RETHINK HIV

Assessment Paper

Sexual Transmission of HIV

Jere R. Behrman and Hans-Peter Kohler

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RUSH
FUNDING DISRUPTIVE IDEAS AGAINST HIV

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Jere R. Behrman[2] and Hans-Peter Kohler[3]

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2 William R. Kenan Jr. Professor of Economics and Sociology, University of Pennsylvania
3 Frederick J. Warren Professor of Demography, Department of Sociology and Population Studies Center,University of Pennsylvania

RethinkHIV: The Project

2011 marks the 30-year anniversary since the Centers for Disease Control and Prevention introduced the world to the disease that became known as AIDS. Despite 30 years of increasing knowledge about transmission, prevention, and treatment, and current annual spending of $15 billion, every day around 7,000 people are infected with the HIV virus and two million die each year. The HIV/AIDS epidemic has had its most profound impact in sub- Saharan Africa, which accounts for 70 percent of new worldwide infections and 70 percent of HIV-related deaths, 1.8 million new infections in children each year, and has 14 million AIDS orphans.

Humanitarian organizations warn that the fight against HIV/Aids has slowed, amid a funding shortfall and donor fatigue. Yet HIV is still the biggest killer of women of reproductive age in the world, and of men aged 15-59 in sub-Saharan Africa. Time is ripe for a reassessment of current policy and expenditure.

The Rush Foundation has asked the Copenhagen Consensus Center to commission a group of leading health academics to analyze HIV policy choices and identify the most effective ways to tackle the pandemic across sub-Saharan Africa.

RethinkHIV identifies effective interventions in the fight against HIV/Aids across sub-Saharan Africa. It applies cost-benefit analysis to highlight investments and actions that can make a significant difference.

The Copenhagen Consensus Center has commissioned eighteen research papers by teams of top health economists, epidemiologists, and demographers who examine the cost-effectiveness of a range of responses to HIV/AIDS in sub- Saharan Africa under the following topics:

- Efforts to Prevent Sexual Transmission
- Efforts to Prevent Non-Sexual Transmission
- Treatment and Initiatives to Reduce the Impact of the HIV/AIDS Epidemic
- Research and Development Efforts
- Social Policy Levers
- Initiatives to Strengthen Health Systems

A panel of five eminent economists, including recipients of the Nobel Prize, convenes in the fall of 2011 to carefully consider the research and engage with the authors. The Expert Panel is tasked with answering the question:

If we successfully raised an additional US$10 billion over the next 5 years to combat HIV/AIDS in sub-Saharan Africa, how could it best be spent?

After deliberating in a closed-door meeting, the Nobel Laureate Expert Panel provides their answer, highlighting investments and actions that could be most effective avenues for additional funding. Their findings and reasoning are released in the fall of 2011, and published in full alongside all of the research in a collated volume in 2012.

RethinkHIV will generate global discussion regarding responses to HIV/AIDS in sub-Saharan Africa. To participate in a dialogue on the research and findings within sub-Saharan Africa, a Civil Society Conference and forums for youth are held following the Expert Panel meeting in late 2011.

The Civil Society Conference is a means of creating a dialogue with African civil society and to agree on a set of bold new actionable priorities with society politicians, civil society organizations, influential thought-leaders, and others within sub-Saharan Africa.

It is hoped that the project will motivate donors to direct more money to the investments and actions that are demonstrated to be most effective to curtail the pandemic in sub-Saharan Africa.

All of the research papers, and many different perspectives on priorities can be found online at the project's website:
www.rethinkhiv.com

You are invited to join the dialogue and provide your own perspective on priorities for action in Africa.

The Copenhagen Consensus Center

The Copenhagen Consensus Center is a Danish state-funded think- tank that commissions and promotes research highlighting the most effective responses to global challenges. The Center is led by author Bjorn Lomborg, named 'one of the 100 Top Global Thinkers' by Foreign Policy in 2010, 'one of the world's 75 most influential people of the 21st century' by Esquire in 2008, and 'one of the 50 people who could save the planet' by the Guardian in 2008. The Copenhagen Consensus Center is implementing the project, which follows the format of past projects such as Copenhagen Consensus 2004, Consulta de San José in 2007, Copenhagen Consensus 2008, and Copenhagen Consensus on Climate in 2009.
www.copenhagenconsensus.com

The Rush Foundation

The Rush Foundation, based in Lausanne, is dedicated to providing fast, effective funding for innovative thinking addressing the HIV/AIDS epidemic in sub-Saharan Africa. The Rush Foundation is the sponsor of the project. The Rush Foundation was launched in 2010 to fund sustainable projects in sub-Saharan Africa focused on alleviating the pandemic through innovative thinking, and to shake up the status quo in HIV thinking by spearheading thought leadership projects and debates that will help reframe HIV policy. Among other initiatives, the Rush Foundation is currently designing a grant programme with ActionAid in Africa aimed at generating new, sustainable HIV initiatives on the ground.
www.rushfoundation.org

The Papers

The body of research for RethinkHIV comprises 18 research papers. The series of papers is divided into Assessment Papers and Perspective Papers. Each Assessment Paper outlines the costs and benefits of at least three of the most promising responses, interventions, or investments to HIV/AIDS in Sub-Saharan Africa within the respective category. Each Perspective Paper reviews the assumptions and analyses made within the Assessment Paper. In this way, a range of informed perspectives are provided on the topic.

Contents

Introduction

The purpose of the RethinkHIV project is to identify and highlight the most cost-effective responses to HIV/AIDS in Sub-Saharan Africa (SSA) with economic analyses of the benefits and costs of specific interventions in six categories of responses to HIV/AIDS. This is the Assessment Paper on the first of the six topics: Prevention of Sexual Transmission of HIV.

As is well-known, sexual infections are a major source of the spread of HIV/AIDS generally (UNAIDS 2010), and are thought to be by far the most important source of the spread of HIV/AIDS in SSA, though there also are other sources of spread of the disease such as maternal-child infection and the use of contaminated blood or needles. Sexual interactions may directly result in the transmission of HIV but they also may increase the vulnerability to the HIV virus through transmitting other sexually transmitted diseases. Interventions to reduce sexual infections broadly speaking can work through reducing the frequency of such interactions or through reducing the risks of sexual infection per sexual encounter. Selection of partners, including with respect to age and risk behaviors of the partner, condom use or other risk reduction strategies with a specific partner, and biomedical interventions that affect HIV transmission can all affect HIV infection risks. Interventions have been proposed to work through both of these channels, though with greater emphasis probably on the latter.

In this Assessment Paper, we first discuss how we identified solutions through preventing sexual infections suggested by the literature. We then discuss benefit-cost analyses to help provide a framework for understanding what information is necessary for evaluating possible interventions. We then turn to assumptions for our estimated benefit-cost ratios for those solutions through preventing sexual infections suggested by the literature and then present the estimated benefit-cost ratios and cost-effectiveness estimates for averting infections and per DALY.

The current debate about preventing HIV infections through sexual relations

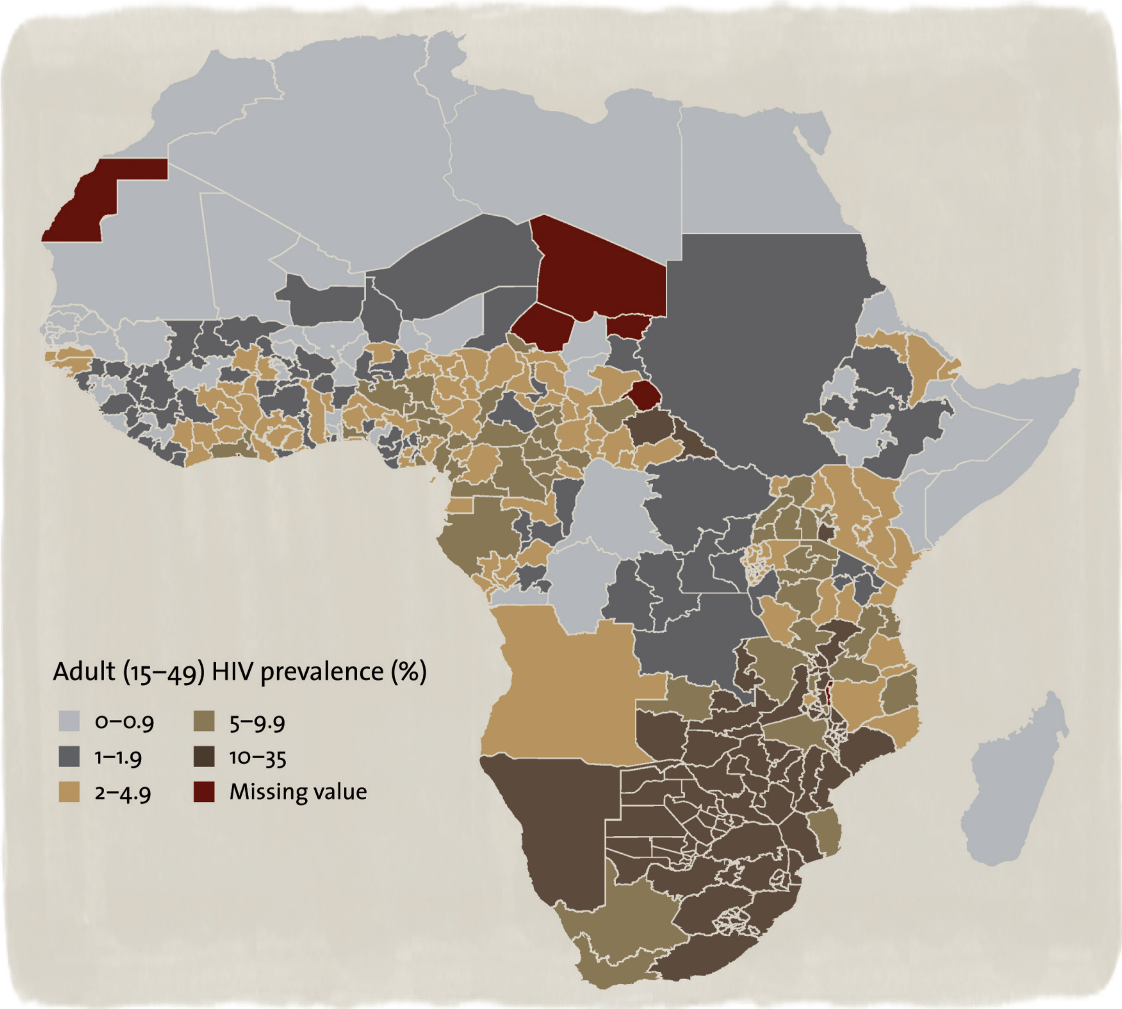
Sexual transmission accounts for more than 80 percent of new HIV infections worldwide, with the rate in SSA being even higher. While paid sex is an important source of new HIV infections in SSA countries with relatively low prevalence, the vast majority of HIV infections in high prevalence countries is not related to paid sex. For example, while an estimated 32% of new HIV infections are attributed to paid sex in Ghana, where adult HIV prevalence is 1.8%, only about 10–14% of new infections are linked to sex work in Kenya and Uganda where adult HIV prevalence is 6.3–6.5%. Urban data from Zambia suggests that 60% of people newly infected through heterosexual transmission acquired HIV within marriage or cohabitation, compared to 50%–65% in Swaziland, 35%–62% in Lesotho and 44% in Kenya. Studies in eastern and southern Africa found that, among all couples tested who had at least one HIV-1 infected partner, the proportion of couples that were HIV-1-discordant varied by study sites from 36 to 85%, with an overall rate of 49%, indicating that discordant couples can succeed in effectively reducing HIV transmission to the uninfected spouses.

Table 1: HIV prevalence, HIV incidence and number of persons living with HIV in sub-Saharan Africa, 2009

	HIV prevalence (Age 15–49)	HIV incidence (Age 15–49)	Number of persons living with HIV (in '000)	Proportion of all HIV+ Persons in SSA	Cumulative Prop. of all HIV+ Persons in SSA
Swaziland	25.9%	2.66	180	0.8%	0.8%
Botswana	24.8%	1.56	320	1.5%	2.3%
Lesotho	23.6%	2.58	290	1.3%	3.7%
South Africa	17.8%	1.49	5,600	25.9%	29.6%
Zimbabwe	14.3%	0.84	1,200	5.6%	35.2%
Zambia	13.5%	1.17	980	4.5%	39.7%
Namibia	13.1%	0.43	180	0.8%	40.5%
Mozambique	11.5%	1.19	1,400	6.5%	47.0%
Malawi	11.0%	0.95	920	4.3%	51.3%
Uganda	6.5%	0.74	1,200	5.6%	56.8%
Kenya	6.3%	0.53	1,500	6.9%	63.8%
Tanzania	5.6%	0.45	1,400	6.5%	70.3%
Cameroon	5.3%	0.53	610	2.8%	73.1%
Gabon	5.2%	0.43	46	0.2%	73.3%
Equatorial Guinea	5.0%	n.a.	20	0.1%	73.4%
Central African R.	4.7%	0.17	130	0.6%	74.0%
Nigeria	3.6%	0.38	3,300	15.3%	89.3%
Chad	3.4%	n.a.	210	1.0%	90.3%
Congo	3.4%	0.28	77	0.4%	90.6%
Cote d'Ivoire	3.4%	0.11	450	2.1%	92.7%
Burundi	3.3%	n.a.	180	0.8%	93.5%
Togo	3.2%	0.27	120	0.6%	94.1%
Rwanda	2.9%	0.18	170	0.8%	94.9%
Guinea-Bissau	2.5%	0.21	22	0.1%	95.0%
Angola	2.0%	0.21	200	0.9%	95.9%
Gambia, The	2.0%	n.a.	18	0.1%	96.0%
Ghana	1.8%	0.15	260	1.2%	97.2%
Sierra Leone	1.6%	0.14	49	0.2%	97.4%
Liberia	1.5%		37	0.2%	97.6%
Guinea	1.3%	0.1	79	0.4%	98.0%
Benin	1.2%	0.1	60	0.3%	98.2%
Burkina Faso	1.2%	0.07	110	0.5%	98.8%
Mali	1.0%	0.06	76	0.4%	99.1%
Mauritius	1.0%	n.a.	9	0.0%	99.1%
Senegal	0.9%	0.08	59	0.3%	99.4%
Eritrea	0.8%	0.03	25	0.1%	99.5%
Niger	0.8%	0.08	61	0.3%	99.8%
Mauritania	0.7%	n.a.	14	0.1%	99.9%
Madagascar	0.2%	n.a.	24	0.1%	100.0%
Comoros	0.1%	n.a.	<1	< 0.1%	100.0%

