THE HEALTH AND ECONOMIC BENEFITS OF INVESTING IN HIV PREVENTION: A REVIEW OF GLOBAL EVIDENCE TO INFORM POLICY DIALOGUE IN VIETNAM

July 2018
This publication was produced for review by the United States Agency for International Development.
It was prepared by Yoriko Nakamura and Michael Chaitkin for the Health Finance and Governance Project.

The Health Finance and Governance Project
USAID's Health Finance and Governance (HFG) project helps to improve health in developing countries by expanding people's access to health care. Led by Abt Associates, the project team works with partner countries to increase their domestic resources for health, manage those precious resources more effectively, and make wise purchasing decisions. The six-year, $209 million global project is intended to increase the use of both primary and priority health services, including HIV/AIDS, tuberculosis, malaria, and reproductive health services. Designed to fundamentally strengthen health systems, HFG supports countries as they navigate the economic transitions needed to achieve universal health care.

July 2018

Cooperative Agreement No: AID-OAA-A-12-00080

Submitted to: Scott Stewart, AOR
Office of Health Systems
Bureau for Global Health

Recommended Citation: Nakamura, Yoriko and Chaitkin, Michael. 2018. *The health and economic benefits of investing in HIV prevention: a review of global evidence to inform policy dialogue in Vietnam*. Washington, DC: Health Finance & Governance Project, Results for Development Institutle.

Abt Associates Inc. | 6130 Executive Boulevard | Rockville, Maryland 20852
T: 301.347.5000 | F: 301.652.3916 | www.abtassociates.com

Avenir Health | Broad Branch Associates | Development Alternatives Inc. (DAI) |
| Johns Hopkins Bloomberg School of Public Health (JHSPH) | Results for Development Institute (R4D)
| RTI International | Training Resources Group, Inc. (TRG)

THE HEALTH AND ECONOMIC BENEFITS OF INVESTING IN HIV PREVENTION: A REVIEW OF GLOBAL EVIDENCE TO INFORM POLICY DIALOGUE IN VIETNAM

CONTENTS

List of Tables

ACRONYMS

AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal care
ART	Antiretroviral therapy
ARVs	Antiretrovirals
BCR	Benefit-cost ratio
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
DALY	Disability adjusted life year
FSW	Female sex worker
HIV	Human immunodeficiency virus
HTC	HIV testing and counseling
ICER	Incremental cost-effectiveness ratio
MMT	Methadone maintenance therapy
MoF	Ministry of Finance
MoH	Ministry of Health
MPI	Ministry of Planning and Investment
MSM	Men who have sex with men
NSP	Needle-syringe programs
OST	Opioid substitution therapy
PEPFAR	United States President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV
PMTCT	Prevention of mother to child transmission
PrEP	Pre-exposure prophylaxis
PWID	People who inject drugs
QALY	Quality adjusted life year
ROI	Return on investment
sdNVP	Single dose nevirapine
SHI	Social Health Insurance
TasP	Treatment as prevention
USAID	United States Agency for International Development
USD	US dollar
VCT	Voluntary counseling and testing
VAAC	Vietnam Administration of HIV/AIDS Control
VSS	Vietnam Social Security

ACKNOWLEDGMENTS

This work was conducted under the Health Finance and Governance (HFG) Project, which is supported by the U.S. Agency for International Development (USAID). The HFG project in Vietnam works closely with the Ministry of Health (MoH) and Vietnam Administration of HIV/AIDS Control (VAAC) in the areas of health financing and domestic resource mobilization for HIV, as PEPFAR transitions out of direct service delivery in Vietnam.

The report was authored by Yoriko Nakamura and Michael Chaitkin of Results for Development Institute (R4D). The authors gratefully acknowledge Daniel Arias, Katie Shepard and Sydney Taylor for supporting the literature review and helping to draft some sections, as well as Lane Goodman and Amanda Kabonero for their skillful formatting. They also thank the HFG Vietnam country team, let by Ted Hammett, and R4D's Marty Makinen for their review of the report. Finally, they thank participants for their feedback during the April 12, 2018 technical meeting on 'Sharing global experience and economic evidence for HIV prevention intervention package and strategy,' co-hosted by VAAC and HFG in Hanoi.

EXECUTIVE SUMMARY

The Government of Vietnam is in the process of reforming its approach to financing preventive health services, including consideration of eventually covering preventive services through the social health insurance (SHI) scheme. Financing for prevention services is important, as health systems that ensure widespread access to and utilization of high-quality preventive services can lead to healthier future populations and reduce spending on costlier curative care. Yet in Vietnam, only seven percent of recurrent health expenditure was spent on preventive services in 2013.[1] The focus on financing for preventive services is also timely in Vietnam because donors contribute to about half of prevention spending, but are beginning to transition their support, leaving preventive services for largely donor-funded areas, like HIV/AIDS, in a vulnerable position.

This report aims to inform the discourse on the composition and financing strategy for HIV prevention by synthesizing the global evidence on the health and economic benefits of HIV preventive interventions, highlighting key considerations for Vietnam. Economic evaluations, such as cost-effectiveness and cost-benefit analysis, can provide useful evidence for health policy decision-making, an answer questions such as: how much does it cost to deliver an intervention? how much net fiscal or monetary benefit is generated by an intervention? and which intervention among several offers greatest value for money?

A rich body of international evidence exists on the health and economic impact of HIV preventive interventions, including some studies set in Vietnam. This report synthesizes the evidence on eight key HIV prevention interventions, which can be categorized by who bears the costs of these interventions and the scope of the benefits (see Table 1). This categorization may be useful for framing dialogue for different audiences (e.g., within MOH vs. with MOF or other sectors).

Table 1. Categorization of HIV prevention interventions

Who bears the costs? Scope of the benefits?	Intervention
Costs borne predominantly by health system Benefits mainly relate to HIV	HIV counseling and testing (HCT) Prevention of mother-to-child transmission (PMTCT) Pre-exposure prophylaxis (PrEP) Post-exposure prophylaxis (PEP)* Treatment as prevention (TasP)
Costs borne predominantly by health system Benefits go beyond HIV	Voluntary medical male circumcision (VMMC) Condoms distribution and use Harm reduction (costs could be spread across sectors)
Costs spread across sectors Benefits go beyond HIV	Social-behavioral and structural interventions Combination prevention (costs could be borne partially or fully by the health system depending on the included interventions)

* No economic evaluations were found for PEP published during the period covered by this review.

Overall, the global evidence summarized in this report provides compelling evidence, that investments in HIV prevention provide good value for money (see Table 2). Most HIV prevention interventions, implemented alone or in combination, are cost-effective or cost-saving over time across a range of different settings.[i] In some cases, cost-effectiveness estimates are dependent on certain assumptions, such as removing barriers that hinder access to or retention in care.

Table 2. Description of interventions and key takeaways from economic evaluations

Intervention	Key takeaways from economic evaluations
HIV counseling and testing (HCT, elsewhere labeled voluntary counseling and testing, or VCT)	• Large scale, routine HIV testing can yield a positive return on investment (ROI) • Community-based testing may be more cost-effective than facility-based testing by better accessing hard-to-reach groups • Routine testing for high-risk groups can occur frequently (e.g., annually) while still being cost-effective • Cost-effectiveness of testing depends on high linkage to care rates – i.e., ensuring that HIV patients access medical care once diagnosed with HIV
Treatment as prevention	• Initiating antiretroviral therapy (ART) at higher CD4 counts is very cost-effective or even cost-saving compared to starting ART at lower CD4 counts, and provides benefits to both people living with HIV and uninfected individuals • Cost-effectiveness depends on good adherence, retention in care, and early detection of virologic failure (i.e. access to viral load testing)
Pre-exposure prophylaxis	• Generalized use of PrEP, even among key populations, may not be cost-effective compared to no PrEP use • Targeted PrEP to the most at-risk groups may be more cost-effective, but it may be challenging and costly to identify individuals in these groups • Potential for PrEP to become more cost-effective if the price of PrEP is reduced • Cost-effectiveness of PrEP also depends on good adherence to PrEP
Voluntary medical male circumcision	• Voluntary medical male circumcision is cost-effective, and even cost-saving, particularly in contexts with generalized HIV epidemics and low prevalence of male circumcision even when there is scale-up of ART • Targeting VMMC to adolescents and young adults is most cost-effective, although the specific age range depends on the time horizon over which cost-effectiveness is assessed, as well as the feasibility of scaling up VMMC coverage
Condom distribution and use	• Expanding the distribution and use of male and female condoms is highly cost-effective

[i] An intervention is defined as being cost-effective when the ratio of the incremental costs to incremental benefits between two interventions falls below a specified or proposed willingness-to-pay threshold. An intervention is cost-saving when the intervention of interest is more effective and less costly than the comparator intervention.

Intervention	Key takeaways from economic evaluations
Social-behavioral and structural interventions	• Estimating the health impact attributed to social-behavioral and structural interventions alone is challenging, but some economic evaluations exist • Individual and community-based behavioral interventions may yield a positive ROI • Structural interventions targeted to vulnerable groups (e.g. female sex workers, orphan girls) is cost-effective, and may provide important societal benefits beyond health
Harm reduction	• Harm reductions strategies are generally considered to be cost-effective interventions • A study in Vietnam determined that offering methadone maintenance therapy is cost-effective compared to a scenario with no other prevention strategies, and would cost USD 97 million to scale up over four years to reach 65 percent of PWID[2] • Another study in Vietnam found that methadone maintenance therapy (MMT) use decreased health service utilization and reduced out-of-pocket spending [3]
Prevention of mother-to-child transmission	• Universal, routine testing is cost-effective, and even cost-saving (in countries with high burden of HIV) • In settings with lower HIV prevalence (like Vietnam [4]), rescreening pregnant women later in their pregnancy can be cost-effective compared to screening only once at the start of pregnancy, but targeted rescreening for high-risk pregnant women may be a more cost-effective alternative • Option B+ (immediate, lifelong ART for HIV pregnant women) can be cost-effective compared to other available ARV-based options, especially if health benefits to the mother are considered • A study found that Option B+ is cost-saving in Vietnam if averted transmission to infants and sexual partners are accounted for among the benefits[5]
Combination prevention	• Interventions that reduce the risk of PLHIV transmitting HIV may be more cost-effective than interventions for uninfected individuals from contracting HIV • Targeting interventions to high-risk groups can be a more cost-effective strategy, especially for high-cost interventions like PrEP • A study in Can Tho province found that annual testing and immediate treatment initiation for key populations (rather than the general population), along with the scale-up of MMT and condom use would reduce new infections by 81 percent and require an additional investment of USD 0.8 million compared to the status quo over 40 years[6] • Another study from Vietnam found that together, the following approaches – NSP and MMT for PWID; condoms for FSWs and their clients, as well as for MSM; and ART – led to a 34 percent reduction in new HIV infections between 2006 and 2010, and was highly cost-effective compared to a scenario without these interventions[7]

This report provides information for the Government of Vietnam to consider as it develops an HIV prevention package that is effective, efficient, and affordable. However, the process of defining this package and advocating for HIV (and other) preventive services to be covered by SHI will require further discussions with key stakeholders and additional evidence, including economic analyses that are specific to Vietnam's context and needs. Economic evidence can be a powerful tool to converse with important actors, such as the Ministry of Finance or the National Assembly, and decisionmakers will want to consider other important considerations beyond the evidence contained in this report, such as budget impact, equity, social values, and system readiness to deliver.

To sustain the gains Vietnam has achieved in combating HIV, it will be important to find a sustainable approach for financing HIV prevention services. The findings from this report underscore the value and potential savings from investments in HIV prevention, whose benefits may extend beyond the health sector. Successes in preventing new HIV infections may also help encourage broader investments in prevention.

Box: What recommendations can be made for Vietnam based on this review?

Based on the evidence presented in this report, it is recommended that Vietnam continue to pursue a *combination prevention* approach, which is also the international standard. In determining an HIV prevention package, Vietnam should focus more of its decision-making process on determining how much to invest in each of the available prevention interventions depending on epidemic reality at the national and sub-national levels, rather than debating which interventions to include or not include. For example, Vietnam should consider the inclusion of newer prevention interventions in the HIV prevention package, such as oral PrEP, but it may be most efficient to target PrEP to key populations.

The main conclusions from the global evidence summarized in this report will be valuable in guiding Vietnam as it designs and implements an HIV prevention package. However, the numeric incremental cost-effectiveness ratios (ICERs) and other economic evaluation metrics reported in the studies should be interpreted with caution, as these values are specific to study assumptions and country contexts. The table below presents the ICERs from studies in Vietnam, which may be more informative than studies from other countries. However, it will be important for Vietnam to continue to build on the findings synthesized in this report, by producing its own evidence that is specific to the Vietnamese context. Numeric findings from studies in other settings can be found in Appendix B.

Intervention	Why is the intervention important?	Economic evaluation metric
Expanding the distribution and use of male condoms	Can reduce HIV infections and other sexually transmitted infections	Closing the annual condom gap (335 million) could avert approximately 2.5 million DALYs and nearly 160,000 new infections at a total cost of USD 1.2 billion over 15 years[8]
Methadone maintenance therapy	Can reduce HIV incidence among PWID and help them overcome their addictions	Compared to status quo (no MMT), MMT strategy costs over a one-year time horizon:[2] - USD 1,964 per QALY - USD 3,324 per HIV infection averted
Targeted rescreening of pregnant women for HIV and Option B+	Can avert HIV infections in infants and the pregnant women's sexual partners	Compared to a focused testing strategy for medium/high burden areas, universal testing cost over a 20-year time horizon:[4] - USD 125 per QALY gained Compared to Option A, Option B+ is cost-saving if accounting for total costs per total infections (MTCT and sexual) over a lifetime horizon[5]

1. INTRODUCTION AND OBJECTIVES

Facing enduring and emerging infectious disease epidemics, mounting burdens of non-communicable diseases and mental illness, and a rapidly aging population, the effectiveness and financial sustainability of Vietnam's health system will increasingly depend on investments in prevention. However, preventive services accounted for only six percent of health expenditure, while 79 percent of health expenditure was on curative services in 2015[ii].[9]

Vietnam's Health Financing Strategy 2016–25 seeks to address the "[i]mbalance of health expenditure between preventive and curative services" by prioritizing prevention in state budget allocations and ultimately incorporating preventive services into the social health insurance (SHI) benefits package.[10] However, the strategy offers few details on how the Government will determine the appropriate level of prevention spending or prioritize among the many available interventions. These issues are increasingly urgent as Vietnam's access to external funding for health diminishes—donors contribute roughly half of prevention spending.

The national HIV/AIDS response is especially vulnerable to decreasing foreign aid. In the next five years, Vietnam will lose much of its financial and programmatic support from the Global Fund and PEPFAR.[11] While the Government has already committed to covering HIV care and treatment services via SHI (Circular No. 15/2015/TT-BYT[iii]), the fate of historically donor-funded HIV prevention activities is less clear. This report aims to inform the Government of Vietnam's approach to financing preventive health services by addressing three interrelated questions:

1. **What approaches are commonly used to evaluate the benefits of HIV prevention interventions?** Numerous analytic methods are employed globally to assess the health, economic, and fiscal benefits of health interventions, including those with preventive aims.
2. **How can evidence inform choices about what interventions to include in an HIV prevention package and efforts to mobilize resources for them?** Findings from economic evaluations of HIV preventive interventions can help to optimize prevention packages and the allocation of resources within them so the Government can achieve the greatest gains with a given prevention budget. Moreover, quantifying the benefits can help to motivate greater investment in HIV prevention, whose results are often less visible than those of curative services.
3. **What can Vietnam learn from the global evidence on HIV prevention?** A review of current evidence can guide the definition of an HIV prevention package and highlight considerations for future revisions to Vietnam's prevention priorities more generally.

The report contributes to deliberations in Vietnam over the composition of and financing strategy for a package of HIV preventive services, including within the Ministry of Health (MoH) and Vietnam Administration of HIV/AIDS Control (VAAC); among the MoH, VAAC, Ministry of Finance (MoF), Ministry of Planning and Investment (MPI), and Vietnam Social Security (VSS); between ministries and the National Assembly; between national and provincial authorities; and between the Government

[ii] In some cases, services cannot easily be categorized as being only preventive or only curative. For instance, spending on antiretroviral therapy (ART) is typically classified as curative even though ART generates substantial preventive benefits.

[iii] This circular provides guidance on medical examination and treatment covered by health insurance for HIV-positive people and people using HIV/AIDS-related health care services.

and development partners. It also serves as a useful resource for decision-makers in other countries considering investments in HIV prevention.

2. ECONOMIC EVALUATION APPROACHES IN HEALTH

Evidence from economic evaluations can play an important, though rarely decisive, role in health policy. Economic evaluations answer a range of questions, including: how much does it cost to deliver an intervention? how much net fiscal or monetary benefit is generated by an intervention? and which intervention among several offers greatest value for money? In turn, these answers can inform various policy efforts, including:

- Advocating for resource mobilization based on estimated needs and established service coverage targets;
- Designing and updating health benefits policies, accounting for cost-effectiveness and budget impact;
- Optimizing resource allocations within and between priority programs; and
- Enhancing dialogue among ministries of health, finance, planning, and more.

Economic evaluation requires simultaneously undertaking two types of analysis: (1) costing the intervention and (2) measuring and/or valuating the resultant benefits. There are several methods and associated data requirements for each type, and choices about which to employ depend on the types of decisions evaluators seek to inform, available time and resources, feasibility of data collection, and more.

This section describes the two main families of economic evaluations for health—cost-effectiveness analysis (CEA) and cost-benefit analysis (CBA)—including their main features, strengths, and limitations. Both families of analysis can yield estimates of the return on investment (ROI) in one or more interventions. There are many resources for detailed guidance on economic evaluation, including overall methods, the role of economic evaluation in defining and updating health benefits policies, costing, and measuring and valuating health benefits.[12–15] Evidence from economic evaluations should be used alongside other considerations, including equity, budget impact, and system readiness.

2.1 Cost-effectiveness analysis[iv]

CEA involves quantifying the costs of health interventions and their benefits in terms of *gains to health*. Health gains can be captured in many ways, from simple measures like averted deaths to sophisticated ones like quality-adjusted life years (QALYs) gained or disability-adjusted life years (DALYs) averted.[v] The results of CEAs are typically expressed in two ways. First, the ratio of cost to health benefit (e.g., dollars per QALY gained) can be reported for individual interventions. These findings are useful when comparing interventions that meet different health needs, such as two novel medicines that have been proposed for inclusion in a health benefits package or national formulary.

[iv] Some texts differentiate between cost-effectiveness analysis and cost-utility analysis, labeling as the latter studies that use quality-adjusted outcome measures as opposed to quantity-only measures. This report uses CEA as an umbrella term for studies relating costs to any measure of health outcome.

[v] For more information on DALYs and QALYs, see: Gold MR, Stevenson D, Fryback DG. HALYs and QALYs and DALYs, Oh My: Similarities and Differences in Summary Measures of Population Health. *Annual Review in Public Health* 2002; 23: 115-34.

Second, CEA results are often presented through a comparative metric called the incremental cost-effectiveness ratio (ICER). The ICER captures the differential costs and health benefits between two interventions serving the same patient population (Equation 1). For instance, the section below on prevention of mother-to-child transmission (PMTCT) reports the ICER of universal HIV testing compared to targeted testing for pregnant women.

$ICER = \frac{C_A - C_B}{H_A - H_B}$, where C_i and H_i are the cost and health gain, respectively, of intervention i. (1)

Countries factor CEA evidence into decision-making in a variety of ways. Some compare an intervention's cost-effectiveness to a threshold based on international normative guidelines or benchmark services for which society has already demonstrated a willingness to pay. For example, US studies often compare results to a threshold of USD 100,000–150,000 per QALY gained based on the cost-effectiveness of renal dialysis. Meanwhile thresholds of up to 3 times GDP per capita are common for studies in low- and middle-income countries, based on value-for-money principles previously endorsed by the World Health Organization (WHO)[16], but there is growing recognition of the need for cost-effectiveness thresholds more grounded in individual country context.[17,18] Increasingly, analysts develop 'league tables' through which they rank interventions by cost-effectiveness and incorporate complementary data on budget impact and service delivery feasibility.[19]

In addition to informing choices about what interventions to cover, CEA evidence can also guide resource allocation within priority health programs, such as a country's response to the HIV epidemic. Optimization often entails sophisticated, data-intensive modeling exercises that account for epidemiological trends, policy targets, and budget constraints. Some countries adapt existing models, such as the World Bank's Optima tool[vi], while others develop their own[vii].

2.2 Cost-benefit analysis

In contrast to CEA, CBA involves quantifying the benefits resulting from an intervention in *monetary terms*. This has some advantages as an alternative or companion to CEA evidence. Monetizing outcome measures enables comparisons of CBA results between health and other sectors, useful to policy makers charged with allocating finite public resources across numerous social investment opportunities. Additionally, CBAs allow for emphasizing in present terms both the costs and benefits that accrue over long time horizons. This casts analysis in a format familiar to ministries of finance and planning that might otherwise disregard long-term health gains resulting from short-term investments.

CBA results are commonly reported as benefit-cost ratios (BCRs), which relate the costs to the monetized benefits of an intervention (Equation 2).[viii]

$BCR = \frac{B_A}{C_A}$, where B_i and C_i are the cost and benefit, respectively, of intervention i. (2)

[vi] For more information on the Optimal tool, see: http://optimamodel.com/

[vii] For example, see Department of Health, South Africa, & South African National AIDS Council. (2016). *South African HIV and TB Investment Case: Reference Report Phase 1*. Retrieved from http://sanac.org.za/2016/03/22/investment-case-report/.

