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Research Paper

Cost-effectiveness of HIV Prevention Interventions in Sub-Saharan Africa: A Systematic Review

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ABSTRACT

Background: Sub-Saharan Africa carries the highest HIV burden globally. It is important to understand how interventions cost-effectively fit within guidelines and implementation plans, especially in low- and middle-income settings. We reviewed the evidence from economic evaluations of HIV prevention interventions in sub-Saharan Africa to help inform the allocation of limited resources.

Methods: We searched PubMed, Web of Science, Econ-Lit, Embase, and African Index Medicus. We included studies published between January 2009 and December 2018 reporting cost-effectiveness estimates of HIV prevention interventions. We extracted health outcomes and cost-effectiveness ratios (CERs) and evaluated study quality using the CHEERS checklist.

Findings: 60 studies met the full inclusion criteria. Prevention of mother-to-child transmission interventions had the lowest median CERs ($1144/HIV infection averted and $191/DALY averted), while pre-exposure prophylaxis interventions had the highest ($13,267/HIA and $799/DALY averted). Structural interventions (partner notification, cash transfer programs) have similar CERs ($3576/HIA and $392/DALY averted) to male circumcision ($2965/HIA) and were more favourable to treatment-as-prevention interventions ($7903/HIA and $890/DALY averted). Most interventions showed increased cost-effectiveness when prioritizing specific target groups based on age and risk.

Interpretation: The presented cost-effectiveness information can aid policy makers and other stakeholders as they develop guidelines and programming for HIV prevention plans in resource-constrained settings.

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1. Introduction

Sub-Saharan Africa (SSA) has experienced a large reduction in new HIV infections over the last decade, with the number of incident infections dropping over 30% since 2010 [1]. This decrease in burden reflects the accomplishment of a global effort focused on a region in which approximately 70% of all people living with HIV reside [2,3]. Despite this success, the decline in incidence is slowing, and gaps in the scale-up of HIV prevention services persist throughout SSA [3].

US$4.5 billion was allocated for HIV prevention investments in 2016 by the international community; however, a recent UNAIDS report stated that an additional annual investment of US$7 billion is urgently needed to meet the 2030 Sustainable Development Goals targets [4–6]. To improve the efficiency of programming for HIV prevention, optimizing limited financial resources is crucial to scale up high-quality, cost-effective interventions to maximize HIV prevention [7].

In addition to evidence-based prevention tools such as voluntary medical male circumcision (VMMC) and prevention of mother-to-child transmission (PMTCT) strategies, new prevention methods such as HIV pre-exposure prophylaxis (PrEP) have been heralded for their remarkable clinical results in the reduction of HIV transmission. However, it is important for policy- and decision-makers to identify where and how such costly interventions fit within regional and national HIV implementation plans and budgets, particularly in resource-limited countries [8].

Ascertaining the cost-effectiveness of prevention interventions is necessary for optimal resource allocation and for identifying inefficiencies within prevention programs [7].

A systematic review of HIV prevention intervention cost-effectiveness was published in 2009 by Galarraga et al., which concluded that the number and quality of cost-effectiveness studies were insufficient and too limited at that time to aid decision making and

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Research in context

Evidence Before This Study

There is an increasing interest in cost-effectiveness of HIV programming among stakeholders. The last systematic review on the cost-effectiveness of all HIV prevention interventions was published nearly ten years ago. At that time, cost-effectiveness studies were limited and often unavailable for specific interventions. A 2013 systematic review presented evidence from studies specifically on pre-exposure prophylaxis and concluded that the intervention's impact relied highly on contextual assumptions. In the past decade, an increasing number of cost-effectiveness studies in HIV prevention literature have become available, but there has not yet been a single review that synthesizes the evidence from all of these studies. We conducted a systematic review for cost-effectiveness studies on HIV prevention interventions. We searched PubMed/MEDLINE, Web of Science, Econ-Lit, Embase, and African Index Medicus, for studies published between January 1, 2009 and December 31, 2018. Search terms included "HIV", "prevention" or "control"; "sub-Saharan Africa"; "cost" or "cost-effectiveness".

Added Value of This Study

This is the first review that provides a comprehensive and update look at the cost-effectiveness of all HIV prevention interventions targeted towards HIV- individuals. Additionally, this review focuses solely on sub-Saharan Africa, the region that carries the vast majority of the global disease burden. We show that voluntary medical male circumcision (VMMC) and prevention of mother-to-child transmission (PMTCT) interventions are cost-effective in almost all contexts. We provide evidence of cost-effectiveness of other newer biomedical interventions, including pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP). We hope that the evidence from this review will aid various stakeholders, including Ministries of Health, program implementers, and international donors, in their decision-making regarding resource allocation policy for HIV prevention.

Implications of All the Available Evidence

The number of studies included in this review reflects the increasing importance of considering cost-effectiveness when designing or implementing HIV prevention programs in sub-Saharan Africa. Numerous studies focused on new biomedical interventions, and many of these studies used mathematical modeling to provide evidence of these interventions' cost-effectiveness since they have not yet been scaled up in sub-Saharan Africa. However, this review shows that most interventions can be cost-effective in specific contexts. As such, we encourage others to use the results of this review with caution. Future economic and costing studies on HIV prevention should include more realistic scenarios so that these data are more accessible and relevant to policymakers and other stakeholders.

policy recommendations [9–10]. However, since 2009, many studies have been published on the cost-effectiveness of various prevention interventions, including newer PrEP technologies and treatment-as-prevention [8].

No systematic review to date has evaluated these newer prevention interventions with a focus on SSA. Such a review would provide important information on HIV prevention costs, outcomes, and effectiveness to support policies and decision-making [8,9]. The purpose of this review is to systematically review published analyses of the cost-effectiveness of HIV prevention interventions in SSA settings. We aim to 1) review evidence from studies published in the last decade that have evaluated cost and outcome metrics for HIV prevention interventions, 2) compare the costs and effects of specific prevention interventions, and 3) understand the assumptions driving cost-effectiveness in order to inform allocation of limited HIV prevention resources.

2. Methods

2.1. Search Strategy and Selection Criteria

We conducted this systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. We searched PubMed/MEDLINE, Web of Science, Econ-Lit, Embase, and African Index Medicus. Additionally, we reviewed reference lists of retrieved articles as well as governmental and organizational reports to complement our search. We limited studies published between January 1, 2009 and December 31, 2018. The following keywords were used: "HIV"; "prevention" or "control"; "cost" or "cost-analysis" or "cost-effectiveness"; "sub-Saharan Africa". The full search strategy, including keywords for each database, can be found in the supplemental material.

Inclusion criteria included full articles that were peer-reviewed and published in English, and reported cost and outcome measures or analysed cost-effectiveness of an HIV prevention intervention. Interventions included, but were not limited to: VMMC, PMTCT, TasP, PrEP, behavioral interventions, vaccinations, and microbicides. As a multi-pronged strategy, two types of PMTCT interventions were considered: Prong II, interventions to prevent unintended pregnancies of HIV-positive women, and Prong III, interventions providing services to reduce HIV transmission from HIV-positive women to their infants. Geography was limited to country settings within SSA, as defined by the United Nations [11]. A full list of eligible country settings can be found in the supplemental material. Studies that focused on HIV treatment with no prevention aspect, systematic reviews, meta-analyses, conference abstracts, and guideline reports were excluded. Studies assessing cost-effectiveness of an intervention's combined impact for both HIV-positive and HIV-negative persons and studies that did not describe costing analyses and effectiveness measures were excluded. Two reviewers aggregated a list of articles produced by the database search and conducted independent screenings based on title and abstract. All discrepancies were resolved by a third reviewer.

2.2. Quality Assessment and Data Extraction

Two reviewers independently extracted data from each of the selected studies using a prepared data form, and an independent crosscheck by a third reviewer was conducted to identify and resolve any disagreements or uncertainties. We developed the data form using guidance from Emory colleagues and prior systematic reviews on similar topics. We assessed the quality of studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement, which contains a 24-point checklist to assess economic evaluation studies [12].

We extracted data on intervention type, study design or model type, geographic setting, HIV transmission method, population, intervention description, perspective, and time horizon. Additional extracted information included scenario descriptions, intervention effectiveness, cost-effectiveness metric results, and discounting rates for effects and costs. We categorized studies by prevention intervention type to compare intervention-specific results. The primary measures of interest were cost per HIV infection averted (HIA), cost per disability-adjusted life year (DALY) averted, cost per quality-adjusted life year (QALY) gained, and cost per life year gained (LYG). We converted study cost-effectiveness results to 2018 US$ using the Consumer Price Index

(CPI) Inflation Calculator and compared them to the International Monetary Fund 2018 estimates of gross domestic product (GDP) per capita for each study setting [13,14].

For each intervention type, we calculated median CERs. Separate medians were calculated for studies reporting cost per HIA estimates and studies reporting cost per DALY averted, QALY gained, or LYG. For studies that explored more than one geographic setting, we considered results from the different settings as individual estimates if they were reported as such within a single study; these results were considered separately when we calculated median CERs.

3. Results

We identified and screened 1115 articles, of which 146 met criteria to be assessed for eligibility. The 969 articles that were initially excluded were deemed ineligible based on the article title and abstract and did not meet either the geographic setting or intervention criteria. Out of the 146 articles, 60 met the full inclusion criteria (Fig. 1). These 60 peer-reviewed studies provided cost-effectiveness results for the following HIV prevention interventions: 14 studies on VMMC, 13 studies on PrEP, five studies on TasP, 15 studies on PMTCT, nine studies on other biomedical interventions, one study on behaviour change, and three studies on structural interventions [15–74]. Among PMTCT studies, 14 considered Prong III strategies, while one focused on Prong II.

Table 1 describes characteristics of each study, including study design or model type, geographic setting, method of transmission, target population, time horizon, HIV prevalence of the target population, perspective, and description of the intervention assessed. Studies focused on heterosexual transmission among the general population except for studies exploring prevention of mother-to-child-transmission. Costs were predominately assessed through a healthcare payer perspective. Two studies included results from countries outside of SSA; non-SSA results were excluded from this review [56,62].

We extracted and converted each study's reported cost-effectiveness measure and converted them to 2018 US$. Table 2 describes these measures. Most studies provided discounted results, with discounting ranging from 0%–5% for the base case scenario, as is standard in cost-effectiveness literature [37]. Outcome measures were presented as number of HIV infections averted (HIA) for a specific scenario, with fewer studies reporting quality-adjusted life years (QALYs) gained or disability-adjusted life years (DALYs) averted. A number of studies did not provide numerical values for cost-effectiveness measures but rather stated whether an intervention was a dominant (cost-savings with better outcomes) or dominated (costlier with poorer outcomes) strategy [55,58,67]. The most cost-effective interventions included -$8356 per HIA for a microbicide intervention in South Africa, —$312 per HIA for a PMTCT intervention in Malawi, and $470 per HIA for a VMMC intervention in Uganda [18,49,62].

The median CERs for each intervention type were as follows: $2967 per HIA and $-388/DALY averted for VMMC, $13,267 per HIA and $799 per QALY gained for PrEP, $7903 per HIA and $890 per DALY averted for TasP, $1421 per HIA and $191 per DALY averted or QALY gained for PMTCT, $1143 per HIA and $392/DALY averted for other biomedical interventions (microbicides, vaccination, praziquantel treatment, combination prevention, condom distribution), and $3575/HIA and $345/DALY averted for structural interventions (partner notification, cash transfer programs). For several of the intervention types, scenarios that prioritized specific sub-populations based on age and/or risk factors were more cost-effective than scenarios that targeted the general population (Figs. 2–7).

Table 3 and Fig. 8 provide the results of the quality assessment of each study using the CHEERS checklist.

4. Discussion

This review summarizes the evidence to date on recent studies of the cost-effectiveness of HIV prevention interventions and serves as an SSA-specific update to the 2009 review by Galarraga et al. [9] Results from this review illustrate that established interventions, such as VMMC and PMTCT, remain cost-effective, as previously found in the 2009

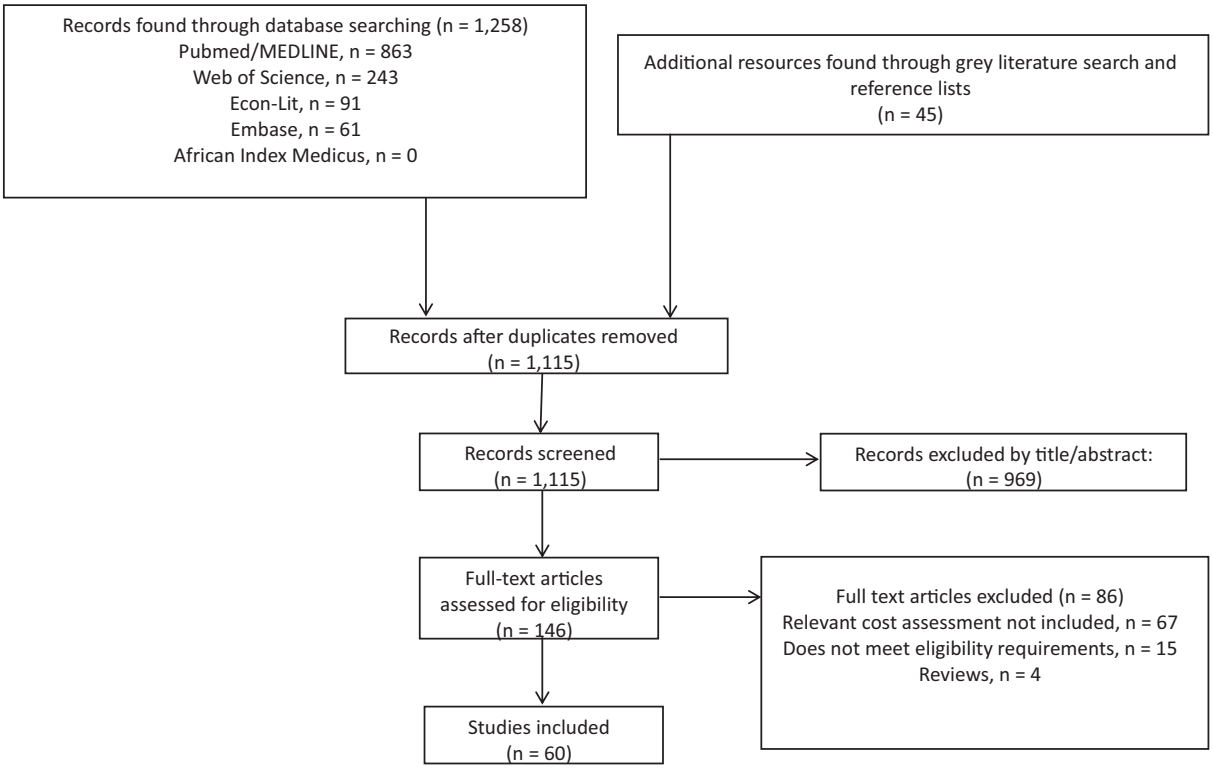

Fig. 1. Flowchart diagram for study selection.