Source: AIDSinfo (http://www.aidsinfoonline.org), retrieved 8/4/2011
Note: HIV incidence = new HIV infections per 100 person years

Figure 1: Sub-national estimates of HIV prevalence among adults (age 15–59) in sub-Saharan Africa, 2001–2010



NOTE: Subnational data not available for Angola, Eritrea, Gabon, the Gambia, Guinea-Bissau, Madagascar, Mauritania, Namibia, Somalia, Sudan and Togo.
Source: UNAIDS (2011, page 74)

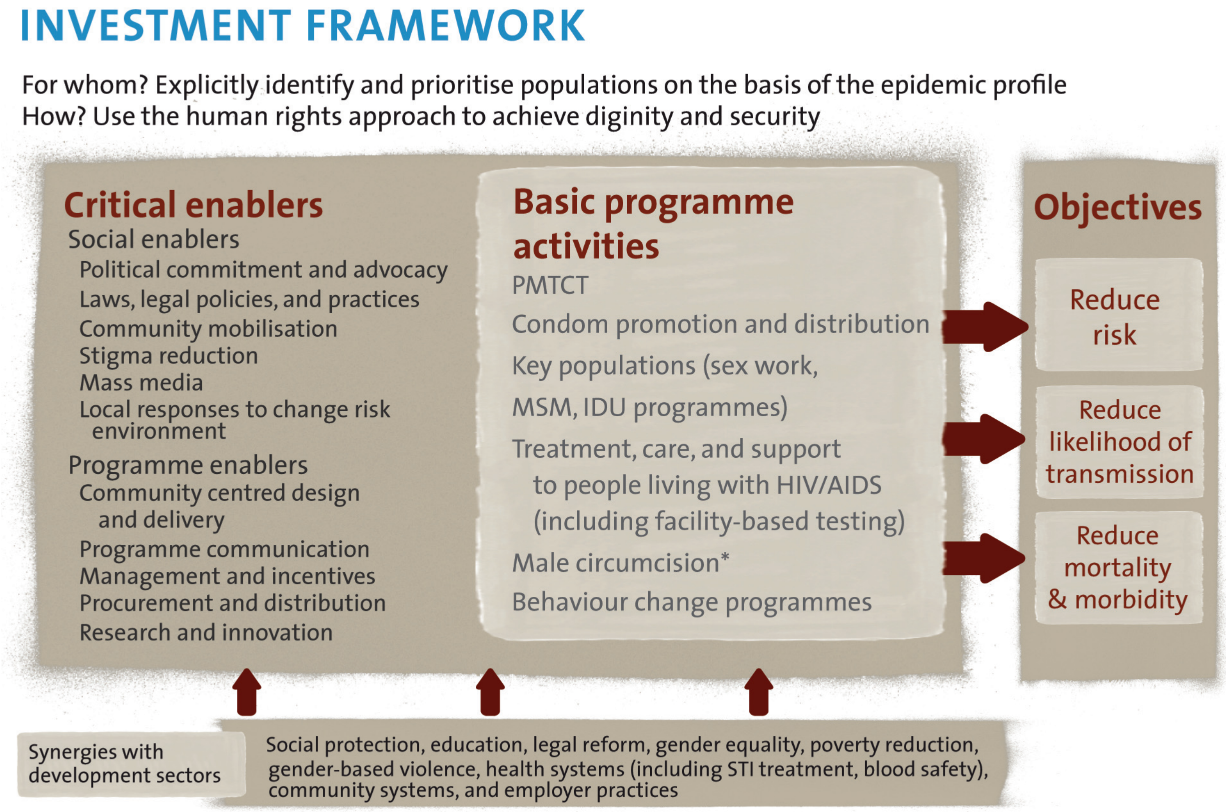
The strategic goal of UNAIDS is to reduce sexual transmission by half, including among young people, by 2015 (UNAIDS 2010, 2011). While there is no doubt that the HIV/AIDS epidemic in SSA continues to be devastating with about 1.8 million annual new infections in 2009, 20 million individuals living with HIV, constituting about 2/3 of the global total, and national adult prevalence ranging up to 25% in Swaziland, Botswana and Lesotho (Table 1), and variance in regional prevalence being even higher, see Figure 1), there is also increasing evidence that the tide of the epidemic has shifted. UNAIDS (2010) for example points out that: (*i*) in SSA, the number of people newly infected with HIV fell from 2.2 million [1.9 million–2.4 million] people in 2001 to 1.8 million [1.6 million–2.0 million] in 2009. (*ii*) In 22 SSA countries, the HIV incidence rate declined by more than 25% between 2001 and 2009; (*iii*) among the five SSA countries with the largest HIV epidemics in terms of the numbers of infected individuals, four—Ethiopia, South Africa, Zambia and Zimbabwe—reduced new HIV infections by more than 25% between 2001 and 2009, while Nigeria's HIV epidemic stabilized. HIV prevalence in Kenya fell from about 14% in the mid-1990s to 5% in 2006, and since 2001, HIV prevalence in Uganda has stabilized between 6.5% and 7%; and HIV prevalence in West and Central Africa remained relatively low in 2009, at or under 2% in 12 countries.

Based on these trends and recent progress in prevention strategies, the 30th anniversary of HIV coincides with a new optimism about the available mix of policies and interventions that aim at reducing HIV infections, and in particular, reducing the sexual transmission of HIV. The Economist recently heralded "The end of AIDS?", concluding that "Thirty years on, it looks as though the plague can now be beaten, if the world has the will to do so" (The Economist 2011). Padian et al. (2011) argue that "we have entered a new area in HIV prevention" where a rapidly changing landscape of HIV prevention suggests a new path of interventions that focuses on efficient combination strategies to turn the tide in the HIV epidemic. Medical male circumcision (MC) has been shown in several randomized controlled trials in SSA to reduce the risk of HIV acquisition by men (Auvert et al. 2005; Bailey et al. 2007; Gray et al. 2007), and while the effect on infection risks during sex with a HIV-positive partner remains somewhat controversial, MC has emerged as one of the core pillars of HIV prevention programs in SSA (Schwartländer et al. 2011; UNAIDS 2010). Recent estimates suggest population-level reductions in HIV infections for men *and* women as high as 28% in Zimbabwe (Hallett et al. 2011), where the reductions in infection risks for men result from the combined effect of a lower HIV prevalence among male partners and possible long-term direct reductions of male-to-female HIV transmission risks that are suggested by recent studies to result from circumcision after the wound healing is completed. Based on the recent evidence about the effectiveness of MC, Potts et al. (2008) argue that resources should be redirected from potentially ineffective interventions—including HIV testing, treatment of STIs and abstinence programs—towards MC and selected other behavioral interventions that have been shown to effectively reduce HIV risks.

In addition to MC, new biomedical developments promise new approaches to substantially reducing the risk of transmitting HIV by offering antiretroviral treatment (ART) to HIV+ individuals as soon as they are infected (NIAID 2011; Smith et al. 2011). This *test-and-treat* strategy is based on the premise that reductions in viral load caused by ART will decrease an individual's infectiousness and advocates regular, widespread HIV testing and immediate initiation of ART for infected people. Findings from the HPTN 052 study (NIAID 2011) for example showed a 96% reduction of HIV transmission attributed to the use of antiretroviral drugs. Some studies have claimed that a comprehensive test-and-treat program could reduce HIV incidence and mortality to less than one case per 1000 people per year by 2016 (Granich et al. 2009), and reduce the prevalence of HIV to less than 1% within 50 years. Based on this recent evidence, it is likely that ART will serve as a cornerstone of combination prevention of HIV-1 in the near future. Continued research will be essential to measure anticipated benefits and to detect implementation barriers and untoward consequences of such a program, especially increases in primary ART resistance. Skeptics of this approach, however, point out that the important role of recent HIV infections in propagating HIV—with studies claiming that up to 40% of HIV infections in urban Malawi are attributable to sexual contact with individuals with early infection (< 6 months) (Cohen and Corbett 2011; Powers et al. 2011), i.e., individuals who are highly infectious but unlikely to be covered by test-and-treat programs in resource-poor countries. Thus, without near-complete coverage, interventions during chronic infection will probably have incomplete effectiveness unless complemented by strategies targeting individuals with early HIV infection, or by interventions that not only reduce HIV transmission risks but also strategies that result in behavioral changes and the adoption of risk-reduction strategies.

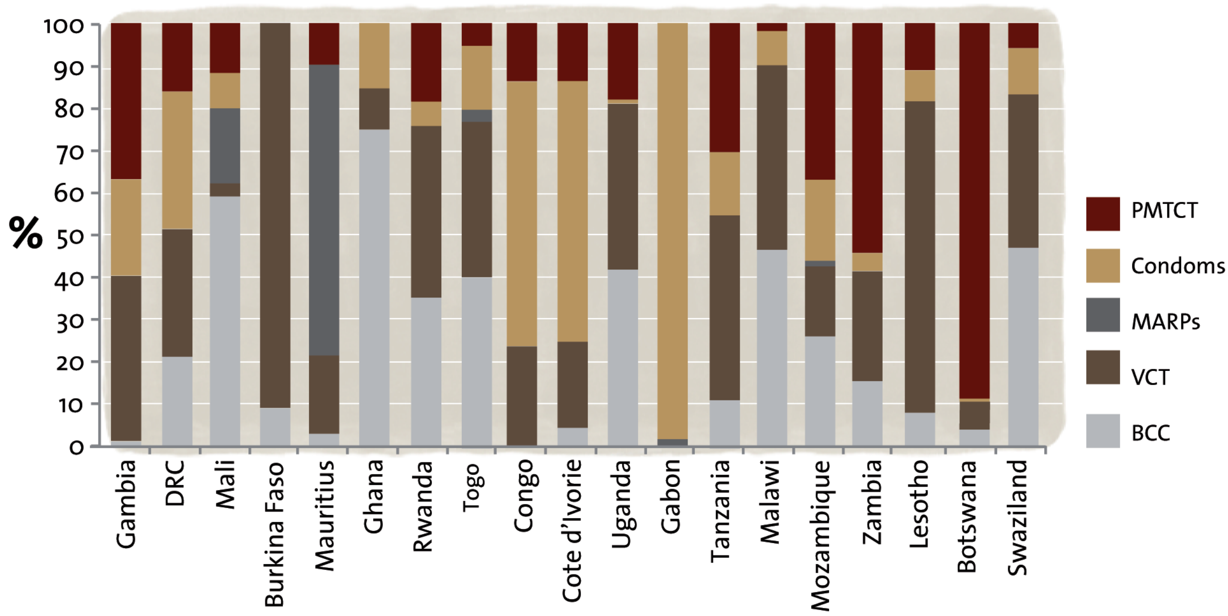
How do behavioral prevention programs fit into the policy mix? Behavioral strategies to prevent the sexual transmission of HIV include programs that aim to delay age of sexual debut, decrease the number of sexual partners and concurrent partnerships, increase the proportion of protected sexual acts, increase acceptance of HIV testing and counseling (HTC), and improve adherence to successful

Figure 2: "Investment approach" to HIV prevention that combines community mobilization, synergies between program elements, and benefits of the extension of antiretroviral therapy for prevention of HIV transmission



Notes: *Applicable in generalized epidemics with a low prevalence of male circumcision. MSM = men who have sex with men. IDU = injecting drug user. PMTCT = prevention of mother-to-child transmission. STI = sexually transmitted infection.
Source: Schwartländer et al. (2011)

Figure 3: Allocation of resources to HIV prevention in sub-Saharan Africa



Notes: BCC = behavior change communication. VCT = voluntary testing and counseling. MARPs = most at-risk populations. PMTCT = prevention of mother to child transmission.
Source: Forsythe et al. (2009), with data from UNAIDS (2008)

biomedical prevention strategies, such as condom use (Coates et al. 2008; McCoy et al. 2010). While biomedical interventions and their promise in reducing HIV infection risk have recently been dominating the headlines in both the scientific and policy-oriented discussion about alternative HIV prevention strategies, Halperin et al. (2011) and Coates et al. (2008) conclude based on their analyses of declining HIV incidence in several SSA countries that behavioral change must remain the core of prevention efforts. In particular, although there have been promising breakthroughs in biomedical interventions to reduce HIV infection risks (notably MC), given the limitations and challenges of biomedical interventions in terms of scaling-up, resource requirements and potential reductions in effectiveness due to drug resistance, these biomedical programs cannot constitute the sole prevention efforts in resource poor contexts such as SSA. Behavioral change programs and structural interventions facilitating behavior change are therefore widely recognized to be an important and essential—but not necessarily sufficient—part of comprehensive HIV prevention programs in SSA (Coates et al. 2008; Padian et al. 2011). The UNAIDS Strategy 2011–2015 concludes that evidence is mounting that comprehensive sexuality education empowers young people to make informed decisions regarding their sexual health and behavior while playing a part in combating damaging beliefs and misconceptions about HIV and sexual health (UNAIDS 2010).

