additional ART uptake thereafter). In the comparison group without CVCT, 55% are ART users at baseline, increasing by 5% per year thereafter. The prevention impact of ART/TasP in discordant relationships is 96%, irrespective of CVCT.

[a]Cumulative expenditure calculations for nationwide CVCT: 7 931 000 adults x 59% in couples = 4 679 290 divided by two people/couple = 2 339 645 couples; 2 339 645 x [(10% tested in implementation phase x $75) + (10% tested in expansion phase x $50) + (20% tested in first maturation phase x $25) + (30% tested in second maturation phase x $25) + (10% tested in maintenance phase x $30)] = $65 510 060.

[b]Cumulative expenditure calculations for TasP for discordant couples identified by nationwide CVCT:2 339 645 x 11% couples discordant = 257 361 couples.

Year 1 (initiation phase): 257 361 x 10% tested and ART/TasP increases from 20.0% before CVCT to 50.6% after CVCT at $442/year/patient: year 1 total $3 480 859.

Year 2 (expansion phase): 257 361 x 10% tested and ART/TasP increases from 20.0% before CVCT to 50.6% after CVCT at $442/year/patient = $3 480 859 plus year-1 TasP patients continue and each add another 5% ART/TasP uptake: year 2 total $6 961 718.

Year 3 (first maturation phase): 257 361 x 20% tested and ART/TasP increases from 20.0% before CVCT to 50.6% after CVCT at $442/year/patient = $10 442 577 plus years-1–2 TasP patients continue and each add another 5% ART/TasP uptake: year 3 total $13 923 435.

Year 4 (second maturation phase): 257 361 x 30% tested and ART/TasP increases from 20.0% before CVCT to 50.6% after CVCT at $442/year/patient = $10 442 577 plus years 1–3-TasP patients continue and each add another 5% ART/TasP uptake: year 4 total $24 366 013.

Year 5 (maintenance phase): 257 361 x 10% of couples tested and ART/TasP increases from 20.0% before CVCT to 50.6% after CVCT at $442/year/patient = $6 961 718 plus years 1–4-TasP patients continue and each add another 5% ART/TasP uptake: Year 5 total $27 846 872.

Total years 1–5: $76 578 898.

[c]Cumulative expenditure calculations for population TasP for all HIV+ cohabiting men and women identified by individual testing: 7 931 000 adult population x 59% adults in heterosexual couples x 13.5% adult HIV prevalence = 631 704 HIV+ individuals.

Year 1: 631 704 x 20% of adults testing and ART/TasP increases from 20.0% to 50.6% at $442/year/patient: year 1 total $17 065 513.

Year 2: 631 704 x 20% of adults testing and ART/TasP increases from 20.0% at baseline to 50.6% at $442/year/patient = $17 065 513 plus year 1-TasP patients continue and each add another 5% ART/TasP uptake: year 2 total $34 131 026.

Year 3: 631 704 x 20% of adults testing and ART/TasP increases from 20.0% at baseline to 50.6% at $442/year/patient = $17 065 513 plus years 1–2-TasP patients continue and each add another 5% ART/TasP uptake: year 3 total $51 196 539.

Year 4: 631 704 x 10% of adults testing and ART/TasP increases from 20.0% at baseline to 50.6% at $442/year/patient = $8 532 756 plus years 1–3-TasP patients continue and each add another 5% ART/TasP uptake: year 4 total $59 729 295.

Year 5: 631 704 x 10% of adults testing and ART/TasP increases from 20.0% at baseline to 50.6% at $442/year/patient = $8 532 756 plus years 1–4-TasP patients continue and each add another 5% ART/TasP uptake: year 5 total $68 262 052.

Total years 1–5: $230 384 424.