Table 1
Study design and setting overview.

Reference	Study design	Setting	Population	Time horizon	HIV prevalence[a]	Perspective[b]	Intervention description
VMMC							
Binagwaho et al. (2010) [15]	Deterministic compartmental simulation	Rwanda	0-49 yo[c], male population	Lifetime	2.7%	Health care payer	Scale-up of VMMC to infants, adolescents, and adults
Njeuhmeli et al. (2011) [16]	Deterministic compartmental simulation	Sub-Saharan Africa	15-49 yo, general population	Lifetime	4.8%	Health care payer	Scale-up of VMMC
Uthman et al. (2011) [17]	Probabilistic decision analysis	Sub-Saharan Africa	15 + yo, male population	Lifetime	5.5%	Health care payer	Uptake of VMMC
Duffy et al. (2013) [18]	Cross-sectional descriptive cost-analysis	Uganda	18 yo and older, male population	Lifetime	5.9%	Health care payer	PrePex device for VMMC
Menon et al. (2014) [19]	Impact analysis	Tanzania	10-49 yo, male population	Lifetime	4.5%	Health care payer	Scale-up of VMMC
Awad et al. (2015) [20]	Deterministic compartmental simulation	Zimbabwe	10-49 yo, male population	15 years	13.3%	Health care payer	Prioritisation of VMMC subpopulations by age, geographic location, sexual risk profile
Awad et al. (2015) [21]	Deterministic compartmental simulation	Zambia	10-49 yo, male population	15 years[c]	11.5%	Health care payer	Prioritisation of VMMC subpopulations by age, geographic location, sexual risk profile
Haacker et al. (2016) [22]	Deterministic compartmental simulation	South Africa	15-59, male population	Lifetime	18.8%	Health care payer	Age prioritised VMMC scale up
Kripke et al. (2016) [23]	Deterministic compartmental simulation	Malawi	10 + yo; male population	15 years	9.6%	Health care payer	Age prioritised VMMC scale up
Kripke et al. (2016) [24]	Deterministic compartmental simulation	Zimbabwe	20-29 yo; male population	15 years	13.3%	Health care payer	Age prioritised VMMC scale up
Kripke et al. (2016) [25]	Deterministic compartmental simulation	Sub-Saharan Africa	10-49 yo; male population	15 years	4.8%	Health care payer	Age prioritised VMMC scale up
Kripke et al. (2016) [26]	Deterministic compartmental simulation	Eswatini	10-49 yo; male population	15 years	27.4%	Health care payer	Age prioritised VMMC scale up
Kripke et al. (2016) [27]	Deterministic compartmental simulation	Malawi, South Africa, Eswatini, Tanzania, Uganda	10-49 yo; male population	15 years	9.6% (Malawi) 18.8% (South Africa) 27.4% (Eswatini) 4.5% (Tanzania) 5.9% (Uganda)	Health care payer	Age prioritised VMMC scale up
Njeuhmeli et al. (2016) [28]	Deterministic compartmental simulation	Zimbabwe	Male infants	36 years	13.3%	Health care payer	Early infant male circumcision
PrEP							
Pretorius et al. (2010) [29]	Deterministic compartmental simulation	South Africa	15-49 yo, general population	10 years	18.8%	Health care payer	PrEP is scaled up to recruit all uninfected individuals
Hallett et al. (2011) [30]	Microsimulation	South Africa	HIV serodiscordant couples	Lifetime	18.8%	Health care payer	PrEP for uninfected partner in serodiscordant relationships
Cremin et al. (2013) [31]	Deterministic compartmental simulation	KwaZulu-Natal, South Africa	15-54 yo, general population	10 years	27.0% (KZN[c])[ref]	Program	Combination prevention strategies of VMMC, early ART, and PrEP
Nichols et al. (2013) [32]	Deterministic compartmental simulation	Macha, Zambia	12 + yo, general population	10 years	7.7% (Macha)	Health care payer	Prioritisation of PrEP
Verguet et al. (2013) [33]	Deterministic compartmental simulation	Sub-Saharan Africa	15-49 yo, general population	5 years	4.8%	Health care payer	PrEP intervention to pre-existing levels of MC, ART, and condom use
Alistar et al. (2014) [34]	Dynamic compartmental simulation	South Africa	15-49 yo, general population	20 years	18.8%	Health care payer	PrEP is scaled up to recruit all uninfected individuals
Nichols et al. (2014) [35]	Deterministic compartmental simulation	Macha, Zambia	12 + yo, general population	40 years	7.7% (Macha)	Health care payer	Uptake of PrEP and TasP in combination
Cremin et al. (2015) [36]	Deterministic compartmental simulation	Nyanza province, Kenya	General population	5 years	13.9% (Nyanza)	Health care payer	Dynamic interaction between key determinants of PrEP impact and cost-effectiveness
Cremin et al. (2015) [37]	Deterministic compartmental simulation	Gaza province, Mozambique	Adult male mine workers	5 years	30.0% (female) 17.0% (male)	Health care payer	Time-limited PrEP uptake among sexual partners of miners
Ying et al. (2015) [38]	Micro-costing analysis	Uganda	HIV serodiscordant couples	10 years	7.1%	Program	Targeted PrEP for serodiscordant couples
Glaubius et al. (2016) [39]	Deterministic compartmental simulation	South Africa	15-54 yo, general population	1) 10yrs 2) lifetime	18.8%	Societal	Long-acting injective antiretrovirals used for PrEP
Walensky et al. (2016) [40]	Deterministic compartmental	South Africa	18-25 yo, high risk women	5 years	Incidence: 5.0%	Program	Long-acting PrEP

(continued on next page)

Table 1 (*continued*)

Reference	Study design	Setting	Population	Time horizon	HIV prevalence[a]	Perspective[b]	Intervention description
	simulation				(high risk women)		
Cremin et al. (2017) [41]	Deterministic compartmental simulation	Nairobi, Kenya	Key populations	10 years	4.8%	Health care payer	PrEP provided to FSW
TasP							
Barnighausen et al. (2012) [42]	Discrete time mathematical model	South Africa	15 + yo, general population	10 years	18.8%	Health care payer	Increased coverage of TasP, ART under the current WHO eligibility guidelines, and MMC
Granich et al. (2012) [43]	Deterministic compartmental simulation	South Africa	15 + yo, general population	1) 5 years 2) 40 years	18.8%	Program	Enhanced combination prevention strategy
Smith et al. (2015) [44]	Individual-based simulation modelling study	KwaZulu-Natal, South Africa	18 + yo, general population	10 years	27.0% (KZN)[ref]	Health care payer	Home HIV counselling and testing
Bershteyn et al. (2016) [45]	Individual-based simulation modelling study	South Africa	General population	20 years	18.8%	Health care payer	Age-targeting outreach with HIV treatment and prevention
Ying et al. (2016) [46]	Dynamic compartmental model	KwaZulu-Natal, South Africa	General population	10 years	27.0% (KZN)[ref]	Program	Home HIV testing and counselling
PMTCT							
Halperin et al. (2009) [47]	Modelling analysis	Sub-Saharan Africa	Pregnant, HIV-infected women	1 year	4.8%	Service delivery	Antiretroviral prophylaxis programs and family planning programs
Nakakeeto et al. (2009) [48]	Forecasting model	Burkina Faso, Cameroon, Cote d'Ivoire, Malawi, Rwanda, Tanzania, and Zambia	HIV-infected women, HIV-exposed infants	8 years	0.8% (Burkina Faso) 3.7% (Cameroon) 2.8% (Cote d'Ivoire) 9.6% (Malawi) 2.7% (Rwanda) 4.5% (Tanzania) 11.5% (Zambia)	Health care payer	PMTCT package including: family planning, HIV testing and counselling, and provision of antiretroviral and cotrimoxazole prophylaxis
Orlando et al. (2010) [49]	Cost-effectiveness analysis	Malawi	Pregnant, HIV-infected women	42 months	16.9% (ANC)	Societal and Private	HAART-based intervention
Robberstad et al. (2010) [50]	Decision analysis	Tanzania	Pregnant, HIV-infected women	18 months	6.6% (ANC)	Health care payer	HAART-based intervention
Shah et al. (2011) [51]	Decision-based analytical model	Nigeria	Pregnant, HIV-infected women	1 year	2.8%	Health care payer	2009 WHO PMTCT guidelines (long-course ART)
Kuznik et al. (2012) [52]	Cost-effectiveness analysis	Uganda	Pregnant, HIV-infected women	19.3 years	7.1%	Health care payer	Combination ART
Binagwaho et al. (2013) [53]	Cost-effectiveness analysis	Rwanda	HIV-infected pregnant women and their infants	Lifetime	2.7%	Health care payer	Dual ARV and short course HAART prophylaxis with breastfeeding or replacement feeding
Fasawe et al. (2013) [54]	Decision analysis	Malawi	Pregnant, HIV-infected women	10 years	16.9% (ANC)	Health care payer	Implementation of Option B +
Maredza et al. (2013) [55]	Cost-effectiveness analysis	South Africa	Pregnant, HIV-infected women	24 months	28.0% (ANC) 5.9% (Kenya)	Health care payer	HAART-based intervention
Gopalappa et al. (2014) [56]	Deterministic compartmental simulation	Kenya, South Africa, Zambia	15-49 yo, female population	Lifetime	18.8% (South Africa) 11.5% (Zambia)	Program	Implementation of Option B +
Ishikawa et al. (2014) [57]	Decision analysis	Zambia	Pregnant, HIV-infected women	18 months	11.5%	Health care payer	Comparison between Option A, Option B, and Option B +
Yu et al. (2014) [58]	Decision analysis	South Africa	Pregnant, HIV-infected women	18 months	28.0% (ANC)	Health care payer	1) tested and treated promptly at any time during pregnancy (promptly treated cohort), 2) no testing or treatment until after delivery and appropriate standard treatments were offered (remedy treated cohort)
Zulliger et al. (2014) [59]	Cost-effectiveness analysis	South Africa	Pregnant, HIV-infected women	1 year	28.0% (ANC)	Health care payer	Expedited initiation onto lifelong ART in pregnant women who met South African ART eligibility criteria
Price et al. (2016) [60]	Decision analysis	Zambia	Pregnant women	Lifetime	11.5%	Health care payer	Daily oral PrEP during pregnancy and breastfeeding
Tweya et al. (2016) [61]	Individual-based simulation modelling study	Malawi	Primigravida women	50 years	16.9% (ANC)	Health care payer	Option B vs. Option B +
Other biomedical							
Verguet et al. (2010) [62]	Cost-effectiveness analysis	South Africa	15-49 yo, female population	1 year	26.3% (Female)	Health care payer	Impact of microbicides distributed alongside condoms
Williams et al. (2011) [63]	Dynamic compartmental model	South Africa	General population	20 years	18.8%	Health care payer	Tenofovir gel uptake by sexually

							active women
Long et al. (2013) [64]	Dynamic compartmental simulation	South Africa	15-49 yo, general population	10 years	18.8%	Health care payer	HIV screening and counselling, ART, VMMC, microbicides
Mbah et al. (2013) [65]	Dynamic compartmental simulation	Zimbabwe	15-49 yo, female population	10 years	13.3%	Health care payer	Praziquantel as a preventive anthelminthic chemotherapy
Terris-Prestholt et al. (2014) [66]	Deterministic compartmental simulation	Gauteng Province, South Africa	15-49 yo, general population + FSW and their partners	15 years	17.6% (Gauteng)	Health care payer	Uptake of tenofovir gel by women
Mvundura et al. (2015) [67]	Impact analysis	Sub-Saharan Africa	15-49 yo, general population	1 year	4.8%	Health care payer	Distribution of 100,000 female condoms
Moodley et al. (2016) [68]	Semi-Markov simulation	South Africa	Adolescents enrolled in school	Lifetime	10.2% (females 15-24) 3.9% (males 15-24)	Health care payer	Hypothetical HIV vaccination provided to adolescent students
Moodley et al. (2016) [69]	Semi-Markov simulation	South Africa	Adolescents girls enrolled in school	Lifetime	10.2% (females 15-24) 3.9% (males 15-24)	Health care payer	National implementation of hypothetical HIV vaccination to adolescents
Wall et al. (2018) [70]	Cost-benefit analysis and cost-effectiveness analysis	Zambia	HIV serodiscordant couples	5 years	11.5%	Donor	Couples' testing and counselling with TasP for seropositive partner
Behavior change							
Enns et al. (2011) [71]	Stochastic network simulation	Eswatini, Tanzania, Uganda, Zambia	15-49 yo, general population	10 years	27.4% (Eswatini) 4.7% (Tanzania) 7.1% (Uganda) 11.5% (Zambia)	Program	Concurrency reduction campaigns focused on behaviour change scenario: 1) increased monogamy, 2) high-risk partnership reduction, 3) untargeted partnership reduction
Structural							
Fieno et al. (2014) [72]	Cost simulation	South Africa	Women aged 15-20 yo, bottom quarter of income distribution	6 years	18.8%	Health care payer	Cash transfers
Remme et al. (2014) [73]	Cost-benefit analysis and cost-effectiveness analysis	Malawi	Adolescent girls attending school	18 months	9.6%	Health care payer	Cash transfers
Rutstein et al. (2014) [74]	Decision-tree model	Malawi	15-49 yo, partners of STI clinic indexes	1 year	9.6%	Health care payer	Partner notification

[a] World Bank 2017 HIV prevalence estimates

[b] Health care payer perspective refers to costs incurred or saved by the governmental healthcare system; Donor perspective refers to costs incurred of saved by international donors; Program and service delivery perspective refers to costs incurred by a stakeholders implementing HIV program; Societal perspective refers to all of society regardless of the payer; Private perspective takes into account the costs incurred by service providers

[c] Abbreviations: ANC = antenatal care clinic; ARV = antiretrovirals; ART = antiretroviral therapy; FSW = female sex worker; HAART = highly active antiretroviral therapy; KZN = KwaZulu-Natal, South Africa; MC = male circumcision; MMC = medical male circumcision; PMTCT = prevention of mother-to-child transmission; PrEP = pre-exposure prophylaxis; TasP = treatment as prevention; VMMC = voluntary medical male circumcision; WHO = World Health Organization; yo = years old.