While recognizing this important role of behavioral change programs, Schwartländer et al. (2011) argue that the policy mix needs to change from a "commodity approach" that encourages scaling-up of numerous strategies in parallel, irrespective of the evidence about the relative effects of these programs, towards a strategic "investment approach" that incorporates major efficiency gains through community mobilization, synergies among program elements, and benefits of the extension of ART for prevention of HIV transmission (Figure 2). This framework proposes three categories of investment, consisting of six basic programmatic activities, interventions that create a facilitating environment to achieve maximum effectiveness ("critical enablers"), and programmatic efforts in other health and development sectors related to HIV/AIDS. Four of the six program components focus on reducing the transmission of HIV through sexual relationships, that is, prevention strategies that are within the scope of the analyses in this paper. The investment approach in Figure 2 also emphasizes the role of "critical enablers", i.e., the complementary program activities that are necessary to increase the effectiveness of prevention efforts. Social enablers include outreach for HIV/AIDS testing and HIV/AIDS treatment literacy, stigma reduction, advocacy to protect human rights, and monitoring of the equity and quality of program access and results and mass communication designed to raise awareness and support change in social norms. Program enablers include incentives for program participation, methods to improve retention of patients on antiretroviral therapy, capacity building for development of community-based organizations, strategic planning, communications infrastructure, information dissemination, and efforts to improve service integration and linkages from testing to care. As we will argue below, the cost of these enablers are often inadequately represented in studies assessing the costs of program interventions, despite the fact that they may constitute an important part of the overall program costs (e.g., up to 35% in the initial years of the investment approach in Figure 5). Based on their evaluation of this investment approach, Schwartländer et al. (2011) claim that at yearly cost of achievement of universal access to HIV prevention, treatment, care, and support by 2015 at no less than US$22 billion, this program can globally avert 12.2 million new HIV infections and 7.4 million deaths from AIDS between 2011 and 2020 compared with continuation of present approaches, and result in 29.4 million life-years gained.

In addition to emphasizing a multi-faceted approach to HIV prevention that combines biomedical, behavioral and structural components, as for instance in the investment approach in Figure 2, there is also a broad recognition that the HIV/AIDS epidemic is heterogeneous—globally, but also within SSA—and that interventions need to be specific to local contexts (e.g., Wilson and Halperin 2008). The most important distinction is between the generalized epidemics in high-prevalence SSA countries, where interventions need to change behaviors and/or infection risks on the population level, versus the more concentrated or mixed epidemics in much of the rest of the world and in low-prevalence SSA countries(note in Table 1 there are eight SSA countries with prevalence at 1% or less and 17 SSA counties with prevalences at 2% or less) where interventions can often be more targeted towards the highest risk groups. While programs clearly need to be adjusted to local contexts, even across different SSA countries, based on a nuanced understanding of the local social, economic, institutional and epidemiological context, Coates et al. (2008) also warns of the dangers of extensive modifications to local contexts that are often based on weak empirical evidence about cross-country differences and that may undermine the synergies and scale effects that can be achieved if interventions are applied on a large scale. Evidence that this might be occurring is provided in Figure 3 (Forsythe et al. 2009), which reports the allocation to HIV prevention in different SSA countries that are arranged from low prevalence (left) to high prevalence (right). While one would expect that the allocation of prevention effort varies by HIV prevalence, the pattern in Figure 3 appears quite random with substantial variations across countries that seem to face relatively similar HIV epidemics. For example, focusing on the two highest prevalence countries, Botswana and Swaziland, the resources allocated to prevention efforts appears to be markedly different. In Botswana, most prevention resources are allocated to PMTCT, whereas in Swaziland, the majority of resources are spent on behavioral change communication (BCC), two interventions that are allocated a much smaller proportion of all resources in Botswana. Of course there are other huge differences between markets, policies, and level of development between Botswana and Swaziland that may account for the variations in resource allocations to HIV prevention in the two countries. But if these factors account for the difference, the comparison between these two countries points to the importance of heterogeneities of other types even in countries with similar prevalences.

Assessing the evidence about the effectiveness and cost-effectiveness of interventions

Ideally, the interventions considered to reduce the sexual transmission of HIV would be based on solid empirical evidence about their effectiveness, and resources would be allocated efficiently to different programs. While there is a growing agreement that contemporary HIV prevention programs should adopt a multi-pronged approach combining biomedical, behavioral and structural approaches (Section 2), diverging advice exists in the current literature as to how to allocate resources to the different components. Forsythe et al. (2009) conclude based on an analysis of how resources are allocated to prevention efforts that "there are clear indications that most countries are not allocating their HIV and AIDS resources in a way which is likely to achieve the greatest possible impact" (see also the discussion of Figure 3). And while evidence is often far from conclusive, several criteria to improve allocation decisions exist: Schwartländer et al. (2011) argue that in their investment approach, "basic program activities [that] have a direct effect on reduction of transmission, morbidity, and mortality from HIV/AIDS, [...] should be scaled up according to the size of the affected population." Potts et al. (2008), in agreement with other studies (e.g., Padian et al. 2011; Schwartländer et al. 2011) argue that intervention with established effectiveness in preventing HIV infection should be scaled-up, while programs that have not been shown to reduce HIV should be faded out. Forsythe et al. (2009) propose an "evidence-based allocation strategy" as the overarching principle in which resources are spent in a way that is, based on the best currently available evidence, likely to achieve the greatest possible result in terms of preventing new infections, providing care and treatment, and mitigating impact. Basic economic theory (Behrman and Knowles 1998) suggests programs should be scaled-up until their social marginal benefits equal their social marginal costs, while others have argued that programs with the largest cost effectiveness (Drummond et al. 1997; Musgrove and Fox-Rushby 2006) or highest benefit-cost ratios (Brent 2010a) should receive priority. Equating social marginal benefits with social marginal costs as suggested by Behrman and Knowles implies that programs should be scaled-up or scaled-down to the point at which benefit-cost ratios are one. Political constraints on governmental budgets, high adjustment costs and effective interest groups may preclude scaling-up or scaling-down all interventions so that all benefit-cost ratios are equal to one so values different from one may be observed in for real world programs. Tools such as the *Resource Needs Model* (RNM), which can provide policymakers with a clearer idea of resource requirements, the *Male Circumcision: Decision Makers' Program Planning Tool* (DMPPT), or the *Goals and Allocation by Cost-Effectiveness* (ABCE) models that can also provide decision makers with a clearer vision of how they might reallocate funds. These different criteria and/or tools lead to different priorities in prevention efforts. The economic approaches, for example, may lead to much different allocations among interventions than some of the other "rules" for allocation suggested above because they focus on costs as well as impacts at the margin. Cost effectiveness estimates, for another example, focus by definition on one objective rather than considering multiple objectives as in cost-benefit analysis.

In addition to possible disagreements about the general principles guiding the allocation of resources to different programs, there is considerable uncertainty about the efficacy and/or effectiveness of program interventions to reduce the sexual transmission of HIV. Ultimately, under any of the criteria stated above, only programs that reduce HIV risk behaviors, HIV infection risks and/or HIV incidence should be considered. However, despite the substantial resources devoted to evaluating such interventions, the evidence remains weak (Padian et al. 2010; Ross 2010). For example, restricting studies to the "gold standard" of randomized controlled trials (RCTs) with biological outcome measures (HIV incidence), a systematic review of late phase RCTs evaluating interventions for the prevention of sexual transmission of HIV by Padian et al. (2010) identified only 37 HIV prevention RCTs reporting on 39 unique interventions. Only six RCTs, all evaluating biomedical interventions, demonstrated definitive effects on HIV incidence. Five of the six RCTs significantly reduced HIV infection: all three male circumcision trials, one trial of sexually transmitted infection treatment and care, and one vaccine trial. Njeuhmeli et al. (2011) evaluate the potential population-level impacts of MC using the *Male Circumcision: Decision Makers' Program Planning Tool* (DMPPT) to model the impact and cost of scaling-up adult MC in Botswana, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe, and Nyanza province in Kenya. At a cost of about US$80 per circumcision, the scaling-up adult MC to reach 80% coverage in these countries by 2015, and maintaining 80% coverage thereafter, would entail performing 20.33 million circumcisions between 2011 and 2015 and an additional 8.42 million between 2016 and 2025. Such a scale-up would result in averting 3.36 million new HIV infections and 386,000 AIDS deaths through 2025, and this scale-up would result in net savings (due to averted treatment and care costs) amounting to US$16.55 billion. However, in contrast to the clear evidence documented for MC, almost 90% of HIV prevention trials reviewed in Padian et al. (2010) had 'flat' results, i.e., the RCTs did not indicate statistically significant declines in HIV and/or STI incidence as a result of the intervention. In some cases, these flat results may be attributable to trial design and/or implementation, including for example inadequate sample sizes to detect changes in incidence, especially in light of the often lower-than-expected incidence in both arms of the RCTs, the requirement to provide "diluted" forms of the intervention to the control arm, or the "diffusion" of the intervention into the control group. An update of this review of RCTs (Padian et al. 2011) has further strengthened the evidence for biomedical interventions—MC and ART as prevention ("test-and-treat")—and also points to the potentials of structural interventions such as microfinance programs (Pronyk et al. 2006, 2008) or conditional cash transfers (Baird et al. 2010; Kohler and Thornton forthcoming) that are discussed in more detail below. Behavioral interventions that have been evaluated in RCTs include some combination of risk reduction counseling, condom promotion and referral and treatment for STIs that exceed the local standard of care. But even the updated analyses in Padian et al. (2011) fail to identify effective behavioral interventions and all seven RCTs reviewed in the study did not find statistically significant reductions in HIV incidence. In summary, therefore, while for some biomedical interventions—and in particular, male circumcision—strong evidence about their efficacy and sometimes their effectiveness exists, outside of these biomedical interventions, the empirical evidence often needs to be supported by circumstantial evidence, evidence from observational studies—which generally do not establish causal effects—or studies that use behavioral outcomes rather than HIV incidence itself in trying to establish the effectiveness of interventions.

The aforementioned limited evidence from RCTs about the effectiveness of behavioral strategies to reduce the sexual transmission of HIV is in sharp contrast with the important role that is often attributed by others to behavioral changes in reducing HIV incidence in SSA (e.g., UNAIDS 2010). Analyzing comprehensive data from Zimbabwe, Gregson et al. (2010) and Halperin et al. (2011) for example document that HIV incidence may have peaked in the early 1990s, and fallen during the 1990s. Household survey data shows that this decline in HIV incidence in Zimbabwe is linked to reductions in reported casual partners from the late 1990s onwards, and in increases in condom use in non-regular partnerships between 1998 and 2007. Gregson et al. (2010) claim that this study provides the first convincing evidence of an HIV decline accelerated by changes in sexual behavior in a southern African country. Declines in HIV prevalence have been linked to behavioral changes also in other SSA countries (Hallett et al. 2006; The International Group on Analysis of Trends in HIV Prevalence and Behaviours in Young People in Countries most Affected by HIV 2010; UNAIDS 2010). Increases in AIDS mortality may have been a key factor driving behavioral changes, and in the specific case of Zimbabwe, another key factor may have been the adverse economic conditions that prevailed during this period. In terms of interventions and behavioral change programs, Halpern et al. identify condom distribution and promotion programs, and community-based interventions as plausibly making major contributions to the HIV decline in Zimbabwe, while they discount an important role related to HIV testing and counseling. Interpersonal communication about HIV/AIDS and risk reduction strategy is likely to have been an important facilitating factor (see also Behrman et al. 2009; Kohler et al. 2007). Potts et al. (2008) also argue that policies targeted at the reduction of multiple concurrent partnerships were one intervention that may have contributed substantially to declines in HIV in SSA, with potentially much greater effectiveness if this prevention strategy had been adopted more broadly.

In contrast, in a somewhat pessimistic summary about behavioral interventions to reduce HIV infections in the context of generalized epidemics such as HIV in SSA, Wilson and Halperin (2008) observe that the most "trusted interventions"—including HIV testing and counseling, condom promotion, and school and youth (including abstinence programs)—are "at best unproven, and at worst disproven, for reducing HIV incidence". Based on the mixed evidence that emerges from the above review, no single behavioral HIV prevention approach has therefore emerged as the leading behavioral intervention in SSA, and the claims that these efforts contributed importantly to the recent declines in HIV in some SSA countries are often based on indirect—and sometimes weak—evidence. While behavioral change programs continue to be emphasized in most agendas aiming at reducing HIV infections (Bertozzi et al. 2006; Schwartländer et al. 2011; UNAIDS 2010), the evidence of dramatic behavioral changes as a response to these programs in SSA remains controversial (McCoy et al. 2010).

In reviewing the evidence about policy intervention, HIV testing and counseling (HTC) deserves specific attention. HIV testing and counseling, and in particular, the component of HTC formerly referred to as voluntary testing and counseling (VCT), has been key component of AIDS control programs for several years, predating the rise of "test-and-treat" interventions in which HIV testing is central for identifying HIV-positive individuals and enrolling them in ART treatment. For example, an Op-Ed piece in the New York Times several years ago declared that HTC is the "missing weapon" in the battle against AIDS (Holbrooke and Furman 2004), based on the argument that those who learn they are *not* infected will be more strongly motivated to avoid infection in the future, and those who learn that they *are* infected will be motivated to avoid infecting others. Yet, at least several RCT studies evaluating HTC programs have shown no consistent reduction for those who test HIV-negative, although risk reduction in some who test positive has occurred, and the studies found no population-level impact of HTC on HIV and/or STI incidence (Corbett et al. 2007; Denison et al. 2008; Metcalf et al. 2005; Sherr et al. 2007; The Voluntary HIV-1 Counseling and Testing Efficacy Study Group 2000). There is also little evidence, among HIV-negative individuals, of HTC impacts on behavioral risk reduction (e.g., condom use or reduction in the number of sexual partners) or even subjective risk assessments about being HIV positive (Delavande and Kohler forthcoming; Matovu et al. 2006), and selectivity in HTC uptake and/or study participation may have affected the findings of existing studies (Glick 2005). Only one recent study by Cremin et al. (2010) documented that both HIV-positive and HIV-negative women receiving HTC have sustained significant reductions in the number of sexual partnerships (the reductions existed for males, but were not statistically significant). Based on the existing evidence, Ross (2010) speculates that HIV testing and counseling might be effective persuading HIV-positive individuals to reduce their risk of onward transmission of HIV to their partners, but potentially leads to relative disinhibition among those who test HIV-negative along the lines of "I have taken risks in the past and have not been infected, so maybe I can continue with my previous behaviors"?