[viii] Some studies compute BCRs but report them as ROIs, suggesting a lack of consensus or consistency among researchers regarding the definition and use of the two terms.

The benefits of an intervention outweigh the costs when the BCR is greater than 1. On their own, such calculations are most useful for eliminating individual investments from consideration (e.g., if their estimated BCR is less than 1). When selecting from a menu of possible investments, it is important to compare estimated CBRs across them, as well as to account for other considerations noted above, such as budget impact and service delivery feasibility.

There are three main ways to monetize benefits. First, health gains themselves can be valuated, though it is challenging both normatively and empirically to assign monetary value to an extra year of life expectancy or a decrement in physical ability. However, it is worth noting that health interventions of value do not always have a BCR greater than 1, especially when health gains are not or cannot be easily valuated monetarily. Second, financial (or fiscal) benefits can be determined based on costs averted as the result of an intervention. For example, in addition to modelling health impacts of increased access to modern contraceptives, the ImpactNow tool[ix] tabulates unrealized expenditure linked to avoided pregnancies and their complications. Third, some studies seek to estimate the broader economic impact of interventions by linking health gains to changes in important socioeconomic indicators like educational attainment, labor force participation, and productivity.

[ix] For more information on the ImpactNow tool, see: http://www.healthpolicyplus.com/impactnow.cfm

3. GLOBAL ECONOMIC EVIDENCE FOR HIV PREVENTIVE INTERVENTIONS

This section synthesizes international evidence on the health and economic impact of globally recommended HIV preventive interventions (Table 3, details on the literature review can be found in Appendix A). The sub-sections below provide some contextual information on each of the interventions, before summarizing the literature on whether these interventions offer good value for money (with additional information from the studies contained in Appendix B). While these economic evaluations provide useful information for policymakers, it is important to underscore that despite the use of rigorous methods, findings from these studies are derived from mathematical models that simplify actual contexts and rely on certain assumptions. Thus, as mentioned before, these findings should be discussed alongside other types of evidence and other considerations including equity, budget impact, and system readiness.

Table 3. Overview of articles reviewed

Intervention	Countries examined
HIV testing (15 studies)	India, Indonesia, Malawi, Netherlands, South Africa, UK, US, Zimbabwe
Treatment as prevention (4 studies)	India, US, South Africa
Oral pre-exposure prophylaxis (14 studies, 2 systematic reviews)	Australia, Canada, Netherlands, Peru, US, Zambia
Oral post-exposure prophylaxis (no studies found)	
Voluntary medical male circumcision (10 studies)	Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe (and two studies on multiple sub-Saharan African countries)
Condoms (5 studies)	US (as well as global assessment of 81 countries and study on 13 sub-Saharan African countries)
Social-behavioral and structural interventions (4 studies, 1 commentary, 1 systematic review)	Benin, Canada, India, Zimbabwe
Harm reduction (12 studies, 1 systematic review)	Australia, Canada, Indonesia, Mexico US, Vietnam
Prevention of mother-to-child (PMTCT) (12 studies, 3 systematic reviews)	Haiti, Ghana, India, Kenya, Namibia, South Africa, Uganda, Vietnam Zambia, Zimbabwe
Combination prevention (12 studies)	China, Nigeria, South Africa, Ukraine, US, Vietnam

3.1 HIV counseling and testing[x]

HIV testing is an important intervention that can provide both individual and societal benefits. Knowledge of HIV status is essential for linking people living with HIV (PLHIV) to treatment, which can extend their lives and reduce the onward transmission of HIV. The consistent use of antiretroviral therapy (ART) helps to suppress viral loads (i.e. copies of HIV in the body) and reduces the likelihood of transmitting the disease to others. The potential impact of HIV testing as a prevention strategy is dependent on the ability to link and retain PLHIV in care. In Vietnam, it is estimated that 80 percent of PLHIV are aware of their status according to VAAC's annual report in 2017.[20] While this represents a considerable portion of PLHIV, reaching and testing more PLHIV will be necessary to meet the Government of Vietnam's commitment to achieve the 90-90-90 targets[xi] by 2020.

Many types of HIV tests and modalities for providing testing services exist. Historically, HIV tests required blood draws at a facility, which were then sent to a laboratory for testing to detect the presence of antibodies against HIV. Receipt of results following an HIV antibody test could take a few days or longer and could only detect HIV infection that had been present for several weeks or months. However, advancements in HIV testing technologies have led to the availability of HIV RNA tests that are able to detect early HIV infection, as well as rapid tests that do not require laboratory analysis and can provide results in 30 minutes. The latter innovation has enabled HIV testing to occur in clinical settings that do not have easy access to laboratories, as well as non-clinical settings.

Recent studies that have evaluated the economic benefits of HIV testing have largely focused on comparing different testing modalities, as well as the frequency of providing HIV testing (Appendix Table B1). However, one study assessed the return on investment of a large-scale HIV testing initiative in the US – a three-year program implemented by the US Centers for Disease Control that targeted geographic areas with a high incidence of AIDS.[21] The study found that the program yielded USD 1.95 in benefits for every dollar spent, accounting only for the benefits gained from infections averted. The study also noted that this BCR was above those estimated from US investments in the treatment of heart attack (BCR USD 1.10), stroke (BCR USD 1.49), and type 2 diabetes (BCR USD 1.55). Thus, HIV testing in Vietnam, particularly targeted testing, may also yield a positive return on investment.

HIV testing modalities

Several studies have found that HIV testing focused at the community level can be a cost-effective or even cost-saving option compared to facility-based testing, because it can better serve hard-to-reach populations and link them to care. This is aligned with efforts to expand community-based HIV testing in Vietnam via mobile testing delivered by providers, non-provider based testing, and even self-testing, which was recently included as a recommended HIV testing approach by the WHO.[22–24]

In Indonesia, the scale-up of rapid VCT at public community health centers was found to be very cost-effective over 20 years compared to the status quo, where HIV testing primarily occurs at hospitals.[25] While scale-up of community-based VCT was found to be cost-effective, it would cost

[x] Also referred to as voluntary counseling and testing

[xi] The "90-90-90" target was launched by UNAIDS in 2014 and calls for the achievement of the following targets by 2020: 90% of PLHIV aware of their status, 90% of PLHIV aware of status on ART, and 90% of PLHIV on ART are virally suppressed (viral load of <200 copies/mL).

USD 60 million over 20 years compared to USD 37 million to maintain current practice. Indonesia, like Vietnam, has a concentrated HIV epidemic among key populations (female sex workers (FSW), men who have sex with men (MSM), people who inject drugs (PWID)),

Other studies focused on community-based (i.e. nonclinical) HIV testing modalities outside of facility settings, including: home testing and counseling, mobile testing, testing offered by community-based organizations, testing in substance abuse treatment programs. and self-testing. Many of these options can be more expensive compared to facility-based testing. However, in South Africa, studies have found that both home testing and counseling and mobile testing are very cost-effective interventions compared to the status quo, even when accounting for uncertainty in model parameters.[26–28] However, South Africa has a generalized HIV epidemic and a lower share of PLHIV aware of their HIV status than in Vietnam. A study in the US that examined non-facility based HIV testing strategies for MSM found that venue-based testing — testing in locations attended by MSM other than for medical, mental health or social services — was cost-saving across 15 US cities.[29] Another study in the US that focused on different testing modalities for PWID found that offering a one-time test in community-based substance abuse treatment centers (no counseling, information about the test only) was more efficient[xii] than referring patients to off-site testing sites.[30] One study also assessed the cost-effectiveness of self-testing in Zimbabwe, and estimated that self-testing could result increase the proportion of people tested for HIV in the past year by seven percentage points (50 to 57 percent). If self-testing cost less than the cost of a provider-delivered HIV negative test[xiii], the study found that self-testing could be a cost-effective option.[31] These findings suggest that community-based HIV testing modalities can be more cost-effective compared to facility-based testing, and that offering a range of testing modalities may be desirable. However, further research is needed to determine the right mix of testing modalities in the Vietnamese context.

Frequency of HIV testing

While the health benefits of HIV testing are clear, an important implementation question is whether to routinely test all population groups and what group at what interval. Economic evaluations that have examined these questions have found that it may be cost-effective to screen high risk groups more frequently than the general population. For example, in India, which has a concentrated epidemic among key populations and in select districts, one study found that screening the general population (HIV prevalence: 0.3%) for HIV every five years and annually in (1) high prevalence districts (HIV prevalence: 0.8%) and (2) high risk groups (HIV prevalence: 5%) is cost-effective.[32] In higher income countries like the US, other studies suggested that even more frequent testing (e.g. every three or six months) among high risk groups could still be cost-effective.[33,34] In many of these studies, sensitivity analysis demonstrated that if linkage to care and adherence were improved or if ART costs were reduced, or both, the cost-effectiveness of more frequent testing would further increase. Thus, more frequent testing for key populations and areas with high prevalence in Vietnam may be cost-effective, but additional analysis is necessary to estimate the optimal testing frequency for these groups.

[xii] Additional cost per QALY gained of off-site referral was higher than one-time test in community-based substance abuse treatment center.
[xiii] The cost per HIV test is higher for HIV positive patients compared to HIV negative patients, due to the more extensive counseling (and associated costs) needed for HIV positive diagnoses.

Partner notification

Partner notification is an intervention related to HIV testing that, with the consent of newly diagnosed PLHIV, seeks to inform recent partners of newly diagnosed PLHIV are informed of their exposure to HIV and encourages them to also get tested.[35] PLHIV may be encouraged by providers to share their HIV status to partners and encourage them to get tested (passive referral). However, providers may work with PLHIV to disclose this information through anonymous notification systems or by directly contacting the partners themselves. Partner notification has successfully been used to control other diseases, such as syphilis, and may help identify more PLHIV. Making voluntary partner notification services available was also recommended by the WHO in 2016.[24]

Two recent studies have examined the cost-effectiveness of partner notification. One study in Malawi compared contract notification, and provider notification with passive referral[xiv], and found that contract notification resulted in a much lower cost per infection averted than provider notification[35] The second study focused on the duration of use of an online partner notification system in the Netherlands.[36] It found that the cost-effectiveness of partner notification increased considerably over time (5 vs. 20 years), and also estimated that partner notification would become more cost-effective as ART costs declined. Thus, provider-based partner notification may be a cost-effective intervention, particularly over time; however, additional evidence may be useful validate these findings.

3.2 Treatment as prevention

Treatment as Prevention (TasP) refers to the use of ARVs among PLHIV to suppress their viral loads, thereby reducing the risk of onward HIV transmission. In the past, international guidelines and national policies promoted PLHIV initiating ART when their CD4 counts dropped below 350 or 200 cells/mm^3 or if they presented with symptoms of advanced HIV or AIDS. However, in recent years, strong evidence has emerged demonstrating the health benefits of earlier ART initiation in terms of not only mitigating HIV morbidity and mortality, but also preventing new transmissions of HIV.[37] As a result, the WHO revised its guidelines in 2015 to recommend, "initiating ART among all adults living with HIV regardless of WHO clinical stage or at any CD4 cell count."[38] Vietnam recently adopted these guidelines and now strives to initiate treatment for any newly diagnosed individual right after their confirmatory test, regardless of clinical stage or CD4 status (Decision No. 5418, 01 December 2017).[39]

Earlier ART initiation provides an opportunity for HIV prevention and treatment advocates to come together, but scaling up ART to a larger portion or all PLHIV also requires a sizeable financial investment. Studies that have examined the economic impact of TasP have found that it is cost-effective or even cost-saving both in the short- and long-term and is robust to changes in key model parameters (Appendix Table B2). A study in India, which found TasP to be very cost-effective under both optimistic and realistic HIV continuum of care scenarios, estimated that implementing TasP would only require an additional USD 517 million over 20 years — a four percent increase in overall HIV spending in India. Thus, TasP may be a cost-effective investment, as long as it is paired with efforts to ensure good adherence to ART and retention in care, as well as early detection of virologic failure (which includes access to routine viral load testing).[40–42]

[xiv] The study defined these strategies as: "provider notification (provider attempts to notify indexes' locatable partners), contract notification (index given 1 week to notify partners then provider attempts notification) and passive referral (index is encouraged to notify partners, standard of care)."

3.3 Oral pre-exposure prophylaxis

Pre-exposure prophylaxis (PrEP) is an HIV prevention strategy that involves the use of ARVs by HIV-negative individuals who are at risk of acquiring HIV infection. Over the last ten years, several clinical trials have demonstrated the efficacy of consistently taken oral PrEP[xv] in preventing HIV transmissions among MSM, PWID, and serodiscordant couples.[43–46] Based on this evidence, the WHO first issued guidance in 2014 that recommended offering PrEP to MSM.[47] These guidelines were expanded in 2015 to recommend offering PrEP to all high-risk population groups (HIV incidence of 3 per 100 person-years or higher).[38] In Vietnam, the MOH and PEPFAR launched a pilot program in June 2017 to offer PrEP to key populations (MSM, transgender women, and HIV-negative partners in a serodiscordant relationship) in June 2017.[48]

While results from Vietnam's PrEP pilot program will not be available until September 2018, several studies have examined the cost-effectiveness of oral PrEP, particularly among MSM in high-income countries (Appendix Table B3). Despite differences in methods and model parameters, several studies have found that offering PrEP to a wide population may not be cost-effective given the high cost of PrEP[xvi], particularly where HIV prevalence is low. A few studies estimated that there would need to be substantial reductions in the cost of PrEP for it to become cost-effective or possibly a cost-saving strategy for general use.[49,50] Estimates of cost-effectiveness were also dependent on model assumptions such as baseline HIV prevalence, adherence to PrEP, prevalence of male circumcision, and condom use (more favorable in scenarios with high HIV prevalence, good adherence, low male circumcision prevalence and condom use). Very few studies examined the impact of drug resistance — an area that is still not very well understood in the context of PrEP. However, systematic reviews of earlier economic evaluations of PrEP found that drug resistance assumptions did not substantially affect cost-effectiveness results.[51,52]

PrEP may be more cost-effective if targeted to specific populations, such as individuals at highest risk of acquiring HIV infection (e.g. highest risk decile of MSM based on sexual activity) or HIV uninfected partners in serodiscordant relationships, particularly if the HIV infected partner is not yet on ART).[49,52–59] However, while targeted PrEP might be a more cost-effective strategy, a few studies cautioned that a targeted strategy may be difficult to implement given the costs and difficulty associated with identifying these highest risk individuals.[56,57] Importantly, none of the reviewed studies accounted for the costs of finding these individuals. PrEP may also be cost-effective if administered "on demand," which involves taking PrEP 24 hours before, during, and after sexual activity. One study that examined "on-demand" PrEP for one year found that it was a cost-saving strategy because it extended life expectancy and cost less than the lifetime costs of living with HIV.[60] Thus, while general use of PrEP may not be a cost-effective intervention, alternative PrEP implementation strategies may provide good value for money.

3.4 Voluntary medical male circumcision

Voluntary medical male circumcision (VMMC) is an effective intervention in preventing HIV infections (and other sexually transmitted infections) that is administered to men. Clinical studies have shown that VMMC may reduce the risk of acquiring HIV by 60 percent among men.[61] Unlike many other HIV prevention interventions, VMMC is a one-time intervention, which means that it

[xv] PrEP has also been tested topically (in the form of a vaginal microbicide gel); however, clinical trials have produced mixed efficacy results.

[xvi] Estimated annual PrEP costs ranged from USD 200 in low-income countries to > USD 10,000 in higher income countries.

does not require any routine follow-up or adherence to the regimen to be fully effective. In 2007, the WHO recommended the inclusion of VMMC as part of comprehensive prevention packages, particularly in countries with generalized HIV epidemic and low prevalence of male circumcision.[62,63]

Most studies have examined VMMC in sub-Saharan African countries that have been prioritized by the WHO as countries that would benefit from the scale-up of VMMC. Compared to the lifetime cost of ART, VMMC is an affordable intervention (average unit cost around USD 100). Studies have shown that VMMC is not only a cost-effective intervention, but also cost-saving in many contexts. Even if with improvements to ART scale-up, VMMC will likely remain an important intervention to include as part of the HIV prevention package in many countries.[63,64]

Studies that have analyzed the economic benefits of VMMC as an intervention have also focused on examining different strategies for targeting VMMC programs, particularly by age, but also by geography. Most studies suggest that focusing scale-up of VMMC coverage among men 30 years and older is not as cost-effective of an approach compared to efforts to scale up VMMC coverage among younger adults and children. This is because the potential impact from VMMC in averting HIV infections is diminished in older adults, who generally have a lower lifetime risk of acquiring HIV compared to a younger person.[62] Many studies suggested that targeting VMMC to men ages 10–34 is a cost-effective approach (especially around the age(s) associated with sexual debut and high HIV incidence). In the short-term, targeting men in their twenties appears to be a cost-effective approach that will have the greatest impact in reducing HIV incidence.[62,63,65] One study from South Africa noted that the return on investment of VMMC is highest when targeting men between the ages of 20 and 25.[62] However, another study cautioned that the health and economic benefits from VMMC among men in their twenties depends on high coverage of VMMC, which may require additional programmatic costs.[65]

VMMC program data has shown that fewer adults, especially those ages 25 and above, access VMMC services compared to younger cohorts—this may be because they may be more sensitivities among older adults (e.g., around privacy, worries about pain, loss of income or time due to accessing VMMC services, stigma, etc.)[60,60] When looking at a longer time horizon, there may be health and economic benefits associated with scaling-up VMMC among individuals between ages 10 and 19 (and even younger) as well, as it may be easier to achieve better VMMC coverage among this age group.[63–67] While VMMC is an important part of HIV prevention packages in contexts with generalized HIV epidemics and low prevalence of male circumcision, it may not be as relevant in Vietnam, given the nature of its HIV epidemic.

3.5 Distribution and use of condoms

Condom distribution and promotion initiatives have been part of Vietnam's safe-sex campaigns.[68] With a high prevalence of HIV among female sex workers and their clients, condom distribution in Vietnam has recently increased in high-risk venues, such as hotels and guesthouses where there is a higher frequency of extramarital sex, and, consequently, a higher frequency of STI transmissions.[69] In addition, the development of markets for condoms and other HIV-related goods and services in Vietnam has been a component of USAID and PATH's Healthy Markets project, which aims to build a private market for condoms and other commodities that historically have been primarily donor funded.[70,71]

Male condom distribution

Male condoms are an effective means of preventing pregnancy and sexually transmitted infections, including HIV, and cost much less than the ARVs used to prevent and treat HIV.[xvii] Condom distribution programs may include the distribution of condoms, alongside education and counseling regarding safe sex and proper condom use.

Global evidence indicates that the distribution of male condoms is cost-effective, yet inadequate to meet present demand. A recent global analysis estimated that the annual gap between current use of male condoms and "desired use"[xviii] of male condoms worldwide approaches 11 billion condoms, with more than 6 billion needed for HIV/STI prevention.[8] By scaling up distribution to meet the total gap, countries could avert 240 million DALYs between 2015-2030, at a cost of roughly USD 115 per DALY averted, which is highly cost-effective under all modeled condom usage scenarios.[8] The same study found that Vietnam could avert nearly 2.5 million DALYs and nearly 160,000 new HIV infections by closing a 355 million annual condom gap.[8] Completely closing the condom gap was found to be highly cost-effective for Vietnam, at a total cost[xix] of USD 1.3 billion between 2015 and 2030.[8]

Recent studies from the US and the UK have suggested that targeted male condom distribution for vulnerable and high-risk populations—such as MSMs, sex workers, youths, and inmate populations—could yield substantial societal cost savings and reduce the transmission of STIs, as well as reduce the rate of unplanned pregnancies (Appendix Table B4).[73,74] These studies emphasize that even modest changes in condom usage can have profound impacts on the cost-effectiveness of a male condom distribution program, given the high lifetime costs of HIV treatment and the impacts of HIV on quality of life and life expectancy.[73] Consequently, countries pay close attention to not only the procurement and distribution of condoms, but also efforts to stimulate demand and utilization among at-risk populations.

Female condom distribution

Females condoms offer similar protective benefits to male condoms, reducing the risk of unwanted pregnancy and preventing STIs, including HIV, by forming a physical barrier to conception and STI transmission.

Studies on female condom distribution indicate that it can be very cost-effective or even generate cost savings.[75,76] An analysis of female condom distribution programs in 13 sub-Saharan African countries found that female condom distribution was very cost-effective across all settings compared to no contraceptive use.[76] Compared to male condom distribution, female condoms can have a higher cost per DALY averted.[8] However, both have been found to be cost-effective contraceptive and prophylactic measures compared to no contraceptive use or current levels of contraceptive use.

[xvii] In 2015, the price of condoms purchased at pharmacies, grocery stores and roadside stalls was estimated to range from 2,000 to 8,000 Vietnamese dong (USD 0.10–0.40).[55]

[xviii] "Desired use" in this study is defined as condom use to meet unmet family planning needs and the total need for condoms for HIV and STI protection (assumed 90 percent condom use among risk groups).[72]

[xix] This accounted for the costs associated with providing condoms, including supplies, labor, and program costs.