Table 2
Intervention cost and output results.

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
VMMC						
Binagwaho et al. (2010) [15]	Infants	1288 HIA[l]	Cost-saving	--	3%	Rwanda: $800·21
	Adolescents	1283 HIA	CER[l] = $3,932/HIA	$4,698/HIA		
	Adults	859 HIA	CER = $4,949/HIA	$5,914/HIA		
Njeuhmeli et al. (2011) [16]	80% VMMC coverage in 13 countries	9 VMMCs/1 HIA	$809/HIA	$927/HIA	NR	SSA: $1,620·00
Uthman et al. (2011) [17]	All adult males	15·5 DALY[l] averted/HIA	$-325/DALY averted (cost savings)	$-388/DALY averted	3%	SSA: $1,620·00
Duffy et al. (2013) [18]	Surgical circumcision method	NR[m]	$430/HIA	$470/HIA	NR	Uganda: $717·50
	PrePex circumcision method	NR	$580/HIA	$634/HIA		
Menon et al. (2014) [19]	Scale-up and maintenance of 80% VMMC coverage	NR	$3,200/HIA	$3,668/HIA	3%	Tanzania: $1,090·00
Awad et al. (2015) [20]	Current VMMC scale-up program	326,000 HIA 11 VMMCs/1 HIA (2010-2025)	$1,010/HIA	$1,072/HIA	3%	Zimbabwe: $1,270·00
	VMMC program with subpopulation prioritization	10-53 VMMCs/1 HIA	$811-$5,518/HIA	$861-$5,861/HIA		
Awad et al. (2015) [21]	Current VMMC scale-up program	306,000 HIA 23 VMMCs/1 HIA (2010-2017) 12 VMMCs/1 HIA (2017-2025)	$1,089/HIA	$1,156/HIA	3%	Zambia: $1,145·00
	VMMC program with subpopulation prioritization	11-36 VMMCs/1 HIA	$888-$3300/HIA	$943-$3505/HIA		
Haacker et al. (2016) [22]	VMMC at 0 yo	4·2 VMMCs/HIA	$859/HIA	$919/HIA	5%	South Africa: $6,560·00
	VMMC at 20 yo	4·4 VMMCs/HIA	$659/HIA	$705/HIA		
	VMMC at 55 yo	214·2 VMMCs/HIA	$24,157/HIA	$25,846/HIA		
Kripke et al. (2016) [23]	60% coverage among 10-29 yo	79 HIA	$5,100/HIA	$5,307/HIA	3%	Malawi: $349·13
	60% coverage among 10–34 yo	92 HIA	$4,600/HIA	$4,786/HIA		
	60% coverage among 10–49 yo	106 HIA	$4,600/HIA	$4,786/HIA		
	60% coverage among 15–49 yo	104 HIA	$3,600/HIA	$3,746/HIA		
	80% coverage among 15–49 yo	148 HIA	$3,500/HIA	$3,642/HIA		
Kripke et al. (2016) [24]	80% Scenario: Scale up to 80% among 10-29 yo	87,000 HIA	$4,800/HIA	$4,994/HIA	3%	Zimbabwe: $1,270·00
	Base Scenario: Scale up to 80% among 10-19 yo	63,000 HIA	$6,000/HIA	$6,243/HIA		
	Scenario A: 80% Scenario with 2x unit cost for 20-29 yo	78,000 HIA	$6,600/HIA	$6,867/HIA		
	Scenario B: 80% Scenario with 2x unit costs for 20-24 yo and 3x unit costs for 25-29 yo	83,000 HIA	$7,200/HIA	$7,492/HIA		
Kripke et al. (2016) [25]	Actual VMMC performance through 2014	240,000 HIA (229,000, 572,000)	$4,400/HIA (median over 14 countries)	$4,578/HIA	3% (costs only)	SSA: $1,620·00
	80% coverage among 15-49 yo	1,082,000 HIA (744,000, 1,839,000)	NR	--		
Kripke et al. (2016) [26]	50% EIMC coverage/80% coverage among 10-24 yo	20,000 HIA (14,000, 24,000)	$1,500/HIA ($1,100, $1,900)	$1,560/HIA ($1,144, $1,977)	3%	Eswatini: $4,090·00
	50% EIMC coverage/80% coverage among 10-29 yo	27,000 HIA (19,000, 34,000)	$1,300/HIA ($900, $1,600)	$1,352/HIA ($936, $1,664)		
	50% EIMC coverage/80% coverage among 10-34 yo	29,000 HIA (21,000, 38,000)	$1,200/HIA ($900, $1,600)	$1,248/HIA ($936, $1,664)		
Kripke et al. (2016) [27]	80% coverage among 10-49 yo	Malawi: 149,000 HIA	$4,600/HIA	$4,600/HIA		Malawi: $349·13
		South Africa: 375,000 HIA	$2,700/HIA	$2,700/HIA		South Africa: $6,560·00
		Eswatini: 31,500 HIA	$1,200/HIA	$1,200/HIA		Eswatini: $4,090·00
		Tanzania: 53,400 HIA	$5,800/HIA	$5,800/HIA		Tanzania: $1,090·00
		Uganda: 486,000 HIA	$1,500/HIA	$1,500/HIA		Uganda: $717·50
	80% coverage among 15-49 yo	Malawi: 148,000 HIA	$3,500/HIA	$3,500/HIA		
		South Africa: 372,000 HIA	$2,200/HIA	$2,200/HIA		
		Eswatini: 32,200 HIA	$900/HIA	$900/HIA		
		Tanzania: 50,500 HIA	$4,100/HIA	$4,266/HIA		
		Uganda: 475,000 HIA	$1,100/HIA	$1,144/HIA		
	80% coverage among 15-24 yo	Malawi: 82,000 HIA	$4,300/HIA	$4,474/HIA		
		South Africa: 182,000 HIA	$2,500/HIA	$2,601/HIA		
		Eswatini: 18,900 HIA	$1,000/HIA	$1,040/HIA		
		Tanzania: 28,300 HIA	$4,900/HIA	$5,098/HIA		
		Uganda: 241,000 HIA	$1,400/HIA	$1,456/HIA		
	80% coverage among 15-29 yo	Malawi: 109,000 HIA	$3,700/HIA	$3,850/HIA		
		South Africa: 246,000 HIA	$2,200/HIA	$2,289/HIA		
		Eswatini: 25,700 HIA	$900/HIA	$936/HIA		
		Tanzania: 36,200 HIA	$4,300/HIA	$4,474/HIA		
		Uganda: 324,000 HIA	$1,200/HIA	$1,248/HIA		
	80% coverage among 15-34 yo	Malawi: 128,000 HIA	$3,500/HIA	$3,642/HIA		
		South Africa: 303,000 HIA	$2,100/HIA	$2,185/HIA		

Table 2 (*continued*)

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
		Eswatini: 29,700 HIA	$900/HIA	$936/HIA		
		Tanzania: 43,200 HIA	$4,000/HIA	$4,162/HIA		
		Uganda: 388,000 HIA	$1,100/HIA	$1,144/HIA		
	80% coverage among 10-24 yo	Malawi: 83,000 HIA	$6,100/HIA	$6,347/HIA		
		South Africa: 190,000 HIA	$3,600/HIA	$3,746/HIA		
		Eswatini: 19,600 HIA	$1,400/HIA	$1,456/HIA		
		Tanzania: 31,300 HIA	$7,800/HIA	$8,116/HIA		
		Uganda: 256,000 HIA	$2,100/HIA	$2,185/HIA		
	80% coverage among 10-29 yo	Malawi: 110,000 HIA	$5,100/HIA	$5,307/HIA		
		South Africa: 250,000 HIA	$3,000/HIA	$3,121/HIA		
		Eswatini: 26,300 HIA	$1,200/HIA	$1,248/HIA		
		Tanzania: 38,700 HIA	$6,800/HIA	$7,076/HIA		
		Uganda: 337,000 HIA	$1,700/HIA	$1,769/HIA		
Njeuhmeli et al. (2016) [28]	Scale up of VMMC among adolescents	266,000 HIA	$4,127/HIA	$4,415/HIA	3%	Zimbabwe: $1,270·00
	Introduction of EIMC into existing VMMC program	268,000 HIA	$5,256/HIA	$5,623/HIA		
PrEP						
Pretorius et al. (2010) [29]	Targeted PrEP for 25-35 yo women	NR	$12,500 - $20,000/HIA	$14,328 - $22,924/HIA	NR	South Africa: $6,560·00
Hallett et al. (2011) [30]	PrEP always used after HIV diagnosis in serodiscordant couple	15% - 52% HIA	$0 - $26,000/HIA	$0 - $28,944/HIA	3%	South Africa: $6,560·00
	PrEP used up through ART initiation for HIV infected partner	11% - 36% HIA	$-2,200 - $21,000/HIA	$-2,449 - $26,025/HIA		
	PrEP used only during periods of trying to conceive a pregnancy and during pregnancy	1% - 2% HIA	$-6,000 - $8,000/HIA	$-6,679 - $8,906/HIA		
Cremin et al. (2013) [31]	PrEP provided to 7.3% of uninfected 15-24 yo	3·2% HIA	$10,540/HIA	$11,362/HIA	3%	South Africa: $6,560·00
	PrEP provided to 4.4% of uninfected 15-54 yo	3·6% HIA	$9,390/HIA	$10,122/HIA		
Nichols et al. (2013) [32]	Non-prioritized PrEP	2,333 HIA; 23,571 QALYs[l] gained	$1,843/QALY gained	$2,051/QALY gained	3%	Zambia: $1,145·00
	Prioritized PrEP	3,200 HIA; 36,216 QALYs gained	$323/QALY gained	$359/QALY gained		
Verguet et al. (2013) [33]	PrEP intervention	200 - 94,100 HIA 3,300 - 1,266,000 DALYs averted	$550 - $44,600/DALY averted	$612 - $49,651/DALY averted	NR	SSA: $1,620·00
Alistar et al. (2014) [34]	10% Guidelines ART, 50% Focused PrEP	1,837,744 HIA	CER = cost saving	CER = cost saving	3%	South Africa: $6,560·00
	10% Guidelines ART, 100% Focused PrEP	3,084,508 HIA	CER = cost saving	CER = cost saving		
	50% Guidelines ART, 100% General PrEP	3,642,543 HIA	$163/QALY gained	$174/QALY gained		
	100% Guidelines ART, 100% Focused PrEP	3,840,111 HIA	$229/QALY gained	$245/QALY gained		
	50% Universal ART, 100% Focused PrEP	4,468,827 HIA	$276/QALY gained	$295/QALY gained		
	100% Universal ART, 100% Focused PrEP	4,663,411 HIA	$302/QALY gained	$323/QALY gained		
	10% Guidelines ART, 50% General PrEP	2,998,344 HIA	$1,172/QALY gained	$1,253/QALY gained		
	10% Guidelines ART, 100% General PrEP	3,381,214 HIA	$1,158/QALY gained	$1,239/QALY gained		
Nichols et al. (2014) [35]	Treatment available at CD4 <500 cells/μL	3388 HIA; 40,643 QALYs gained	CER = $62/QALY gained ($46–$75) ICER = $62/QALY gained ($46–$75)	CER = $69/QALY gained ($51–$83) ICER = $69/QALY gained ($51–$83)	3%	Zambia: $1,145·00
	Prioritized PrEP (most sexually active)	1502 HIA; 13,611 QALYs gained	CER = $4,103/QALY gained ($2,890–$5,803) ICER[l] = dominated	CER = $4,567/QALY gained ($3,217 – $6,460) ICER = dominated		
	Prioritized PrEP (mostly sexually active and treatment available at CD4 <500 cells/μL)	4494 HIA; 50,936 QALYs gained	CER = $1,153/QALY gained ($686–$1,756) ICER = dominated	CER = $1,283/QALY gained ($763–$1,954) ICER = dominated		
	Non-prioritized PrEP (randomly distributed)	4053 HIA; 40,318 QALYs gained	CER = $3,730/QALY gained ($2,454–$5,691) ICER = dominated	CER = $4,152/QALY gained ($2,731–$6,335) ICER = dominated		
	Non-prioritized PrEP (randomly distributed and treatment available at CD4 <500 cells/μL)	5894 HIA; 67,835 QALYs gained	CER = $2,253/QALY gained ($1,672–$3,188)	CER = $2,508/QALY gained ($1,861–$3,549) ICER = dominated		

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Table 2 (*continued*)