It is important, however, to recognize that the contemporary context in which HIV testing and counseling is expanded is often substantially different from the context in which the above studies were conducted (Gersovitz 2011), as voluntary counseling is increasingly complemented by routine testing within health care settings, home-based testing and counseling or even self-testing (Ganguli et al. 2009; Helleringer et al. 2009; Weinreb and Stecklov 2009). New testing possibilities, including more frequent testing and home-based testing, and a decreasing stigmatization of testing HIV positive, and new incentives to get tested to gain access to ART for both treatment and prevention, may have changed the impact of HTC on behavioral risk reduction and behavioral change in SSA. Couple-based HIV testing and counseling (Painter 2001), incentives for getting tested (Thornton 2008), or programs facilitating the communications of HIV test results between spouses or with sexual partners (Anglewicz and Chitsanya 2011) may also enhance the effectiveness of HIV testing and counseling in reducing HIV infection risks, and community-based interventions using mobile technologies can be used to substantially increase the uptake of HIV testing services (Sweat et al. 2011). Despite the somewhat mixed evidence, therefore, UNAIDS Strategy 2011–2015 continues to emphasize the scaling-up of HIV testing and counseling as an essential component of prevention strategies, including particular foci for improving access to HIV testing and counseling among youth and HTC for couples. UNAIDS (2010), and Cremin et al. (2010) conclude that "[HTC in the form of] VCT arguably represents the best opportunity for encouraging sexual behavior[al] change, which is essential if the transmission of HIV is to be abated and the provision of treatment is to be sustainable". This conclusion is conditional on HTC leading to sustained risk reduction among both infected and uninfected individuals. This outcome is only likely if HTC is widespread, possibly relatively frequent, combined with high-quality counseling.

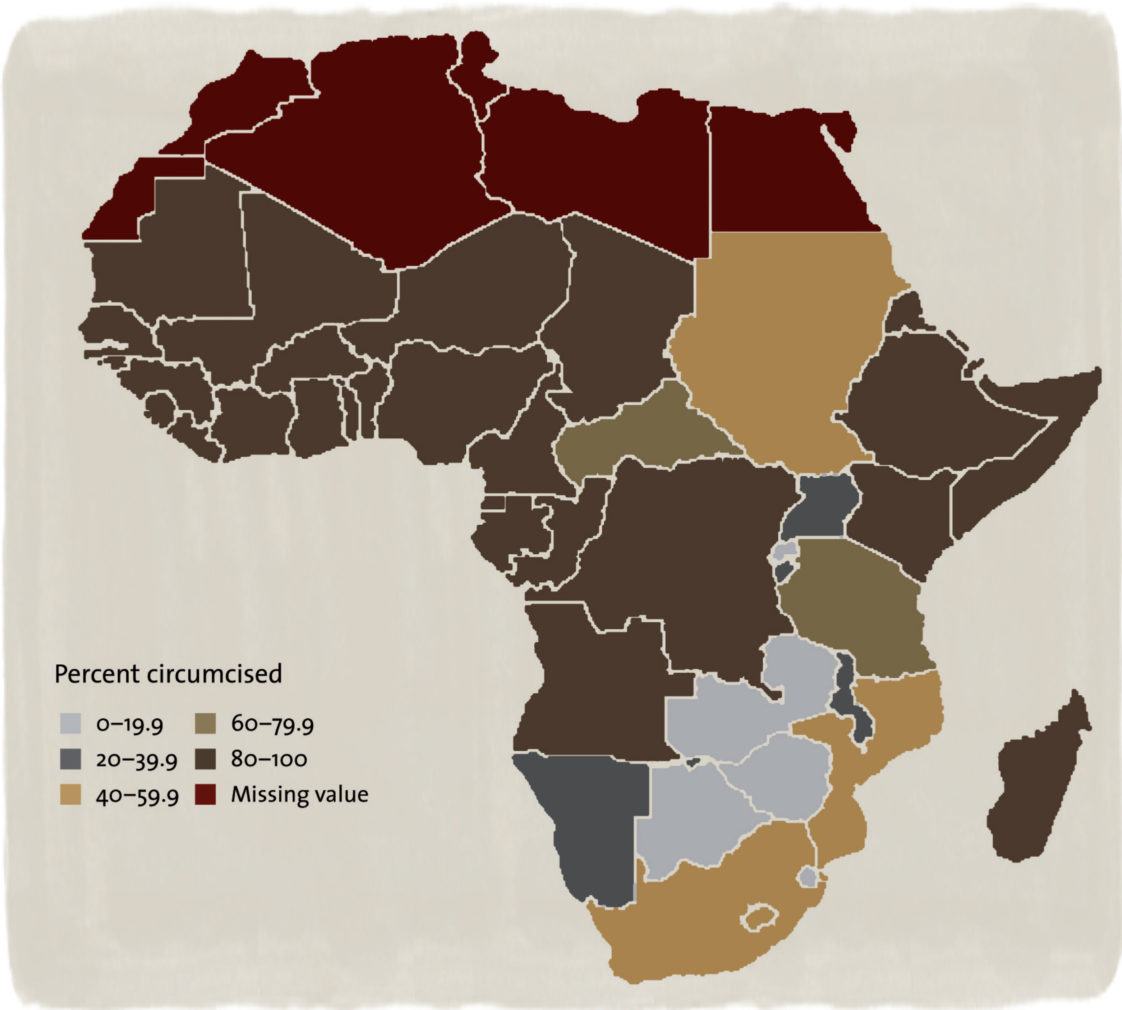
In addition to offering some revisionist perspectives on HIV testing and counseling, some recent studies also provide a more optimistic perspective within the otherwise generally inconclusive or controversial empirical evidence about the effectiveness of behavioral interventions. For example, cell phones and related technologies may offer new ways for delivering information campaigns, and for interacting with young adults in SSA, in ways that can reduce HIV risks (Swendeman and Rotheram-Borus 2010). A recent school-level randomized experiment has also provided information on the relative risk of HIV infection by partner's age, and documented that the sexual behaviors of teenagers are responsive to HIV risk information. In particular, this randomized study documented a 28% decrease in teen pregnancy, an objective proxy for the incidence of unprotected sex (Dupas 2011), among teenagers who received information about the local prevalence of HIV disaggregated by age and gender group, i.e., important—but generally not available—information that can affect partner selection and the adoption of condoms or other risk-reduction behaviors with a specific partner, while the official abstinence-only HIV curriculum had no impact on teen pregnancy. Besides offering HIV-related education and training in schools, some recent studies also suggest that encouraging school attendance by adolescents—and in particular girls—through monetary incentives can not only reduce school dropouts but can also reduce HIV infection risks by delaying sexual debut and/or other reducing risk factors associated with infection with human immunodeficiency virus (Baird et al. 2010; Cho et al. 2011; Hallfors et al. 2011). In addition, several other programs that deviate from the more conventional behavioral intervention programs that have been the focus of much of the above literature, have emerged as potential HIV prevention approaches. For example, Pronyk et al. (2006, 2008) document with a large-scale RCT that the IMAGE Program in South Africa, which combines microfinance for women with gender training and community mobilization, resulted in increases in household economic well-being and women's empowerment, a 50% reduction in intimate partner violence, and reduced HIV risk behavior among young women participants. The program has scaled-up to reach more than 12,000 women in South Africa. In addition, several studies have suggested the possibility that conditional cash transfers can effectively be implemented to reduce HIV infection risks, including a program that gave financial rewards for testing negative for non-HIV sexually transmitted diseases every few months in Tanzania (RESPECT) (de Walque et al. 2011; World Bank 2010b) and a program for adolescents in Mexico (Galarraga and Gertler 2010). Another program in Malawi found that conditional and unconditional cash transfers for adolescent girls were associated with lower rates of marriage (Baird et al. 2010) and HIV (World Bank 2010a). Recent press releases have heralded these conditional cash incentive programs as potentially promising and innovative approaches to HIV/AIDS prevention. The UC Berkeley news release about the RESPECT program for example begins "Giving out cash can be an effective tool in combating sexually transmitted infections in rural Africa" (Yang 2010). Kohler and Thornton (forthcoming), drawing on a program offering financial incentives for individuals to maintain their HIV status in Malawi, however raise some concerns about the potential effectiveness of CCT programs for HIV prevention, and conclude that CCT programs that aim to motivate safe sexual behavior in Africa need to take into account that money given in the present may have much stronger effects than rewards in the future, and any effect of these programs may be fairly sensitive to the specific design of the program, the local and/or cultural context and the degree of agency individuals have with respect to sexual behaviors.

In summary, current empirical evidence clearly points to MC as a promising intervention, with possible additional effective interventions being comprehensive testing and counseling, effective information and peer group campaigns and possibly programs that encourage schooling or incentivize HIV risk reductions. Translating these findings into policy interventions, however, requires prioritization among different possible prevention approaches, as well as decisions about resource allocations to different components in multi-faceted approaches such as the "investment approach" in Figure 2. In choosing among these effective interventions, additional criteria are necessary to guide resource allocations and aid the prioritization of prevention strategies. Cost-effectiveness analyses and benefit-cost analyses can both fill this gap, and especially the former has been extensively applied to HIV prevention programs.

To provide guidance about the allocation of resources to prevention efforts, an extensive body of literature has emerged that studies the cost-effectiveness of interventions targeted towards reducing HIV infections through sexual relations. Cost-effectiveness is defined to yield the effectiveness in terms of some specific goal for the use of some specific amount of resources, often using summary measures of effectiveness such as the quality- or disability-adjusted life years (QALYs/DALYs) gained/averted through the same resources used in different interventions (Drummond et al. 1997). Cost-effectiveness analysis (CEA) is then used to compare two or more alternatives in terms of their costs and effectiveness through a cost-effectiveness ratio that is computed as the difference in costs over the difference in effectiveness. In the context of HIV/AIDS, the costs per HIV infection averted and the costs per DALY/QALY are also often used as the outcome variables. A recent review by Galarraga et al. (2009), for example, conducted a systematic identification of publications through several methods: electronic databases, internet search of international organizations and major funding/implementing agencies, and journal browsing. Inclusion criteria included: HIV prevention intervention, publication in 2005–2008, setting in low- and middle-income countries, and cost-effectiveness estimation (empirical or modeling) using outcomes in terms of cost per HIV infection averted and/or cost per disability-adjusted life year (DALY) or quality-adjusted life year (QALY). The study found 21 studies analyzing the cost-effectiveness of HIV-prevention interventions published in 2005–2008. Seventeen cost-effectiveness studies analyzed biomedical interventions; only a few dealt with behavioral and environmental/structural interventions. Sixteen studies focused on SSA, and only a handful on Asia, Latin America and Eastern Europe. They summarize the results of these studies to show that many HIV-prevention interventions are very cost-effective in absolute terms (using costs per DALY averted), and also in country-specific relative terms (in cost per DALY measured as percentage of GDP per capita). They also note that there are several types of interventions for which cost-effectiveness studies are still not available or insufficient, including surveillance, abstinence, school-based education, universal precautions, prevention for positives and similar structural interventions. They further conclude that the sparse cost-effectiveness evidence is not easily comparable due to a lack of uniform reporting of costs and outcomes, and, thus, not very useful for decision making. There is still much work to be done both on costs and effectiveness to adequately inform HIV prevention planning. Some key findings of Galarraga et al.'s (2009) review, which are relevant for the discussions within the framework of RethinkHIV about the prevention of sexual infections, are reported in Table 2 (for a related study, see Uthman et al. 2010).

Based on their review of the literature, Galarraga et al. (2009) conclude that MC stands out as highly cost-effective given the levels of efficacy suggested by recent RCTs, and whereas no clear picture emerges for behavioral and structural interventions (see also Shepherd et al. 2010). For behavioral interventions, there is a lack of demonstrated efficacy in reducing HIV infections, and even where such evidence exists, careful cost-effectiveness data are often missing. A similar conclusion is

Figure 4: Male circumcision prevalence in sub-Saharan Africa, 2010



Source: UNAIDS (2011, page 65)

obtained with respect to HCT, where cost-effectiveness results are strongly affected by the mixed findings about the extent to which HCT can reduce HIV. A possibly more optimistic perspective of the cost-effectiveness of HTC is suggested by a recent study (Waters et al. 2011) that has cost-effectiveness of alternative HIV retesting frequencies, with testing frequencies ranging from 3 months to 30 years. The benefits of HTC occur as persons testing HIV+ receive treatment, thereby reducing the further transmission probabilities (no behavioral change is assumed to result from HTC in this study). For example, accounting for secondary infections averted, the most cost-effective testing frequency was every 7.5 years for 0.8% incidence, every 5 years for 1.3% incidence, and every 2 years for 4.0% incidence. At a testing frequency of 7.5 years, the overall cost per QALY gained was $701, and the total cost per HIV-infected case identified was $2030. Thus, even in low prevalence populations, regular HTC (re-)testing could be cost-effective—even if there are no behavioral changes resulting from HTC itself as all the benefits occur in Waters et al. (2011) through ART treatment of HIV+ individuals. In terms of structural interventions, Galarraga et al. (2009) primarily identify conditional cash transfer (CCT) programs as potentially cost-effective interventions, based on further studies confirming existing evidence about their effectiveness, while in many other structural interventions no clear conclusions about their cost effectiveness could be established.