3.6 Social-behavioral and structural interventions

In addition to the biomedically focused interventions described above, social-behavioral and structural interventions can also play an important role in preventing HIV (Table 4). In the context of HIV prevention, social-behavioral interventions seek to encourage behaviors that mitigate risky behaviors, such as using condoms or adhering to PrEP or ART. Interventions can be individually focused, such as counseling services or targeted for larger groups, such as community outreach events or mass media campaigns. In contrast, structural interventions focus on the underlying reasons that influence behaviors and make individuals or groups susceptible to HIV.[77] In other words, structural interventions "promote health by altering the context in which people function, eliminating barriers to health behavior, and facilitating the ability and motivation to make better health decisions."[78] Socio-behavioral and structural interventions often require a concerted effort across multiple sectors (e.g. education, criminal justice, law enforcement, and others). Thus, adding these interventions to a package in Vietnam should be done alongside with a process for engaging and working collaboratively with these sectors.

Table 4. Examples of social-behavioral and structural HIV prevention interventions

Social-behavioral	Structural
• Education, outreach, and community campaigns • Mass media (radio, print media, billboards) • Counseling • (Peer) support groups • Case management	• Community mobilization • Gender empowerment • Links to other social programs, such as housing and food-assistance programs • Cash transfers (particularly for young women) • Laws decriminalizing drug use, sex work, homosexuality

Estimating the health impact attributed to social-behavioral and structural interventions alone can be challenging, which makes it difficult to conduct economic evaluations of these interventions.[79] Nonetheless, a few economic evaluations have assessed a range of social-behavioral and structural interventions, finding that there may be health and economic benefits to including these types of interventions in HIV prevention programs (Appendix Table B5). For example, one study in Canada found that a government-funded, community-based HIV program that provided a set of social-behavioral and structural interventions (e.g., mass media programs for HIV prevention, medication and adherence support, and social support and social inclusion sessions) saved approximately five Canadian dollars for every dollar invested.[80] Another commentary argued that despite prevailing views that individual social-behavioral interventions are inefficient, the benefits of these interventions may outweigh the costs particularly for high-risk MSM. [81] The study cited evidence that many high-risk MSM suffer from psychosocial issues[xx] contribute to risky behaviors that require social-behavioral interventions.

In terms of structural interventions, existing economic evaluations have focused on interventions targeted to vulnerable women, such as FSWs, and adolescent orphans, where structural

[xx] Some studies have found in their sample population of HIV positive MSM, that approximately 50 percent have psychiatric disorders and/or mood and anxiety disorders.[81]

interventions particularly have the potential to reduce the number of new infections.[82] In India, a study found that the addition of a community mobilization and empowerment intervention[xxi] for FSW to the Avahan[xxii] initiative's HIV prevention program was very cost-effective (or cost-saving if including the savings from averted ART use).[83] Another study found that providing financial assistance to keep orphan girls in school was a very cost-effective intervention in Zimbabwe.[78] Finally a systematic review found that the following gender-based interventions were shown to be cost-effective: couple counseling for the prevention of vertical transmission; gender empowerment; community mobilization; female condom promotion for FSWs; expanded female condom distribution for the general population; and post exposure HIV prophylaxis for rape survivors.[84] It is also worth noting that many structural interventions provide societal benefits beyond averted HIV infections, such as reduced gender-based violence and increased retention in school.

3.7 Harm reduction for people who inject drugs

In Vietnam, 44 percent of new HIV infections are among PWID, and 21 percent of PWID live with HIV.[22] Intravenous drug use is also a key contributor to the spread of HIV globally, particularly outside of sub-Saharan Africa. PWID are susceptible to acquiring (and transmitting) HIV through sharing infected needles, in addition to sexual transmission. Thus, harm reduction strategies play an essential role in preventing new infections among PWID, alongside other HIV prevention strategies.

Needle-syringe programs

Among the available strategies to prevent HIV among PWID, needle-syringe programs (NSPs) are one of the least costly to implement (Table 5).[85] NSPs help prevent the transmission of HIV by providing clean needles and syringes to PWID, which reduces the frequency of shared needle use. NSPs may also provide ancillary services, such as HIV testing and counseling, referrals to HIV and drug treatment, and condom provision.[86]

Studies have found that NSPs are a cost-effective intervention for preventing HIV among PWID (Appendix Table B6).[85,87] Recent studies from the US and Australia have shown that NSPs can yield a positive return on investment over time, when accounting for the savings in lifetime HIV treatment costs from averted HIV infections.[86,87] The study from the US found that investing an additional 10 million over a year to expand NSP programs would result in a ROI of USD 7.58 for every dollar spent.[86] Meanwhile, the study from Australia found that investing AUD 240 million over 10 years would result in an ROI of AUD 1.3-5.5 for every dollar spent (depending on rates of receptive syringe sharing).[87]

[xxi] Community mobilization and empowerment interventions may include: community involvement in program management and services, violence reduction, and addressing legal policies and practices." Vassal, et al. also define empowerment as "the *process* by which those who have been denied the ability to make choices (the disempowered) to acquire such an ability."[83]

[xxii] Avahan is a large-scale HIV prevention initiative in India funded by the Bill and Melinda Gates Foundation.

Table 5. Annual per patient costs of providing NSPs, OST, and ART (global estimates)[85]

Strategy	Annual per person costs
NSPs	USD 23-71
Opioid substitution therapy	USD 363-1057 (methadone)
ART	USD 1000-2000

Opioid substitution therapy

Opioid substitution therapy (OST)[xxiii] is a method of treating opioid addiction, where medication (most often methadone or buprenorphine) is provided to alleviate drug withdrawal symptoms. Unlike NSPs, OST may help PWID overcome their addictions and stop drug use.[88] With respect to HIV, methadone maintenance therapy (MMT), a form of OST, has been shown to decrease HIV-related risk behaviors, HIV screening rates, and adherence to treatment.[2,88,89]

In Vietnam, Hanoi Medical University's Institute of Preventive Medicine and Public Health has conducted and published evaluations demonstrating both the cost-effectiveness of MMT and its benefits to health utility[xxiv], health utilization, and out-of-pocket spending among PWID. A 2012 study evaluated the cost-effectiveness and budgetary impact of MMT programs.[2] Using data from the 2008 MMT pilot in Vietnam, it concluded that from the Vietnamese health care perspective, MMT is a cost-effective strategy over a one-year period (ICER: USD 3,324 per HIV infection averted; USD 1,964 per QALY gained) compared to the status quo, where no other prevention strategies were accounted for. The estimated cost was approximately USD 97 million for Vietnam to scale up MMT between 2011 and 2015 to achieve 65 percent coverage of PWID[xxv]. In 2013, another economic evaluation of MMT found that MMT increased health utility among PWID and decreased health service utilization by 46 percent (48 percent decrease in inpatient service utilization and 32 percent decrease in outpatient service utilization).[3] The study also attributed a 67 percent reduction in OOP spending to enrollment in MMT, which suggests that MMT may help minimize financial vulnerability among PWID.

Behavioral interventions among PWID

In addition to biomedical interventions, two studies have explored the cost-effectiveness of behavioral interventions that promote safer-sex and injection practices among PWID.[91,92] One study in the US analyzed the health benefits and cost-effectiveness of implementing the Holistic Health Recovery Program (HHRP+), an HIV risk reduction and health promotion intervention for HIV-infected PWID supported by US Centers for Disease Control.[92] The study projected that over 10 years, expanding HHRP+ to 80 percent of PWID in the US could reduce HIV prevalence among PWID by 0.68 percentage points compared to the status quo (PWID OST coverage: 13 percent; PWID with HIV access to ART: 33 percent). It also found that expanding HHRP+ to 80 percent of

[xxiii] Also referred to as opioid agonist therapy (OAT).
[xxiv] Health utility is a way of measuring quality of life that reflects how "a respondent *values* a state of health, not just the characteristics of that health state."[90] The cited study used the EuroQOL instrument to measure health utility.
[xxv] Based on target coverage of 70 percent that was defined in the *National HIV/AIDS Strategic Plan 2011-2020,* issued by the Vietnam Ministry of Health.[2]

PWID in the US was a very cost-effective intervention compared to the status quo (ICER: USD 7,777 per QALY gained, used WHO recommended willingness-to-pay thresholds). However, another study suggested that the additional value of behavioral risk reduction interventions may become less cost-effective when added to other harm reduction strategies, such as NSPs .[91]

Supervised injection facilities

Supervised injection facilities (SIFs) are spaces where PWID can inject their own drugs under the supervision of medical professionals. SIFs facilitate the safe injection of drugs and because medical staff are present, they can also prevent fatal overdoses. Staff at SIFs may also become, "a trusted, stabilizing force in many hard-to-reach PWID's lives, persuading many to enter addiction treatment." While the establishment of SIFs is controversial, they present a promising, non-punitive approach to supporting PWID. The first legally sanctioned SIF opened in Vancouver, Canada in 2003, and since then, many cities worldwide have begun to open SIFs.

Several economic evaluations have examined the costs and benefits of establishing SIFs in various North American sites, including four studies that used similar methods (Table 6). These studies all found that the benefits of opening one SIF in each of these cities outweighed the costs of operating the SIF, especially when considering averted HIV and hepatitis C infections. Another study that focused on identifying the optimal number of SIFs to open in two Canadian cities found that it would be cost-effective to open up to three facilities in Toronto and two in Ottawa (assuming a willingness to pay threshold of CAD 50,000 per QALY gained).[93]

Table 6. Costs and benefits of establishing a SIF

Location	Key parameters	Cost-benefit ratio
Montreal, Canada[94]	**HIV prevalence among PWID:** 19% **Rate of needle sharing:** 35% **Annual SIF cost:** CAD 2.2 million **Lifetime HIV treatment cost**[xxvi]**:** CAD 210,555	1.35 (accounts for HIV benefits)
Ottawa, Canada[95]	**HIV prevalence among PWID:** 12% **Rate of needle sharing:** 14% **Annual SIF cost:** CAD 2.2 million **Lifetime HIV treatment cost:** CAD 210,555	0.48 (accounts for HIV benefits) 1.26 (accounts for HIV and Hepatitis C Virus benefits)
Saskatoon, Canada[96]	**HIV prevalence among PWID:** 15% **Rate of needle sharing:** 24% **Annual SIF cost:** CAD 2.2 million	1.44 (accounts for HIV benefits)

[xxvi] Note: these lifetime HIV treatment costs are most likely much higher in Canada compared to the Vietnam.

Location	Key parameters	Cost-benefit ratio
	Lifetime HIV treatment cost: CAD 210,555	
Baltimore, US[97]	**HIV prevalence among PWID:** 18% **Rate of needle sharing:** 3% **Annual SIF cost:** USD 1.8 million **Lifetime HIV treatment cost:** USD 402,000	4.35 (accounts for HIV and HCV benefits)

* All studies noted above assumed that SIFs would lead to a 70 percent reduction in needle sharing

3.8 Prevention of mother-to-child transmission

HIV can also be vertically transmitted from HIV-infected women to their children. Transmissions can occur during pregnancy, childbirth, and after childbirth through breastfeeding. However, early detection and treatment of HIV in pregnant women, as well as prophylactic measures administered to newborns can considerably reduce the risk of vertical transmissions. Recent initiatives to strengthen PMTCT interventions in Vietnam include adopting a policy of immediate, lifelong ART for all pregnant women diagnosed with HIV (Option B+) and ongoing efforts to integrate PMTCT services with maternal and child health services.[22,98] This includes the addition of HIV testing for pregnant women into the antenatal care (ANC) package[xxvii], which may help improve HIV testing coverage for pregnant women (49.7 percent in 2013) given that greater than 90 percent of women have at least one antenatal care visit in Vietnam[xxviii].[22,39,98]

Most economic evaluations have focused on assessing HIV testing during pregnancy or the use of ARVs for PMTCT. However, one study estimated the return on investment of New York state's spending on PMTCT services (including HIV testing, repeat testing, and administering ARVs) over a 16-year period. The study found that every dollar New York state invested in PMTCT services yielded a return of USD 3.96, and would have yielded a positive return even if the estimated number of infections averted had been 25 percent less.[99]

HIV testing in pregnant women

As mentioned in Section 3.1, HIV testing is an important intervention that identifies PLHIV and ideally links them to care. For pregnant PLHIV, identification of HIV status is important both for the mother and newborn child's health. It is especially important to ensure that pregnant PLHIV receive ARVs before, during, and after delivery to prevent transmitting HIV to her child.

Economic evaluations of HIV testing among pregnant women have primarily focused on two areas: whether to test all pregnant women and whether to provide more than one HIV test during

[xxvii] See National Guidelines on Reproductive Health (Decision No. 4128 dated 29 July 2016), which recommends HIV counseling and testing for all pregnant women at their first antenatal care visit.

[xxviii] Another issue for Vietnam to address is covering the cost of HIV testing. Circular No. 15 (26 June 2015) states that social health insurance will pay for *provider-initiated* HIV testing. In practice, many providers only initiate testing if they know women are at higher risk. In accordance with international evidence and guidelines, universal HIV testing of pregnant women is in proposed revisions to both Decision No. 5418 and Circular No. 15, but these have not yet been enacted.

pregnancy. Systematic reviews have found that universal, routine[xxix] HIV testing for pregnant women is cost-effective, and in higher burden areas, cost-saving (Appendix Table B7).[100,101] An "opt-out" approach[xxx] is favorable compared to a voluntary testing approach, as it can lead to higher uptake of HIV testing. In terms of whether to provide testing to all pregnant women or to target testing to specific groups, universal testing even in settings with low HIV prevalence has been found to be cost-effective. A study that looked at one-time, universal testing in Vietnam found that this was very cost-effective approach (USD 125 per QALY gained) compared to targeted testing.[102]

In many settings, HIV testing is provided to women only at their first ANC visit. However, studies have also shown that rescreening pregnant women later in their pregnancy is cost-effective, particularly in areas with high HIV incidence and prevalence.[101,103] In settings with lower HIV incidence and prevalence, rescreening can also be cost-effective, but targeted rescreening may provide a more cost-effective alternative.[101]

Finally, one study in India assessed the cost-effectiveness of offering HIV screening at the primary healthcare level, which was a result of efforts to integrate the PMTCT component of its National AIDS Control Programme with the maternal and child health component of its National Rural Health Mission. The study found that this intervention increased the number of women screened for HIV and improved linkage to care at a cost of less than USD 1 per pregnant woman tested.[104] Together, this evidence underscores the health and economic benefits of providing good access to HIV testing services for pregnant women.

Use of ARVs for PMTCT

One of the early applications of using ARVs prophylactically was to prevent mother-to-child prevention of HIV. Over time the recommended approach for using ARVs for PMTCT has evolved (Table 7). Since 2013, the WHO has recommended Option B+—lifelong ART regardless of CD4 cell count or clinical stage for all HIV-infected pregnant and breastfeeding women—given the health benefits to the mother and for preventing HIV transmission both via pregnancy and sexually. In 2015, the WHO adopted Option B+ as the recommended approach for the use of ARVs for PMTCT.[38] Over the past few years, many countries have adopted Option B+, including Vietnam, which adopted this policy nationwide in 2016.[22]

Table 7. Options for giving ARVs to pregnant women and newborns (copied from WHO PMTCT guidelines[105])

	Mother receives		Infant receives
	Treatment (CD4 count ≤ 350 cells/mm^3)	**Prophylaxis** (CD4 count > 350 cells/mm^3)	
Option A	Triple ARVs as soon as diagnosed, *continued for life*	**Antepartum:** AZT starting as early as 14 weeks gestation	Daily NVP from birth through 1 week beyond complete cessation of breastfeeding; or, if not breastfeeding or if mother

[xxix] Routine testing refers to "provider-initiated HIV testing and counseling with the option to decline (opt-out)"[100]
[xxx] An "opt out" HIV testing approach is one where providers offer and provide an HIV test, unless a patient asks to not get tested.

	Mother receives		Infant receives
		Intrapartum: at onset of labor, sdNVP and first dose of AZT/3TC **Postpartum:** daily AZT/3TC through 7 days postpartum	is on treatment, through age 4–6 weeks
Option B	Triple ARVs starting as soon as diagnosed, continued for life	Triple ARVs starting as early as 14 weeks gestation and continued intrapartum and through childbirth if not breastfeeding or until 1 week after cessation of all breastfeeding	Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method
Option B+	Regardless of CD4 count, triple ARVs starting as soon as diagnosed, continued for life		Daily NVP or AZT from birth through age 4–6 weeks regardless of infant feeding method

Although the provision of lifelong ART requires a large investment, all studies that assessed the cost-effectiveness of Option B+ compared to no PMTCT or single dose nevirapine (sdNVP) found Option B+ to be cost-effective. When Option B+ was compared to Option B, some studies did not find Option B+ to be a cost-effective approach, but several studies did note that Option B+ may be easier to implement because CD4 testing is not necessary.[106,107,102]

One analysis examined scenarios with no PMTCT, Option A, Option B, and Option B+ in Vietnam.[5] This study found that Option B+ cost USD 9,834 per infant infection averted compared to Option A (assuming ART initiation at CD4 count less than 500 cells/mm^3). However, when sexually transmitted infections averted were incorporated in the same analysis, the study found that no PMTCT, Option A, and Option B cost more and were less effective in comparison to Option B+, which was found to be cost-saving. Thus, most studies suggest that Option B+ is cost-effective compared to other available options, especially when the full range of benefits are considered, including health benefits to the infant and mother, as well as averting other HIV transmissions.

3.9 Combination prevention

Most of the studies summarized above have focused on comparing a single HIV prevention intervention to the status quo. However, there is broad recognition that a combination prevention approach that integrates a variety of the interventions mentioned above is necessary to substantially reduce the number of new HIV infections.[108] While global evidence may be useful in informing the types of interventions to include in an HIV prevention package, the optimal combination of interventions will ultimately depend on many local factors such as the country's HIV epidemiological profile, available financial resources, sociopolitical issues, and more.

Several studies have examined the cost-effectiveness of different combinations of HIV prevention interventions (Appendix Table B8). Some studies have found that interventions that reduce the risk of PLHIV transmitting the disease are more cost-effective than interventions aimed at preventing

uninfected individuals from contracting HIV.[109,110] Many studies also found that, when possible, targeting interventions to high-risk groups could be a more cost-effective strategy, particularly for high-cost interventions like PrEP.[109–112] While PrEP is viewed as an important intervention for preventing new HIV infections, many studies found that unless PrEP were targeted to high-risk groups, it may not be cost-effective to add to a combination prevention strategy until other interventions have been included or scaled-up (as seen in Table 8). A study in South Africa found that a combination prevention package that included circumcision, screening, expanded ART, microbicides could offer 90 percent of the health benefits at less than 25 percent of the cost of providing the same package with PrEP.[108] Treatment as prevention (earlier ART initiation) was also shown to be a more cost-effective strategy compared to delayed ART—however, one study in South Africa did suggest that despite this, a combination of scaling-up guidelines-based ART[xxxi] and medical male circumcision could also achieve the same reduction in HIV incidence as TasP alone for USD 5 billion less over eleven years.[113]

Table 8. Optimal cost-effectiveness path from studies looking at combination prevention

Nigeria[114] **Serodiscordant couples**	**South Africa[111]** **Adult population**	**South Africa[108]** **Adult population**	**South Africa[112]** **Adult population**	
DALYs averted[xxxii] + Condom promotion + TasP + Short-term PrEP *Infections averted* + Condom promotion + Short-term PrEP + Replace short with long-term PrEP + TasP	+ Focused PrEP + Universal ART *Focused PrEP infeasible* + Universal ART + General PrEP	+ Circumcision (75%*) + Screening (annual) + Expanded ART (75%) + Microbicides (50%) and PrEP (50%)	*QALYs gained* + Expanded ART (40%) + Expanded ART (80%) + PrEP 15-24y (40%) + PrEP 15-24y (80%) + PrEP 15-54y (80%) *Infections averted* + Expanded ART (40%) + Expanded ART (80%) + Replace expanded ART with early ART (80%) + PrEP 15-24y (40%) + PrEP 15-24y (80%) + PrEP 15-54y (80%)	*Increasing budget* ↓

* Percentage in the parentheses indicates coverag

[xxxi] In this study, guidelines-based ART refers to the treatment of ART according to the WHO treatment guidelines (in this case, initiation of ART at CD4 <350 cells/mm^3 since the study was conducted in 2012).
[xxxii] DALYs and QALYs can capture health benefits both to uninfected and infected individuals, whereas using infections averted as the outcome measure captures benefits to uninfected individuals only. Thus, the optimal path of cost-effectiveness even within the same study may differ based on whether the health benefit is measured in infections averted or DALYs/QALYs.

Combination prevention in Vietnam

One of the identified studies assessed different implementation scenarios of a routine "test and treat" intervention combined with other HIV prevention interventions (guidelines-based ART, MMT, and condoms) in Can Tho province, Vietnam.[6] The most cost-effective strategy was annual testing and immediate treatment for key populations, along with the scale-up of MMT and condom use (coverage of 50 percent and 60-85 percent, respectively). This strategy was estimated to cost USD 78 per DALY averted and to reduce new infections by 81 percent compared to the status quo over 40 years. Implementing this strategy in Can Tho province would require an investment of USD 22.7 million over 40 years, but in comparison, maintaining the current set of interventions would cost USD 22.1 million. The same study also underscored the importance of leveraging existing synergies in successful implementing a "test and treat" approach, noting that "peer educators working for NSP and condom promotion would likely be the most effective agents who can directly reach key populations and facilitate early uptake of HIV diagnosis and treatment." It also called for the need to remove the social and structural factors that currently prevent key populations, particularly PWID, from accessing HIV services.