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
			ICER = dominated			
Cremin et al. (2015) [36]	Standard PrEP intervention ($20 million budget)	24,603 (~11%) HIA (3,750 - 49,450)	$2,060 - $36,360/HIA	$2,293 - $40,478/HIA	3%	South Africa: $6,560·00
Cremin et al. (2015) [37]	All uninfected women eligible to receive PrEP	NR	$15,647/HIA	$17,419/HIA	3%	Mozambique: $481·25
	Providing PrEP only to partners of miners	NR	$71,374/HIA	$79,458/HIA		
	Providing PrEP only to partners of miners and only during the last six weeks of the year	NR	$9,538/HIA	$10,618/HIA		
Ying et al. (2015) [38]	40% overall ART coverage[b]; 10% coverage for persons with CD4 350-500 cells/μL	94,000 HIA	Ref.	--	3%	Uganda: $717·50
	Increase ART Coverage (50% coverage for persons with CD4 350-500 cells/μL)	104,000 HIA	Dominated	--		
	Targeted PrEP and ART to 90% serodiscordant couples	120,000 HIA	$1,340/HIA	$1,466/HIA		
Glaubius et al. (2016) [39]	Optimistic scenario, Non-prioritized PrEP	1·6% - 9·1% HIA	$20,905 - $22,022/HIA $176,755 - $181,734/LYG	$22,874 - $24,096/HIA $192,313 - $198,856/LYG	3%	South Africa: $6,560·00
	Optimistic scenario, Age-prioritized PrEP	2·9% - 17·2% HIA	$10,880 - $11,094/HIA $84,418 - $85,105/LYG	$11,905 - $12,139/HIA $92,371 - $93,123/LYG		
	Optimistic scenario, Risk-prioritized PrEP	8·1% HIA	$11,094/HIA $85,105/LYG	$12,139/HIA $93,123/LYG		
	Conservative scenario, Non-prioritized PrEP	1·0 - 5·5% HIA	$35,090 - $37,137/HIA $276,605 - $284,781/LYG	$38,396 - $40,635/HIA $302,665 - $311,611/LYG		
	Conservative scenario, Age-prioritized PrEP	1·8 - 10·3% HIA	$18,429 - $19,213/HIA $133,428 - $135,695/LYG	$20,165 - $21,023/HIA $145,999 - $148,479/LYG		
	Conservative scenario, Risk-prioritized PrEP	4·4% HIA	$1,242/HIA $11,568/LYG	$1,359/HIA $12,657/LYG		
Walensky et al. (2016) [40]	Standard PrEP	127 HIA	$10,100/HIA Cost saving (vs. no PrEP)	$10,806/HIA	3%	South Africa: $6,560·00
	Long-acting PrEP	156 HIA	$12,400/HIA Cost saving (vs. no PrEP)	$13,267/HIA		
Cremin et al. (2017) [41]	50% PrEP coverage to all FSW	NR	$65,160/HIA (95% CI: $43,520 - $95,250)	$66,404/HIA (95% CI: $44,351 - $97,069)	0%	Kenya: $1,870·00
	50% PrEP coverage to high-risk FSW	NR	$10,920/HIA (95% CI: $4,700 - $51,560)	$11,128/HIA (95% CI: $4,789 - $52,544)		
TasP						
Barnighausen et al. (2012) [42]	Coverage: 70% ART, 20% TasP, 45% MMC[l]	650,000 HIA (compared to 50% ART and 45% MMC)	$7,157/HIA	$7,813/HIA	3%	South Africa: $6,560·00
	Coverage: 80% ART, 40% TasP, 45% MMC	1,000,000 HIA	$7,482/HIA	$8,186/HIA		
	Coverage: 80% ART, 60% TasP, 45% MMC	1,100,000 HIA	$7,937/HIA	$8,684/HIA		
	Coverage: 80% ART, 80% TasP, 45% MMC	1,260,000 HIA	$8,370/HIA	$9,158/HIA		
Granich et al. (2012) [43]	ART initiation at CD4 count ≤350 cells/μL vs. ≤200 cells/μL	200,000-1,400,000 HIA	NR	--	3%	South Africa: $6,560·00
	ART initiation at CD4 count <500 cells/mm^3 vs. ≤350 cells/μL	200,000-1,500,000 HIA	$182/DALY averted	$199/DALY averted		
	ART initiation at all CD4 levels vs. CD4 count ≤500 cells/μL	300,000-1,400,000 HIA	$1,381/DALY averted	$1,510/DALY averted		
Smith et al. (2015) [44]			High ART cost | Low ART cost		3%	South Africa: $6,560·00
	ART initiation at ≤200 cells/μL (vs. status quo)	2,000 DALYs averted	$22,300/HIA | $12,900/HIA $1,230/DALY averted | $414/DALY averted	$24,400/HIA | $14,115/HIA $1,345/DALY averted | $453/DALY averted		
	ART initiation at ≤350 cells/μL	3,100 DALYs averted	$10,400/HIA | $4,210/HIA $1,020/DALY averted | $788/DALY averted	$11,379/HIA | $4,606/HIA $1,116/DALY averted | $851/DALY averted		
	ART initiation at <500 cells/μL	3,300 DALYs averted	$8,910/HIA | $2,780/HIA $1,090/DALY averted | $342/DALY averted	$9,749/HIA | $3,041/HIA $1,192/DALY averted | $374/DALY averted		
	Universal ART	3,300 DALYs averted	$8,190/HIA | $1,960/HIA $1,300/DALY averted |	$8,961/HIA | $2,144/HIA $1,422/DALY averted | $339/DALY averted		

Table 2 (*continued*)

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
			$310/DALY averted			
Bershteyn et al. (2016) [45]	Targeting 10-30 yo	NR	$6,238/HIA	$6,491/HIA	3%	South Africa: $6,560·00
	Targeting 20-30 yo	NR	$5,031/HIA	$5,235/HIA		
	Targeting 22-27 yo	NR	$4,279/HIA	$4,452/HIA		
	Targeting 25-27 yo	NR	$3,967/HIA	$4,128/HIA		
	Targeting to full population	NR	$10,812/HIA	$11,250/HIA		
Ying et al. (2016) [46]	Base case (36% of HIV-infected people achieving viral suppression)	Ref.	Ref.	--	3%	South Africa: $6,560·00
	Home HTC (48% of HIV-infected people achieving viral suppression)	152,000 HIA	$3,290/HIA	$3,546/HIA		
	Home HTC + High Viral Load (60% ART uptake if CD4>350 cells/μL and VL>10,000 copies/mL)	183,000 HIA	$3,320/HIA	$3,579/HIA		
	Home HTC + CD4 (60% ART uptake if CD4 350–500 cells/μL)	195,000 HIA	$2,960/HIA	$3,190/HIA		
PMTCT						
Halperin et al. (2009) [47]	Perinatal HIV transmission prevention program	241,596 HIA	$543/HIA	$631/HIA by perinatal infection	NR	SSA: $1,620·00
	Services to prevent unintended pregnancies	72,000 HIA	$359/HIA	$417/HIA by unintended pregnancy		
Nakakeeto et al. (2009) [48]	Meeting UNGASS[l] targets for PMTCT by 2010	NR	Burkina Faso: $2,292/HIA	$2,741/HIA	3%	Burkina Faso: $734.03
			Cameroon: $1,366/HIA	$1,633/HIA		Cameroon: $1,540·00
			Cote d'Ivoire: $1,391/HIA	$1,663/HIA		Cote d'Ivoire: $1,790·00
			Malawi: $965/HIA	$1,154/HIA		Malawi: $349·13
			Rwanda: $1,085/HIA	$1,297/HIA		Rwanda: $800·21
			Tanzania: $1,068/HIA	$1,277/HIA		Tanzania: $1,090·00
			Zambia: $829/HIA	$991/HIA		Zambia: $1,145·00
Orlando et al. (2010) [49]	PMTCT program with VCT, HAART, treatment of malnutrition, TB, malaria, STDs (private perspective)	370 HIA 10,449 DALYs averted	$998/HIA $35·36/DALY averted	$1,193/HIA $42·30/DALY averted	3%	Malawi: $349·13
	PMTCT program with VCT, HAART, treatment of malnutrition, TB, malaria, STDs (public perspective)	370 HIA 10,449 DALYs averted	$-261/HIA $-16·55/DALY averted	$-312/HIA $-19·80/DALY averted		
Robberstad et al. (2010) [50]	Single-dose NVP[l]	0·00051 HIA (per pregnancy) 0·0129 DALYs averted	$26,826/HIA $1,071/DALY averted	$20,749/HIA $1,227/DALY averted	NR	Tanzania: $1,090·00
	PMTCT Plus[c]	0·00267 HIA (per pregnancy) 0·067 DALYs averted	$7,204/HIA $287/DALY averted	$8,257/HIA $328/DALY averted		
Shah et al. (2011) [51]	Current PMTCT Coverage (10% of all HIV-infected women)	1400 HIA	$3,620/HIA	$4,149/HIA	3%	Nigeria: $2,050·00
	Current ANC Coverage (58% of HIV-infected women)	7680 HIA	$3,203/HIA	$3,671/HIA		
	Full PMTCT Coverage (100% of HIV-infected women)	14400 HIA	$3,167/HIA	$3,630/HIA		
Kuznik et al. (2012) [52]	18 months ART vs. sdNVP[l]	5·21 DALYs averted	$46/DALY averted	$51/DALY averted	3%	Uganda: $717·50
	18 months ART vs. DT[l]	3·22 DALYs averted	$99/DALY averted	$110/DALY averted		
	18 months ART vs. no treatment	8·58 DALYs averted	$34/DALY averted	$37/DALY averted		
	Lifetime ART vs. sdNVP	19·2 DALYs averted	$205/DALY averted	$228/DALY averted		
	Lifetime ART vs. DT	11·87 DALYs averted	$354/DALY averted	$394/DALY averted		
	Lifetime ART vs. no treatment	31·6 DALYs averted	$172/DALY averted	$191/DALY averted		
Binagwaho et al. (2013) [53]	Dual ARV + breastfeeding	NR	Dominated	--	3%	Rwanda: $800·21
	Dual ARV + replacement feeding	NR	Dominated	--		
	Sc-HAART + 6 mo. breastfeeding	NR	Dominated	--		
	Sc-HAART + 12 mo. breastfeeding	9,837 HIV uninfected children still alive	--	--		
	Sc-HAART + 18 mo. breastfeeding	9,292 HIV uninfected children still alive	ICER = $11,882/HIA (compared to 12 mo.)	$12,882/HIA		
	Sc-HAART + replacement feeding	NR	Dominated	--		
Fasawe et al. (2013) [54]	Current Practice	4,503 HIA	$816/HIA $37/QALY gained	$935/HIA $42/QALY gained	3%	Malawi: $349·13
	Option A	15,606 HIA	$844/HIA $37/QALY gained	$967/HIA $42/QALY gained		
	Option B	15,997 HIA	$1,331/HIA $60/QALY gained	$1,525/HIA $68/QALY gained		
	Option B+	15,997 HIA	$1,265/HIA $57/QALY gained	$1,450/HIA $65/QALY gained		
Maredza et al.	Increase coverage of extended	220 DALYs averted	Dominant	Dominant	3%	South Africa: $6,560·00

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Table 2 (*continued*)

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
(2013) [55]	NVP to infants (rural)					
	Promote formula feeding (rural)	420 DALYs averted	$1,300/DALY averted	$1,490/DALY averted		
		Promote breastfeeding (rural)	160 DALYs averted	Dominant		
		--				
		Increase coverage of extended NVP to infants (urban)	90 DALYs averted	Dominant		
		--				
Promote formula feeding (urban)		160 DALYs averted	Dominant	--		
Promote breastfeeding (urban)	-240 DALYs averted[d]	$3,200/DALY averted	$3,667/DALY averted			
Gopalappa et al. (2014) [56]	Option B+ vs. Option A	NR[e]	Kenya: $6,015/ HIA South Africa: $22,987/HIA Zambia: $6,778/HIA	Kenya: $6,763/HIA South Africa: $25,590/HIA Zambia: $7,545/HIA	3%	Kenya: $1,870·00 South Africa: $6,560·00 Zambia: $1,145·00
Ishikawa et al. (2014) [57]	Option B	7,176 HIA	$1,023/HIA	$1,094/HIA	3%	Zambia: $1,145·00
	Option B+	7,318 HIA	$1,254/HIA	$1,341/HIA		
Yu et al. (2014) [58]	Remedy cohort[f]	110 infant HIA	Extended dominated[g]	--	3%	South Africa: $6,560·00
	Remedy cohort, breastfeed	421 infant HIA	Extended dominated	--		
	Remedy cohort, replacement feed	11 infant HIA	Extended dominated	--		
	Promptly treated cohort[h]	698 infant HIA	Undominated[i]	--		
	Promptly treated cohort, breastfeed	360 infant HIA	Extended dominated	--		
	Promptly treated cohort, replacement feed	883 infant HIA	Undominated	--		
Zulliger et al. (2014) [59]	Rapid initiation of ART in Pregnancy pilot program	16.88 QALYs saved	$1,160/QALY gained	$1,291/QALY gained	3%	South Africa: $6,560·00
Price et al. (2016) [60]	Oral PrEP at first ANC visit with HIV- test and end with breastfeeding cessation	381 HIA	$965/DALY averted	$1,025/DALY averted	3%	Zambia: $1,145·00
Tweya et al. (2016) [61]	Option B+ vs. Option B	133 DALYs averted	$841/DALY averted	$875/DALY averted	3%	Malawi: $349·13
Other biomedical						
Verguet et al. (2010) [62]	Access to condoms and microbicide effective at 55%	1,908 HIA	$-6,712/HIA	$-8,356/HIA	NR	South Africa: $6,560·00
Williams et al. (2011) [63]	Tenofovir 25% Coverage	250,000 HIA (20,000 – 380,000)	$2,392/HIA ($562-$4,222)	$2,662/HIA ($625-$4,700)	3%	South Africa: $6,560·00
	Tenofovir 90% Coverage	1,100,000 HIA (60,000 – 2,040,000)	$1,701/HIA ($420-$2,982)	$1,893/HIA ($467-$3,319)		
Long et al. (2013) [64]	Scale-up of VMMC to 75% of all men	12·1% HIA	Cost-saving	--	NR	South Africa: $6,560·00
	Tenofovir gel used by 50% of women	14·1% HIA	$526/QALY gained	$602/QALY gained		
	Use of PrEP by 50% of all uninfected persons	28·4% HIA	$9,009/QALY gained	$10,326/QALY gained		
	VMMC, microbicide, and PrEP	43·5% HIA	$5,739/QALY gained	$6,578/QALY gained		
Mbah et al. (2013) [65]	Praziquantel treatment received during childhood	21,120 HIA	$259/HIA	$314/HIA	3%	Zimbabwe: $1,270·00
	Praziquantel treatment received during childhood and FGS[l] prevalence is reduced relative to those who did not receive treatment	41,500 HIA	$132/HIA	$174/HIA		
Terris-Prestholt et al. (2014) [66]	72% microbicide gel use consistency and 54% HIV efficacy	55,366 HIA	$297/DALY averted	$392/DALY averted	3%	South Africa: $6,560·00
Mvundura et al. (2015) [67]	Distribution of 100,000 female condoms	273 HIA	Lower Bound: Cost Savings[j] Higher Bound: $154/DALY averted[k]	-- Higher Bound: $168/DALY averted	NR	SSA: $1,620·00
Moodley et al. (2016) [68]	HIV vaccine intervention for school-based adolescents	4·36 QALYs gained in lifetime	$43/QALY gained	$47/QALY gained	3%	South Africa: $6,560·00
Moodley et al. (2016) [69]	60% coverage at $12 per vaccine dose	NR	$4·98/LYG (95%: $2·77–$11·61)	$5·45/LYG (95%: $3·03–$12·70)	3%	South Africa: $6,560·00
Wall et al. (2018) [70]	Nationwide CVCT	166,153 HIA	$394/HIA	$394/HIA	0%	Zambia: $1,145·00
	TasP for serodiscordant couples identified by CVCT	9,656 HIA	$7,930/HIA	$7,930/HIA		
	Population TasP for all HIV+ cohabitating men and women identified by individual HTC	17,872 HIA	$12,891/HIA	$12,891/HIA		