Table 2: Cost per DALY and cost per infection averted for selected interventions in sub-Saharan Africa

Cost (US$) per				
	DALY	**infection averted**	**Region/ country**	**Source**
HCT	82	1,315 483*	SSA Kenya	Hogan et al. (2005) John et al. (2008)
Treatment of STIs	17–121	321–3,635	E. Africa	Oster (2005); Vickerman et al. (2006); White et al. (2008b)
School-based interventions	376–530	6,704–9,448	Africa	Hogan et al. (2005)
Male circumcision	–	176–3,554	SSA	Gray et al. (2007); Martin et al. (2007); White et al. (2008a)
Empowerment/ social/ peer-based programs/ mass media	3	599	SSA	Hogan et al. (2005)

Sources: Adapted from Galarraga et al. (2009)
Note: * focuses on averting infant infections

Beyond cost-effectiveness analyses, there is also a nascent literature on cost-benefit analyses for setting priorities for HIV/AIDS interventions (Brent 2010a). This cost-benefit approach considers benefits more broadly, including the subjective well-being of individuals, and tries to account for the fact that individuals make conscious choices with respect to sexual relations and other behaviors that affect their HIV infection risks (Philipson and Posner 1993). Brent (2010b), for example, evaluate the costs and benefits of scaling-up HCT programs in Tanzania, formulating a welfare function based on an individual's, or in the case of couple-HCT, two individuals' expected utility functions and estimating the benefits the averted lives lost whenever discordant couples are revealed, while the costs also include the utility costs of behavioral changes based on new information about one's (and possibly one's spouse's) HIV status. The study finds that the existing HCT program is only marginally worthwhile, while scaling-up the program, and particular, also scaling-up couple-HCT, could increase the benefit-cost ratio to over three. A related study also finds that the benefits of education through delaying the onset of sexual activity outweigh the costs of the program and the possible positive effects of higher education on risk-taking behaviors (Brent 2009).

RethinkHIV: Possible solutions for the prevention of HIV infections through sexual relations

Our guidelines for selecting possible solutions for RethinkHIV that aim for the reduction of HIV infection through sexual relations are as follows: First, we focused on potential interventions for which there is reasonably strong empirical evidence from multiple SSA countries about the efficacy—and possibly even effectiveness—of the intervention. Second, we focused on interventions that are seen as important elements in the HIV/AIDS prevention efforts in SSA by international organizations and local governments. Third, we restricted ourselves to interventions for which reasonable estimates about both the benefits and costs of the intervention could be obtained. The later requirement, for example, ruled out the consideration of test-and-treat programs, as the efficacy of this possible intervention has just recently been established and the effectiveness of the intervention outside the context of randomized trials, as well as the challenges—and costs—of a scale-up of these interventions, are currently unknown.

Based on these guidelines, the three solutions for the prevention of HIV infections through sexual relations for which cost-benefit and cost-effectiveness estimates are presented in this Assessment Paper are:

Male circumcision (MC)

MC is currently the policy intervention with the strongest empirical evidence based on randomized controlled trials in SSA that have carefully assessed effectiveness in preventing sexually-transmitted HIV. Extensive studies have also been conducted to assess the costs and challenges of implementing and scaling-up MC. Multiple studies have suggested that this scale-up of MC is cost-effective. MC is also an important element of the prevention agenda promoted by UNAIDS as well as many governments or NGOs in SSA. The prevalence of MC continues to be relatively low in many countries most affected by the HIV/AIDS epidemic (Figure 4), and MC has been scaled-up in many SSA countries and seems to be accelerating rapidly. For example, UNAIDS (2011) reports that more than 100,000 men were circumcised in eight priority countries (Kenya, Malawi, Namibia, Rwanda, South Africa, Swaziland, Zambia, Zimbabwe) in 2009, up from less than 50,000 in 2006, and more than 350,000 men were circumcised during 2010 in these eight countries. While some scholars have argued that behavioural disinhibition, that is, the adoption of riskier sexual behaviours among circumcised men, may reduce the effectiveness of MC for reducing HIV incidence, current empirical evidence suggests that behavioural disinhibition is unlikely to be a major factor that will substantially reduce the effectiveness of MC (for one of many related discussions on the validity of the evidence supporting MC and its potential for HIV reductions in SSA, see Geen et al, 2011, and Banerjee et al, 2011). For example, data from the three RCTs on MC (Auvert et al., 2008; Bailey et al., 2007; Gray et al, 2007) and one prospective cohort study (Mattson et al., 2008) found no overall increases in risk behavior following circumcision. Among the Kenya RCT participants, Mattson et al. (2008) found that risk behavior actually decreased over the course of 12 months.

Most existing studies of MC have focused on circumcision of adolescents and young adults, and this focus is attractive because adolescents and young adults often represent the age groups most at risk of contracting HIV. It is clear, however, that MC can be performed at a variety of ages, including at very young ages. Evidence from Botswana suggests that infant MC may be very acceptable to mothers (Plank et al, 2010). Infant or neonatal circumcision is relatively easily performed in context where a large fraction of births occur within hospital contexts, or neonatal follow-ups in hospitals are common, and the marginal costs of performing a neonatal MC in the context of a hospital delivery might be small. Bollinger et al (2009) for example estimate for Botswana that the costs of neonatal MC are about 20% lower than the costs of adult MC due to lower complication rates and lower costs for commodities, and some studies–in the specific case for Rwanda–estimate costs for neonatal or infant circumcision that are only about 25% of the costs of adult MC (studies in the US suggest that the costs of neonatal/infant MC are only about 10% of the costs of adult MC, but the applicability of these estimates to SSA is questionable given the generally less developed health systems in SSA). The primary disadvantage of neonatal/infant MC as compared to adult MC is that the primary benefits in terms of reduced HIV incidence will occur 20-30 years in the future when individuals who were circumcised as infants reach their primary ages of sexual activity. We will discuss these pros and cons of neonatal/infant MC as compared to adult MC further in the context of our discussion of the benefit-cost ratios for MC. For example, White et al.'s (2008a) simulations suggest that circumcising neonates would begin to reduce HIV incidence in the general population after 20–30 years in men and 30–40 years in women, whereas circumcising most men before sexual debut or in early adulthood would have much quicker impacts.

Although tens of millions of men remain uncircumcised in SSA, it is also important to recognize that the prevalence of MC is already fairly high in several countries and regions with high HIV prevalence (Figures 1 and 4), raising some doubts whether scale-ups in MC are a realistic effective scenario in all SSA contexts with severe epidemics.

HIV testing and counseling (HTC)

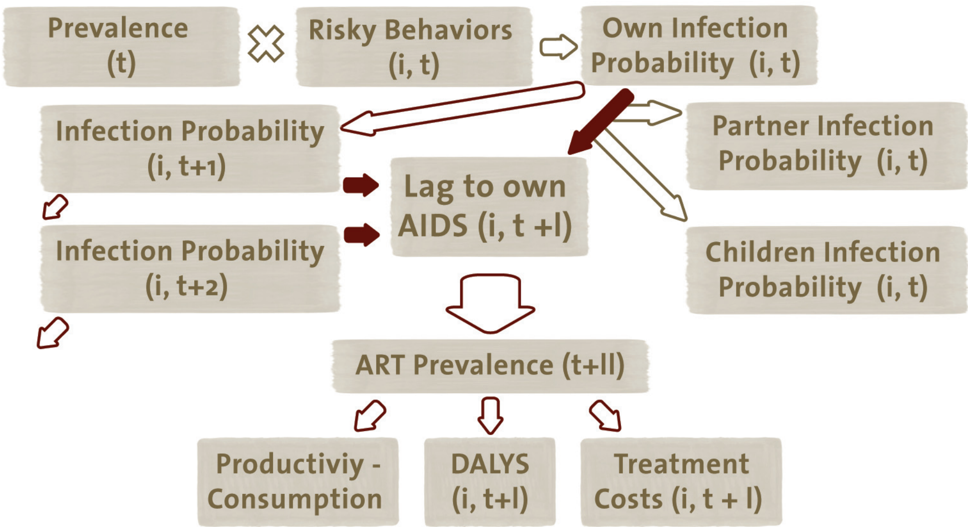
We consider HTC as a possible solution for the prevention of sexual transmission of HIV, even though the empirical evidence to date is mixed. HTC is likely to remain an important component of HIV prevention, especially given that it is a crucial element in providing HIV-positive individuals with ART for both treatment and possibly prevention. In addition, technological progress has changed the options for HTC substantially from the context in which earlier HTC programs were evaluated, thereby improving access to HTC as well as potential frequency and convenience of testing and the possible expansion of couple-based HTC. Relatively comprehensive repeated home-based HTC is therefore a realistic option in SSA, and recent studies suggest that such programs can lead to reductions in the sexual transmission of HIV. It is important to emphasize, however, that benefit-cost calculations for HTC are more speculative than those for MC as both estimates of the program effects, and the costs of HTC programs to achieve these program effects, have great uncertainty.

Information campaigns through mass media and peer groups (IC)

Our consideration of information campaigns through mass media and peer groups (IC) is based on the fact that, despite the uncertain empirical evidence about their effectiveness, these programs continue to constitute an important component of HIV prevention strategies. While the alleged effectiveness of some of the "conventional" media and peer group campaigns are not generally backed by careful empirical evidence, more recent studies suggest that more innovative program designs—including for instance school-based interventions, information campaigns that provide specific local information relevant to risk reduction (e.g., the local HIV prevalence by age), or programs that rely on cell phones and related technologies—are effective in reducing HIV infections among young adults. As with HTC, it is important to emphasize that benefit-cost calculations for IC are more speculative than those for MC as both estimates of the program effects, and the costs of HTC programs to achieve these program effects have great uncertainty.

The above policy options are attractive to consider in the context of the RethinkHIV Project because the potential solutions cover a broad range of empirically and theoretically attractive interventions: First, our analyses include a biomedical intervention (male circumcision) that results in a long-term irreversible reduction in infection risk as a result of a one-time medical procedure; risk reductions are potentially stronger for female-to-male and male-to-male transmissions, but may also be important for male-to-female transmissions. The second option considers HTC campaigns that focus on information that individuals have about their own HIV status though HIV testing and counseling, where both theoretical and empirical arguments suggest that providing individuals with accurate information about their own—and possibly also their spouses' and/or other sexual partners' HIV status—should result in less risky decisions about sexual behaviors and sexual relationships. Finally, the third option focuses on information campaigns through mass media and

Figure 5: Conceptual framework for the benefit-cost analyses of interventions to reduce the sexual transmission of HIV: Possible sequences for individual *i* starting at year *t*



peer groups that aim at reducing risk behaviors in populations affected by HIV by providing more information about HIV/AIDS and potential prevention strategies; information campaigns have also integrated peer groups and community mobilization for prevention efforts, and these aspects seem important for attaining program effectiveness.

Some readers may wonder why condom distribution is not an obvious solution to consider. The answer is that we have not been able to find systematic studies, such as RCTs, that provide persuasive evidence that interventions that focus primarily on condom distribution are likely to be high benefit-cost interventions.

Benefit-Cost Analyses for Policy Interventions: Some General Considerations

The remainder of this paper focuses on establishing benefit-cost ratios, as well as cost-effectiveness estimates, for the above interventions to reduce the sexual transmission of HIV in SSA. The approach that we pursue in this context combines several of the important themes discussed above: we focus on interventions for which there is reasonable evidence about their effectiveness. We adopt an explicit life-cycle perspective in which both the costs and benefits of the interventions occur throughout an individual's life, and we explicitly consider survival probabilities and levels of income and consumption as they occur across the life-cycle. We also consider how interventions are likely to affect the course of the HIV/AIDS epidemic, and how the benefits of an intervention may change as a result of the fact that the intervention affects the future HIV prevalence within which individuals will make decisions about sexual and related behaviors.

Within the scope of the present paper, however, it was also necessary to accept several limitations. First, some epidemiological models for cost-effectiveness analyses are based on fairly detailed models that derive the disease dynamics from assumptions about sexual behaviors, including mixing between different subpopulations, and model changes in prevalence as the combined effect of mortality, changes in infection risks and behavioral change. But because of the scarcity of information our framework is more limited. We capture the effects of mortality, program interventions and behavioral changes on prevalence by making reasonable assumptions about disease dynamics, rather than deriving the disease dynamics from micro-foundations. In addition, in order to estimate the benefits of interventions, we account for the additional DALYs lived by individuals in the presence of interventions to reduce the sexual transmission of HIV across the life-course, and we include the costs/benefits from losses in productivity and consumption through mortality and morbidity. Second, we do not derive individual behavior based on an explicit utility maximization model and a derived welfare function for individuals or couples, nor do we explicitly allow for behavioral changes in responses to interventions that would in part reduce the effectiveness of the intervention (e.g., increases in risky sex in response to the reduced HIV infection risks after circumcision are not explicitly modeled). We do, however, base our reductions of infection risks on empirical studies that have identified the net (or reduced form) consequences of different interventions, and these program effects tend to reflect the extent to which individuals have modified their risk-taking behaviors in response to interventions. Third, we also do not consider intergenerational perspectives, such as are relevant to account for the consequences of preventing a person's HIV infection on reduced mother-to-child transmission or the human capital investments of children in the person's household. Fourth, we also do not explicitly account for altruism. Several of these limitations can be addressed in future research. Despite these limitations, however, the benefit- cost approach utilized in this paper is an important contribution to the existing literature evaluating different interventions to reduce the sexual transmission of HIV because we ground our analysis in a systematic integration of the available evidence within a dynamic life-cycle perspective in which an individual faces evolving risks and ART prevalences, with age-specific survival probabilities and with the incorporation of age-specific productivity and consumption effects in addition to DALYS.

Within the framework outlined above, benefit-cost analyses differ from studies of cost effectiveness in several important dimensions, and benefit-cost analyses are likely to be preferable for guiding policy decisions about how to allocate scarce resources to different possible interventions. Benefit-cost analysis, or the equivalent in the present case of internal rates of returns, is the appropriate tool for prioritizing among solutions that many have multiple impacts, such as those considered in this paper. The alternative of cost-effective analysis for only one impact is only partial and may be misleading if major impacts are ignored. For example the cost per life saved or per DALY saved may be quite misleading if there are impacts on other outcomes such as productivity, as appears to be the case for HIV/AIDS. Therefore we focus in this paper on benefit-cost analysis, though we make some comparisons below with cost-effectiveness estimates to see whether or not the focus in cost-effectiveness analysis on single impacts leads to similar rankings of interventions.