All monetary units are in USD.
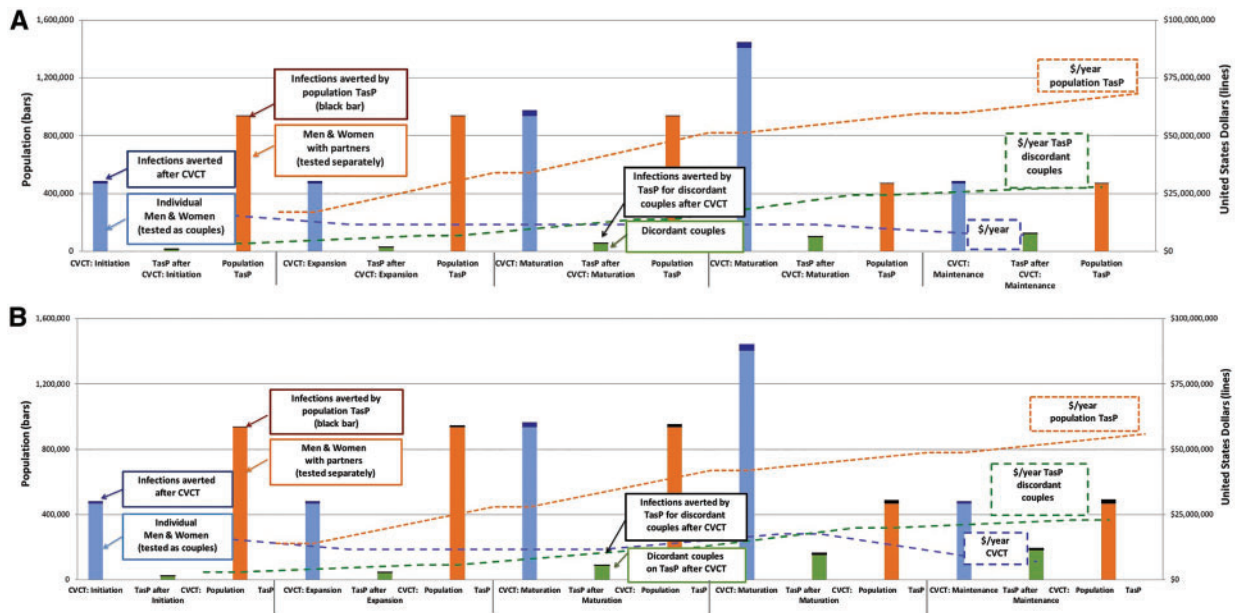
Figure 2. Persons tested, HIV infections averted, and expenditures for hypothetical nationwide implementations of CVCT, TasP for discordant couples identified by CVCT and population TasP for HIV+ cohabiting men and women identified by individual testing. A. Primary analysis results. B. Sensitivity analysis results. Model inputs are shown in Table 2 and cumulative results and calculated costs-per-infection averted are shown in Table 3. Columns indicate the number of individuals (left-axis). Lines indicate expenditures (right-axis). All monetary units are in USD.

CVCT assumptions (to reach 80% of adult couples): in the initiation phase, 10% of couples test at $75 per couple; in the expansion phase, an additional 10% of couples test at $50 per couple; in the first maturation phase, an additional 20% of couples test at $25 per couple; in the second maturation phase, an additional 30% of couples test at $25 per couple; and in the maintenance phase, 10% of residual and new couples test at $30 per couple. We similarly assume that individual HIV counselling and testing reached 80% of adult individuals in couples over the time horizon.

Panel A: Primary analyses (using estimates observed during the 73 Zambian government clinics implementation, see Table 2).

- CVCT: The prevention impact of CVCT is 79% for discordant couples on ART, 63% for discordant couples not on ART and 47% for concordant negative couples.
- TasP after CVCT: 20.0% of HIV+ partners in discordant couples are ART users before CVCT, increasing to 50.6% at 12 months after CVCT (with 5% per year ART/TasP uptake thereafter). The prevention impact of ART/TasP in discordant relationships before CVCT was 34%, increasing to 63% after CVCT.
- Population TasP: 20.0% of HIV+ individuals are on ART, increasing to 50.6% 12 months after testing. The prevention impact of population TasP for HIV+ cohabiting men and women identified by individual testing is 34%.

Panel B: Sensitivity analyses (using worst-case estimates of CVCT impact and best-case estimates of ART/TasP uptake and impact, see Table 2).

- CVCT: The prevention impact of CVCT is 50% for discordant couples and 30% for concordant negative couples.
- TasP after CVCT: 55% of HIV+ partners in discordant couples are ART users before CVCT, increasing to 80% at 12 months after CVCT (with 5% per year ART/TasP uptake thereafter). The prevention impact of ART/TasP in discordant relationships is 96%.
- Population TasP: 55% of HIV+ individuals are on ART, increasing to 80% at 12 months after testing. The prevention impact of population TasP for HIV+ cohabiting men and women identified by individual testing is 96%.

biomedical prevention trials which have not quantified the independent prevention impact of CVCT provided during eligibility screening to identify discordant couples.[25,34] As an illustration, our observed post-CVCT HIV incidence rate in non-ART-using discordant couples is similar to that in the delayed treatment arm of HIV Prevention Trials Network 052 ((HPTN-052)[25]—this finding represents a substantial reduction in incidence after CVCT and before treatment. In another example, observational studies in the same region that later hosted the Partners PrEP trial suggest a similar reduction after CVCT (10/100 PY in

uncounselled discordant couples to 2/100 PY in the counselled but untreated control arm) with a residual reduction from 2/100 PY to 0.50–0.65/100 PY attributable to PrEP.[34]

The potential for self-selection into the cohort based on recent risk behaviour is possible. A comprehensive study using Demographic and Health Surveys [DHS] data from 23 sub-Saharan African countries estimated median incidence in discordant couples ranged from 7.5/100 PY to 19.5/100 PY in low and high prevalence countries, respectively (Zambian median was 19.5/100 PY).[35] This estimate is higher than our

calculated pre-CVCT incidence. Assuming that our pre-CVCT incidence is biased downward, this could lead us to underestimate CVCT prevention impact among discordant couples. Background HIV incidence in concordant negative couples in Zambia is less well established. However, incidence in concordant negative couples has been estimated at 0.6–0.8/100 PY in Kenya, Tanzania and Uganda.[36–39] Though one would expect incidence in concordant negative couples to be higher in Zambia due to higher HIV prevalence, these estimates are lower than our calculated pre-CVCT incidence, which could lead us to overestimate CVCT prevention impact among concordant negative couples.