Table 2 (*continued*)

Reference	Scenario	Outcome measure	Cost-effectiveness measure reported in publication (US$)	Cost-effectiveness measure (US$ 2018)	Discount rate	Country GDP per capita (current US$), 2018[a] [76]
Behaviour change						
Enns et al. (2011) [71]	Increased monogamy	77 (8·7%) HIA	NR	--	3%	Eswatini: $4,090·00
	High-risk partnership reduction	115 (11·7%) HIA	NR	--		Tanzania: $1,090·00
	Untargeted partnership reduction	76 (8·9%) HIA	NR	--		Uganda: $717·50
						Zambia: $1,145·00
Structural						
Fieno et al. (2014) [72]	Cash transfer at $5 monthly benefit	3,400 HIA	$1,650/HIA	$1,919/HIA	NR	South Africa: $6,560·00
	Cash transfer at $10 monthly benefit	4,250 HIA	$2,640/HIA	$3,071/HIA		
	Cash transfer at $20 monthly benefit	5,100 HIA	$4,400/HIA	$5,118/HIA		
Remme et al. (2014) [73]	Long-term benefits of 18-month cash transfer trial	93,600 HIV DALYs averted	$297/HIV DALY averted	$345/HIV DALY averted	NR	Malawi: $349·13
Rutstein et al. (2014) [74]	Passive Referral	Ref.	Ref.	--	NR	Malawi: $349·13
	Provider Notification	27·5 HIA	ICER = $3,560/HIA	$4,080/HIA		
	Contract Notification	0·4 HIA	ICER = $51,421/HIA	$58,941/HIA		

[a] Country GDP estimates retrieved from International Monetary Fund, World Economic Outlook.
[b] ART coverage means HIV treatment for people with CD4 <350 cells/μL and TasP coverage means HIV treatment for people with CD4 ≥ 350 cells/μL.
[c] PMTCT Plus refers to a HAART intervention for all HIV infected women during pregnancy and lactation, regardless of CD4 count, according to 2009 WHO guidelines.
[d] Negative value indicates an intervention was less effective than base case.
[e] Not reported for infant only infections averted.
[f] Women in remedy cohort received HIV testing and standard treatment only after delivery.
[g] Extended dominated excludes any intervention that has a higher ICER than more effective interventions.
[h] Women in the promptly treated cohort received HIV testing and treatment at some point during pregnancy.
[i] Undominated refers to strategies that are more cost-effective.
[j] The intervention was cost-saving in the following countries: Botswana, South Africa, Eswatini, Zambia, Zimbabwe.
[k] Cost($)/DALY averted for other included countries: Cameroon (43), Kenya (110), Lesotho (9), Malawi (114), Mozambique (154), Namibia (9), Tanzania (73), Uganda (25).
[l] Abbreviations: DT = dual therapy (zidovudine and lamivudine); ANC = antenatal care clinic; ARV = antiretrovirals; ART = antiretroviral therapy; CI = confidence intervals; DALY = disability-adjusted life year; EIMC = early infant male circumcision; FGS = female genital schistosomiasis; FSW = female sex worker; HAART = highly-active antiretroviral therapy; HIA = HIV infections averted; LYG = life years gained; NVP = nevirapine; PMTCT = prevention of mother-to-child transmission; PrEP = pre-exposure prophylaxis; QALY = quality-adjusted life year; Sc-HAART = short-course highly-active antiretroviral therapy; sdNVP = single dose nevirapine; SSA = sub-Saharan Africa; STD = sexually transmitted disease; TB = tuberculosis; UNGASS = UN General Assembly Special Session on AIDS; VCT = voluntary counselling and testing; VMMC = voluntary medical male circumcision; yo = years old.
[m] Abbreviations: NR = not reported; in certain instances, studies may have 1) reported cost-effectiveness measure without stating an effectiveness measure or 2) presented visualized cost-effectiveness results without stating the numeric value of the cost-effectiveness measure. These instances would lead to an 'NR'.

review. For newer prevention strategies, such as PrEP and TasP, many of the studies relied on various assumptions and scenarios that may not reflect reality.

The review found that PMTCT and VMMC interventions were the most cost-effective. Studies on PMTCT interventions, including HAART, infant feeding methods, expedited ART, and Option B+ suggest that these strategies are very cost-effective [47,49,50,54,56,57,59]. These studies provide evidence supporting WHO guidelines of transitioning from Option A and of recommending PMTCT Option B and Option B+. When WHO began the policy transition from Option B to Option B+ in 2013, the agency conducted a preliminary cost analysis to estimate the incremental cost of switching to the new policy [75]. The authors argued that researchers should develop additional cost-effectiveness models to appropriately evaluate the cost of the policy with programmatic data. A number of studies have since provided evidence supporting the policy decisions around Option B+ [56,57]. However, stakeholders should be mindful that implementation of strategies like Option B+ raises concerns since many of these studies do not take into account initial costs and upfront investment required to scale up PMTCT programs to a level that can be considered cost-effective over an extended time period [61,75]. Additionally, while the majority of PMTCT studies included in this review focused on Prong III, only one study addressed PMTCT Prong II by studying the expansion of family planning services as a cost-effective method to avert HIV infections through the prevention of unintended pregnancies [47]. This focus may reflect recent programmatic shifts towards PMTCT Prong III and treatment of HIV infected women, even though family planning is effective in reducing MTCT.

The VMMC studies included in this review agreed that the intervention was cost-effective. Seven different studies developed models that estimated cost effectiveness of VMMC at 80% coverage, which is a common target for many HIV prevention programs; however, achieving this level of coverage is often not feasible in many settings [16,19,23–27]. Additional studies exploring cost effectiveness at various levels of VMMC coverage may help inform decision makers in areas where 80% coverage would be difficult to attain. Multiple studies explored scenarios targeting VMMC at different age groups, with a consensus that prioritizing younger males is more favourable and cost-saving compared to targeting the general male adult population [15,22,24].

Similarly, a common conclusion was that PrEP strategies targeting specific risk groups were more cost-effective than general PrEP strategies [29,32,34,35,39]. Four studies found that PrEP was most cost-effective when using a prioritization strategy aimed at young individuals who are most at-risk, including having more than four partners and reporting low condom use [32,34,39,41]. The majority of included PrEP studies were set in South Africa, a country that could perhaps better absorb the higher costs of PrEP implementation compared with others in the region. However, three studies in Zambia and Mozambique agreed that prioritizing high-risk individuals would create the most effective scenario for PrEP implementation, adding to the evidence that a targeted PrEP strategy could be feasible across country settings [32,35,36].

The assumption of 100% PrEP coverage considered in many studies may be difficult to implement [11,14]. This scenario implies that every eligible individual would receive PrEP, which may not be realistic in settings where universal treatment has not even been realized. Many

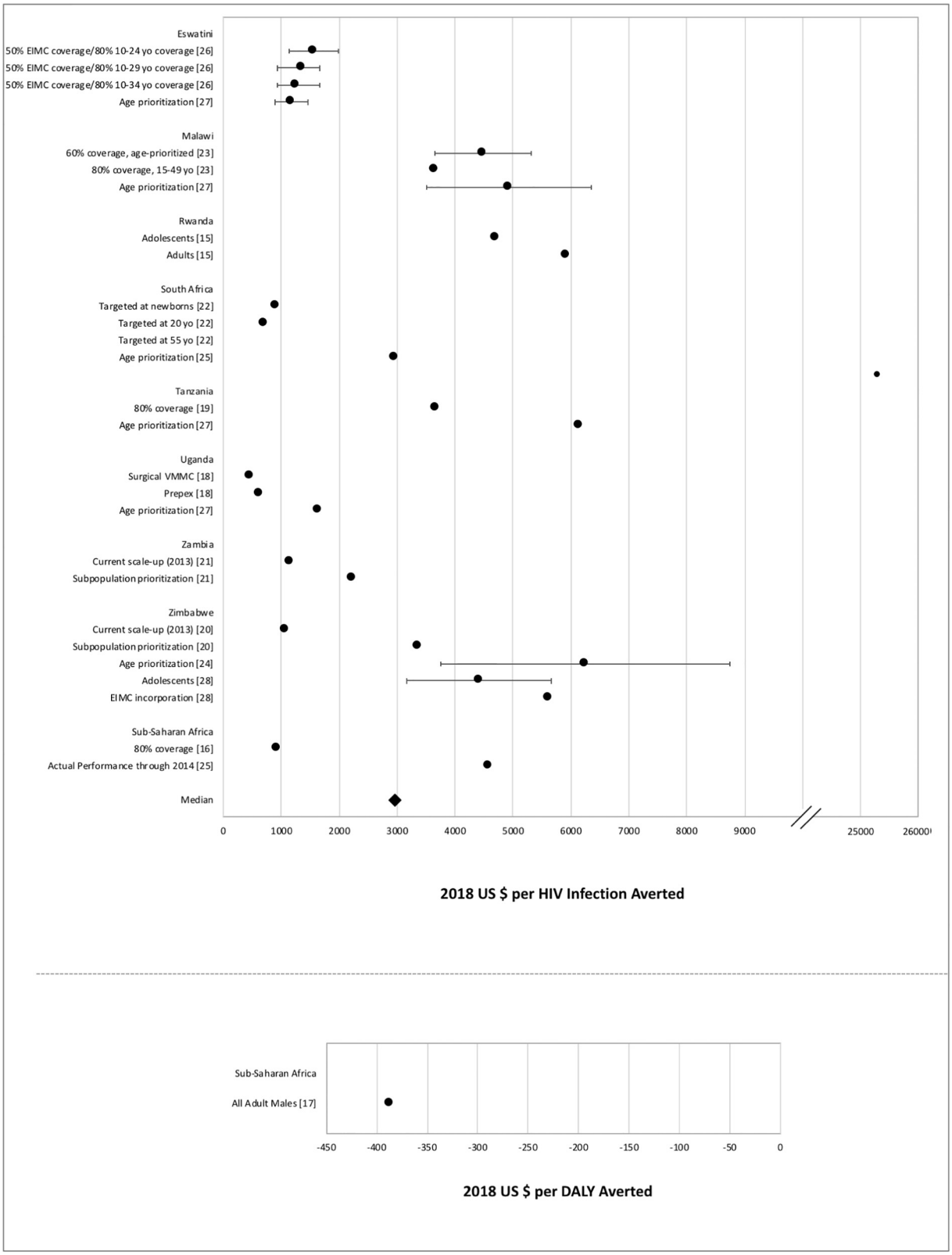


Fig. 2. Cost-effectiveness measures of VMMC interventions. Data points reflect the measures from VMMC studies reporting cost per HIV infection averted (above) and cost per DALY averted (below). Points represent study-specific cost-effectiveness estimates; error bars represent estimate ranges, if provided in study results.

studies point out that achieving such a high level of PrEP coverage would be less cost-effective than simply increasing ART coverage. Accordingly, WHO issued recommendations in 2015 to provide PrEP as a prevention option to individuals at substantial risk of acquiring HIV in settings with high HIV incidence [76]. Although studies have shown that PrEP can be cost-effective when targeted towards high-risk groups and when assuming high adherence, it remains a challenging intervention due to high costs, ethical issues, and inequitable distribution [8].