Conceptually, benefit-cost analysis is straightforward. Simply compare the benefits with the costs - if the benefits exceed the costs, or equivalently the benefit-cost ratio exceeds one, then an intervention is warranted. The benefits are simply the sum of the present discounted values of the weighted impacts of the interventions. Likewise the costs are simply the sum of the present discounted values of the costs of the intervention. The devil—and the challenges—however, as usual are in the details. Some examples follow:[4]

Applying this general concept of benefit-cost analyses to the prevention of the sexual transmission of HIV requires the adoption of a life-cycle perspective in which both infection risks, as well as the costs and benefits of being HIV-negative or becoming infected with HIV, are dependent on an individual's life-cycle. Figure 5 illustrates some of the complexities with a representation of

4 Several of these issues are also relevant in the context of other mathematical models that are used to evaluate HIV prevention or treatment programs. For example, in a review of the key messages emerging from mathematical models of HIV/AIDS interventions, Johnson and White (2011) identify several themes and challenges that are common to these models: the positive (or possibly negative) effects of interventions beyond the groups in which they are introduced, the importance of intervening early, the potential for behavioral changes towards more risky behaviors to reverse gains made in HIV prevention, and the emerging threat of drug resistance.

the dynamics of the process. The individual starts in year *t* unaffected when s/he is a given age and gender, say a 20 year-old male for concreteness, and in a particular context that reflects the prevalence of HIV at that time and his behaviors that put him at risk. The right-side of this figure gives the benefits for a 20 year old male of averting infection in terms of DALYs that would be lost, ART and other treatment costs, loses of production minus consumption – all of which occur with lags due to the latency period before HIV leads to AIDS and the probabilities of all of which depend on survival probabilities in the absence of AIDS and the prevalence and timing of ART among those infected with HIV. The left-side gives the dynamics over subsequent ages, depending on the nature of the intervention including how it affects the HIV prevalence in the relevant population. In addition to the effects on the 20 year old male as he ages, as indicated in the upper right side of the figure there are effects on partners and possible intergenerational transmission of effects to children (for males, through infecting female partners prior to pregnancies). We elaborate on the particular assumptions that we make for our estimates, consistent with this figure, in Sections 6.1 and 6.2 below. We focus in Section 6 on a particular age and gender for our estimates because, as discussed below, the probable costs and effects are age- and gender-specific. We consider interventions focused on 20 year olds because that age is likely to be an age in which the interventions have close to their maximum effectiveness. We focus on males because one of the leading possible solutions for reducing the sexual transmission of HIV/AIDS is MC.

The costs of an intervention are basically the real resource costs that are incurred to change the probability of infection through altering risky behaviors. The prevalence depends upon the rest of society and is likely to change over time, increasing during the spread of the epidemic and declining if there are effective means to reduce the epidemic that are adopted by others.[5] The prevalence that a 20 year old male faces and his risky behaviors determine the probability of he becoming infected in the year when he is 20. If he is not infected, then he faces infection probabilities the next year ($t + 1$) when he is 21, and if not infected that year, the infection probabilities of being infected in the subsequent year ($t + 2$) when he is 22, etc. The blue arrows to the left in Figure 5 illustrate this sequence.

Of course in any year he may become infected. The red arrows in Figure 5 indicate what happens if he is infected. Once infected, there is increased probability of infecting sexual partners and (if the individual is a female) transferring the infection to new children, as indicated by the two green arrows. For our estimates in this Assessment Paper we assume that the impact on the individual's sexual partners' infection probabilities is captured on average by the changing prevalence. For the infected individual himself, there is a latency period (*l*) of on average of about ten years before he develops AIDS (Morgan et al. 2002). Once he develops AIDS (the pentagon in the figure), the impact on average depends on the prevalence at that time (e.g., 10 years after infection) of ART treatment, which also is likely to change over time if, for example, coverage is extended by expanded efforts by governments or international organizations. The benefits of not being infected for those who would not receive ART include avoiding disability and mortality, as captured for example by DALYS, and losses of productivity above own consumption. Note that even if the value per year of premature disability and mortality as represented by DALYS is assumed to be independent of age, the loss (gain) to the rest of society because an individual would have produced more (less) than he consumed over the rest of his life is likely to be very dependent on age (see the next paragraph). The benefits of not being infected for those who would receive ART include the cost of ART for the rest of their lives. Based on Economist (2011b, 90), we assume that the cost of one year of ART is

5 Vernon Smith suggested in personal correspondence that the average HIV incidence within a period in a population (or subpopulation) can be viewed to depend on the interaction between the size of the infected and the size of the uninfected populations at the start of the period. Our simulations of individual behaviors are similar in spirit to this suggestion.

$500, the sum of $100 for a year's course of drugs plus around $400 for the cost of administration (for related estimates, see Galarraga et al. 2011; Schwartländer et al. 2011). We assume that the ART prevalence is initially 25%, and increases by 1 percentage point each year.

There are several important life-cycle patterns in these processes. (1) Risky behaviors are likely to increase in adolescence and reach a maximum in late adolescence and early adulthood and then decline. (2) Productivity is likely to be zero and then very low in childhood but increase during adolescence to reach a maximum in mature adulthood and then decline when the individual becomes elderly in an inverted U-shaped pattern. (3) Own consumption is likely to also follow an inverted U-shaped pattern but with less sharp age patterns and positive consumption (in contrast to productivity) even when very young or very old so that own consumption is likely to be greater than own productivity for the young and the elderly and own productivity is likely to be greater than own consumption for prime-age adults. (4) Survival probabilities affect all the forward-looking relevant outcomes such as future productivity, consumption and ART costs. We incorporate all these life-cycle considerations into our estimates. We note here that they affect the estimated benefits and costs demonstrably, so estimates that ignored them might be quite misleading. We use the UN Population Division estimates of age-specific survival probabilities for SSA uninfected populations to represent the relevant age patterns in mortality for uninfected populations (UN-ESA 2010).

Another factor is that some important dimensions of the costs and benefits are likely to vary importantly across societies depending inter alia on the average per capita income. For this reason we effectively consider two types of economies: lower per capital income economies for which $1,000 per year DALYS are assumed and somewhat higher per capital income economies for which $5,000 per year DALYS are assumed. These alternative DALYS are the alternatives being used by all the Assessment Papers in this project so they assure consistency across the six Assessment Papers with regard to one important assumption. The values of DALYS used themselves are one important difference between these two types of economies, but hardly the only important difference. We also assume parallel differences in life-cycle paths of productivities and consumption and in the short-run costs beyond DALYS of the onslaught of AIDS for individuals not receiving ART in the form of other care by the health system or by their families. To investigate the sensitivity of the estimates to the assumption about the value of DALYS, we also simulate what happens if in an otherwise $1,000 per year DALYS (i.e., relatively poor) economy the appropriate value of the DALYS themselves is $5,000 per year (and vice versa).

Further, as noted above, all the forward-looking costs and benefits from the time of an intervention that affects the probability of infection must be discounted to the same point of time in order to make sensible comparisons of benefits and costs for any particular intervention and across interventions, as well as with other uses of resources ranging from increased schooling to improved environmental protection. We assume, as in the other five Assessment Papers that are part of this project, that alternative discount rates of interest are 3% and 5%.

Finally, an important factor is the initial HIV prevalence. For given risky behaviors, the probability of infection obviously depends on what the HIV prevalence is in the relevant pool of potential sexual partners. We assume two options: First, an initial high prevalence of 25%, which corresponds roughly to the prevalence level in Botswana, Lesotho and Swaziland, i.e., the highest national adult HIV prevalence levels currently observed in SSA (Table 1). Second, a medium level of HIV prevalence of 11%. This level approximately evenly divides the number of HIV+ persons in SSA, with about half living in countries above and one half living in countries below that prevalence, and it broadly represents the cluster of countries that have an adult HIV prevalence between 10–15% in Table 1. We do not calculate benefit-cost ratios for low prevalence countries in SSA, say with a HIV prevalence of 5% or lower, because the prevention agenda in these countries arguable needs to have a different emphasis than in the high prevalence countries, and 3/4 of all HIV+ persons in SSA currently live in countries with a prevalence of 5% or higher. We further assume that these prevalences will decline proportionally each year depending on the assumed success of the intervention. Before we use this framework to evaluate the three possible solutions—MC, HIV testing and counseling, and information campaigns—for reducing sexual transmission of HIV/AIDS, we want to highlight some general considerations that are likely to have substantial impacts on the results of benefit-cost analyses and about which explicit and conscious assumptions need to be made. Uniformity in these assumptions across different studies is necessary for comparability.

1) *Range of Impacts:* Adverting HIV/AIDS for an individual has a number of impacts on that individual over his/her life cycle, depending on the life-cycle stage at which the individual is infected and the latency period between infection and development of HIV/AIDS. Adverting HIV/AIDS not only results in later mortality, but less use of medical resources and increased productivity. Some interventions to lessen HIV/AIDS also may have important other impacts, such as increasing schooling of adolescents. And, in addition, adverting HIV/AIDS has positive impacts through reducing the probability of HIV/AIDS for others, namely individuals' sexual partners and, for women of childbearing ages, their subsequent children. Therefore estimating the benefits is likely to be complicated not only because of the multiple impacts on a particular individual, but also the dependency on the life-cycle stage and the probable impacts on others.

2) *"Prices":* Impacts generally are multiple and measured in different units, but must be combined into the same units (normally monetary units with prices as weights) in order to sum them and in order to compare them with costs. For some impacts conceptually at least the measurements are relatively straightforward—for instance, market prices for the value of increased labor productivity or reduced use of medical goods and services under the assumption that such prices reflect the true social marginal value of the relevant good or service. But for other impacts, this evaluation is much more challenging. The key example for this project is the value of adverting mortality. A range of methods have been proposed in the literature—for example, the lowest-cost alternative means of adverting mortality (Summers 1992, 1994) and the revealed preference as reflected in wage-risk choices in labor markets (Aldy and Viscusi 2007; Hammitt 2007; Robinson 2007; Viscusi 1993, 2010). A related question is what prices should be used. For example, should prices (including wages) be used for a poor SSA developing country or for Denmark—under the argument that a life should be valued the same whether it be in a low- or a high-income country? How these questions are answered can make an enormous difference for the present project in which adverted mortality is a major impact. For example, Summers (1992) reports that the cost of saving a life through measles immunization was on the order of magnitude of $800 per life saved in the early 1990s or about $1250 in 2004 (adjusting for inflation and the costs of raising resources Behrman et al. 2004), while in a recent publication Bartick and Reinhold (2010) use $10.56 million per death in 2007 US dollars. For the present project, all of the Assessment Papers are using the same two alternatives—DALYS of $1,000 per year and $5,000 per year—to assure consistency within the project with regard to this critical assumption.

3) *Range of costs:* What is of interest for the costs are the total true resource costs to society. These are not identical to governmental budgetary expenditures, though often analysts seem to assume

that they are. On one hand governmental budgetary expenditures in some cases include substantial transfer components (e.g., in Conditional Cash Transfer programs), which typically involve some but much smaller resource costs than the amount of the fiscal expenditures. On the other hand, private costs and distortionary costs of raising funds for governmental programs may be considerable. Many programs, for example, may require time inputs from individuals that are not typically covered by governmental expenditures. Distortion costs of raising resources for governmental expenditures also have been estimated to be on the order of magnitude of 25% of those expenditures or more (e.g., Ballard et al. 1985; Devarajan et al. 1997; Feldstein 1995; Harberger 1997; Knowles and Behrman 2003, 2005). Because cost estimates vary considerably, it is important to present estimates that illustrate how robust the benefit-cost ratios are to different cost estimates.

4) *Discounting:* The costs and, probably even more the benefits, may be distributed over a number of years. But the value to society of resources in the future is less than the value of the same resources now because they can be reinvested if they are available now. Therefore future costs and benefits should be discounted to the present for comparability, particularly for costs and benefits that are likely to occur some time into the future. And the discount rate makes a difference. For instance, the present discounted value (PDV) of $1,000 received in 20 years is $553 if the discount rate is 3%, $377 if the discount rate in 5% and $149 if the discount rate is 10% (and for 40 years, the respective PDVs are $306, $142 and $22). However there is a lack of agreement about what discount rates are appropriate, though rates in the 3%–10% range are common for the social sectors. For the present project, all of the Assessment Papers are using the same two alternatives—discount rates of 3% per year and 5% per year—to assure consistency within the project with regard to this critical assumption.

5) *Interaction among solutions:* Of necessity we consider each solution in isolation, not only among those that we consider in this paper but also with regard to the other five categories considered in this project. It might be the case, for example, that "Research and Development" will come up with a cheap and widely-applicable intervention that eliminates infection risks or cures HIV/AIDS. Were that to happen, the impacts of the solutions considered in this paper would change radically in a way that probably would mean that the solutions discussed in this Assessment Paper would become much lower priority. But our estimates are under the assumption that such developments are improbable. Of course over time some of the solutions in the six categories, or other solutions, possibly will have widespread impacts—in which case it may be valuable to undertake again the current exercise in light of the very changed situation.

6) *Scale:* Scale can come into estimation of benefit-cost ratios in at least four ways. First, there may be high benefit-cost interventions that are effective for only a small select population, and therefore are not likely to be of interest for the present project with its broad perspective. Second, there may be interventions that have high benefit-cost ratios on a small scale but that are difficult to scale-up because critical dimensions of the small-scale intervention (e.g., high-quality and particularly dedicated staff) cannot be maintained if the intervention is scaled-up. Third, there may be important aggregate effects on markets if HIV/AIDS is adverted on a large scale, such as increased demands on schooling systems and reduced wage rates along the lines in the opposite direction of Young's (2005) provocative article on "the gift of the dying" due to the HIV/AIDS epidemic in SSA. Fourth, the more an effective intervention is scaled-up within a community, the lower the risk of infection all else equal.

7) *Estimation challenges:* The estimation challenges for obtaining benefit-cost ratios are enormous not only for the reasons noted above, but because of the difficulties in obtaining good response estimates due to endogenous behavioral choices, unobserved variables, selectivity of samples, and different market and policy contexts to which large numbers of academic studies have been devoted. Our above review of the literature reflects these uncertainties. For example, for many behavioral interventions and for the expansion HTC, both program effects and the costs associated with potentially effective programs are difficult to pin down, and scaled-up programs may have different effects and be subject to different costs than programs that have been implemented as part of research studies. One could therefore conclude that the a task of estimating benefit-cost ratios is so difficult that it would be better to abandon it. But that would leave society with little systematic guidance about policy choices in this important area. Therefore, in hopes of improving the basis for policy guidance, we swallow hard and proceed boldly and hopefully creatively (and hopefully not too foolhardily) to make the best estimates that we can given the present very imperfect information and strong assumptions necessary, with some efforts to explore the sensitivity of our estimates to important alternative assumptions.