In 2014, VAAC developed an HIV investment case, which analyzed Vietnam's HIV epidemic and sought to 'identify priorities and solutions to increase the effectiveness, efficiency and sustainability of the national response to HIV.'[115] For this investment case, VAAC modeled five different scenarios to understand their costs and benefits. While the investment case did not calculate the cost-effectiveness of the different scenarios, it did find that a combination approach of harm reduction and other prevention interventions, along with scaling up the 'test and treat' approach would be most effective. Based on these results and other information gathered through stakeholder consultations, the investment case recommended prioritizing these interventions (particularly for key populations), along with increasing domestic funding, integrating and decentralizing HIV service delivery systems, and ensuring sufficient supply of HIV drugs and commodities.

Table 9. Scenarios modeled for Vietnam's HIV Investment Case (2014) [115]

Description of scenario	Total annual investment (in USD)	Total infections averted	Total saved (in USD)
Scenario 1: Baseline + adding 80% coverage of immediate treatment (at CD4<1000) for key populations and treatment at CD4<350 for other PLHIV.	61 million	87,177	4.6 billion
Scenario 2: Halfway to National Targets + 80% coverage of ART (at CD4<1000) for key populations, and treatment at CD4<350 for other PLHIV.	72 million	118,299	6.3 billion
Scenario 3: National Targets + 80% coverage of ART (CD4 <1000) for key populations.	83 million	135,655	7.2 billion
Scenario 4: National Targets + 80% coverage of ART (CD4 1000) for key populations and 80% of ART coverage at CD4<500 for other PLHIV.	88 million	137,385	7.3 billion
Scenario 5: National Targets + 80% treatment coverage for all at CD4<1000, 65% NSP coverage, 35% MMT coverage, and positive prevention for serodiscordant couples.	92 million	152,583	8.1 billion

Finally, another study conducted in Vietnam assessed the impact and cost-effectiveness Vietnam's HIV programs (ART and prevention programs) from 2006 to 2010.7 The study accounted for the following interventions – NSP and MMT for PWID; condoms for FSWs and their clients, as well as for MSM; and ART. Between 2006 and 2010, approximately USD 480 million was invested in HIV programs, which resulted in an estimated 34 percent reduction in new HIV infections. In comparison to a counterfactual scenario where these programs were absent, condom promotion programs for MSM were most cost-effective (USD 130 per DALY averted), followed by ART (USD 164 per DALY averted), condom promotion programs for FSWs and their clients (USD 302 per DALY averted), and NSPs for PWID (USD 1,493 per DALY averted).[xxxiii] When these interventions were considered together, they cost USD 238 per DALY averted, which the study notes is considered 'highly cost-effective' according to most willingness-to-pay thresholds.

Combination prevention for PWID

A few studies also looked at the cost-effectiveness of combination prevention in the context of preventing HIV infection among PWID, an important key population group in Vietnam. Two studies found that the optimal cost-effectiveness path involved starting with opioid substitution therapy, then adding expanded ART or early ART, and finally oral PrEP.[88,116] One study found the addition of PrEP to be very cost-effective in the Ukraine, while another study in the US did not find it to be cost-effective, most likely due to the higher annual PrEP costs and lower HIV prevalence among PWID.

These economic evaluations may raise useful considerations for efficiently prioritizing between different interventions under constrained resources, but one limitation to note is that most of these studies do not account for possible synergies and overlaps that may occur between programs.[88,108,117] Clinical trials and other research studies have only recently been undertaken to study the effectiveness of combination prevention.[117] Thus, information from these trials will allow for better cost-effective estimates of combination prevention in the future.

[xxxiii] Note: this study did not have sufficient information to calculate cost-effectiveness ratios for MMT.

4. CONCLUSIONS

The global evidence summarized in this report demonstrates that most HIV prevention interventions, implemented alone or in combination, are cost-effective or even cost-saving over time across a range of different settings. Efforts to reduce new infections of HIV will continue to be an important aspect of Vietnam's national HIV/AIDS response, and findings from this report show that investments in HIV prevention provide good value for money. While implementing many of these interventions require sizable upfront costs, the potential savings from averted infections will save Vietnam's health system the costs associated with providing lifelong ART. Moreover, several HIV prevention interventions have health and societal benefits beyond averting HIV infections, such as reducing other sexually transmitted diseases and drug overdoses. Thus, as Vietnam increasingly finances its HIV response with domestic resources, it will be important to define an HIV prevention package that is effective, efficient, and affordable and to ensure that the health system, in concert with other relevant actors, is able to sustainably finance and implement the interventions. Some final considerations for Vietnam include:

Table 10. Summary of considerations for Vietnam

Cost-effective interventions backed by global evidence and evidence from Vietnam	• ***Expanding the distribution and use of male condoms*** can not only reduce HIV infections, but also other sexually transmitted infections as well. • ***Methadone maintenance therapy*** will be an important intervention in reducing HIV incidence among PWID, as well as in supporting PWID to overcome their addictions. • ***Targeted rescreening of pregnant women for HIV*** (and even non-targeted rescreening) and ***Option B+*** can help avert HIV infections in infants and the pregnant women's sexual partners. • ***Combination prevention*** and tackling the issue of HIV prevention with different interventions is also a globally favored approach.
Cost-effective interventions backed by robust global evidence, but without specific evidence from Vietnam	• ***Expanding community-based HIV testing efforts and promoting routine testing for high-risk groups*** can help improve awareness of HIV status among PLHIV and prevent new infections. • ***Early ART initiation (i.e. expansion of ART eligibility guidelines)*** paired with systems to ensure adherence, retention in care, and early detection of virologic failure, will improve health outcomes among PLHIV and avert future HIV infections. • ***Needle-syringe programs*** are an important intervention to reduce HIV and other infections transmitted via injection drug use.
Interventions that are likely cost-effective, but could benefit from additional evidence	• ***Targeting Oral PrEP to high-risk individuals*** could be a cost-effective intervention, but further studies should incorporate the costs of identifying and retaining high-risk individuals, as this may diminish the cost-effectiveness of targeted oral PrEP. Data from the ongoing PrEP pilot program in Vietnam could help provide additional evidence to determine whether to include PrEP in the HIV prevention package. • ***Social-behavioral and structural interventions*** may be a cost-effective intervention, but these interventions are often context specific, so Vietnam should assess these important types of interventions with information from its own context (note: estimating the health impact due to these types of interventions alone is challenging).

	• ***Supervised injection facilities*** are an innovative, non-punitive intervention to promote safe injection drug use among PWID. However, opening a SIF in Vietnam (or other countries) may be a controversial decision.
Cost-effective interventions that may not be applicable to Vietnam	• ***VMMC*** is a cost-effective and even cost-saving strategy, but it is recommended for contexts with generalized HIV epidemics and low male circumcision rates.

While this report may inform the Government's decision on the composition and financing strategy for a package of HIV prevention services, it is important to recognize the limitations of this information. Global evidence is a useful input to the decision-making process, but determining the optimal package of HIV preventive services and advocating for HIV (and other) preventive services to be covered by SHI will require considerable consultation and additional evidence, including further economic analyses that are tailored to Vietnam's context and specific needs. Decisions around the HIV prevention package will also need to account for important non-financial factors as well, such as equity and implementation considerations (e.g., system readiness, sociopolitical context).

Vietnam has made great progress over the past several years in reducing the number new HIV infections. Dedicated efforts to create an effective and sustainable approach to financing HIV (and other health) prevention services will result in worthwhile health and economic benefits and help Vietnam to move towards zero new HIV infections.

APPENDIX A

The global evidence summarized in this report was identified through a search of journal articles published over the last five years (January 2012 through July 2017) in PubMed. Combinations of the following search terms were used to identify relevant articles published in English (Appendix Table A1).

Appendix Table A1: Literature review search terms

Categories	Search terms
Disease	HIV; AIDS; HIV/AIDS
Economic analysis	Cost-benefit; cost-effective; cost-utility; return on investment (ROI); economic analysis; impact and cost
Settings	Vietnam FSW; PWID; MSM
HIV prevention strategies	**General:** Prevention; combination prevention **Testing:** HIV testing and counseling; voluntary counseling and testing (VCT); **Condom distribution programs:** condom distribution; condom promotion; condom social marketing (CSM) **Structural and social interventions:** school-based education; abstinence education; information, education and communication (IEC); behavior change **Interventions for IDUs:** needle and syringe exchange; methadone maintenance treatment; opioid substitution therapy; harm reduction; **MTCT:** mother-to-child transmission (PMTCT); Option B+; feeding substitution; **Male circumcision**: male circumcision; voluntary medical male circumcision (VMMC) **ARVs for prevention:** treatment as prevention (TasP); pre-exposure prophylaxis (PrEP); post-exposure prophylaxis (PEP)

149 articles were identified through this search and 97 were included in the literature review. Articles were excluded for a variety of reasons including: focusing on experimental interventions (e.g. microbicides, long-acting PrEP), containing information only on health benefits (and not costs) or focusing on very specific interventions (e.g., HIV/STI/hepatitis intervention for young men leaving prison). A few articles were also excluded due to quality issues, as well as difficulty in accessing the articles. A summary of the articles reviewed is described in Appendix Table A2 below, and details of most studies is contained Appendix B.

Appendix Table A2: Summary of articles reviewed

Intervention	Countries/regions and number of articles from the setting
HIV testing (15 studies)	*General* • US (1) *HIV testing modalities* • Indonesia (1) • South Africa (3) • US (3) • Zimbabwe (1) *Frequency of HIV testing* • India (1) • UK (1) • US (2) *Partner notification* • Malawi (1) • Netherlands (1)
Treatment as prevention (4 studies)	• India (1) • South Africa (1) • US (1) • Multi-country – India and South Africa (1)
Oral pre-exposure prophylaxis (14 studies, 2 systematic reviews)	*Oral PrEP for MSM* • Australia (1) • Canada (2) • Netherlands (1) • Peru (1) • US (4) *Oral PrEP for high risk-groups* • US (1) *Oral PrEP for serodiscordant couples* • Uganda (1) *Oral PrEP for general population* • Zambia (2) • Sub-Saharan Africa - 42 countries (1)
Voluntary Male Medical Circumcision (10 studies)	• Malawi (1) • South Africa (2) • Tanzania (2) • Uganda (1) • Zambia (1) • Zimbabwe (1) • Sub-Saharan Africa – 4 countries (1) • Sub-Saharan Africa – 13 countries (1)
Condoms (5 studies)	*Male condoms* • US (2) • Global - 81 countries (1)

Intervention	Countries/regions and number of articles from the setting
	Female condoms • US (1) • Sub-Saharan Africa – 13 countries (1)
Social-behavioral and structural interventions (4 studies, 1 commentary, 1 systematic review)	• Benin (1) • Canada (1) • India (1) • Zimbabwe (1)
Harm reduction (12 studies, 1 systematic review)	*Needle and syringe programs* • Australia (1) • US (1) *Opioid substitution therapy* • Indonesia (1)Vietnam (2) *Behavioral interventions for PWID* • Mexico (1) • US (1) *Supervised injection facilities* • Canada (4) • US (1)
Prevention of mother-to-child transmission (PMTCT) (12 studies, 3 systematic reviews)	*ROI analysis of PMTCT program* • US (1) *HIV testing in pregnant women* • Haiti, Kenya, Namibia, Vietnam (1) • India (2) • Uganda (1) *ARVs for PMTCT* • Malawi (2) • Ghana (1) • Kenya, South Africa, Vietnam, Zambia (1) • Zambia (1) • Zimbabwe (1) • Uganda (1)
Combination prevention (13 studies)	*Combination prevention for general adult population* • Nigeria (1) • South Africa (4) • US (2) • Vietnam (3) *Combination prevention for PWID* • China (1) • Ukraine (1) • US (1)

APPENDIX B

Appendix Table B1: HIV testing

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
HIV testing modalities						
Indonesia[25]	Compared scale up of VCT at community levels to current practice (60% testing at hospitals)	20 years	**HIV prevalence:** 2% (MSM); 3% (indirect FSW); 12% (FSW); 43% (PWID) **VCT cost:** USD 15-69	Scaling up VCT at community levels reduces overall prevalence by 36% over 20 years.	**ICER:** Scale up of community-based VCT costs USD 248 per HIV infection averted and USD 9.17 per DALY averted *Excluded financial and budgetary impacts of increased need for ART	**Threshold:** WHO recommended WTP thresholds Scale up of community-based VCT is very cost-effective compared with the status quo.
South Africa[26]	Compared ART coverage with home HTC every 5 years (with different ART initiation criteria) to baseline ART coverage	10 years	**HIV prevalence:** 32% **HIV transmission factor for persons with acute HIV infection:** 26 **Home HTC cost:** USD 8-22 **Monthly ART costs:** USD 57	Providing home HTC every 5 years and linkage to care with ART initiation at CD4 ≤350 cells/mm^3 or viral load >10,000 copies/mL decreases HIV incidence by 68% compared with no ART scenario.	**ICER:** Home HTC with ART if CD4 ≤350 cells/mm^3 and/or viral load >10,000 copies/mL was less costly and more effective than the other HTC strategies and cost USD 2,960 per infection averted compared to the baseline ART coverage scenario. Home HTC with ART if CD4 <350 cells/μL and/or viral load >10,000 copies/mL cost USD 1,710	**Threshold:** WHO recommended WTP thresholds Home HTC with expanded ART initiation eligibility is cost-effective compared with Home HTC with current ART eligibility.

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
					per QALY gained compared with Home HTC with ART if CD4 ≤500 cells/ mm^3 Home HTC with ART if CD4 ≤500 cells/ mm^3 cost USD 900 per QALY gained compared with Home HTC with ART if CD4 ≤350 cells/mm^3 Home HTC with ART if CD4 ≤350 cells/mm^3 cost USD 860 per QALY gained compared with baseline ART coverage	
South Africa[28]	Compared home HTC every four years (with different ART initiation criteria) with status quo of facility-based testing	10 years	**Home HTC cost:** USD 9-23 **Facility based testing cost:** USD 20 **Monthly ART costs:** USD 47	Introducing home HTC in addition to current practice would decrease HIV associated morbidity by 10-22% and HIV infections by 9-48% (depending on ART initiation criteria).	**ICER:** Compared with the status quo, Home HTC cost between USD 1,020-1,300 per DALY averted depending on ART initiation criteria.	**Threshold:** WHO recommended WTP thresholds Home HTC under all ART initiation criterion (including universal test and treat) is considered very cost effective.
South Africa[27]	Compared one-time mobile HIV testing to current medical facility-based testing	Lifetime	**HIV prevalence:** 6.6% (of previously undiagnosed individuals)	Introducing one-time mobile HIV test would increase life expectancy from 132.2 to 140.7 months.	**ICER:** Compared with facility-based testing, mobile testing unit cost USD 2,400 per year of life saved	**Threshold:** WHO recommended WTP thresholds

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			Linkage to care: 31-58% (depends on CD4 count and gender) **Mobile HIV test:** USD 29-31 **Facility based testing:** USD 9-14 **Monthly ART costs:** USD 13-40	5-year survival with facility-based testing is 53% and 59% with mobile testing.		Home HTC under all Mobile unit testing is considered very cost-effective compared to facility-based testing.
US[118]	Compared routine and targeted testing at clinics, hospitals, and community-based organizations	1 year	**HIV prevalence:** 2.4% **HIV transmission rate:** 2.72-10.20% (depends on awareness of HIV status)	Targeted testing averted 17.78 transmission per year, while routine testing averted 34.30 transmissions	**Cost per averted transmission:** Routine HIV testing – USD 29.903 (CBO); USD 135,228 (clinic); USD 60,542 (hospital) Targeted HIV testing – USD 32,946 (CBO); USD 35,187 (clinic)	N/A
US[29]	Compared five different testing strategies to existing practice among MSM in 16 cities: 1) venue-based testing (VBT); 2) couples VCT; 3) social network strategy; 4) at home testing; and 5) large scale testing events	9-15 months	**HIV transmission rate (per 100 people):** 1.41-7.3 (depends on awareness of HIV status)	Venue based testing averted 47,532 new infections over 15 months across 15 cities	**Cost per QALY gained:** VBT was cost-saving in all cities	**Threshold:** <USD 100,000 per QALY gained for cost-effectiveness; <USD 20,645 per new HIV diagnosis
US[30]	Compared three HIV testing strategies: 1) off-site testing referral; 2) on-site rapid testing in	Lifetime	**Prevalence of undetected HIV infection:** 0.45%	Compared to no intervention, interventions increase life expectancy by:	**ICER:** Off-site testing was less efficient compared to	**Threshold:** <USD 100,000 per QALY gained

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
	community-based substance abuse treatment programs with information only (no counseling); 3) on-site rapid testing with risk reduction counseling		**HIV test acceptance:** Offsite – 24%; Onsite with risk reduction counseling – 81%; Onsite with information – 86% **Receipt of test results:** Offsite – 76%; Onsite with risk reduction counseling – 98%; Onsite with information – 99% **Linkage to care:** Offsite – 18%; Onsite with risk reduction – 85%; Onsite with counseling – 80%) **Cost of intervention:** Offsite – USD 35; Onsite with information – USD 46; Onsite with counseling – USD 85 **Monthly ART costs:** USD 1,740-4,000	- Off-site testing: 0.8 years - On-site testing with risk reduction counseling: 3.4 years - On-site testing with information: 3.7 years	offering on-site testing with information One-time, onsite testing with information costs USD 60,300 per QALY gained compared to no intervention	One-time, on-site testing with information only is cost-effective.
Zimbabwe[31]	Compared self-testing to provider-delivered HIV testing and counseling	20 years	**Provider delivered HTC:** USD 9-25 **Self-test cost:** USD 3	Self-testing can avert 7,00 DALYs over 20 years if self-testing is introduced	Over 20 years, introduction of self-testing would lead to savings in healthcare costs of USD 75 million and avert 7,000 DALYs	Examined a range of cost-effective thresholds (USD 0 – 10,000) Self-testing was preferred intervention under most scenarios modeled.
Frequency of HIV testing						

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
India[32]	Compared current testing practices, one-time testing, testing every 5 years, and annual testing to the following population groups: 1) general population; 2) high prevalence districts; and 3) high risk groups	Lifetime	**HIV prevalence:** 0.29% (general population); 0.8% (high prevalence districts); 5% (high risk groups) **HIV incidence (per 100 PY):** 0.032 (general population); 0.088 (high prevalence districts); 0.552 (high risk groups) **HIV transmission rate** (per 100 PY): 0.16-9.03 (depends on viral load) **Linkage to care:** 50% **HIV test cost (rapid):** USD 3.33 **Monthly ART costs:** USD 9-55 (ART initiation ≤350 cells/mm^3)	One-time screening resulted in the following decrease in transmissions: 2.5% (general population); 2.4% (high prevalence districts); <1% (high risk) over 6 years	**ICER:** Screening every 5 years among the general population costs USD 1,900 per year of life saved Annual screening among high prevalence districts costs USD 1,900 per year of life saved and USD 1,800 per year of life saved among high risk groups. *Estimates did not account for additional prevention associated with expanded testing.	**Threshold:** WHO recommended WTP thresholds Screening every 5 years among the general population and annually among high prevalence districts and high-risk groups is cost-effective compared to current practice.
UK[119]	Compared universal and targeted high-risk testing (MSM, PWID, and people from HIV endemic countries) at different frequencies to the status quo	10 years	**HIV prevalence:** 0.033% (general population); 1.2% (PWID); 2.5-5% (people from HIV endemic countries); 5% (MSM) **HIV transmission probability per partnership:** 2-40% (depends on gender, sexual orientation, drug use, and stage of HIV) **Fraction starting ART at CD4 ≤350 cells/mm^3:** 6% (PWID); 22% (people from HIV	Annual testing of all adults could avert 5% of new infections (up to 18% if risky behaviors are halved) Annual testing to high risk groups and one-time testing for all other adults could prevent 4-15% of new infections	**ICER:** Annual universal testing costs GBP 80,300 per QALY gained compared to the status quo. Annual high-risk testing and one-time testing for other adults costs GBP 17,500 per QALY gained compared to the status quo.	**Threshold:** UK CE threshold of GBP <20,000 – 30,000 Annual universal testing is not cost-effective. Annual high-risk testing and one-time testing for other adults is cost-effective.