The five studies included in this review were not in agreement with regard to the cost-effectiveness or the feasibility of TasP strategy; one

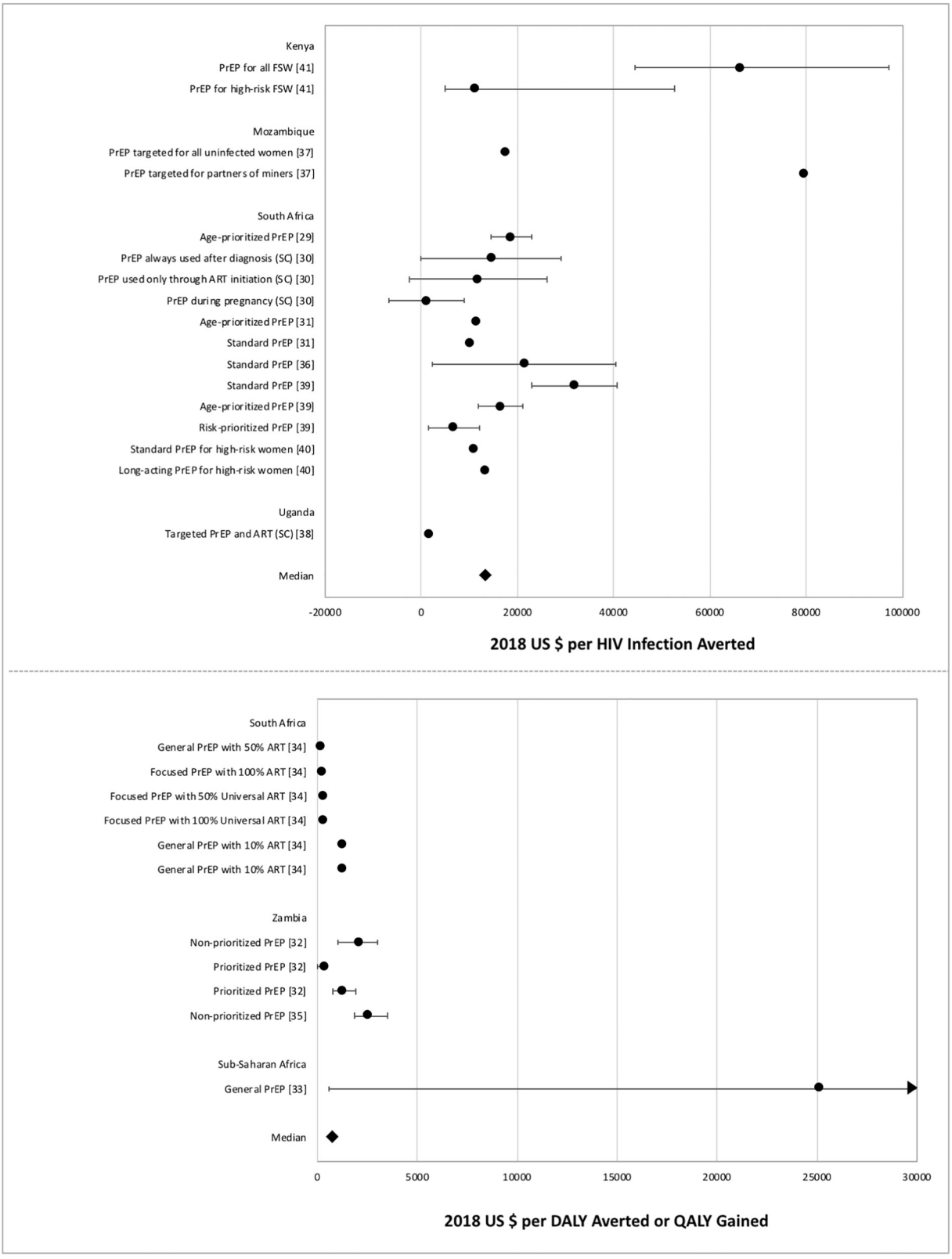


Fig. 3. Cost-effectiveness measures of PrEP interventions. Data points reflect the measures from PrEP studies reporting cost per HIV infection averted (above) and cost per DALY averted or QALY gained (below). Points represent study-specific cost-effectiveness estimates; error bars represent estimate ranges, if provided in study results.

study concluded that TasP was less cost-effective than a combination of VMMC and ART, which is already the standard practice in many sub-Saharan African settings [42]. From this review, it is unclear whether or not TasP would be more cost-effective in certain settings over others. Despite this uncertainty, many countries have already developed and implemented guidelines for TasP and universal test-and-treat (UTT)

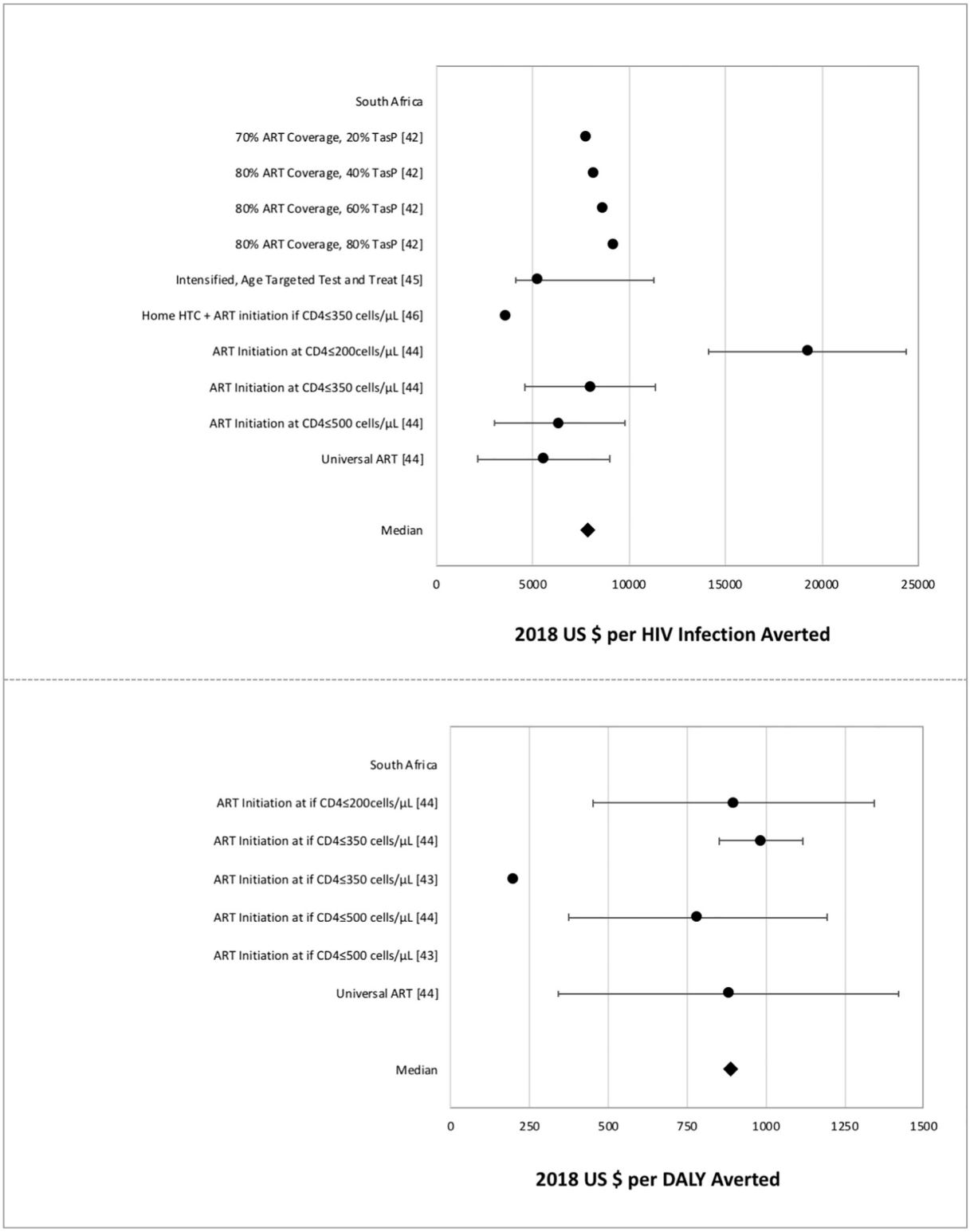
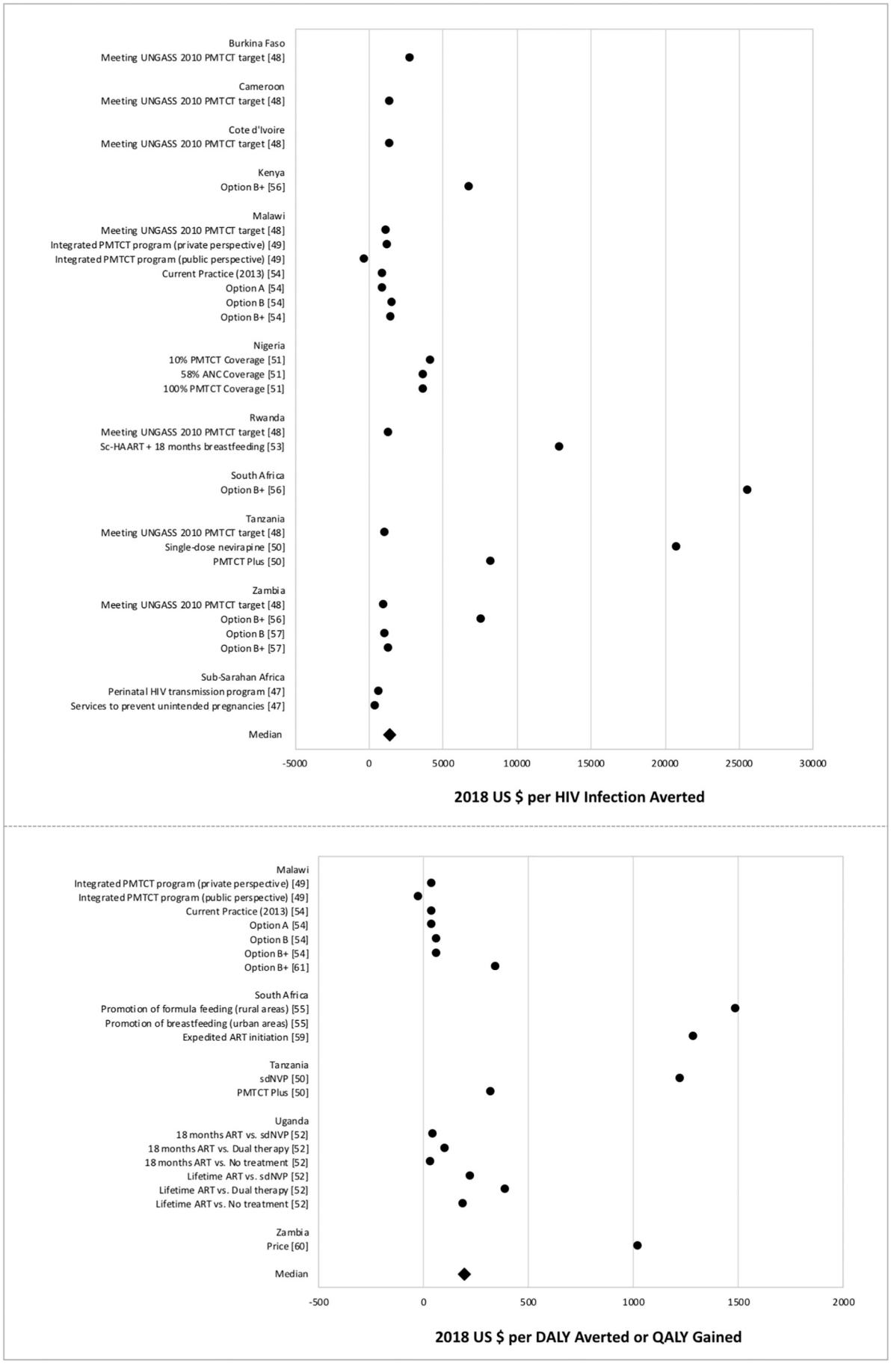


Fig. 4. Cost-effectiveness measures of TasP interventions. Data points reflect the measures from TasP studies reporting cost per HIV infection averted (above) and cost per DALY averted (below). Points represent study-specific cost-effectiveness estimates; error bars represent estimate ranges, if provided in study results.

[77]. Healthcare investment to provide UTT services successfully is substantial, especially in extensive resource-constrained settings [78].

This review also included studies that explored cost-effectiveness of methods that are still in development and not currently available on the market, including long-acting PrEP injections, HIV vaccines, and microbicide gels. The findings from these studies suggest that these interventions would be cost-effective once accessible [62–64,66,68,69]. Only one study included in this review considered the reduction of HIV incidence by estimating the intervention effect of schistosomiasis treatment. Mbah et al. showed that mass praziquantel administration


Burkina Faso
Meeting UNGASS 2010 PMTCT target [48]
Cameroon
Meeting UNGASS 2010 PMTCT target [48]
Cote d'Ivoire
Meeting UNGASS 2010 PMTCT target [48]
Kenya
Option B+ [56]
Malawi
Meeting UNGASS 2010 PMTCT target [48]
Integrated PMTCT program (private perspective) [49]
Integrated PMTCT program (public perspective) [49]
Current Practice (2013) [54]
Option A [54]
Option B [54]
Option B+ [54]
Nigeria
10% PMTCT Coverage [51]
58% ANC Coverage [51]
100% PMTCT Coverage [51]
Rwanda
Meeting UNGASS 2010 PMTCT target [48]
Sc-HAART + 18 months breastfeeding [53]
South Africa
Option B+ [56]
Tanzania
Meeting UNGASS 2010 PMTCT target [48]
Single-dose nevirapine [50]
PMTCT Plus [50]
Zambia
Meeting UNGASS 2010 PMTCT target [48]
Option B+ [56]
Option B [57]
Option B+ [57]
Sub-Sarahan Africa
Perinatal HIV transmission program [47]
Services to prevent unintended pregnancies [47]
Median
-5000
0
5000
10000
15000
20000
25000
30000
2018 US $ per HIV Infection Averted
Malawi
Integrated PMTCT program (private perspective) [49]
Integrated PMTCT program (public perspective) [49]
Current Practice (2013) [54]
Option A [54]
Option B [54]
Option B+ [54]
Option B+ [61]
South Africa
Promotion of formula feeding (rural areas) [55]
Promotion of breastfeeding (urban areas) [55]
Expedited ART initiation [59]
Tanzania
sdNVP [50]
PMTCT Plus [50]
Uganda
18 months ART vs. sdNVP [52]
18 months ART vs. Dual therapy [52]
18 months ART vs. No treatment [52]
Lifetime ART vs. sdNVP [52]
Lifetime ART vs. Dual therapy [52]
Lifetime ART vs. No treatment [52]
Zambia
Price [60]
Median
-500
0
500
1000
1500
2000
2018 US $ per DALY Averted or QALY Gained