We present expenditures that governments, donors or investors would need to make to introduce CVCT. Expenditures in our models did not include clinic space, HIV test kits, condoms or therapeutic ART, which were available as standard care in government clinics. This approach is similar to that used by the President's Emergency Plan for AIDS Relief (PEPFAR) to calculate incurred annual ART costs per patient.[30] Promotions and advocacy are critical expenditures, since many African adults are not aware that cohabiting couples can have different HIV test results and often assume that their results must be the same as their partner's.[3] Funds used towards staffing could be reduced if existing individual testing services included CVCT. Programmatically, this could be a cost-effective way of attaining the first UNAIDS 90–90-90 target.[40]

Weighted analyses resulted in very little difference in our outcome measures. Though ART use was self-reported and we did not capture duration of use, varying ART use by ±10% before and after CVCT changed CHIA estimates by <±1.0%. Additionally, though we had comparatively low power to detect seroincidence differences in ART vs non-ART users before CVCT, varying the prevention impact of ART between 34% and 96% did not substantively change the resulting CHIAs, nor did varying TasP uptake among discordant couples between 50.6% and 80%. Finally, sensitivity analyses confirm that even with optimistic assumptions about ART use, uptake and impact, the CHIA for CVCT remains lower than TasP.

Rwanda exemplifies the potential of nationwide CVCT, which according to previous conservative estimates, prevents ≥70% of new infections in that country;[10] >80% of pregnant women have tested with partners since 2009, and premarital CVCT is a social norm.[13] In contrast, despite feasibility and Ministry of Health endorsement in Zambia, less than one in 10 Zambian couples have been jointly tested and counselled.[14] A nationwide CVCT programme could prevent, at minimum, half of heterosexual HIV infections and would cost 5% of the 2014 PEPFAR budget for 5 years in Zambia.[41] Given that ART adherence would be improved through partner participation, CVCT is a high-impact entry point into treatment and prevention.

Our models do not consider the prevention impact of CVCT or ART in concordant positive couples. We also did not quantify other potential benefits of CVCT, including improved clinical HIV outcomes resulting from increased ART adherence and uptake of family planning (reducing unplanned pregnancies and perinatal HIV infection). Similarly, we did not consider other possible advantages of TasP (clinical benefits, prevention of mother-to-child transmission, among others). More detailed cost-effectiveness analyses including these outcomes, as well as the role of donated and opportunity costs and over longer time horizons, are warranted. Importantly, our implementation scenarios apply averages across a very large population when in fact costs, uptake and treatment effects are likely heterogeneous. Future research on: such heterogeneity; relative sources of attributable CVCT prevention impact (e.g. how much is due to condom use, reduction in concurrent partnerships and STIs, ART uptake and adherence, VMMC uptake etc.); strategies to integrate CVCT into ART programmes cost-effectively; and best practices for providing CVCT (such as home-based, clinic-based, mobile testing, and a possible role for self-testing) would help inform implementation.

Conclusion

CVCT is cost-effective, affordable and WHO-recommended. However, required indicators, targets, dedicated funds and timelines for CVCT implementation do not yet exist. Our strongest recommendations are that: (i) governments and donors make CVCT a required monitoring indicator whether or not ART is available; (ii) targets and timelines be set for CVCT implementation; and (iii) corresponding budgets for CVCT be allocated. Our results suggest that promotion of CVCT in ART clinics should be a priority high-impact strategy to improve the prevention impact of ART. This novel finding suggests that the prevention impact of treatment is considerably bolstered by CVCT. Where affordable, TasP can be implemented after CVCT to more cost-effectively target TasP to discordant couples.

Supplementary data

Supplementary data are available at *IJE* online.

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Author Contributions

K.M.W. 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. M.I. contributed to the concept and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. W.K. contributed to the concept and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. E.K. contributed to the concept and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. B.V. contributed to the concept and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. J.M. contributed to the concept and design of the study, revised the article critically for important intellectual content and gave final approval of the version to be published. R.P. 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. T.S. 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. D.S. 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. A.T. contributed to the study concept and design, revised the article critically for important intellectual content and gave final approval of the version to be published. E.H.

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