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			endemic countries); 46% (MSM); 23-75% (other adults) **HIV test cost:** GBP 8 **Monthly ART costs:** GBP 1,190			
US[34]	Determined the optimal testing frequency for different risk groups. Compared the optimal policy with one-time (for low risk) and annual (for high risk) testing frequency.	Lifetime	**HIV incidence:** 0.01% (low risk); 0.1% (moderate risk); 1% (high risk) **Linkage to care:** 100% **HIV test cost:** USD 14	Not specified separately from ICER	**ICER:** Testing every 2.4 years costs USD 36,342 per QALY gained compared to one-time testing for low risk groups. Testing every 3 months costs USD 45,074 per QALY gained compared to annual testing for high risk groups.	N/A – testing frequencies optimized based on cost-effectiveness threshold of USD 168,904 per QALY gained
US[33]	Compared testing at 3- and 6-month intervals with annual testing using fourth generation and rapid tests in MSM and PWID.	1 year	**HIV incidence:** 0.62% (PWID); 1.27% (MSM) **HIV transmission rate (per person year):** 0.003-1.146 (depends on awareness of status and stage of HIV) **Percent viral suppression:** 36% (PWID); 42% (MSM) **Rapid HIV test cost:** USD 23-98 **Fourth generation test cost:** USD 11-75 **Lifetime HIV test costs:** USD 417,000	Compared to annual testing, use of fourth generation test every 3 or 6 months can avert between 2-3.20 new infections in a cohort of 10,000 MSM Compared to annual testing, use of rapid test every 3 or 6 months can avert between 1.75-2.66 new infections in a cohort of 10,000 MSM Compared to annual testing, use of fourth generation test every 3 or 6 months can avert between 0.39-	**ICER:** For MSM, testing every 3-months using a rapid test compared to testing every 6 months cost USD 48,000) per QALY gained. All other scenarios were cost-saving. For PWID, testing every 6-months using a fourth-generation test compared to annual testing cost USD 133,200 per QALY gained. All other scenarios cost > USD 150,000 per QALY gained.	**Threshold:** <USD 100,000 per QALY gained For MSM, HIV testing was cost saving or cost-effective for all scenarios. For IDU, testing every 6 months compared with annual testing using a fourth-generation test was just above the cost-

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
				0.60 new infections in a cohort of 10,000 PWID Compared to annual testing, use of rapid test every 3 or 6 months can avert between 0.35-0.50 new infections in a cohort of 10,000 PWID		effectiveness threshold, other scenarios were not cost-effective.
Partner notification						
Malawi[35]	Compared three partner notification strategies: 1) provider notification (provider tried to notify locatable partners); 2) contract notification (index partner given 1 week to notify partners, after which provider attempts to contact); 3) passive referral (index encouraged to notify partners, standard of care)	1 year	**Probability of partner return:** - Provider notification: 51% - Contract notification: 18-33% - Passive referral: 24%	Based on 5,000-person cohort, contract and provider notification averted 27.5 and 27.9 new infections, respectively, compared to passive referral over one year	**ICER:** Compared to passive referral, contract notification cost USD 3,560 per infection averted Compared to contract notification, provider notification cost USD 51,421 per infection averted	N/A
Netherlands[36]	Compared use of an online partner notification to identify 5-20% of new diagnoses versus no partner notification among MSM	5-20 years (in 5-year increments)	**Percent of MSM diagnosed with CD4 count ≤350 cells/mm³:** 37% **Outpatient visit for partner notification:** EUR 124	Partner notification can reduce 18 (5% identification of all new diagnoses) to 69 (20% identification) new infections over 5 years Partner notification can reduce 221 (5% identification of all new	**ICER:** Introducing online partner notification costs between EUR 41,716 to 5,887 per QALY gained (with 5% identification, and treatment initiated at <500 cells/mm³)	N/A

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
				diagnoses) to 830 (20% identification) new infections over 20 years	If treatment is initiated immediately, partner notification costs between 41,065 to 5,719 per QALY gained over 5 to 20 years	

Appendix Table B2: Treatment as Prevention

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
India[40]	Compared two early ART initiation scenarios (initiation above CD4 > 350 cells/mm^3) with delayed ART initiation	20 years	**On ART reduction in rate of transmission:** 93% **Percent tested in past 12 months (realistic scenario):** 3-32% **Percent newly diagnosed linked to care (realistic scenario)**: 55-80% **Rate of loss-to-follow up annually:** 0.16-0.195 **Annual cost of ART:** USD 133-329	Early ART can result in 18-38% reduction in new infections depending on optimistic vs. realistic engagement in HIV care	**ICER:** With optimistic engagement in HIV care, early ART cost USD 442 per QALY gained compared to delayed initiation. With realistic engagement in HIV care, early ART cost USD 530 per QALY gained.	**Thresholds:** WHO recommended WTP thresholds Early ART (under both HIV care engagement scenarios) is considered very cost-effective
India and South Africa[41]	Compared early initiation of ART (initiation at CD4 ≤350-550 cells/mm^3) with delayed ART (initiation above CD4 ≤250 cells/mm^{3}L) in serodiscordant couples	5 years and lifetime	**Number of transmissions (per partner per 100 person years) – viral suppression:** 0.010 **Number of transmissions (per partner per 100 person years) – no viral suppression:** 1.48 **Rate of loss to follow up (# per 100 person year):** 3.4 **Annual cost of ART:** USD 135-561	Early ART can result in 66% reduction in new infections over 5 years and 13% reduction over a lifetime compared to delayed ART	**ICER:** Over 5-years, early ART cost 1,800 per life-year saved compared to delayed ART in India Over lifetime, early ART cost USD 530 per life-year saved compared to delayed ART	**Thresholds:** WHO recommended WTP thresholds Early ART is cost effective over 5 years and very cost-effective over a lifetime in India
			Number of transmissions (per partner per 100 person years) – viral suppression: 0.010	Early ART can result in 69% reduction in new infections over 5 years and 13% reduction over a lifetime compared to delayed ART	**ICER:** Over 5-years, early ART was cost-saving compared to delayed ART in South Africa	Early ART is cost saving over 5 years and very cost-effective over a

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			Number of transmissions **(per partner per 100 person years) – no viral suppression:** 1.48 **Rate of loss to follow up (# per 100 person year):** 3.4 **Annual cost of ART:** USD 153-520		Over lifetime, early ART cost USD 590 per life-year saved compared to delayed ART	lifetime in South Africa
South Africa[42]	Compared four ART initiation scenarios: 1) CD4 count ≤200 cells/mm^3 (current practice); 2) CD4 count ≤350 cells/mm^3; 3) CD4 count ≤500 cells/mm^3; 4) all CD4 levels	5 and 40 years	**On ART reduction in rate of transmission:** 92% **Annual cost of ART:** USD 188-595	Expanding ART initiation to CD4 ≤350 cells/mm^3 can prevent 17% and 15% of new infections over 5 and 40 years, respectively compared to current practice Expanding ART initiation to all CD4 levels can reduce 45% of new infections over 40 years	**Net savings:** Compared to current practice, cumulative undiscounted cost savings of USD 7.2, 17.3, and 28.7 billion for ART initiation at CD4 count ≤350 cells/mm^3, ≤500 cells/mm^3, and all CD4 levels, respectively over 40 years	N/A
US[120]	Estimated the effects of early ART initiation on HIV incidence in the US between 1996 and 2009	13 years	**On ART reduction in rate of transmission:** 90%	Early ART averted 188,000 new infections between 1996 and 2009. 4/5 of infections were averted when ART initiation was CD4 ≥500 cells/mm^3 Without early ART, new infections during this period would have been 25 percent higher	Loss in life expectancy avoided through all prevented cases is worth USD 128 billion (if each life year is worth UD 150,000) Benefit of each prevented case of HIV is USD 678,000 (if each of the 4.5 life years saved is worth USD 150,000)	N/A

Appendix Table B3: Oral PrEP

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Population group: MSM						
Australia[53]	Compared the following strategies to no PrEP: 1) PrEP for all MSM; 2) targeted PrEP for MSM with multiple sexual partnerships; 3) targeted PrEP for discordant partnerships	10 years	**Background HIV prevalence:** 10% **PrEP coverage:** 10-30% (general); 15-30% (high risk and discordant partnerships) **Duration on PrEP:** 5 years or until HIV diagnosis **PrEP effectiveness:** 95% (efficacy); 75% (adherence) **Annual PrEP drug costs:** AUD: 9,505	Use of PrEP for 10-30% of all MSM can result in 9 to 30% reduction in HIV infections	**ICER:** AUD >400,000 per QALY gained compared with no PrEP	**Thresholds:** Australian cost-effective thresholds (not specified) Use of PrEP for all MSM and for high risk MSM not considered to be cost-effective compared to no PrEP.
				Targeted PrEP for MSM with multiple sexual partners resulted in 3 to 22% reduction in HIV infections	**ICER:** AUD >100,000 per QALY gained compared with no PrEP	
				Targeted PrEP for MSM in discordant relationships resulted in 7 to 15% reduction in HIV infections	**ICER:** AUD 8,399 to 11,575 per QALY gained compared with no PrEP	
Canada[121]	Compared the following strategies to no PrEP use: 1) PrEP to all MSM; 2) PrEP to highest risk decile; 3) increasing PrEP effectiveness; 4) varying HIV test frequency in susceptible individuals on PrEP	20 years	**PrEP coverage:** 25-100% **PrEP effectiveness:** 44% **Annual PrEP drug costs:** USD 10,012	Use of PrEP for all MSM can avert 1,970 to 4,581 infections	**ICER:** 500,000 to 800,000 CAD per QALY gained compared to no PrEP	**Thresholds:** <20,000 to 100,000 CAD per QALY gained PrEP for all MSM not cost-effective compared to no PrEP
				Targeted PrEP for highest risk MSM can avert 1,116 to 3,012 infections	**ICER:** 35,000 to 70,000 CAD per QALY gained compared to no PrEP	Targeted PrEP for high risk MSM is cost effective compared to no PrEP

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
				PrEP for highest risk MSM (25% coverage) and high PrEP effectiveness (99%) can avert 1,540 infections	**ICER:** 15,000 CAD per QALY gained compared to no PrEP	Highly effective, targeted PrEP for high risk MSM is cost-effective compared to no PrEP
Canada[60]	Compared 1 year of 'on-demand' PrEP to 35.2 years of infection (proxy for lifetime) with varying ART costs	Lifetime	**Duration on PrEP:** 1 year **Annual PrEP drug (and associated) costs:** USD 12,001	Incremental benefits of PrEP compared to HIV infection in QALYs ranged from 2.86-16.99 (depending on discount factor)	**ICER:** 'On-demand' PrEP strategy is cost-saving relative to lifetime costs of treating HIV infection even in the 'expensive' scenario (for annual ART costs) when discount rate is 0% and 3%	**Threshold:** < EUR 20,000/QALY gained
Netherlands[54]	Targeted PrEP to 10% of highly sexually active MSM and compared two strategies to no PrEP: 1) daily PrEP and 2) on-demand PrEP	40 years	**Background HIV prevalence:** Calibrated to Dutch HIV epidemic among MSM **Duration on PrEP:** 5 years or until HIV diagnosis **PrEP effectiveness:** 80% **Annual PrEP drug (and associated) costs:** EUR 7,400 (daily); EUR 3850 (on-demand)	PrEP can avert 1,400 to 2,500 infections depending on PrEP effectiveness (in context of a stable HIV epidemic)	**ICER:** EUR 11,000/QALY gained when used daily or EUR 2,000/QALY gained when used on-demand compared to no PrEP	**Threshold:** < EUR 20,000/QALY gained Daily and on-demand PrEP is cost-effective compared to no PrEP
Peru[51]	Compared various PrEP implementation scenarios to no PrEP (study also included transwomen)	10 years	**PrEP coverage:** 20% **PrEP effectiveness:** 92% (efficacy); 15-95% (adherence) **Annual PrEP drug costs:** USD: 420-600	Coverage of 5%, prioritizing highest risk groups, can avert about 8% of new infections over 10 years	ICER: Scenario with highest cost per DALY averted was USD 1,036 to 4,254 (uniform PrEP coverage at 20%)	**Threshold:** WHO recommended WTP thresholds PrEP is cost-effective compared to no PrEP under all modeled scenarios, but most cost-effective when

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
						prioritized highest risk groups.
US[50]	Compared 1-year duration of PrEP intervention to no PrEP scenario	Lifetime	**Background HIV prevalence:** 19% **Duration on PrEP:** 1 year **PrEP effectiveness:** 56% **Annual PrEP drug costs:** USD 10,711	QALYs gained: - Low adherence: 4.02 - Moderate adherence: 5.53 - Moderate adherence (with moderate HIV prevalence): 10.24 - High adherence: 11.6	**ICER:** One-year of daily PrEP costs 64,000 per QALY gained compared to no PrEP	**Threshold:** < USD 100,000 per QALY gained One-year of daily PrEP is cost-effective compared to no PrEP
US[122]	Compared different test and treat and PrEP strategies to no PrEP scenario	Lifetime	**Background HIV prevalence:** 24% **PrEP coverage:** 25% **PrEP effectiveness:** 44% (efficacy); 28% (adherence) **30-day supply of PrEP:** USD 776	PrEP + test and treat strategy can avert 59% of new infections compared to no PrEP	**ICER:** Compared to no PrEP, PrEP + test and treat strategy costs USD 27,863 per QALY gained *Model also captured secondary infections	**Threshold:** < USD 150,000 per QALY gained PrEP + test and treat is cost-effective compared to no PrEP
US[55]	Compared various PrEP scenarios to no PrEP	Lifetime	**Background HIV prevalence:** 19% **Duration on PrEP:** 1 year **PrEP effectiveness:** 44% (efficacy) **Annual PrEP drug costs:** USD 9,312	For base case PrEP scenario, need to treat 64 people to avert one infection	**ICER:** Compared to no PrEP, PrEP to general MSM population costs USD 160,000 per QALY gained	**Threshold:** < USD 100,000 per QALY gained PrEP is not cost-effective compared to no PrEP

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
US[49]	Compared different coverage rates (20, 50, 100%) of PrEP to no PrEP	20 years	**Background HIV prevalence:** 12% **PrEP coverage:** 20-100% **Duration on PrEP:** 20 years **PrEP effectiveness:** 95% (efficacy); 75% (adherence) **30-day supply of PrEP:** USD 776	PrEP can result in 13% reduction in new infections if initiated in 20% of MSM compared to no PrEP	**ICER:** Compared to no PrEP, ICER ranged from USD 172,090 to 216,480 per QALY gained as PrEP coverage increased PrEP costs USD 52,443/QALY gained for high risk MSM (avg. 5 annual partners)	**Threshold:** <USD 100,000 per QALY gained (not explicitly used in study) If threshold above is applied, PrEP for the general population is not cost-effective compared to no PrEP, but targeted PrEP to high risk MSM is cost-effective
Population group: Other high-risk groups						
US[110]	Compared different PrEP prioritization strategies among all MSM, high-risk MSM, high-risk heterosexuals, and PWID	20 years	**PrEP coverage:** 50% **Duration on PrEP:** 20 years **PrEP effectiveness:** 44% reduction in HIV transmissions **Annual cost of PrEP intervention:** USD 9,672	Compared to no PrEP, prioritized PrEP can result in the following reductions in new infections: - MSM: 19% - High risk MSM: 15% - High risk heterosexuals: 5% - PWID: 2%	**ICER:** Compared to no PrEP, cost-per-infection-averted for prioritization to: - MSM: USD 2.1 million - High risk MSM: 1.1 million - High risk heterosexual: 43 million - PWID: 9 million	N/A
Population group: Serodiscordant couples						
Uganda[123]	Compared ART and PrEP for 90% of high risk serodiscordant couples to current ART coverage	10 years	**ART and PrEP coverage:** 90% of high risk serodiscordant couples **PrEP effectiveness:** 96% (efficacy)	Targeted PrEP and ART scale-up to high risk serodiscordant couples can avert 43% of new infections compared to the status quo	**ICER:** Compared to status quo, targeted PrEP and ART scale-up to high risk serodiscordant couples costs USD 1,340 per	**Threshold:** WHO recommended WTP thresholds Scale-up of ART and use of PrEP as a

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			Duration on PrEP: 6 months **Annual PrEP intervention costs:** USD 408 (research study scenario); 92 (MOH scenario)		infection averted and USD 5,354 per DALY averted	bridge for sustained ART use in serodiscordant couples is cost-effective compared to the status quo
Population group: General population						
42 Sub-Saharan African countries[56]	Compared PrEP to status quo (pre-existing levels of male circumcision and ART)	5 years	**PrEP coverage:** 10% **PrEP effectiveness:** 68% (efficacy); 80% (adherence) **Duration on PrEP:** 5 years **Annual PrEP drug and test costs:** USD 200	Over 5 years, 390,000 new HIV infections can be prevented in sub-Saharan Africa (24% in South Africa alone)	**ICER:** Compared to status quo, PrEP cost between USD 500 per DALY averted (Lesotho) to USD 44,600 per DALY averted (Eritrea)	**Threshold:** WHO recommended WTP thresholds Only cost-effective in countries with high HIV burden and low levels of male circumcision
Zambia[124]	Compared ART initiation at CD4 count ≤500 cells/ mm^3 and PrEP (nonprioritized or prioritized to most sexually active) to status quo (ART initiation at CD4 count ≤350 cells/ mm^3)	40 years	**PrEP coverage:** 5-15% (prioritized); 40-60% (nonprioritized) **PrEP effectiveness:** 20-60% **Annual PrEP drug and test costs:** USD 134	Compared with the baseline, prioritized PrEP and treatment at CD4 count ≤350 cells/ mm^3 can avert 16% of new infections. Nonprioritized PrEP and treatment at CD4 count ≤500 cells/ mm^{3}can avert 59% of new infections.	**ICER:** Compared to ART initiation at CD4 ≤500 cells/ mm^3, nonprioritized PrEP and treatment at CD4 count <500 cells/μL costs USD 5,861 per QALY gained. All other scenarios were weakly or strongly dominated compared to ART initiation at CD4 count <500 cells/μL.	**Threshold:** WHO recommended WTP thresholds Compared to ART initiation at CD4 count ≤500 cells/ mm^3, nonprioritized PrEP and treatment at CD4 count ≤500 cells/ mm^3 is borderline cost-effective

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Zambia[57]	Compared two PrEP strategies to scenario with no PrEP (ART initiation at CD4 count 350 cells/μL): 1) Prioritized PrEP to half of the most sexually active individuals; 2) PrEP to 40-60% of the total population	10 years	**Background HIV prevalence:** 7.7% **PrEP coverage:** 5-15% (prioritized); 40-60% (nonprioritized) **PrEP effectiveness:** 20-60% **Annual PrEP drug cost:** USD 194	Compared with the baseline, prioritized PrEP can avert 31% new infections. Nonprioritized PrEP can avert 23% of new infections.	**ICER:** Compared to status quo, prioritized PrEP cost USD 323 per QALY gained and was less costly and more effective than the prioritized PrEP strategy.	**Threshold:** WHO recommended WTP thresholds Compared to the status quo, prioritized PrEP is very cost-effective

Appendix Table B4: Voluntary medical male circumcision

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
12 VMMC priority countries in sub-Saharan Africa and Nyanza Province, Kenya[64]	Estimated the cost per infection averted for VMMCs conducted through 2014. Assumed countries achieved 90-90-90 treatment goals.	25 years	**Cost of VMMC:** USD 132	Among 240,000 projected HIV Infections averted over 25 years due to VMMC performed through 2014 in 13 priority countries: – Age 10-14: 20% of infections averted – Age 15-19: 32% of infections averted – Age 20-24: 26% of infections averted – Age 25-29: 11% of infections averted – Age 30 and above: 10% of infections averted	**ICER:** Cost per HIV infection averted ranged from USD 1,300 in Swaziland to USD 22,000 in Rwanda Median cost per HIV infection averted was USD 4,400 For 10 of 13 countries, cost per HIV infection averted was less than USD 7,000	Same range as cost per infection of scaling up ART (USD 5,500 – 8,375); Option B+ (USD 6,000-23,000)
Malawi[125]	Compared scenario where VMMC is not scaled up over baseline levels to scenarios including: 1) Scaling VMMC coverage to 60% by different age groups; 2) Scaling VMMC coverage to 60% by geographic areas; 3) Scaling VMMC coverage to 60% by urban vs. rural. Scenario reflecting country's initial target of 80% coverage also modeled	15 years	**Coverage of VMMC:** 60-80% **Cost of VMMC:** USD 100 **Annual cost of ART:** USD 451	Circumcising males ages 10-29 would avert 75% of HIV infections compared to current strategy of circumcising males 15-49 Circumcising males ages 10-34 would avert 88% of HIV infections compared to current strategy of circumcising males 15-49	**ICER:** Scaling up VMMC to 60% coverage costs between USD 176-268 per DALY averted (varies by different target age groups – most cost-effective strategy is to target men 15-49) compared to baseline scenario Scaling up VMMC to 60% coverage costs between USD 140-1,143 per DALY averted (varies by different geographic areas) compared to baseline scenario	**Threshold:** WHO recommended WTP thresholds Cost-effective and cost-saving (compared to cost of lifetime ART)

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
					Circumcising men in urban areas costs USD 120 per DALY averted and USD 355 in rural areas per DALY averted compared to baseline scenario.	
South Africa[126]	Estimated the impact of scaling up VMMC to 80% VMMC coverage by age group compared to baseline scenario	15 years	**Cost of VMMC:** USD 125 **Annual cost of ART:** USD 377	Scaling up VMMC to 80% coverage among males 20-24, 25-29, and 30-34 achieves the greatest reduction in HIV incidence over 5 years Great reduction in HIV incidence over 15 years achieved by circumcising 80% of men ages 15-19 and 20-24 Scaling up VMMC to 80% coverage to men ages 10-34 averts 84% of HIV infections averted	When unit costs are uniform across all age groups, men ages 15-34 are the most cost-effective group to target When costs increase with client age, men ages 15-29 year are the most cost-effective age group	VMMC cost saving compared to lifetime treatment of ART, except in Gauteng province (with VMMC unit cost of USD 225)
South Africa[62]	Estimated the impact over time and across the population of circumcising one male individual at a specific age in a specific year		**VMMC effectiveness:** 60% reduction in acquiring HIV **Cost of VMMC:** USD 52 (infant) – 104 (adult) **Annual cost of ART:** USD 267-531	Circumcising one man up to age 20 prevents 0.2 HIV infections (on average)	**ICER:** Circumcising one male between age 10 and 20 costs USD 450-478 per infection averted **Net savings:** Circumcising one man at age 20 saves USD 617 **Financial rate of return:** Circumcising one male at age 25 yields 14.5% rate of return	N/A