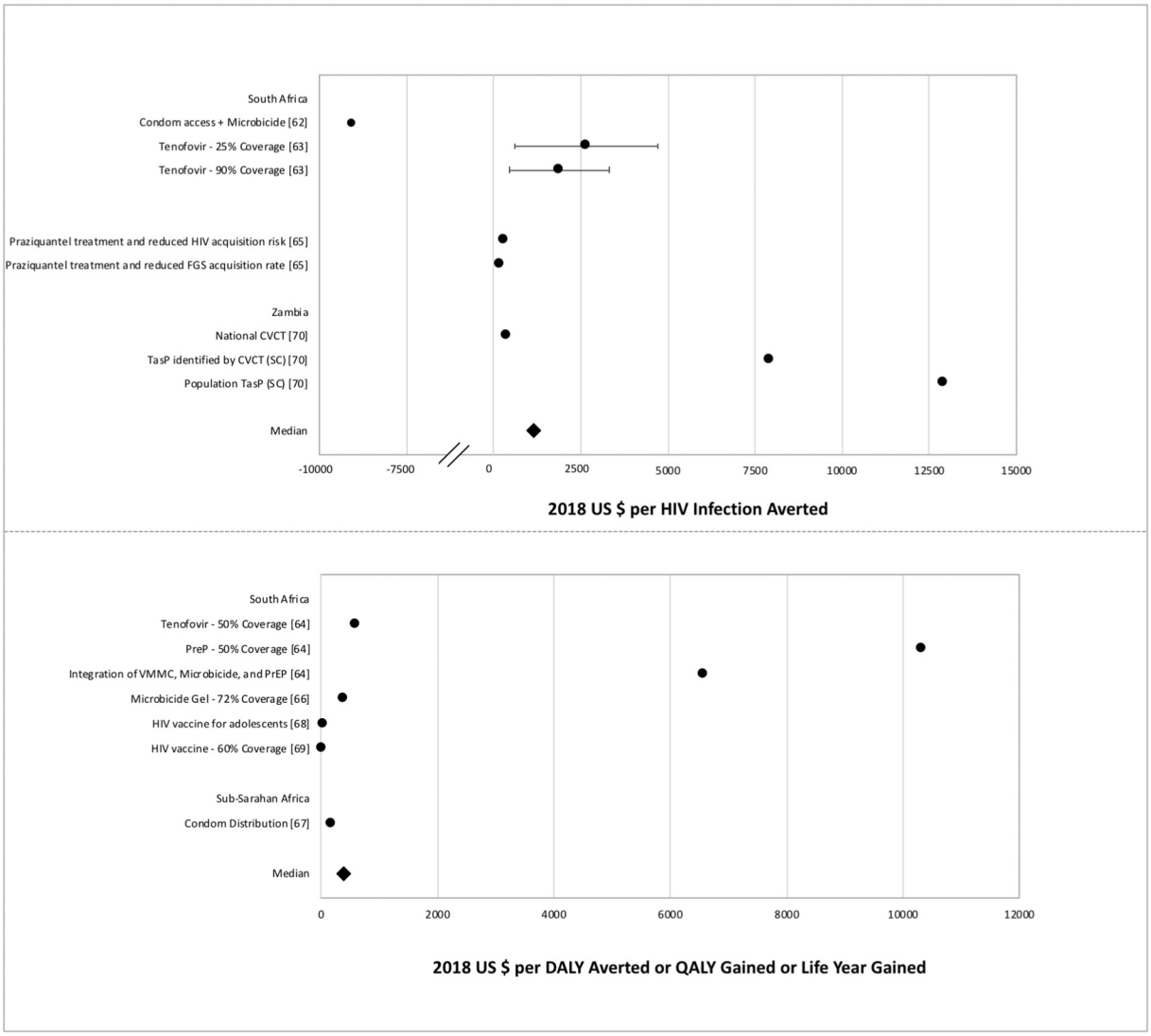


Fig. 6. Cost-effectiveness measures of biomedical interventions. Data points reflect the measures from miscellaneous biomedical studies reporting cost per HIV infection averted (above) and cost per DALY averted or QALY gained (below). Points represent study-specific cost-effectiveness estimates; error bars represent estimate ranges, if provided in study results.

would be a cost-effective approach to reduce HIV transmission. In addition to its affordability, praziquantel treatment is very safe, well tolerated, and easily administered, but it has not been explicitly considered as a HIV prevention intervention, as the link between HIV acquisition and schistosomiasis remains unclear [65].

The vast majority of the included studies determined cost-effectiveness based on the WHO-CHOICE guidance that considers interventions to cost-effective if the cost per DALY averted is between one and three times the study country's GDP per capita [79]. This threshold is becoming increasingly contested, as many experts believe that it does not consider governments' ability to generate the appropriate resources or willingness to pay [80,81]. Some studies have translated HIA to DALYs; we did not find a standard conversion that would be applicable to the various country settings [17]. Moreover, the usefulness of this type of threshold is especially important when discussing high cost interventions, such as PrEP and TasP. Although these prevention strategies may be considered cost-effective under certain assumptions, this may not always translate into feasible implementation. The GDP-based threshold is unrelated to national and donor HIV budgets, both of which are needed to understand an intervention's affordability. Thus, more information is need on whether many SSA countries would be able to implement a large-scale PrEP program, although its use as a main prevention strategy has been heavily emphasized in policy discussion [8]. Many countries are already struggling to provide universal ART, and adding a high-cost strategy may apply further pressure on resource limited prevention programs.

In the 2009 review, Galarraga et al. concluded that not enough information regarding cost-effectiveness of many prevention strategies existed for decision-making or policy change [9]. Their review included many cost-effectiveness studies on interventions for behaviour change, intravenous drug use (IDU) harm reduction, and information, education, and communication. The present review found only two studies

Fig. 5. Cost-effectiveness measures of PMTCT interventions. Data points reflect the measures from PMTCT studies reporting cost per HIV infection averted (above) and cost per DALY averted or QALY gained (below). Points represent study-specific cost-effectiveness estimates.

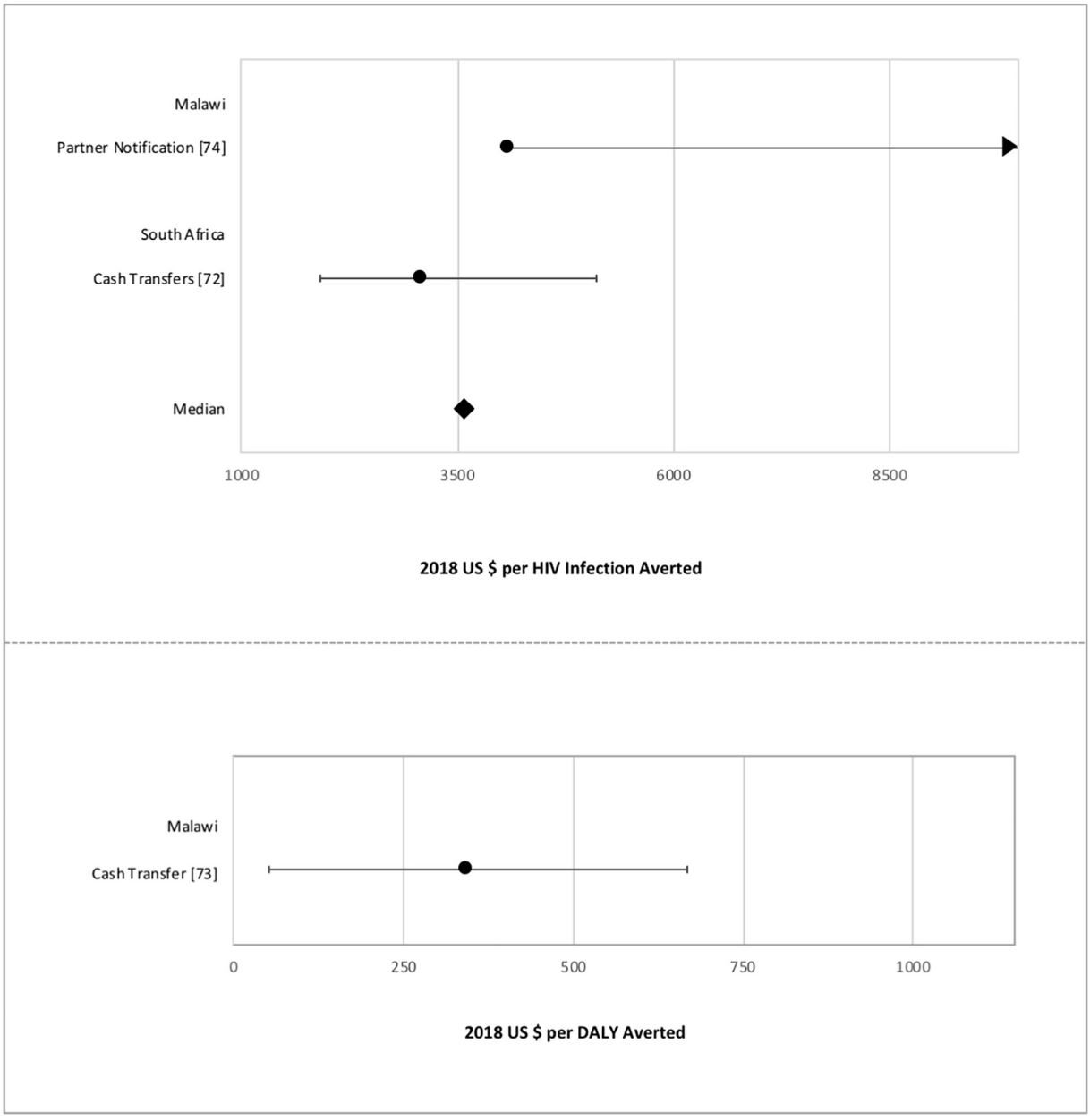


Fig. 7. Cost-effectiveness measures of structural interventions. Data points reflect the measures from structural intervention studies reporting cost per HIV infection averted (above) and cost per DALY averted (below). Points represent study-specific cost-effectiveness estimates; error bars represent estimate ranges, if provided in study results.

on behaviour change and structural interventions, with most recently published studies focusing on biomedical interventions. This shift represents a reflection of changing priorities of the international donor community and emerging technology available from pharmaceutical companies. The authors mentioned the lack of cost-effectiveness studies on vulnerable groups, such as men who have sex with men (MSM) and female sex workers (FSW). Similarly, the current review found only one study focusing on FSWs, although there are published studies on these populations in settings outside of Africa [66,82]. The continuing dearth of studies on these vulnerable populations in sub-Saharan Africa ought to be addressed by future research, as costing studies can inform policymaking.

Several limitations were recognized while conducting this review. First, behavioral and structural interventions, like partner concurrency reduction and condom use, have historically been included in HIV prevention programs [71]. Although the studies in this paper suggest that these strategies are cost-effective, most analyses do not separate the effect of behaviour change on HIV incidence from other interventions, thus not allowing us to understand the effectiveness of these interventions in isolation [67,71]. Second, comparability across studies was difficult since parameters, settings, and assumptions vary. Unless studies present cost-effectiveness estimates using the same assumptions, base year, time horizon, and discount rate, we should take caution when comparing study estimates.

Third, many of the cost-effectiveness studies offer evidence for a specific intervention in a number of scenarios, but few address the potential effects of an intervention in scenarios outside the scope of the study. This makes it difficult to generalize a study's results to other country settings, creating an obstacle for policy makers in determining how and when a single intervention is the most cost-effective for a specific country. The limited geographic coverage among the studies additionally does not allow for broad generalizability. South Africa was the setting in 24 of the 60 studies (40%) and just three countries (South Africa, Zambia, and, Malawi) comprise over 60% of the studies.

Table 3
CHEERS quality assessment, by intervention type.