Additional specific assumptions necessary for the estimates for the three solutions and benefit-cost ratios and cost-effectiveness estimates

Before turning to our estimates of benefit-cost and cost-effectiveness, we first summarize the critical elements in our benefit-cost estimates and then note several specific assumptions, in addition to the general considerations for benefit-cost calculations discussed above, that need to be made for the evaluation of the three possible solutions—male circumcision, HIV testing and counseling and information campaigns through mass media and peer groups—for the reduction of sexual transmission of HIV.

Summary of Procedures Underlying our Estimated Benefit-Cost Ratios

Our general approach to estimating the benefit-cost ratios is the same for all three interventions. Consistent with the conceptual framework in Figure 5, we assumed that the benefits of averting an HIV infection has the following components, all of which are discounted to the time of the intervention to compare with costs of the intervention that are also discounted to the time of the intervention:

- DALYs saved from averting AIDS on average ten years after the infection given age-specific survival patterns in the absence of AIDS;
- Differences in production minus consumption, both of which have life-cycle patterns (e.g., so that for prime-age adults production exceeds consumption, but not for those younger or older) and both of which reflect survival probabilities in the absence of AIDS and the prevalence of ART;
- Treatment costs (other than ART) on average ten years after infection for those who develop AIDS and who not receive ART until they die;
- ART costs that would have been expended on average ten years after the initial infection and continued over the remainder of each infected individual who receives ART remaining life, again adjusted for survival probabilities in the absence of AIDS, that are saved due to reduced HIV infections; and
- Infections averted through the reduction in the HIV prevalence in the broader population (see Section 6.2 for the specific assumptions for the alternative interventions).

These benefits are experienced for the year (male age 20 years) of the intervention and, if the individual is not affected, as he ages year by year, as indicated in the left side of Figure 5. For MC we assume that females benefit from the intervention similarly to males because of the dominance of heterosexual sexual transmissions, and for HTC and information campaigns we assume that females subjected to the intervention would benefit similarly to males. As noted above, there is considerable uncertainty in calculating all of these benefits, as well as the resource costs of the intervention, for which reason we present alternative estimates that illustrate the sensitivity of our estimates to alternative assumptions. But we note that we do not include some possible benefits, in particular the benefits from averting intergenerational transmission of the disease to children ("Children Infection Probability" on upper right side of Figure 5). For this reason, all else equal, our estimates are lower-bound estimates of the true benefits. These benefits are compared to the real resource costs of interventions that vary across the interventions and are discussed in Section 6.2.

Additional Specific Assumptions for Each of the Three Solutions

Male Circumcision (MC): Based on the literature review summarized above, we assume that MC reduces the probability of infection through sexual interaction by 30%. This is a permanent effect of a one-time intervention that lasts over the remaining life time of the circumcised male. We further assume that HIV prevalences will decline proportionally each year to 0.98 of the previous year value due to the changes induced by this proposed solution on the pool of potential sexual partners. That is, although we focus on one individual for our simulation, we assume that the same policy is applied broadly to others, not just for this one individual in isolation. We assume that the direct costs of circumcision are in the range of $40 to $70 based on estimates that have been reported for SSA (Gray et al. 2007; Martin et al. 2007; Schwartländer et al. 2011; White et al. 2008b). These are only the direct costs, and do not cover any cost of pain and suffering or possible infection risks or the costs of campaigns or programs to make men aware of the options and benefits of circumcision and to induce them to elect to do so or additional capital costs that might be required to scale-up the intervention beyond currently existing health clinics or other providers. Because some of the costs of circumcision are likely to depend on local costs and income levels, we assume a cost range of $30–52 for the low per capita economy, and $60–105 for the high per capita economy. Because the scale-up of MC requires expansion of health services as well as information campaigns—and possibly explicit incentives—to achieve a high uptake of MC, we assume in our baseline calculations that the overall costs of one MC on average are twice the direct costs of the medical procedure. In lieu of detailed data on these costs, this assumption seems to be a more reasonable baseline scenario than calculations that focus on the direct costs of circumcision (as is often the case in existing studies). We comment below on the implications of such other costs for our benefit-cost estimates.

HIV Testing and Counseling (HTC): Following recent studies about the population-level effect of HTC programs, we assume that an one-time large-scale HTC program that achieves a very comprehensive coverage can reduce HIV incidence by 20% (Waters et al. 2011), with the effect fading over a 10-year period. This effectiveness of a comprehensive HTC campaign is consistent with the literature reviewed above. This assumed reduction in incidence is the combined effect of behavioral changes in the HIV+ partners who would be identified in a comprehensive HTC campaign as well as reductions in transmission risks that occur because HIV+ individuals could identify treatment as a result of the HTC campaign. We further assume that during the initial 10 year period, the HIV prevalence will decline proportionally each year to 0.99 of the previous year value due to the changes induced by this proposed solution on the pool of potential sexual partners and higher mortality of HIV+ persons; subsequently, HIV prevalence declines each year to .995 of the previous year, essentially as

Table 3. Benefits, Costs and Benefit-Cost Ratios for Three Possible Solutions to Reduce Sexual HIV/AIDS Infections in SA

High Prevalence (25% initially)													
Program Costs													
		Benefits				Direct costs		Total costs		Benefit-Cost Ratios			
		3%, 1K	5%, 1K	3%, 5K	5%, 5K	1K	5K	1K	5K	3%, 1K	5%, 1K	3%, 5K	5%, 5K
Male circumcision	Low C	$1,989	$1,373	$9,945	$6,866	$30	$60	$60	$120	33.1	22.9	82.9	57.2
	High C	$1,989	$1,373	$9,945	$6,866	$52	$105	$104	$210	19.1	13.2	47.4	32.7
HTC	Low C	$322	$237	$1,612	$1,184	$15	$30	$23	$45	14.3	10.5	35.8	26.3
	High C	$322	$237	$1,612	$1,184	$20	$40	$30	$60	10.7	7.9	26.9	19.7
Info Campaign	Low C	$244	$179	$1,219	$895	$30	$60	$30	$60	8.1	6.0	20.3	14.9
	High C	$244	$179	$1,219	$895	$80	$160	$80	$160	3.0	2.2	7.6	5.6
Medium Prevalence (11% initially)													
Program Costs													
		Benefits				Direct costs		Total costs		Benefit-Cost Ratios			
		3%, 1K	5%, 1K	3%, 5K	5%, 5K	1K	5K	1K	5K	3%, 1K	5%, 1K	3%, 5K	5%, 5K
Male circumcision	Low C	$972	$671	$4,862	$3,357	$30	$60	$60	$120	16.2	11.2	40.5	28.0
	High C	$972	$671	$4,862	$3,357	$52	$105	$104	$210	9.3	6.5	23.2	16.0
HTC	Low C	$142	$104	$709	$521	$15	$30	$23	$45	6.3	4.6	15.8	11.6
	High C	$142	$104	$709	$521	$20	$40	$30	$60	4.7	3.5	11.8	8.7
Info Campaign	Low C	$107	$79	$536	$394	$30	$60	$30	$60	3.6	2.6	8.9	6.6
	High C	$107	$79	$536	$394	$80	$160	$80	$160	1.3	1.0	3.4	2.5

Notes: See text for details. 1K and 5K refer respectively to $1,000 and $5,000 DALY economies. 3% and 5% are discount rates.
Low C and High C are the low and high cost assumptions

a result of higher mortality of HIV positive persons. Schwartländer et al. (2011) estimates the costs of HTC in SSA at about $15, and Hausler et al. (2006) report costs for clinic-based tests at $7–10, and Helleringer et al. (2010) estimate the cost of home-based HTC at around $15 in rural Malawi. In order to achieve the effectiveness in reducing HIV incidence that our calculations assume, it is important that the HTC campaign is comprehensive and reaches a majority of the population, and that is accompanied by follow-up for persons who have not yet participated in HTC, a compressive counseling in connection with HTC, and potential referral to ART for those who are identified as HIV+. The direct costs of the HTC program are therefore likely to exceed the estimates that exist in the literature. We therefore assume direct HTC costs in the low per capita economy of $15–20 per HTC, and in the high per capita economy of $30–40. Moreover, because we anticipate that a comprehensive and effective HTC campaign requires some scaling-up of infrastructure as well as additional costs of associated information campaigns, we assume that the total costs of HTC exceed the direct costs by 50%.

Information Campaigns through Mass Media and Peer Groups: The evidence on which to base these estimates is the weakest among the three possible solutions that we consider in this Assessment Paper. A skeptical reading of the literature reviewed above would suggest that the evidence about the effect of information campaigns on HIV incidence is weak, and that currently no proven strategies to reduce HIV incidence through such programs exist. A somewhat more optimistic reading of the literature suggests that some recent innovations in program design, and the possible combination with cell phones, provide new possibilities to design new information campaigns and peer group programs that might reduce incidence. Clearly, there is a considerable amount of speculation, and the existing literature is only of limited help. Similar uncertainty exists with respect to the costs of programs. For example, Hogan et al. (2005) provide some discussion, but it is difficult to figure out the costs per person for these interventions. If one looks at their estimates of costs per infection averted, and compares them to HTCs, then the costs per infection averted range from 0.1 to about 20 times of that of HTCs—a huge range. Schwartländer et al. (2011) estimate $3.38 for community mobilization programs in SSA, but it is unclear what program activities are included the types of programs that they are considering.

To provide at least some guidance about the benefit-cost ratios of information campaigns, we assume that a one-time program intervention can be designed that initially reduces HIV incidence by 15%, and that this effect linearly declines over 10 years. Given the existing evidence, we assume that this effect can be achieved by a fairly intensive campaign that requires a fair amount of time and effort in counseling/training young men and women. The required time substantially exceeds that of HTCs, and the extra time is not compensated by the fact that some of these are group sessions (e.g. many effective programs implement a curriculum that is based on repeated sessions with young adults to teach them about safe sex, etc). Therefore we assume that the costs of information campaigns with the effectiveness noted above is from two to four times the costs of (the least expensive) HTC.

Benefit-Cost Ratios for Interventions that Reduce HIV Infections through Sexual Interactions

Table 3 presents benefit-cost estimates for each of the three possible solutions based on the assumptions discussed above, in each case with alternative estimates for: $1,000 DALY economy and $5,000 DALY economy, 3% and 5% discount rates, 11% (medium) and 25% (high) initial HIV prevalence, and low and high costs for the interventions. By a "$1,000 DALY economy" we mean a relatively low-income economy in general, not only with respect to DALYS; likewise we mean a higher-income economy in general for a "$5,000 DALY economy." As noted, the "high" initial prevalence assumption of 25% is about the average prevalence rate for the three countries in SSA with the highest HIV prevalence in Table 1—Swaziland, Botswana and Lesotho. The "medium" initial prevalence rate of 11.0% is that of Malawi and slightly below Mozambique, Namibia, and Zambia. Though over a third of the SSA countries included in Table 1 have prevalence rates of less than 2% (and over half have prevalence rates of less than 3.5%), we do not consider a "low" prevalence case because it would double the number of estimates presented but not add much information. For all three solutions we assume that the target segments are all 20-year olds, not just some particular subpopulation such as prostitutes or men having sex with men. As noted above, the benefit-cost calculations were performed for males, and it is assumed that females are identically affected by the intervention in the case of HTC and information campaigns; for male circumcision, we assume that females benefit symmetrically through the interaction with circumcised men. Because of this broad targeting to young adults (and young males, for male circumcision), there are assumed to be impacts on the overall prevalence rates over time, as noted. Examination of this Table 3 suggests the following observations:

Table 4: Costs per infection averted and costs per DALY for three possible solutions to reduce sexual hiv/aids infections in SAA

High Prevalence (25% initially)												
		Infections averted (per person)	DALYs Saved (per person)	Costs of treatment		Total costs		Cost per infection averted		Cost per DALY	
				1K	5K	1K	5K	1K	5K	1K	5K
Male circumcision	Low C	0.277	6.72	$30	$60	$60	$120	$216	$433	$4	$9
	High C	0.277	6.72	$52	$105	$104	$210	$375	$758	$8	$16
HTC	Low C	0.025	0.85	$15	$30	$23	$45	$890	$1,779	$18	$35
	High C	0.025	0.85	$20	$40	$30	$60	$1,186	$2,372	$23	$47
Info Campaign	Low C	0.019	0.65	$30	$60	$30	$60	$1,567	$3,133	$46	$93
	High C	0.019	0.65	$80	$160	$80	$160	$4,177	$8,355	$124	$247
Medium Prevalence (11% initially)											
		Infections averted (per person)	DALYs saved (per person)	Costs of treatment		Total costs		Cost per infection averted		Cost per DALY	
				1K	5K	1K	5K	1K	5K	1K	5K
Male circumcision	Low C	0.136	3.28	$30	$60	$60	$120	$443	$886	$9	$18
	High C	0.136	3.28	$52	$105	$104	$210	$768	$1,550	$16	$32
HTC	Low C	0.011	0.38	$15	$30	$23	$45	$2,022	$4,043	$40	$80
	High C	0.011	0.38	$20	$40	$30	$60	$2,696	$5,391	$53	$106
Info Campaign	Low C	0.008	0.28	$30	$60	$30	$60	$3,560	$7,120	$105	$211
	High C	0.008	0.28	$80	$160	$80	$160	$9,494	$18,988	$281	$562

Notes: See text for details. 1K and 5K refer respectively to $1,000 and $5,000 DALY economies. 3% and 5% are discount rates.
Low C and High C are the low and high cost assumptions

First, the estimated benefit-cost ratios are sensitive to some of the critical assumptions that are investigated in the table. The benefit-cost ratios are substantially higher:

- For a $5,000 DALY economy than a $1,000 DALY economy they are about 2.5 times as large,
- For a 3% discount rate than for a 5% discount rate they are about 40% larger,
- For a high (25%) initial HIV prevalence than for a medium (11%) initial HIV prevalence they are a little more than twice as large,
- For our low-cost intervention estimates than for our higher-cost intervention estimates they are about 1.7, 1.3 and 2.7 times as large, respectively, for the three possible solutions.