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Tanzania[66]	Compared scenario with baseline levels of VMMC with those that targeted 80% VMMC coverage over a 4-year period	15 years	**Cost of VMMC:** USD 83 **Annual cost of ART:** USD 145	Over 5 years, circumcising males 20-24, 25-29, and 30-34 is projected to result in greatest reduction in HIV incidence Over 15 years, circumcising males 10-14, 15-19, and 20-24 projected to result in greatest reduction in HIV incidence	**ICER:** Circumcising males ages 20-24, 20-29, of 30-34 would achieve lowest cost per infection averted compared to circumcising males ages 10-49	N/A
Tanzania[127]	Estimated the costs and impact of a scaled up VMMC program	15 years	**Average unit cost of VMMC:** USD 47	Scale up of VMMC to 88% coverage can avert approximately 23,000 new infections between 2010-2015 and 157,500 infections from 2016-2025	**ICER:** VMMC scale up between 2010-2015 costs USD 11,300 per infection averted and USD 3,200 between 2010-2025	
Uganda[67]	Compared four scale-up strategies to reach 80% VMMC coverage compared to a baseline scenario, also accounted for benefits for reduction in sexually transmitted infections and modeled impact on accounting for both males and females	5 and 25 years	**HIV prevalence among males, ages 15-59:** 0.3-9.3% **Baseline male circumcision prevalence:** 23.6% **Cost of VMMC:** USD 17-42 **VMMC efficacy in reducing HIV incidence:** 50%	Increasing VMMC among infants may result in greater long-term impact compared to a strategy focused on adolescents and adults	VMMC may result in cost-savings of USD 0.20M over 5 years of focusing VMMC scale up on adolescents and adults and USD13.71 million after 25 years, increasing scale-up to VMMC among infants **ICER:** Over 5 years, cost per infection averted was USD 5,500-9,200 compared to the baseline scenario, but <USD 500 over 25 years	N/A

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Zambia[63]	Examined prioritizing VMMC to different subpopulations of males based on age, geographic location, and sexual risk profile	7, 15, and 45 years (starting in 2010)	**Baseline male circumcision prevalence:** 12.85% **VMMC effectiveness:** 60% reduction in acquiring HIV **Cost of VMMC:** USD 30 – 110 (depending on age); USD 95-99.75 for males 15-29	80% VMMC coverage by 2017 among males 15-49 can result in 306,000 infections averted If total number of circumcisions to date had been targeted to males 15-29, VMMC program would have averted 51 percent more HIV infections by 2025 Over 15 years, 88% of HIV infections averted by circumcising males 10-34	**ICER:** Cost per infection averted was USD 1,089 for 80% VMMC coverage by 2017 among males 15-49 over 15 years With age prioritization, cost per infection averted ranged from USD 888 to 3,300 with cost increasing with age of circumcision over 15 years	N/A
Zimbabwe[65]	Compared four scenarios: 1) assumed scale up to 80% coverage among males 10-29 with same unit cost for all ages; 2) for different age groups, compared a scenario based on predictions about the level at which coverage would plateau; 3) scenario that assumed annual increase in coverage in males 20-29 was 2x the base scenario (#2) and with 2x higher unit costs; 4) scenario where annual increase in	15 years	**VMMC coverage:** 80% coverage among males in five - year age groups over 4 years **Cost of VMMC:** USD 109	Infections averted between 2015-2029 – **Scenario 1:** 87,000 – **Scenario 2:** 63,000 – **Scenario 3:** 87,000 – **Scenario 4:** 83,000	**ICER**: Cost per infection averted between 2015-2029 – **Scenario 1:** USD 4,800 – **Scenario 2:** USD 6,000 – **Scenario 3:** USD 6,600 – **Scenario 4:** USD 7,200	N/A

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
	coverage in males 20-24 was 2x the base scenario and 2x higher unit costs, for males 25-29, annual increase in coverage was 3x higher with 3x higher unit costs					

Appendix Table B5: Distribution and use of condoms

Country	Intervention	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Male condoms						
UK[73]	Compared condom distribution programs among young people, black ethnic minorities, MSMs, and the general population to no condom distribution programs	Lifetime	Condom effectiveness (relative risk): 1.0001 to 1.5 **Cost of intervention per person:** GBP 0.48	Condom distribution programs for all young people in England could avert 5,123 STI cases per annum	**ICER:** Condom distribution program for all young people costs GBP 17,411 per QALY gained (when RR = 1.23) compared to no condom distribution programs	**Threshold:** National Institute for Health and Care Excellence standards Condom distribution programs for all young people considered cost-effective compared to no condom distribution programs
US[74]	Compared distribution of 1 condom per week to MSM inmates in a Los Angele County jail to no condom distribution	Lifetime (32 years)	**Condom effectiveness:** 85% **Percent sex acts protected by condom:** 51% **Cost of intervention per month:** USD 994	Condom distribution averted 0.2 HIV infections per month	**ROI:** USD 74,777 in averted lifetime HIV treatment costs over 32-year window	N/A
Female condoms						

13 sub-Saharan African countries[76]	Estimated the potential dual health impact and cost-effectiveness of a Woman's Condom distribution program in 13 sub-Saharan African countries with HIV prevalence rates of 0.4% among adults aged 15–49 years	1 year	**Average cost of intervention per condom distributed:** USD 1.41	Distribution of 100,000 female condoms can prevent 21 HIV infections prevented in study population	**ICER:** Distributing female condoms cost per DALY averted ranges from USD 146 for Zimbabwe to USD 303 for Mozambique	**Threshold:** WHO recommended WTP thresholds Condom distribution is very-cost effective compared to no contraceptive use in all 13 countries
US[75]	Conducted a retrospective economic evaluation of a female condom distribution (200,000 condoms) and education program in Washington, DC	1 year	**Condom effectiveness:** 95% **Percent condoms used during sex:** 65% **Cost per female condom used:** USD 3.19	Distribution of 200,000 female condoms can result in 23 infections averted over 1 year in study population	**Net savings:** USD 7.046 million (societal perspective) and USD 5.181 million (payor perspective)	N/A

Appendix Table B6: Social and structural interventions

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Benin	Compared five social marketing behavioral interventions: peer education, radio broadcasts, magazines, public outreach events and billboards	Outcomes measured 28 months after behavioral intervention introduced	**Annual cost in USD:** - **Public outreach events:** 187,783 - **Peer education:** 199,129 - **Radio broadcasts:** 195,173 - **Magazine:** 146,355 - **Billboards:** 64,834 **Impact of exposure on odds of self-reported condom use (95% confidence interval):** - **Public outreach events:** 1.20-1.88 - **Peer education:** 0.93-1.61 - **Radio broadcasts:** 1.16-1.69 - **Magazine:** 1.32-2.62 - **Billboards:** 0.70-1.30	Only magazines, radio broadcasts, and public outreach events were significantly correlated with reported condom use	Radio broadcasts increased self-reported condom use the greatest, followed by magazines and public outreach events Magazines cost the least per person reached, followed by radio broadcasts and magazines Public outreach events seemed to influence condom use less cost-effectively compared to magazines and radio broadcasts	N/A
Canada[80]	Estimated the return on investment of community-based HIV programs	24 years	**Cost of lifetime HIV treatment: CAD** 256,090 (2005) to CAD 286,965 (2011)	From 1987 to 2011, community-based HIV programs prevented 16,672 new HIV infections	**ROI:** From 2005 to 2011, each dollar invested in community-based HIV programs saved approximately CAD 4.8	N/A
India[83]	Evaluated addition of community mobilization and empowerment interventions to core	7 years	**HIV prevalence among FSW:** 16.4% **Annual cost of intervention:** USD 31,690-135,572	Community mobilization and empowerment interventions averted 1,257 and 2,775 new HIV infections over 7 years in two different districts	**ICER:** Addition of community mobilization and empowerment interventions costs USD 13.48-14.12 per DALY averted	**Threshold:** WHO-recommended WTP threshold Addition of community

	HIV prevention services among FSW				If savings from ART accounted for, addition of community mobilization and empowerment are cost saving	mobilization and empowerment interventions are very cost-effective
Zimbabwe[78]	Assessed an orphan assistance intervention that provided school fees, uniforms, school supplies, and a school-based teacher "helper"	3 years	**HIV prevalence among orphan girls 15-17:** 5.3% (vs. 2.3% in non-orphan girls)) **Intervention cost per pupil:** USD 1,025	Orphan assistance resulted in gain of 0.36 QALYs per orphan supported	**ICER:** School support cost USD 6 per QALY gained	**Threshold:** WHO-recommended WTP threshold Providing orphan assistance is very cost-effective

Appendix Table B7: Harm reduction for PWID

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Needle and syringe programs						
Australia[87]	Compared NSP coverage with scenarios that had no NSPs (needle sharing rate of 25-50%) or other available prevention strategies.	10 years	**HIV transmission probability per injection with contaminated syringe:** 0.6-0.8% **Annual ART costs:** 14,613-27,776	NSPs can reduce HIV incidence by 34-70% and result in gain in 20,000-60,000 QALYs compared to no NSP scenario	**ICER:** NSPs cost AUD 416-8750 per QALY gained compared to no NSPs **Future ROI:** AUD 1.3-5.5 in averted healthcare costs for every dollar invested	**Threshold:** AUD <50,000 NSPs are very cost-effective compared to no NSPs
US[86]	Increasing investments in NSPs by US$10 to 50 million	1 year	**Number of new HIV infections due to injection drug use in the US per year:** 2,575	If an additional $10-50 million were invested for NSPs, 194-816 infections could be averted	**ICER:** Increased annual investments in NSPs cost USD 51,601-60,302 per HIV infection averted **ROI:** Return of USD 7.58-6.38 in averted lifetime HIV treatment costs for every dollar invested	N/A
Opioid substitution therapy						
Indonesia[89]	Expanding MMT from 5 to 40% coverage	10 years	**HIV prevalence among PWID:** ~50% **Unit cost per client visit of methadone program:** USD 2.63-6.70 (health care system and societal perspective, respectively)	Expanding MMT coverage can avert 2,400 infections over 10 years	**ICER:** Expanding MMT coverage costs USD269 per DALY averted compared to no MMT expansion In terms cost per infection averted, expanding MMT coverage costs USD 6,817 per HIV infection averted compared to no MMT expansion	**Threshold:** WHO recommended WTP thresholds Expanding MMT is very cost-effective compared to no MMT expansion

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Vietnam[2]	Compared a pilot MMT program with the status quo	1 year	**HIV prevalence among PWID:** 18% **HIV transmission probability per injection with contaminated syringe:** 0.01% **Annual MMT cost:** USD 252 **Annual ART cost:** USD 432-1,477	Pilot MMT program averted 34 infections over 1 year	**ICER:** MMT strategy costs USD 1,964 per QALY compared to status quo (no MMT) MMT strategy costs USD 3,324 per HIV infection averted compared to status quo **Budget impact:** USD 97 million for 65% coverage of PWID from 2011 to 2015	**Threshold:** WHO recommended WTP thresholds MMT strategy is cost-effective compared to status quo
Behavioral interventions						
Mexico	Compared different implementation scenarios of a single session brief behavioral intervention (either didactic or interactive) aimed at promoting safer sex and safer injection practices among female sex workers who injected drugs	Lifetime	**HIV/STI combined incidence per 100 person-year:** 64.3-66.1 **HIV prevalence among used syringes (per 100 exposures):** 12.3% **Intervention efficacy and costs:** Derived from *Mujer Mas Segura* intervention	Not specified separately from ICER.	**ICER:** Interactive safer sex/didactic safer injection intervention cost between USD 4,360 to 5,291 per QALY gained compared to a dually didactic strategy and was the most cost-effective approach (ICER depended on coverage of NSP programs)	**Threshold:** WHO recommended WTP thresholds An interactive safer sex/didactic safer injection intervention is highly cost-effective
US	Compared the implementation of two manual-guided risk reduction and health promotion interventions for HIV-infected PWID (HHRP+ and 3H+), in	10 years	**HIV prevalence among PWID:** 15% **Decrease in shared injections due to HHRP+:** 50% **Coverage:**	Expanding HHRP+ to 80% coverage can avert up to 29,000 infections over 10 years compared to the status quo Expanding 3H+ (less comprehensive intervention than HHRP+) to 80% coverage can avert	**ICER:** Expanding HHRP+ to 80% coverage costs USD 7,777 per QALY gained compared to the status quo Expanding 3H+ to 80% coverage costs USD 7,707 per QALY gained compared to the status quo	**Threshold:** WHO recommended WTP thresholds Expanding HHRP+ and 3H+ is very cost=effective

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
	addition to OST, to the status quo		**- OST: 13% PWID** (also analyzed expansion to 80% alone and in combination with 80% coverage of each of the two behavioral interventions) **- ART:** 30% non-PWID; 33% PWID **- HHRP+:** 40-80% **- 3H+:** 80% **Annual costs per patient:** - OST: USD 2,845 - OST + HHRP+: USD 3,981 - OST + 3H+: USD 3,081 - HHRP+: USD 2,003 - 3H+: USD 1,103	up to 19,000 HIV infections over 10 years compared to the status quo Expanding HHRP+ with broader OST coverage can avert up to 74,000 infections over 10 years compared to the status quo	Expanding HHRP+ with broader OST is less cost-effective than expanding HHRP+ alone	compared to the status quo

Appendix Table B8: PMTCT

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
HIV testing in pregnant women						
Haiti, Kenya, Namibia, Vietnam[4] (results only shown for Vietnam)	Compared the following HIV screening strategies among pregnant women in four countries with high to very low HIV prevalence: 1) current practice; 2) highly focused HIV testing (among high burden areas); 3) focused HIV testing (among high and medium areas); 4) universal testing in all areas.	Accounted for 20 years of pediatric treatment costs for infections not averted	**HIV prevalence:** 0.1% **ANC coverage:** 94-95% (current in Vietnam – 94%) **% tested for HIV at ANC:** 20-95% (current in Vietnam – 72%) **ART coverage among HIV positive pregnant women:** 65-95% (current in Vietnam – 65%) **Maternal ART:** USD 208 (for 14 weeks of pregnancy to 12 months post-natal) **Annual pediatric ART:** USD 136-258 (depending on age) **HIV test:** USD 0.73	Universal testing can lead to ~40% reduction in new infections compared to a focused testing strategy for medium/high burden areas	**ICER:** Compared to a focused testing strategy for medium/high burden areas, universal testing costs USD 125 per QALY gained (Assumed testing at first ANC visit, as well as for HIV-positive pregnant women before initiating ART)	**Threshold:** WHO recommended WTP thresholds Universal testing is very cost-effective compared to a focused testing approach in Vietnam (cost-saving in higher burden countries)
India[128]	Compared one-time testing during pregnancy to the addition of a second HIV test during pregnancy (34 weeks or beyond)	2 years	**HIV incidence per 1000 person women years:** 1.2 **HIV test:** USD 3.33 **Cost of ART for PMTCT:** USD 179 **Cost of pediatric ART:** USD 194	Based on an observational study, 4 additional infections were detected in the two years among five clinical sites.	**ICER:** Addition of a second HIV test during pregnancy was cost-saving compared to one-time testing	N/A

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
India[104]	Evaluated impact among pregnant women of an intervention that offered HIV screening at the primary healthcare level	1 year	Not specified.	Additional 27% of HIV infected women were detected during the intervention period, primarily at the PHC level	**Cost per pregnant woman:** Incremental cost of the intervention was INR 44 per pregnant woman tested (<USD 1)	N/A
Uganda[103]	Compared four HIV screening strategies in hypothetical cohort of 10,000 pregnant women: 1) Rapid HIV antibody test at first visit (current practice); 2) Strategy 1 + HIV RNA test at first visit; 3) Strategy 1 + repeat antibody test at delivery; 4) Strategy 3 + HIV RNA test at delivery	Lifetime	**HIV prevalence:** 10% **HIV incidence:** 3% (during pregnancy); 4% (during breastfeeding) **HIV transmission rate during pregnancy:** 1% (on ART) – 35% (incident HIV infection during pregnancy) **HIV transmission rate during breastfeeding:** 5% (on ART) – 35% (no ART) **Rapid HIV antibody test:** USD 3 **Confirmatory test**: USD 6 **HIV RNA test:** USD 32 **ART costs:** USD 68 (during pregnancy); USD 45 (during breastfeeding)	Addition of repeat HIV antibody test at delivery increases combined maternal and child life years saved by 1,538 compared to one-time HIV antibody test at the first prenatal visit in a hypothetical cohort of 10,000 pregnant women	**ICER:** Addition of a repeat HIV antibody test at delivery cost USD 379 per life-year saved compared to one-time HIV antibody test at the first prenatal visit. This was incrementally, the most cost-effective strategy.	**Threshold:** WHO recommended WTP thresholds Addition of a repeat HIV antibody test at delivery is very cost-effective compared to one-time HIV antibody testing at the first prenatal visit
ARVs for PMTCT						
Ghana[129]	Compared Option B+ to Option B (the	Lifetime	**HIV transmission during pregnancy:** 10% (Option B); 1% (Option B+)	Option B+ resulted in a gain of 0.1 years for maternal life expectancy compared to Option B. It also led to an	**ICER:** Option B+ costs USD 785/QALY gained compared to Option B	**Threshold:** WHO recommended WTP thresholds

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
	current status quo in Ghana)		**HIV Transmission during breastfeeding:** 1% (Option B and B+)	increase in average health benefit per child of 3.2 QALYs. National scale up of Option B+ could results in up to 668 infections averted among children.		Very cost-effective
Kenya, South Africa, Vietnam, Zambia[5] (results only for Vietnam shown)	Compared Option B+ to Option B, Option A and no PMTCT	Lifetime	**HIV transmission during pregnancy:** 2% (Option A and B); 0.5% (Option B+ if ART started before pregnancy) **HIV transmission during breastfeeding:** 0.2% (Option A and B); 0.16% (Option B+ if ART started before pregnancy)	If ART eligibility criteria is CD4 cell count ≤350 cells/mm^3, Option B+ averts 52% more transmissions compared to Option B. If ART eligibility criteria is CD4 cell count ≤500 cells/mm^3, Option B+ averts 24% more transmissions compared to Option B.	**ICER:** Option B+ costs USD 21,500/per infant infection averted compared to Option A (ART eligibility CD4 ≤350 cells/mm^3) Option B+ costs USD 9,800/infant infection averted compared to Option A (ART eligibility CD4 ≤500 cells/mm^3) Option B+ is cost-saving if accounting for total costs per total infections (MTCT and sexual) under both ART eligibility thresholds	**Threshold:** Unspecified
Malawi[130]	Compared Option B+ to Option B.	Lifetime	Not specified.	Option B+ averts one additional vertical infection of HIV per 200 HIV-infected pregnant women if first and second pregnancies are considered.	**ICER:** Option B+ costs between USD 500 and 1,300/DALY averted compared to Option B (depends on certain variables – life expectancy	**Threshold:** WHO recommended WTP thresholds Option B+ can be considered cost-effective in

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
					of infected infant, annual cost of ART)	comparison to Option B under certain scenarios
Malawi[131]	Compared Options A, B, and B+ to current practice (mix of interventions including HIV testing and counseling and ARV prophylaxis for HIV-infected pregnant women)	10 years	**HIV transmission during pregnancy:** 22% (no ARV); 2.7% (Option A); 1.7% (Option B, B+) **HIV transmission during breastfeeding:** 1.04% (no PMTCT); 0.2% (Option A, B, B+)	Option B+ would reduce the number of infants infected by 71% compared to the current practice. The number of HIV infected on ART and alive after ten years would more than double with Option B+.	**Cost per infant infection averted (compared to current practice):** USD 844 (Option A); USD 1,331 (Option B); USD 1,265 (Option B+) **ICER (compared to current practice):** USD 38/QALY gained (Option A); USD 68/QALY gained (Option B); USD 64/QALY gained (Option B+) accounting only for infant infections averted USD 314/QALY gained (Option A); USD 338/QALY (Option B); USD 455/QALY (Option B+) accounting for maternal health outcomes over 10-year time horizon	**Threshold:** WHO recommended WTP thresholds Option B+ is cost-effective compared to current practice.