	1	2	3	4	5	6	7	8	9	10	11a	11b	12	13a	13b	14	15	16	17	18	19	20a	20b	21	22	23	24
Binagwaho et al. (2010) [15]	Y*	Y	Y	Y	Y	Y	Y	Y	Y	N*	Y	N/A*	N/A	N/A	Y	N	P*	Y	N	Y	Y	N/A	Y	N/A	Y	N	Y
Njeuhmeli et al. (2011) [16]	N	Y	Y	Y	Y	Y	N	Y	Y	Y	N/A	Y	N/A	N/A	Y	N	Y	Y	N	Y	Y	N/A	Y	N/A	Y	Y	Y
Uthman et al. (2011) [17]	Y	Y	Y	Y	Y	Y	Y	Y	P	Y	N/A	N	N/A	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	N	N
Duffy et al. (2013) [18]	Y	Y	Y	Y	Y	Y	N	Y	Y	N	P	N/A	N/A	Y	N/A	Y	N	Y	P	P	Y	N/A	N/A	N/A	Y	N	Y
Menon et al. (2014) [19]	N	Y	Y	Y	Y	N	N	P	Y	P	N	N/A	N/A	Y	N/A	Y	Y	Y	N	Y	Y	N	N/A	N/A	Y	Y	Y
Awad et al. (2015) [20]	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N/A	Y	N/A	N/A	Y	N	Y	Y	Y	N	Y	N/A	Y	N/A	Y	Y	Y
Awad et al. (2015) [21]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	N/A	Y	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Haacker et al. (2016) [22]	Y	Y	Y	Y	Y	N	Y	N	Y	P	N/A	Y	N/A	Y	Y	Y	Y	Y	Y	N	Y	N/A	Y	N/A	Y	Y	Y
Kripke et al. (2016) [23]	P	P	Y	Y	Y	P	Y	Y	P	N	N/A	N	P	N/A	Y	N	Y	P	N	N	Y	N/A	P	Y	Y	Y	Y
Kripke et al. (2016) [24]	Y	P	Y	Y	Y	N	Y	Y	P	Y	N/A	Y	N/A	N/A	Y	P	P	P	P	P	P	N/A	Y	N/A	Y	Y	Y
Kripke et al. (2016) [25]	N	P	Y	P	P	N	N	P	P	P	N/A	N	N/A	N/A	Y	P	Y	P	P	N	Y	N/A	Y	Y	Y	Y	Y
Kripke et al. (2016) [26]	N	P	Y	Y	Y	N	P	Y	P	Y	N/A	N	N/A	N/A	Y	P	Y	Y	N	N	P	N/A	Y	Y	Y	Y	Y
Kripke et al. (2016) [27]	N	P	P	Y	Y	N	N	Y	P	Y	N/A	P	N/A	N/A	Y	Y	P	P	Y	N	Y	N/A	Y	Y	Y	Y	Y
Njeuhmeli et al. (2016) [28]	P	P	Y	P	Y	N	Y	Y	P	Y	N/A	P	N/A	N/A	Y	P	Y	P	P	N	Y	N/A	P	N/A	Y	Y	Y
PrEP																											
Pretorius et al. (2010) [29]	Y	Y	Y	Y	Y	N	Y	P	N	P	Y	N/A	N	N/A	P	N	Y	Y	Y	Y	P	N/A	Y	N/A	Y	Y	Y
Hallett et al. (2011) [30]	N	Y	Y	Y	P	N	Y	N	P	Y	N/A	Y	N	N/A	P	N	Y	Y	Y	Y	Y	N/A	P	N/A	Y	Y	Y
Cremin et al. (2013) [31]	N	P	Y	Y	Y	Y	Y	Y	P	P	N/A	Y	N/A	N/A	Y	Y	Y	Y	Y	Y	P	N/A	Y	N/A	Y	Y	Y
Nichols et al. (2013) [32]	Y	Y	Y	Y	Y	P	Y	P	P	P	N/A	P	N	N/A	P	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Verguet et al. (2013) [33]	N	Y	Y	P	Y	N	Y	Y	N	P	N/A	Y	Y	N/A	P	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	N	Y
Alistar et al. (2014) [34]	Y	Y	Y	P	Y	N	Y	Y	P	P	N/A	Y	N	N/A	Y	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Nichols et al. (2014) [35]	Y	Y	Y	Y	Y	N	Y	Y	P	P	N/A	Y	N	N/A	P	N	P	Y	Y	P	Y	N/A	P	N/A	Y	Y	Y
Cremin et al. (2015a) [36]	N	N	Y	Y	Y	Y	Y	Y	P	P	Y	N/A	N/A	N/A	Y	N	Y	Y	P	P	Y	N/A	N	N/A	P	Y	Y
Cremin et al. (2015b) [37]	Y	Y	Y	Y	Y	Y	Y	Y	P	P	N/A	Y	N/A	N/A	P	N	Y	Y	N	Y	Y	N/A	N	N/A	P	Y	Y
Ying et al. (2015) [38]	Y	Y	Y	Y	Y	Y	Y	Y	P	P	Y	N/A	N	N/A	Y	Y	Y	N	P	N	P	N/A	N	N/A	Y	Y	Y
Glaubius et al. (2016) [39]	Y	Y	Y	Y	Y	Y	Y	Y	P	P	N/A	Y	N/A	N/A	Y	Y	P	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Walensky et al. (2016) [40]	Y	Y	Y	Y	Y	Y	Y	Y	P	P	N/A	P	N/A	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Cremin et al. (2017) [41]	N	Y	Y	Y	Y	Y	Y	Y	P	P	N/A	Y	N/A	N/A	Y	P	Y	Y	Y	P	P	N/A	P	N/A	Y	Y	Y
TasP																											
Barnighausen et al. (2012) [42]	P	P	Y	P	Y	N	Y	Y	Y	P	N/A	Y	N/A	N/A	P	N	Y	Y	Y	N	Y	N/A	Y	N/A	Y	N	Y
Granich et al. (2012) [43]	Y	Y	Y	Y	Y	P	Y	Y	Y	Y	N/A	P	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Smith et al. (2015) [44]	Y	Y	Y	Y	Y	Y	Y	Y	P	Y	N/A	Y	P	Y	N/A	P	Y	Y	Y	P	Y	N/A	Y	N/A	Y	Y	Y
Bershteyn et al. (2016) [45]	N	Y	Y	P	Y	N	P	P	P	N	N/A	N	N	N/A	P	N	Y	Y	Y	N	Y	N/A	Y	Y	Y	Y	Y
Ying et al. (2016) [46]	N	P	Y	Y	Y	Y	Y	P	P	P	Y	N/A	N	Y	N/A	Y	P	Y	Y	N	Y	Y	N/A	N/A	Y	Y	Y
PMTCT																											
Halperin et al. (2009) [47]	N	Y	Y	P	P	Y	P	N	N	Y	N/A	Y	N/A	N/A	Y	N	N	Y	Y	Y	Y	N/A	N	N/A	Y	Y	Y
Nakakeeto et al. (2009) [48]	P	P	P	P	P	Y	Y	P	P	Y	N/A	Y	N/A	N/A	Y	Y	Y	Y	N	Y	P	N/A	P	N/A	Y	Y	N
Orlando et al. (2010) [49]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	N	P	P	P	Y	N	N/A	N/A	Y	P	N
Robberstad et al. (2010) [50]	Y	Y	Y	Y	Y	N	Y	N	P	Y	N	N/A	Y	N/A	N	N	P	Y	P	P	P	Y	N/A	N/A	Y	Y	N
Shah et al. (2011) [51]	Y	P	Y	p	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Kuznik et al. (2012) [52]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	N	Y
Binagwaho et al. (2013) [53]	Y	P	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	N/A	Y	P	N	Y	Y	Y	P	N/A	Y	Y	Y	N	N
Fasawe et al. (2013) [54]	Y	Y	Y	Y	Y	Y	Y	Y	P	Y	N/A	Y	P	N/A	Y	P	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	P	N
Maredza et al. (2013) [55]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	N/A	Y	Y	P	Y	Y	Y	Y	N/A	Y	N/A	Y	N	N
Gopalappa et al. (2014) [56]	N	Y	Y	Y	P	N	Y	Y	P	P	N/A	Y	N/A	N/A	Y	P	Y	Y	P	Y	Y	N/A	N	N/A	Y	Y	Y
Ishikawa et al. (2014) [57]	P	Y	Y	Y	Y	Y	Y	Y	P	Y	N/A	P	Y	N/A	Y	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Yu et al. (2014) [58]	Y	Y	Y	Y	Y	N	Y	Y	P	Y	N/A	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Zulliger et al. (2014) [59]	Y	Y	P	Y	Y	N	Y	Y	Y	Y	Y	N/A	Y	Y	N/A	Y	N	Y	P	Y	Y	Y	N/A	N/A	Y	Y	Y
Price et al. (2016) [60]	Y	Y	Y	Y	Y	Y	Y	P	P	Y	N/A	Y	Y	N/A	Y	Y	P	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Tweya et al. (2016) [61]	Y	Y	Y	Y	Y	N	Y	P	P	Y	N/A	Y	N	N/A	P	P	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Other biomedical																											
Verguet et al. (2010) [62]	Y	Y	Y	Y	P	N	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	N	Y
Williams et al. (2011) [63]	N	P	Y	N	N	N	P	P	N	Y	Y	N/A	P	N/A	Y	N	Y	Y	Y	N	Y	N/A	N	N/A	Y	Y	Y
Long et al. (2013) [64]	Y	Y	Y	Y	Y	N	P	Y	N	Y	N/A	Y	Y	Y	N	P	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Mbah et al. (2013) [65]	Y	P	Y	Y	Y	Y	Y	P	Y	Y	N/A	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	P	Y	Y
Terris-Prestholt et al. (2014) [66]	Y	Y	Y	Y	Y	Y	Y	Y	P	Y	N/A	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Mvundura et al. (2015) [67]	Y	Y	Y	N	Y	N	Y	Y	N	Y	N/A	P	N/A	N/A	Y	Y	Y	Y	N	P	Y	N/A	N	N/A	Y	P	Y
Moodley et al. (2016) [68]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Moodley et al. (2016) [69]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Wall et al. (2018) [70]	N	P	Y	P	Y	Y	Y	Y	Y	Y	P	N/A	N/A	Y	N/A	N	N	P	Y	P	Y	Y	Y	N/A	Y	Y	Y
Behaviour Change																											
Enns et al. (2011) [71]	Y	Y	Y	Y	Y	Y	Y	Y	P	P	N/A	Y	N/A	N/A	P	N	Y	Y	Y	Y	Y	N/A	Y	N/A	Y	Y	Y
Structural																											
Fieno et al. (2014) [72]	N	N	P	Y	Y	N	P	P	N	Y	Y	N/A	N/A	Y	N/A	N	P	Y	P	Y	Y	N	N/A	N/A	Y	N	Y
Remme et al. (2014) [73]	N	P	Y	Y	Y	Y	Y	P	P	Y	P	N/A	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	Y
Rutstein et al. (2014) [74]	Y	P	Y	Y	Y	Y	Y	P	N	Y	Y	N/A	N/A	Y	N/A	Y	Y	Y	Y	Y	Y	Y	N/A	N/A	Y	Y	N

Abbreviations: Y = item completely fulfilled; P = item partially fulfilled; N = item not fulfilled; N/A = item not applicable to the study
Item Checklist: 1. Title; 2. Abstract; 3. Introduction 4. Target Population; 5. Setting and Location; 6. Study Perspective; 7. Comparators; 8. Time Horizon; 9. Discount Rate; 10. Choice of health outcomes; 11a. Measurement of effectiveness (single study-based estimates); 11b. Measurement of effectiveness (synthesis-based estimates); 12. Measurement of performance based outcomes; 13a. Estimating Resources and Costs (single study-based economic evaluation); 13b. Estimating Resources and Costs (model-based economic evaluation); 14. Currency, Price, Conversion; 15. Model Choice; 16. Assumptions; 17. Analytical Methods; 18. Study Parameters; 19. Incremental Costs and Outcomes; 20a. Characterizing Uncertainty (single study-based economic evaluation); 20b. Characterizing Uncertainty (model-based economic evaluation); 21. Heterogeneity; 22. Study Findings; 23. Funding; 24. Conflicts of Interest

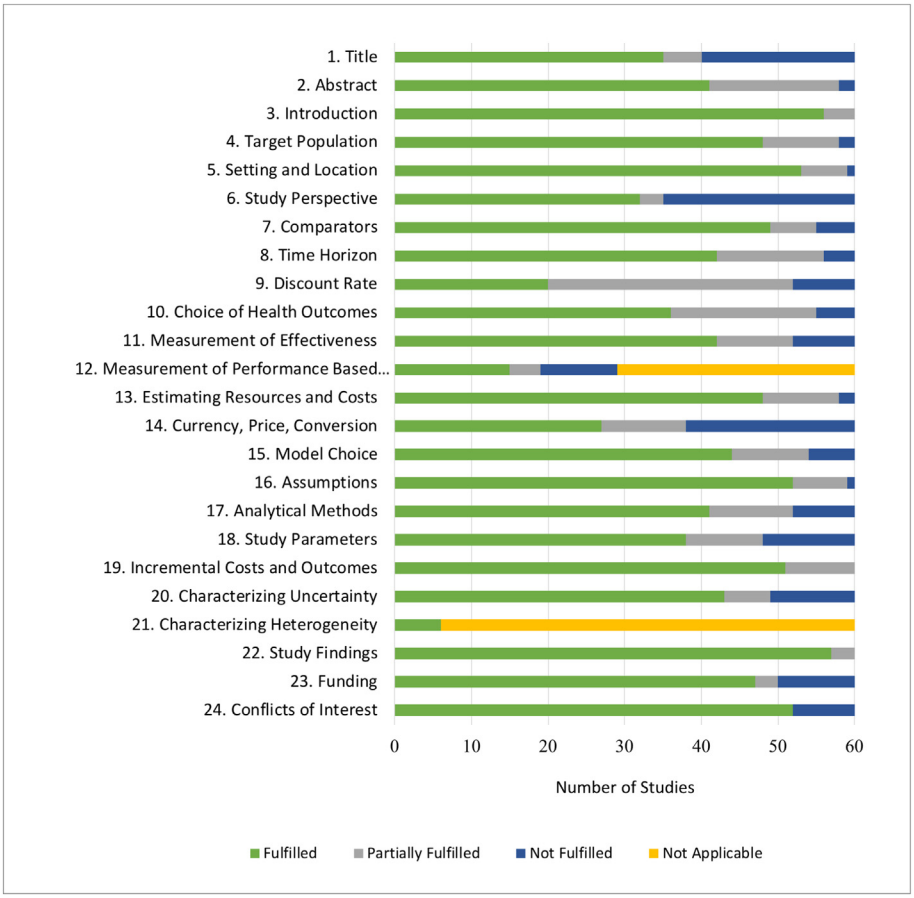


Fig. 8. Visual representation of CHEERS checklist evaluation. Green bars represent the number of studies that completely fulfilled the corresponding item of the CHEERS checklist. Blue bars represent the number of studies that did not fulfill an applicable item. Gray bars represent the number of studies that partially, but did not completely, fulfilled the CHEERS checklist item. Yellow bars represent number of studies for which the item was not applicable.

Lastly, this review is not immune to publication bias. Studies that do not demonstrate interventions as cost-effective are less likely to be submitted to peer-reviewed journals or to be published by journals [83]. It is possible that some cost-effectiveness results of current HIV interventions are not available to key policy makers, which poses a large problem. Despite the aforementioned limitations, this review included studies of good quality, highlighting the strength of the available evidence.

The large number of studies included in this review reflects the increasing importance of considering cost-effectiveness as a factor in implementing HIV prevention interventions in sub-Saharan Africa. The studies demonstrated intervention cost-effectiveness under a variety of scenarios and emphasized interventions targeting high-risk populations. In contrast to the 2009 Galarraga review, which concluded that sufficient cost-effectiveness data did not exist to inform large-scale decision making, the results from emergent, more robust and varied costing studies may serve as an aid to inform evidence-based decisions. Key stakeholders, such as international donors and government agencies, should consider cost-effectiveness results and affordability when developing national guidelines and protocols for HIV prevention to maximize prevention impact under resource constraints. However, important gaps in the research persist: a lack of focus on vulnerable populations remains an important concern in this region, and additional studies that discuss the cost-effectiveness of different combinations of interventions are needed to reflect the reality of HIV programs in this region [84].

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The contents are the responsibility of the authors and do not necessarily reflect the views of sponsors, who had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The corresponding author had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

Contributors

KW conceived the study. SS and SE conducted the literature search. PK, SE, and SC conducted the data extraction. SS wrote the first draft, and KW, PC, SE, SC, and PK reviewed and provided feedback. All authors approved the final paper.

Declaration of Interests

The authors declare that they do not have any competing interests.

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Appendix A. Supplementary Material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.eclinm.2019.04.006.

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