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Uganda[132]	Compared 18 months of ART and lifelong ART to sdNVP and dual therapy for 7 weeks	Lifetime	**HIV transmission during pregnancy and breastfeeding:** 40% (no ARV); 25.8% (sdNVP); 17.4% (dual therapy); 3.8% (Option B and lifelong ART)	Compared with no therapy, single-dose nevirapine, and dual therapy, lifelong ART averted 31.6, 19.2, and 11.9 disability adjusted life years, respectively.	**ICER:** Lifelong ART costs 172 USD/DALY averted when compared to no therapy, 205/DALY averted when compared to sdNVP, and 354/DALY averted when compared to dual therapy	**Threshold:** WHO recommended WTP thresholds Lifelong ART is very cost-effective when compared to no therapy, sdNVP, and dual therapy.
Zambia[102]	Compared Option B+ and Option B to Option A	10 years	**HIV transmission during pregnancy:** 15-37% (no ARV); 2% (Option A, B, B+) **HIV transmission during breastfeeding:** 0.51-1.57% (No ARV); 0.2% (Option A, B, B+)	Adoption of Option B or B+ led to 33% reduction in the risk of HIV transmission among exposed infants compared to Option A. Adoption of Option B resulted in 72% reduction in the risk of HIV transmission to serodiscordant partners over 24 months, and additional 15% reduction with Option B+ compared to Option A.	**Cost per infant infection averted (compared to no PMTCT):** USD 1,034 (Option A); USD 1,140 (Option B); USD 1,406 (Option B+) **Cost per total infections averted:** USD 1,023 (Option B); USD 1,254 (Option B+) **ICER:** USD 88/QALY gained (Option B); USD 155/QALY gained (Option B+) accounting only for infant infections averted	**Threshold:** WHO recommended WTP thresholds Very cost-effective. When future treatment costs included, Option B and B+ were cost saving. Option B+ in comparison to Option B was not cost-effective.
Zimbabwe[107]	Compared Option A, B, and B+ to sdNVP (current practice).	Lifetime	**HIV transmission during pregnancy:** 17.5-27.3% (no ARV); 7.3-17.6% (sdNVP);	Replacing sdNVP with Option A results in increase in combined maternal and child life	**ICER:** Option B+ costs USD 1370/YLS compared with Option B.	**Threshold:** WHO recommended WTP thresholds

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			3.6-13.6% (Option A); 1-3.3% (Option B, B+) **HIV transmission during breastfeeding (rate per 100 PY):** 2.9-9.1 (no PMTCT); 2.7 (sdNVP); 2.2-4.0 (Option A, B, B+)	expectancy from 36.97 to 37.89 years. Option B increases combined LE to 38.32 years and Option B+ to 39.04 years).		Option B+ is not cost-effective compared with Option B (just over the cost-effective threshold)

Appendix Table B9: Combination prevention

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Combination prevention for general adult population						
Nigeria[114]	Compared the following interventions: 1) TasP; 2) PrEP; and 3) condom promotion for serodiscordant couples	20 years	**Condom efficacy:** 70% **Reduction in non-condom protected acts following condom promotion:** 52% **PrEP effectiveness (efficacy x adherence):** 70% **Reduction in HIV transmission due to ART:** 92% **Male circumcision efficacy:** 68% **Annual cost of condom promotion:** USD 19 **Annual cost of PrEP:** USD 233 **Annual cost of ART:** USD 365	Compared with baseline of offering ART to all HIV-positive individuals at CD4 <≤350 cells/mm^3, long-term PrEP averted the 15% of new infections, followed by condom promotion (10%), short-term PrEP (10%) and TasP (10%)	**ICER:** Compared with baseline of offering ART to all HIV-positive individuals at CD4 ≤350 cells/mm^3, condom promotion cost USD 1,206 per DALY averted. Adding TasP to condom promotion cost USD 1,607 per DALY averted. Adding short-term PrEP to TasP and condom promotion cost USD 7,870 per DALY averted. Switching to long-term PrEP cost USD 19,054 per DALY averted. When measuring impact in terms of infections averted, condom promotion was the most cost-effective strategy followed by short-term PrEP, long-term PrEP, and then adding TasP.	**Threshold:** WHO recommended WTP thresholds Condom promotion and the addition of TasP to condom promotion are both very cost-effective. Adding short-term PrEP to condom promotion and TasP is cost-effective. Switching to long-term PrEP is not cost-effective.

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
South Africa[111]	Compared expanded ART coverage and oral PrEP to status quo in adult population	20 years	**HIV prevalence:** 18% **PrEP effectiveness:** 60% **Reduction in HIV transmission due to ART:** 95% **Coverage of PrEP and ART:** 10-100% **Annual cost of PrEP:** USD 80 **Annual cost of ART:** USD 150	Compared to status quo, 100% scale up of universal ART alone can avert 75% of new infections. 100% scale up of PrEP alone can avert 63% of new infections.	**ICER:** If Focused PrEP is feasible, focused PrEP alone is the most cost-effective strategy compared to the status quo, followed by the addition of universal ART. If only general PrEP is possible, universal ART is the most effective strategy compared to the status quo, followed by the addition of general PrEP	**Threshold:** WHO recommended WTP thresholds Focused PrEP compared to the status quo is cost-saving All other strategies are cost-effective
South Africa[108]	Compared the following interventions alone and in combination: 1) HIV screening and counseling; 2) ART (initiation at CD4 ≤ 350 cells/mm^3); 3) male circumcision; 4) PREP; 5) microbicides	10 years	**Reduction in HIV transmission due to male circumcision:** 50% **Reduction in HIV transmission due to PrEP:** 21-67% **Reduction in HIV transmission due to microbicides:** 39% **Reduction in HIV transmission due to ART:** 96%	Comprehensive portfolio of expanded screening, ART, male circumcision, microbicides, and PrEP can avert 62% of new infections and reduce HIV prevalence from 14 to 10% In terms of infections averted, PrEP can avert the largest number of infections.	**ICER:** Comprehensive portfolio of expanded screening (annual screening), ART (75% coverage), male circumcision (75% coverage), microbicides (50% coverage), and PrEP (50% coverage) costs USD 9,900 per QALY gained Compared to the status quo, male circumcision is cost-saving – most cost-effective strategy following that is screening, screening and ART, and then a comprehensive portfolio of all five interventions	**Threshold:** WHO recommended WTP thresholds Comprehensive portfolio is cost-effective compared to a screening + ART strategy

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
					Compared to status quo – male circumcision is cost-saving; screening costs USD 150 per QALY gained; microbicides cost USD 526 per QALY gained; scale up of ART costs USD 1,149 per QALY gained; PrEP costs USD 9,009 per QALY gained	
South Africa[112]	Analyzed different combinations of expanding ART coverage, early ART and PrEP in the adult population	10 years	**Efficacy of ART in reducing risk of transmission:** 96% **Effectiveness of PrEP: 70%** (assumed high adherence) **Annual ART costs:** USD 600 **Annual PrEP costs:** USD 250	In terms of infections averted, expanding ART to all eligible (CD4 count ≤350 cells/mm^3), then to all HIV infected (early ART) can reduce 35% infections In terms of QALYs gained, scaling up earlier should be prioritized initially, however impact of early ART (all HIV infected) is not as beneficial under this perspective	In terms of infections averted, expanding ART to all eligible individuals is most cost-effective, then switching to early ART, and then adding PrEP In terms of QALYs gained, expanding ART to all eligible individuals and then adding PrEP is most cost-effective (early ART is costlier and less effective)	N/A
South Africa[113]	Compared increased coverage of: 1) TasP; 2) expansion of guidelines-based ART (CD4 count <350 cells/mm^3); 3) male circumcision	11 years	**ART coverage:** 50-80% **TasP coverage:** 20-80% **MMC coverage:** 45-80%	Not specified.	**ICER:** Scale up of male circumcision alone costs USD 1,096 per infection averted and USD 5,198 per death averted compared to status quo Scale up of ART costs USD 6,790 per infection averted and USD 5,604 per death	N/A

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
					averted compared to status quo Scale up of TasP costs USD 8,735 per infection averted and USD 7,739 per death averted compared to status quo	
US[110]	Compared combinations of the different interventions to identify the optimal package. Interventions include: clinical and non-clinical testing; condom distribution; post-exposure prophylaxis; linkage to care; care coordination; STD screening; partner notification services; behavioral risk reduction; linkage to support services; social marketing; community-level interventions; prioritized use of surveillance data; social services; screening for alcohol users; screening and treatment for cofactors	20 years	**HIV prevalence:** 1.6% **Effect sizes of intervention (relative risk benefits on pathway):** - Condom use/distribution: 12.3% increase - Community based HIV testing: 10.2% increase - PEP utilization: 42% increase - Linkage to care: 10% increase - Care coordination/mgmt.: 20% increase -STD care and treatment: 28% decrease - Partner services intervention: 2.8% increase - IDU risk reduction: 67.4% decrease - Risky sexual practices: 25% decrease	Package to prevent most infections includes community-level interventions, STD screening for high risk HIV infected persons, partner services, and linkage to support interventions. This package can avert 34% of new HIV infections.	**ICER:** Package to prevent the most infections costs USD 106,378 per infection averted **Cost savings:** Total cost savings would be USD 250 million per year (using cost-saving threshold of USD 360,000 per infection averted)	N/A

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Vietnam[6]	Examined the impact of general and targeted HIV testing and counseling and early ART combined with other HIV prevention interventions (baseline ART coverage, MMT, condoms) in the adult population	40 years	**Baseline coverage of ART:** 25% Of PLHIV (64% of eligible adults) Baseline coverage of MMT: 7.4% in MMT **Baseline condom use:** FSW/MCF: 80%; MSM: 40% **Efficacy of ART in reducing sexual transmissions:** 96% **Efficacy of ART on needles sharing transmissions:** 96% **Efficacy of MMT on needle-sharing transmissions:** 90% **Efficacy of condoms on transmissions:** 20-36% **Coverage of testing and immediate treatment:** 70% PWID and MSM, 80% FSW **Annual ART costs:** USD 415 **HIV testing and counseling costs:** USD 7.20	Annual HTC and immediate treatment for key populations, combined with scale up of MMT (50% coverage) and condom use (60-85%)will reduce new infections by 81% and cost USD 22.7 million. This strategy will reduce incidence to less than 1 per 100,000 in 14 years and result in a relative cost saving after 19 years	**ICER:** Most cost-effective scenario was combination prevention scale-up with annual testing and immediate treatment for key populations, which cost USD 78 per DALY averted compared to the status quo (dominated other strategies, except combination prevention scale up with standard ART)	N/A
Vietnam[7]	Analyzed the impact and cost-effectiveness of HIV programs (NSPs and MMT for PWID, condoms for FSWs/clients and for MSM, and ART) from 2006-2010 using a retrospective modeling approach		**Efficacy of condom use:** 95% **Efficacy of ART:** 96%	Between 2006-2010, HIV investments have averted 50,570 infections (34% reduction) and 42,557 deaths (35% reduction). Most effective interventions in reducing new infections were: 1) ART; 2) condoms for FSWs/clients; 3) condoms for MSM/clients; 4) NSPs for PWID	**ICER:** Entire HIV investment cost USD 9,498 per HIV Infection averted, USD 11,287 per HIV-related death averted, USD 1,196 per DALY averted in comparison to counterfactual scenario	Considered highly cost-effective according to 'most willingness-to-pay thresholds'

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
				Prevention programs estimated to have led to 401,550 fewer DALYs	Direct investments in HIV prevention and ART cost USD 1,972 per HIV infection averted, USD 2,344 per HIV-related death averted, USD 248 per DALY averted Condom program for MSM cost USD 103 per DALY averted; ART cost USD 164 per DALY averted; Condom promotion for FSW/clients cost USD 302 per DALY averted; NSP cost USD 1,493 per DALY averted	
Combination prevention for PWID						
China[133]	Assessed VCT, ART, and harm reduction treatment programs individually and in combination	30 years	**PWID HIV prevalence:** 9.3% **Sexual transmission reduction on ART:** 90% **Needle sharing transmission reduction on ART:** 50% **Annual costs per patient (USD)** - ART: 4,781 - MMT: 532 - NSP: 192	Not specified.	**ICER:** Expanding ART costs int'l dollar 4,840 per QALY gained compared to the base case Harm reduction costs int'l dollar 5,090 per QALY gained compared to the base case In combination, starting with expanding ART, then harm reduction, then VCT	N/A

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
Ukraine[116]	Examined strategies that used oral PrEP in combination with MMT and ART	20 years	**PWID HIV prevalence:** 42% **Sexual transmission reduction on ART:** 96% **Needle sharing transmission reduction on ART:** 50% **Reduction in injection equipment sharing on MMT:** 85% **MMT graduation:** 5% **Sexual transmission reduction on PrEP:** 49% **Needle sharing transmission reduction:** 49% **Coverage of intervention:** **Annual per patient (USD)** **- ART costs:** 450-950 **- MMT costs:** 368 - **PrEP costs:** 950	ART combined with MMT and PrEP (50% coverage) averted the most infections	**ICER:** Most cost-effective combination was adding MMT first, then ART, then PrEP (25% coverage) – addition of PrEP to MMT and ART cost USD 1,700 per QALY gained	**Threshold:** WHO recommended WTP thresholds Addition of PrEP to MMT and ART is still very cost-effective
US[88]	Assessed four interventions on their own and in combination: 1) opioid agonist therapy; 2) needle-syringe exchange programs; 3) HIV testing and treatment; 4) oral PrEP	20 years	**PWID HIV prevalence:** 9.8% **Reduction in injection equipment sharing due to OAT:** 54.7% **OAT graduation:** 3.6% **Needle sharing reduction:** 45% **Transmission reduction if injecting partner on ART:** 59%	Compared to the status quo and assuming 50% coverage of the intervention of interest: - OAT can reduce HIV prevalence by 16% - NSP can reduce HIV prevalence by 17% - Test and treat can reduce HIV prevalence by <1% - PrEP can reduce HIV prevalence by 26%	**ICER:** Compared to the status quo and assuming 50% coverage of the intervention of interest: - OAT costs USD 18,000 per QALY gained - NSP costs USD 25,000 per QALY gained - Test and treat costs USD 27,000 per QALY gained - PrEP costs USD 3000,000 per QALY gained	**Threshold:** <USD 50,000 50% coverage of OAT, NSP, and test and treat is cost-effective

Country	Intervention(s)	Time horizon	Key parameters	Health outcome	Economic evaluation metric	Cost-effective?
			Transmission reduction if sexual partner is on ART: 90% **PrEP injection and sexual transmission reduction:** 48.9% **Annual cost per patient (USD)** **- ART: 23,000** **- OAT: 7,000 (recurrent)** **- NSP: 615** **- PrEP: 10,000 + 800 (screening)**	If interventions can be combined, 50% coverage of OAT, NSP and test treat can reduce HIV prevalence by 27%	If interventions can be combined, 50% coverage of OAT followed NSP and then test and treat would be the most cost-effective approach (<USD 50,000 per QALY gained)	

REFERENCES

1 Viet Nam 2013 General Health Accounts and Disease Expenditures with Sub-analysis of 2013 HIV/AIDS Expenditure. Hanoi: Government of Vietnam. Ministry of Health, 2016 https://www.hfgproject.org/vietnam-2013-general-health-accounts-disease-expenditures-sub-analysis-2013-hivaids-expenditure/ (accessed Nov 8, 2017).

2 Tran BX, Ohinmaa A, Duong AT, *et al.* The cost-effectiveness and budget impact of Vietnam's methadone maintenance treatment programme in HIV prevention and treatment among injection drug users. *Glob Public Health* 2012; **7**: 1080–94.

3 Tran BX, Nguyen LT. Impact of methadone maintenance on health utility, health care utilization and expenditure in drug users with HIV/AIDS. *Int J Drug Policy* 2013; **24**: e105-110.

4 Ishikawa N, Dalal S, Johnson C, *et al.* Should HIV testing for all pregnant women continue? Cost-effectiveness of universal antenatal testing compared to focused approaches across high to very low HIV prevalence settings. *J Int AIDS Soc* 2016; **19**: 21212.

5 Gopalappa C, Stover J, Shaffer N, Mahy M. The costs and benefits of Option B+ for the prevention of mother-to-child transmission of HIV. *AIDS Lond Engl* 2014; **28 Suppl 1**: S5-14.

6 Kato M, Granich R, Bui DD, *et al.* The potential impact of expanding antiretroviral therapy and combination prevention in Vietnam: towards elimination of HIV transmission. *J Acquir Immune Defic Syndr 1999* 2013; **63**: e142-149.

7 Pham QD, Wilson DP, Kerr CC, *et al.* Estimating the Cost-Effectiveness of HIV Prevention Programmes in Vietnam,. *PloS One* 2015; **10**: e0133171.

8 Stover J, Rosen JE, Carvalho MN, *et al.* The case for investing in the male condom. *PloS One* 2017; **12**: e0177108.

9 Viet Nam 2014-2015 Health Accounts (draft). .

10 Vietnam Health Financing Strategy Period 2016-2025. Ministry of Health, 2016.

11 Teixeira H, Jaymond M, Kerr L, *et al.* Progress in Peril? The Changing Landscape of Global Health Financing. ACTION Global Health Advocacy Partnership. ACTION Global Health Advocacy Partnership, 2017 http://www.action.org/uploads/documents/Progress_in_Peril_web_updated_103017.pdf (accessed Nov 8, 2017).

12 Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the Economic Evaluation of Health Care Programmes, Fourth. Oxford: Oxford University Press, 2015.

13 Glassman A, Giedion U, Smith PC, editors. What's In, What's Out: Designing Benefits for Universal Health Coverage. Washington, DC: Center for Global Development, 2017.

14 Costing of Health Services for Provider Payment: A Practical Manual Based on Country Costing Challenges, Trade-offs, and Solutions. Joint Learning Network for Universal Health Coverage http://www.jointlearningnetwork.org/resources/costing-of-health-services-for-provider-payment-a-practical-manual.

15 Brazier J, Ratcliffe J, Tsuchiya A, Salomon J. Measuring and Valuing Health Benefits for Economic Evaluation, Second. Oxford: Oxford University Press, 2017.

16 The World Health Report 2002: Reducing risks, promoting healthy life. World Health Organization, 2002 http://www.who.int/whr/2002/en/ (accessed Jan 3, 2018).

17 Leech AA, Kim DD, Cohen JT, Neumann PJ. Use and Misuse of Cost-Effectiveness Analysis Thresholds in Low- and Middle-Income Countries: Trends in Cost-per-DALY Studies. *Value Health* DOI:10.1016/j.jval.2017.12.016.

18 Bilinski A, Neumann P, Cohen J, Thorat T, McDaniel K, Salomon JA. When cost-effective interventions are unaffordable: Integrating cost-effectiveness and budget impact in priority setting for global health programs. *PLoS Med* 2017; **14**: e1002397.

19 Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S. Thresholds for the cost-effectiveness of interventions: alternative approaches. *Bull World Health Organ* 2015; **93**: 118–24.

20 Vietnam Administration for HIV/AIDS Control. Báo cáo công tác phòng, chống HIV/AIDS năm 2017 và nhiệm vụ trọng tâm năm 2018. 2017 http://vaac.gov.vn/solieu/Detail/Bao-cao-cong-tac-phong-chong-HIV-AIDS-nam-2017-va-nhiem-vu-trong-tam-nam-2018.

21 Hutchinson AB, Farnham PG, Duffy N, *et al.* Return on public health investment: CDC's Expanded HIV Testing Initiative. *J Acquir Immune Defic Syndr 1999* 2012; **59**: 281–6.

22 Vietnam Country Operational Plan (COP/ROP) 2017. PEPFAR, 2017 https://www.pepfar.gov/documents/organization/272025.pdf.

23 HIV testing services in Vietnam move closer to high-risk groups. https://www.usaid.gov/results-data/success-stories/lay-providers-bring-hiv-testing-directly-communities (accessed Jan 7, 2018).

24 Guidelines on HIV self-testing and partner notification - supplement to consolidated guidelines on HIV testing services. World Health Organization http://apps.who.int/iris/bitstream/10665/251655/1/9789241549868-eng.pdf?ua=1 (accessed Jan 7, 2018).

25 Tromp N, Siregar A, Leuwol B, *et al.* Cost-effectiveness of scaling up voluntary counselling and testing in West-Java, Indonesia. *Acta Medica Indones* 2013; **45**: 17–25.

26 Ying R, Sharma M, Celum C, *et al.* Home testing and counselling to reduce HIV incidence in a generalised epidemic setting: a mathematical modelling analysis. *Lancet HIV* 2016; **3**: e275-282.

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

28 Smith JA, Sharma M, Levin C, *et al.* Cost-effectiveness of community-based strategies to strengthen the continuum of HIV care in rural South Africa: a health economic modelling analysis. *Lancet HIV* 2015; **2**: e159-168.

29 Zulliger R, Maulsby C, Solomon L, *et al.* Cost-utility of HIV Testing Programs Among Men Who Have Sex with Men in the United States. *AIDS Behav* 2017; **21**: 619–25.

30 Schackman BR, Metsch LR, Colfax GN, *et al.* The cost-effectiveness of rapid HIV testing in substance abuse treatment: results of a randomized trial. *Drug Alcohol Depend* 2013; **128**: 90–7.

31 Cambiano V, Ford D, Mabugu T, *et al.* Assessment of the Potential Impact and Cost-effectiveness of Self-Testing for HIV in Low-Income Countries. *J Infect Dis* 2015; **212**: 570–7.

32 Venkatesh KK, Becker JE, Kumarasamy N, *et al.* Clinical impact and cost-effectiveness of expanded voluntary HIV testing in India. *PloS One* 2013; **8**: e64604.

33 Hutchinson AB, Farnham PG, Sansom SL, Yaylali E, Mermin JH. Cost-Effectiveness of Frequent HIV Testing of High-Risk Populations in the United States. *J Acquir Immune Defic Syndr 1999* 2016; **71**: 323–30.

34 Lucas A, Armbruster B. The cost-effectiveness of expanded HIV screening in the United States. *AIDS Lond Engl* 2013; **27**: 795–801.

35 Rutstein SE, Brown LB, Biddle AK, *et al.* Cost-effectiveness of provider-based HIV partner notification in urban Malawi. *Health Policy Plan* 2014; **29**: 115–26.

36 Nichols BE, Gotz HM, van Gorp ECM, *et al.* Partner Notification for Reduction of HIV-1 Transmission and Related Costs among Men Who Have Sex with Men: A Mathematical Modeling Study. *PloS One* 2015; **10**: e0142576.

37 Cohen MS, Chen YQ, McCauley M, *et al.* Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; **365**: 493–505.

38 Guideline on when to start antiretroviral therapy and pre-exposure prophylaxis for HIV. World Health Organization, 2015 http://apps.who.int/iris/bitstream/10665/186275/1/9789241509565_eng.pdf?ua=1 (accessed Dec 22, 2017).

39 Ministry of Health, Vietnam. Hướng dẫn điều trị và chăm sóc HIV/AIDS ban hành theo Quyết định số 5418/QĐ-BYT. 2017 http://vaac.gov.vn/Cms_Data/Contents/Vaac/Folders/DocumentLaw/Vanban/~contents/YL52A6DBD4E8SDUV/14-1-Huong-dan-Dieu-tri-va-cham-soc-HIV-VAAC-final-Web.pdf.

40 Maddali MV, Dowdy DW, Gupta A, Shah M. Economic and epidemiological impact of early antiretroviral therapy initiation in India. *J Int AIDS Soc* 2015; **18**: 20217.

41 Walensky RP, Ross EL, Kumarasamy N, *et al.* Cost-effectiveness of HIV treatment as prevention in serodiscordant couples. *N Engl J Med* 2013; **369**: 1715–25.

42 Granich R, Kahn JG, Bennett R, *et al.* Expanding ART for treatment and prevention of HIV in South Africa: estimated cost and cost-effectiveness 2011-2050. *PloS One* 2012; **7**: e30216.

43 Grant RM, Lama JR, Anderson PL, *et al.* Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; **363**: 2587–99.

44 Thigpen MC, Kebaabetswe PM, Paxton LA, *et al.* Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med* 2012; **367**: 423–34.

45 Baeten JM, Donnell D, Ndase P, *et al.* Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med* 2012; **367**: 399–410.

46 Choopanya K, Martin M, Suntharasamai P, *et al.* Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet Lond Engl* 2013; **381**: 2083–90.

47 Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. World Health Organization, 2014 http://apps.who.int/iris/bitstream/10665/128048/1/9789241507431_eng.pdf?ua=1&ua=1 (accessed Dec 30, 2017).

48 United States and Vietnam launch oral pre-exposure option to reduce new infections. 2017; published online June 12. https://www.usaid.gov/vietnam/press-releases/jun-12-2017-united-states-and-vietnam-launch-oral-hiv-pre-exposure.

49 Juusola JL, Brandeau ML, Owens DK, Bendavid E. The cost-effectiveness of preexposure prophylaxis for HIV prevention in the United States in men who have sex with men. *Ann Intern Med* 2012; **156**: 541–50.

50 McKenney J, Chen A, Hoover KW, *et al.* Optimal costs of HIV pre-exposure prophylaxis for men who have sex with men. *PloS One* 2017; **12**: e0178170.

51 Gomez GB, Borquez A, Caceres CF, *et al.* The potential impact of pre-exposure prophylaxis for HIV prevention among men who have sex with men and transwomen in Lima, Peru: a mathematical modelling study. *PLoS Med* 2012; **9**: e1001323.

52 Schackman BR, Eggman AA. Cost-effectiveness of pre-exposure prophylaxis for HIV: a review. *Curr Opin HIV AIDS* 2012; **7**: 587–92.

53 Schneider K, Gray RT, Wilson DP. A cost-effectiveness analysis of HIV preexposure prophylaxis for men who have sex with men in Australia. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2014; **58**: 1027–34.

54 Nichols BE, Boucher CAB, van der Valk M, Rijnders BJA, van de Vijver DAMC. Cost-effectiveness analysis of pre-exposure prophylaxis for HIV-1 prevention in the Netherlands: a mathematical modelling study. *Lancet Infect Dis* 2016; **16**: 1423–9.

55 Chen A, Dowdy DW. Clinical effectiveness and cost-effectiveness of HIV pre-exposure prophylaxis in men who have sex with men: risk calculators for real-world decision-making. *PloS One* 2014; **9**: e108742.

56 Verguet S, Stalcup M, Walsh JA. Where to deploy pre-exposure prophylaxis (PrEP) in sub-Saharan Africa? *Sex Transm Infect* 2013; **89**: 628–34.

57 Nichols BE, Boucher CAB, van Dijk JH, *et al.* Cost-effectiveness of pre-exposure prophylaxis (PrEP) in preventing HIV-1 infections in rural Zambia: a modeling study. *PloS One* 2013; **8**: e59549.

58 Gomez GB, Borquez A, Case KK, Wheelock A, Vassall A, Hankins C. The cost and impact of scaling up pre-exposure prophylaxis for HIV prevention: a systematic review of cost-effectiveness modelling studies. *PLoS Med* 2013; **10**: e1001401.

59 Kessler J, Myers JE, Nucifora KA, *et al.* Evaluating the impact of prioritization of antiretroviral pre-exposure prophylaxis in New York. *AIDS Lond Engl* 2014; **28**: 2683–91.

60 Ouellet E, Durand M, Guertin JR, LeLorier J, Tremblay CL. Cost effectiveness of 'on demand' HIV pre-exposure prophylaxis for non-injection drug-using men who have sex with men in Canada. *Can J Infect Dis Med Microbiol J Can Mal Infect Microbiol Medicale* 2015; **26**: 23–9.

61 Kripke K, Reed J, Hankins C, Smiley G, Laube C, Njeuhmeli E. Impact and Cost of Scaling Up Voluntary Medical Male Circumcision for HIV Prevention in the Context of the New 90-90-90 HIV Treatment Targets. *PloS One* 2016; **11**: e0155734.

62 Haacker M, Fraser-Hurt N, Gorgens M. Effectiveness of and Financial Returns to Voluntary Medical Male Circumcision for HIV Prevention in South Africa: An Incremental Cost-Effectiveness Analysis. *PLoS Med* 2016; **13**: e1002012.

63 Awad SF, Sgaier SK, Tambatamba BC, *et al.* Investigating Voluntary Medical Male Circumcision Program Efficiency Gains through Subpopulation Prioritization: Insights from Application to Zambia. *PloS One* 2015; **10**: e0145729.

64 Kripke K, Njeuhmeli E, Samuelson J, *et al.* Assessing Progress, Impact, and Next Steps in Rolling Out Voluntary Medical Male Circumcision for HIV Prevention in 14 Priority Countries in Eastern and Southern Africa through 2014. *PloS One* 2016; **11**: e0158767.

65 Kripke K, Hatzold K, Mugurungi O, *et al.* Modeling Impact and Cost-Effectiveness of Increased Efforts to Attract Voluntary Medical Male Circumcision Clients Ages 20-29 in Zimbabwe. *PloS One* 2016; **11**: e0164144.

66 Kripke K, Perales N, Lija J, *et al.* The Economic and Epidemiological Impact of Focusing Voluntary Medical Male Circumcision for HIV Prevention on Specific Age Groups and Regions in Tanzania. *PloS One* 2016; **11**: e0153363.

67 Kacker S, Frick KD, Quinn TC, Gray RH, Tobian AAR. Financial implications of male circumcision scale-up for the prevention of HIV and other sexually transmitted infections in a sub-Saharan African community. *Sex Transm Dis* 2013; **40**: 559–68.

68 Hoang L. Playing it safe. Latit. Views World. 2013; published online April 3. https://latitude.blogs.nytimes.com/2013/04/03/free-condom-campaign-is-a-pragmatic-shift-in-vietnams-approach-to-safer-sex/ (accessed Oct 25, 2017).

69 Measurable results: condom social marketing in Vietnam. PSI http://www.psi.org/wp-content/uploads/drupal/sites/default/files/publication_files/Condom%20Social%20Marketing%20Fact%20Sheet.pdf (accessed Oct 25, 2017).

70 Vietnam figures out a new way to distribute condoms. Goats Soda. 2015; published online June 24. https://www.npr.org/sections/goatsandsoda/2015/06/24/397101875/vietnam-is-having-condom-problems-and-thats-a-good-thing (accessed Jan 3, 2018).

71 Vietnam country program. PATH. http://sites.path.org/vietnam/emerging-and-epidemic-diseases/usaid-healthy-markets/ (accessed Oct 25, 2017).

72 Stover J, Hallett TB, Wu Z, *et al.* How can we get close to zero? The potential contribution of biomedical prevention and the investment framework towards an effective response to HIV. *PLoS One* 2014; **9**: e111956.

73 Sadler S, Tosh J, Pennington R, *et al.* A cost-effectiveness analysis of condom distribution programmes for the prevention of sexually transmitted infections in England. *J Epidemiol Community Health* 2017; **71**: 897–904.

74 Leibowitz AA, Harawa N, Sylla M, Hallstrom CC, Kerndt PR. Condom distribution in jail to prevent HIV infection. *AIDS Behav* 2013; **17**: 2695–702.

75 Holtgrave DR, Maulsby C, Kharfen M, *et al.* Cost-utility analysis of a female condom promotion program in Washington, DC. *AIDS Behav* 2012; **16**: 1115–20.

76 Mvundura M, Nundy N, Kilbourne-Brook M, Coffey PS. Estimating the hypothetical dual health impact and cost-effectiveness of the Woman's Condom in selected sub-Saharan African countries. *Int J Womens Health* 2015; **7**: 271–7.

77 HIV prevention programmes overview. https://www.avert.org/professionals/hiv-programming/prevention/overview (accessed Jan 8, 2018).

78 Miller T, Hallfors D, Cho H, Luseno W, Waehrer G. Cost-effectiveness of school support for orphan girls to prevent HIV infection in Zimbabwe. *Prev Sci Off J Soc Prev Res* 2013; **14**: 503–12.

79 Hsu J, Zinsou C, Parkhurst J, N'Dour M, Foyet L, Mueller DH. Comparative costs and cost-effectiveness of behavioural interventions as part of HIV prevention strategies. *Health Policy Plan* 2013; **28**: 20–9.

80 Choi SKY, Holtgrave DR, Bacon J, *et al.* Economic Evaluation of Community-Based HIV Prevention Programs in Ontario: Evidence of Effectiveness in Reducing HIV Infections and Health Care Costs. *AIDS Behav* 2016; **20**: 1143–56.

81 Safren SA, Perry NS, Blashill AJ, O'Cleirigh C, Mayer KH. The cost and intensity of behavioral interventions to promote HIV treatment for prevention among HIV-positive men who have sex with men. *Arch Sex Behav* 2015; **44**: 1833–41.

82 Shannon K, Strathdee SA, Goldenberg SM, *et al.* Global epidemiology of HIV among female sex workers: influence of structural determinants. *Lancet Lond Engl* 2015; **385**: 55–71.

83 Vassall A, Chandrashekar S, Pickles M, *et al.* Community mobilisation and empowerment interventions as part of HIV prevention for female sex workers in Southern India: a cost-effectiveness analysis. *PloS One* 2014; **9**: e110562.

84 Remme M, Siapka M, Vassall A, *et al.* The cost and cost-effectiveness of gender-responsive interventions for HIV: a systematic review. *J Int AIDS Soc* 2014; **17**: 19228.

85 Wilson DP, Donald B, Shattock AJ, Wilson D, Fraser-Hurt N. The cost-effectiveness of harm reduction. *Int J Drug Policy* 2015; **26 Suppl 1**: S5-11.

86 Nguyen TQ, Weir BW, Des Jarlais DC, Pinkerton SD, Holtgrave DR. Syringe exchange in the United States: a national level economic evaluation of hypothetical increases in investment. *AIDS Behav* 2014; **18**: 2144–55.

87 Kwon JA, Anderson J, Kerr CC, *et al.* Estimating the cost-effectiveness of needle-syringe programs in Australia. *AIDS Lond Engl* 2012; **26**: 2201–10.

88 Bernard CL, Owens DK, Goldhaber-Fiebert JD, Brandeau ML. Estimation of the cost-effectiveness of HIV prevention portfolios for people who inject drugs in the United States: A model-based analysis. *PLoS Med* 2017; **14**: e1002312.

89 Wammes JJG, Siregar AY, Hidayat T, *et al.* Cost-effectiveness of methadone maintenance therapy as HIV prevention in an Indonesian high-prevalence setting: a mathematical modeling study. *Int J Drug Policy* 2012; **23**: 358–64.

90 Hunink M, Glasziou P, Siegel J, *et al.* Decision making in health and medicine: integrating evidence and values. Cambridge: Cambridge University Press, 2012.

91 Burgos JL, Patterson TL, Graff-Zivin JS, *et al.* Cost-Effectiveness of Combined Sexual and Injection Risk Reduction Interventions among Female Sex Workers Who Inject Drugs in Two Very Distinct Mexican Border Cities. *PloS One* 2016; **11**: e0147719.

92 Song DL, Altice FL, Copenhaver MM, Long EF. Cost-effectiveness analysis of brief and expanded evidence-based risk reduction interventions for HIV-infected people who inject drugs in the United States. *PloS One* 2015; **10**: e0116694.

93 Enns EA, Zaric GS, Strike CJ, Jairam JA, Kolla G, Bayoumi AM. Potential cost-effectiveness of supervised injection facilities in Toronto and Ottawa, Canada. *Addict Abingdon Engl* 2016; **111**: 475–89.

94 Jozaghi E, Reid AA, Andresen MA. A cost-benefit/cost-effectiveness analysis of proposed supervised injection facilities in Montreal, Canada. *Subst Abuse Treat Prev Policy* 2013; **8**: 25.

95 Jozaghi E, Reid AA, Andresen MA, Juneau A. A cost-benefit/cost-effectiveness analysis of proposed supervised injection facilities in Ottawa, Canada. *Subst Abuse Treat Prev Policy* 2014; **9**: 31.

96 Jozaghi E, Jackson A. Examining the potential role of a supervised injection facility in Saskatoon, Saskatchewan, to avert HIV among people who inject drugs. *Int J Health Policy Manag* 2015; **4**: 373–9.

97 Irwin A, Jozaghi E, Weir BW, Allen ST, Lindsay A, Sherman SG. Mitigating the heroin crisis in Baltimore, MD, USA: a cost-benefit analysis of a hypothetical supervised injection facility. *Harm Reduct J* 2017; **14**: 29.

98 Optimizing Viet Nam's HIV response: and investment case. Ministry of Health, 2014.

99 Laufer FN, Warren BL, Pulver WP, Smith LC, Wright RL, Birkhead GS. Return on Investment From Expenditures Incurred to Eliminate Mother-To-Child Transmission Among HIV-Infected Women in New York State: 1998-2013. *J Acquir Immune Defic Syndr 1999* 2016; **71**: 558–62.

100 Ibekwe E, Haigh C, Duncan F, Fatoye F. Economic impact of routine opt-out antenatal human immune deficiency virus screening: A systematic review. *J Clin Nurs* 2017; published online March 2. DOI:10.1111/jocn.13787.

101 Bert F, Gualano MR, Biancone P, *et al.* HIV screening in pregnant women: A systematic review of cost-effectiveness studies. *Int J Health Plann Manage* 2017; published online May 29. DOI:10.1002/hpm.2418.

102 Ishikawa N, Shimbo T, Miyano S, *et al.* Health outcomes and cost impact of the new WHO 2013 guidelines on prevention of mother-to-child transmission of HIV in Zambia. *PloS One* 2014; **9**: e90991.

103 Kim LH, Cohan DL, Sparks TN, Pilliod RA, Arinaitwe E, Caughey AB. The cost-effectiveness of repeat HIV testing during pregnancy in a resource-limited setting. *J Acquir Immune Defic Syndr 1999* 2013; **63**: 195–200.

104 Bindoria SV, Devkar R, Gupta I, *et al.* Development and pilot testing of HIV screening program integration within public/primary health centers providing antenatal care services in Maharashtra, India. *BMC Res Notes* 2014; **7**: 177.

105 Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. World Health Organization, 2012 http://www.who.int/hiv/PMTCT_update.pdf (accessed Jan 7, 2018).

106 Karnon J, Orji N. Option B+ for the prevention of mother-to-child transmission of HIV infection in developing countries: a review of published cost-effectiveness analyses. *Health Policy Plan* 2016; **31**: 1133–41.

107 Ciaranello AL, Perez F, Engelsmann B, *et al.* Cost-effectiveness of World Health Organization 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2013; **56**: 430–46.

108 Long EF, Stavert RR. Portfolios of biomedical HIV interventions in South Africa: a cost-effectiveness analysis. *J Gen Intern Med* 2013; **28**: 1294–301.

109 Lin F, Farnham PG, Shrestha RK, Mermin J, Sansom SL. Cost Effectiveness of HIV Prevention Interventions in the U.S. *Am J Prev Med* 2016; **50**: 699–708.

110 Kessler J, Myers JE, Nucifora KA, *et al.* Averting HIV infections in New York City: a modeling approach estimating the future impact of additional behavioral and biomedical HIV prevention strategies. *PloS One* 2013; **8**: e73269.

111 Alistar SS, Grant PM, Bendavid E. Comparative effectiveness and cost-effectiveness of antiretroviral therapy and pre-exposure prophylaxis for HIV prevention in South Africa. *BMC Med* 2014; **12**: 46.

112 Cremin I, Alsallaq R, Dybul M, Piot P, Garnett G, Hallett TB. The new role of antiretrovirals in combination HIV prevention: a mathematical modelling analysis. *AIDS Lond Engl* 2013; **27**: 447–58.

113 Barnighausen T, Bloom DE, Humair S. Economics of antiretroviral treatment vs. circumcision for HIV prevention. *Proc Natl Acad Sci U S A* 2012; **109**: 21271–6.

114 Mitchell KM, Lepine A, Terris-Prestholt F, *et al.* Modelling the impact and cost-effectiveness of combination prevention amongst HIV serodiscordant couples in Nigeria. *AIDS Lond Engl* 2015; **29**: 2035–44.

115 Vietnam Administration for HIV/AIDS Control. Optimizing Viet Nam's HIV Response: An Investment Case. 2014.

116 Alistar SS, Owens DK, Brandeau ML. Effectiveness and cost effectiveness of oral pre-exposure prophylaxis in a portfolio of prevention programs for injection drug users in mixed HIV epidemics. *PloS One* 2014; **9**: e86584.

117 Walensky RP. Combination HIV prevention: the value and interpretation of mathematical models. *Curr HIV/AIDS Rep* 2013; **10**: 195–8.

118 Castel AD, Choi S, Dor A, *et al.* Comparing Cost-Effectiveness of HIV Testing Strategies: Targeted and Routine Testing in Washington, DC. *PloS One* 2015; **10**: e0139605.

119 Long EF, Mandalia R, Mandalia S, Alistar SS, Beck EJ, Brandeau ML. Expanded HIV testing in low-prevalence, high-income countries: a cost-effectiveness analysis for the United Kingdom. *PloS One* 2014; **9**: e95735.

120 Goldman DP, Juday T, Seekins D, Linthicum MT, Romley JA. Early HIV treatment in the United States prevented nearly 13,500 infections per year during 1996-2009. *Health Aff Proj Hope* 2014; **33**: 362–9.

121 MacFadden DR, Tan DH, Mishra S. Optimizing HIV pre-exposure prophylaxis implementation among men who have sex with men in a large urban centre: a dynamic modelling study. *J Int AIDS Soc* 2016; **19**: 20791.

122 Drabo EF, Hay JW, Vardavas R, Wagner ZR, Sood N. A Cost-effectiveness Analysis of Preexposure Prophylaxis for the Prevention of HIV Among Los Angeles County Men Who Have Sex With Men. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2016; **63**: 1495–504.

123 Ying R, Sharma M, Heffron R, *et al.* Cost-effectiveness of pre-exposure prophylaxis targeted to high-risk serodiscordant couples as a bridge to sustained ART use in Kampala, Uganda. *J Int AIDS Soc* 2015; **18**: 20013.

124 Nichols BE, Baltussen R, van Dijk JH, *et al.* Cost-effectiveness of PrEP in HIV/AIDS control in Zambia: a stochastic league approach. *J Acquir Immune Defic Syndr 1999* 2014; **66**: 221–8.

125 Kripke K, Chimbwandira F, Mwandi Z, *et al.* Voluntary Medical Male Circumcision for HIV Prevention in Malawi: Modeling the Impact and Cost of Focusing the Program by Client Age and Geography. *PloS One* 2016; **11**: e0156521.

126 Kripke K, Chen P-A, Vazzano A, *et al.* Cost and Impact of Voluntary Medical Male Circumcision in South Africa: Focusing the Program on Specific Age Groups and Provinces. *PloS One* 2016; **11**: e0157071.

127 Menon V, Gold E, Godbole R, *et al.* Costs and impacts of scaling up voluntary medical male circumcision in Tanzania. *PloS One* 2014; **9**: e83925.

128 Joshi S, Kulkarni V, Gangakhedkar R, *et al.* Cost-effectiveness of a repeat HIV test in pregnancy in India. *BMJ Open* 2015; **5**: e006718.

129 VanDeusen A, Paintsil E, Agyarko-Poku T, Long EF. Cost effectiveness of option B plus for prevention of mother-to-child transmission of HIV in resource-limited countries: evidence from Kumasi, Ghana. *BMC Infect Dis* 2015; **15**: 130.

130 Tweya H, Keiser O, Haas AD, *et al.* Comparative cost-effectiveness of Option B+ for prevention of mother-to-child transmission of HIV in Malawi. *AIDS Lond Engl* 2016; **30**: 953–62.

131 Fasawe O, Avila C, Shaffer N, *et al.* Cost-effectiveness analysis of Option B+ for HIV prevention and treatment of mothers and children in Malawi. *PloS One* 2013; **8**: e57778.

132 Kuznik A, Lamorde M, Hermans S, *et al.* Evaluating the cost-effectiveness of combination antiretroviral therapy for the prevention of mother-to-child transmission of HIV in Uganda. *Bull World Health Organ* 2012; **90**: 595–603.

133 Li J, Gilmour S, Zhang H, Koyanagi A, Shibuya K. The epidemiological impact and cost-effectiveness of HIV testing, antiretroviral treatment and harm reduction programs. *AIDS Lond Engl* 2012; **26**: 2069–78.

BOLD THINKERS DRIVING
REAL-WORLD IMPACT