Therefore it might be very misleading to assume away the heterogeneity in these various dimensions by considering, for example, only central values for DALYs, discount rates, HIV prevalence and costs. Instead it is important to be sensitive to how the estimates vary with plausible variations in all of these dimensions. Then it is desirable to try to pin down as much as possible which of these assumptions are appropriate for any particular situation being considered in order to inform the decision as to which benefit-cost ratios are most likely to be appropriate for that particular context. Of course in terms of prioritizing interventions, the patterns in our estimates suggest higher benefit-cost ratios the higher are DALYS, the lower are discount rates, the higher is HIV prevalence and the lower are costs.

Second, nevertheless, overall these benefit-cost estimates tend to be high and all but one exceed one (the exception is the high-cost information campaign in a $1,000 DALY economy with a 5% discount rate, in which case the benefit-cost ratio is 1.0), suggesting substantial possibilities for interventions that reduce the transmission of sexually-transmitted HIV/AIDS. Note that in many cases the benefit-cost ratios would be relatively high even if the benefits are overestimated or the costs underestimated. For example if the costs of MC were underestimated by a factor of 10 because of the exclusion of the costs of pain and suffering, the costs of informing and inducing men to participate, and the capital costs of scaling-up beyond mere marginal additions to existing health clinics, the benefit-cost ratios still would be from 2.3 to 8.3 in high prevalence areas—though they would be around 2.0 or less for high-cost interventions in $1,000 DALY economies.

Third, MC of young adults emerges as the intervention with the highest benefit-cost ratios in both the high and medium prevalence context, for both 1K and 5K economies and independent of the discount rate. This dominance of MC over other interventions analyzed in this paper is due to the long-term sizable reduction in HIV infection risks resulting from a one-time procedure that can be performed at relatively moderate costs, and the fact that females benefit from the male-centered intervention through changes in the prevalence among their male partners and possible reductions in female to male transmission rates. While we do not analyze neonatal or infant MC in detail, the general tendency in the comparison of the benefit-cost ratios between adult and neonatal/infant MC can be easily established. At a discount rate of 3%, delaying the effect of reducing HIV infections 2-3 decades into the future would reduce benefits by about 45-60%. If the costs of neonatal/infant MC are less than 45-60% of the costs of adult circumcision, then the benefit-cost ratio for infant/neonatal MC would exceed that for adult MC; to the extent that the cost savings are less, adult MC would have higher benefit-cost ratios. Because there continues to be considerably uncertainty about the relative costs of neonatal/infant as compared to adult MC in SSA, and because most of the studies that point to very high cost savings by conducting infant/neonatal as compared to adult MC pertain to countries with contexts where a high fraction of births occur in hospitals and/or neonatal hospital follow-up is common, we conclude at this point that – at least broadly speaking – the benefit-cost ratios for infant/neonatal MC in a SSA context are likely to be relatively similar to that of adult MC (where young adults are the primary target).

Fourth, the benefit-cost ratios change some in predictable ways if a high value of DALYS is used for low-DALYS economies and vice versa (estimates not presented), but basically give similar patterns. The benefits, and thus the benefit-cost ratios, increase if for the poorer economies DALYS are valued at $5,000 and decrease if for the better-off economies DALYS are valued at $1,000.

Cost-effectiveness Estimates for Interventions that Reduce HIV Infections through Sexual Interactions

Table 4 presents the costs per HIV infection averted (HIA) and the costs per DALY that are implied by our calculations of the benefit-cost ratios above. The first observation is that these costs per HIA and DALY are broadly consistent with other estimates in the literature (e.g., Galarraga et al. 2009; Table 2), and the broad conclusions obtained from the cost-effectiveness calculations in Table 4 are similar to those obtained from the benefit-cost analyses in Table 3. For example, MC is the most

Table 5: Application to selected high- and medium -prevalence countries - Botswana and Mozambique

	Scenario	
	High Prevalence	**Medium Prevalence**
Assumed initial HIV prevalence for benefit-cost caclulatins	**25%**	**11%**
Largest SSA country with HIV prevalence near scenario assumptions	**Botswana**	**Mozambique**
Total number of HIV+ persons aged 15-49 in above country (2009, in '000)	320	1,400
Total number of young adults aged 15-25 in above country (2010, in '000, male and females)	444	4,606
Fraction (already) circumcised	12%	51%
Intervention I: Male Circumcision		
Number of beneficiaries, infections averted and total benefits resulting from $10 million spent on intervention		
Total beneficiaries (= number of male circumcisions, in '000)	61	122
Number of infection avoided (in '000)	16.8	16.5
Total benefits of intervention (in million $)	603	119
Benefit-cost ratio	60.3	11.9
Intervention II: HTC		
Number of beneficiaries, infections averted and total benefits resulting from $10 million spent on intervention		
Total beneficiaries (= number of HTCs (for males and females), in '000)	190	381
Number of infection avoided (in '000)	4.8	4.2
Total benefits of intervention (in million $)	307	54
Benefit-cost ratio	30.7	5.4
Intervention III: Information Campaign		
Number of beneficiaries, infections averted and total benefits resulting from $10 million spent on intervention		
Total beneficiaries (= number of persons reached by info campaign (males and females), in '000)	91	182
Number of infection avoided (in '000)	1.7	1.5
Total benefits of intervention (in million $)	111	19
Benefit-cost ratio	11.1	1.9

Notes:
Benefits are based on 3% discount rate.
Botswana is considered as a 5K economy, Mozambique as a 1K economy.
Costs of the intervention are the average of the low and high scenarios.
Number of infections avoided per person reached by intervention is obtained from Table 4.
Benefits per person reached by intervention is obtained from Table 3.
Total number of young adults is obtained from UN World Population Prospects 2010.
Number (already circumcised) is obtained from http://aidsinfoonline.org.

cost-effective intervention, both in terms of costs per infection averted and cost per DALY averted, in both the high- and medium-prevalence scenarios. HTC is also cost-effective if the program is sufficiently comprehensive and well-designed to result in the reductions of HIV infection risks that we have assumed in our calculations. Information campaigns are least cost-effective intervention based on our calculations, with considerable uncertainty about the costs per DALY and HIA.

Comparing Tables 3 and 4, however, also reveals some important differences between the benefit-cost approach (Table 3) and the cost-effectiveness approach (Table 4). For example, based on cost-effectiveness calculations, MC always dominates HTC, and MC is between 3–4 times more cost–effective than HTC (the costs per DALY and HIA for MC are between 25%–33% those for HTC). This ratio by which MC dominates HTC is somewhat less in the benefit-cost analyses. This results from the fact that the benefits are discounted, and while both programs result in sizable reduction in infection risks in the short-term, they fade for HTC during 10 years; for MC they remain throughout the life-course, but the additional DALY's and HIV occur further in the future, as well as potentially at stages of the life-course where consumption exceeds production, which reduces the benefits in the benefit-cost considerations but does not affect the cost-effectiveness considerations. Hence, benefit-cost considerations reflect the timing of the DALYs saved as a result of the interventions through discounting, and they reflect the stage of the life-cycle - and the consumption and production profiles corresponding to these stages of the life-cycle - at which DALYs are saved as a result of the intervention. These aspects, which can be important for prioritizing interventions, are not reflected in cost-effectiveness analyses. A further advantage of benefit cost analyses is that they help to compare the costs of the intervention to the benefits on the same metric; for example, based on cost-effectiveness calculations one could wonder, assuming that more cost-effective interventions have already been exploited or are not available, if an intervention that can avert an HIV infection of costs of close to $10,000 or more is worth-while. The benefit-cost considerations, which include an evaluation of life - combining both the valuation of DALYs and the patterns of production and consumption - reflect this valuation of life and show that even interventions that can avert an HIV infection of costs of close to $10,000 have benefit-cost ratios that exceed one. Moreover, benefit-cost calculations, but not the cost-effectiveness calculations in Table 4, reflect how different rates of intertemporal trade-offs (discount factors) affect the priority setting in HIV prevention and resource allocation to different programs.

Especially for biomedical interventions, for which substantial shares of program costs are spent on not–locally-produced program inputs (e.g., drugs and medical technology), the costs of intervention are likely to vary less than proportionally with the income levels of the economy. Our assumptions about program costs reflect this. As a result, the benefit-cost calculations reflect generally strongly increasing benefit-cost ratios in comparing a $1,000 economy with a $5,000 economy, and for all interventions, the benefit-cost ratios are about 2.5 as high in the latter than the former. In cost-effectiveness calculations, however, higher income levels affect only the cost side—at least in our calculation as we use a uniform life table that reflects mortality in the absence of AIDS across all calculations. As a result, interventions become *less* cost-effective in higher income contexts as compared to lower income contexts, in sharp contrast to the benefit-cost ratios, that increase with income levels under our assumptions in our basic benefit-cost estimates that link DALYS to the overall income levels of the economies.

Application to selected high- and medium-prevalence countries

The interventions discussed in this paper focus on young adults. To provide an idea about the potential number of beneficiaries in SSA for these interventions, we observe that there are currently about 148 million individuals ("young adults") in their 20s in SSA, and about 215 million individuals will enter their 20s in the next decade. Considering current young adults, and individuals becoming young adults over the next decade, as the primary target of interventions to reduce the transmission of HIV therefore suggests that there are more than 350 million potential beneficiaries of such interventions over the next decade. About half of these individuals are male, of which a significant proportion - varying from less than 10% to more than 80% (Figure 4) - are circumcised based on existing cultural and/or religious norms and practices. Prevalence of circumcision tends to be lower in countries with high prevalence of HIV (Figures 1 and 4).

In the broadest sense, therefore, the potential pool of beneficiaries in SSA of such interventions targeted at young adults is very large. As is emphasized in our analyses, however, SSA countries vary importantly in their HIV prevalence, the prevalence of circumcision, the income levels, and other demographic and socioeconomic characteristics and trends. Policies are therefore likely to need to be prioritized differently to specific countries, policy mixes are likely to need to be adjusted to the specific contexts, and the feasibility, costs and benefits of interventions will differ across different SSA countries.

Table 5 provides an illustrative example of the number of infections averted and the total benefits incurred if the three interventions – MC, HTC and information campaigns – were implemented in selected high- and medium-prevalence countries. Based on the review of the literature, there is considerable uncertainty about the scale to which these interventions can be rolled-out and implemented. Most clearly for MC, and to a lesser extent for HTC, the interventions require the expansion of health infrastructure for their implementation that may limit the short-term scale-up of these interventions. For MC, the implementation also requires overcoming possible cultural or normative inertias towards MC in countries where MC has not been widely practiced so far (see Figure 4). There is also considerable uncertainty about the scale of the intervention and the disease dynamics resulting from the intervention and other socioeconomic, demographic and behavioral changes that occur parallel to the intervention. To illustrate the benefits resulting from the interventions in a comparable fashion, we therefore present summary calculations of the infections averted and the total benefits incurred assuming that a total amount of $10 million were devoted to each of these interventions as part of a broad HIV intervention across several years targeted at young adults. Because of the considerable heterogeneities among the high-prevalence countries and among the medium-prevalence countries in these and other relevant dimensions, we focus on the countries with the largest population corresponding to the high- and medium-prevalence levels for our calculations (see also Table 1 for a list of countries by HIV prevalence): Botswana for the high-prevalence scenario, and Mozambique for the medium-prevalence scenario (South Africa has larger population, but is a combination of areas with difference prevalences and an overall average between our high-prevalence and medium-prevalence country groups; see Figure 1). Reflecting the very different income levels, we consider Botswana as corresponding to a "5K economy" in our calculations, and Mozambique as a "1K economy". We use the average of the high and low cost scenario to represent costs and the benefits based on the calculations in Table 3 with a discount rate of 3%.

Based on our calculations, for example, $10 million devoted to MC of young males would result in approximately 61 thousand male circumcisions in Botswana, resulting in approximately 17 thousand averted HIV infections among both men and women and incurring about $600 million of benefits (benefit-cost ratio approximately 60) in terms of discounted DALYs saved, averted treatment costs and net production. In contrast, the same amount devoted to MC in Mozambique would result in about 122 thousand male circumcisions, more than in Botswana due to assumed lower costs in Mozambique as compared to Botswana. Because of the lower prevalence in Mozambique as compared to Botswana, there would be fewer HIV infections averted in Mozambique as compared to Botswana (16.5 thousand as compared to 16.8 thousand), and combined with lower income levels in Mozambique that affect the valuation of benefits, the total benefits are only about one fifth of those in Botswana (119 as compared to 603 million $s). While MC continues to generate benefits that vastly exceed the costs, the benefit-cost ratio in Mozambique is "only" 11.9 as compared to more than 60 in Botswana.

Table 5 also reports analogous calculations for HTC and information campaigns. While $10 million allocated to these interventions would reach a larger number of individuals due to the lower costs of the intervention than of MC, the infections averted, the total benefits incurred and the benefit-cost ratios would be lower for these interventions as compared to MC. Nevertheless, both of these interventions have benefit-cost ratios larger than one – and often substantially so – in both Botswana and Mozambique.

Conclusions

HIV/AIDS is primarily spread through sexual interactions in SSA. Therefore it is natural to ask what are the relative merits of possible solutions to the HIV/AIDS epidemic in SSA that work through reducing infections spread by sexual interactions. This Assessment Paper addresses three such possible solutions for which there is sufficient information to suggest that they might be quite promising:

1. Male Circumcision (MC),
2. HIV Testing and Counseling (HTC) and
3. Information Campaigns through Mass Media and Peer Groups.

Even though there is more information on these possible solutions than on some other possibilities, the information is limited and the challenges of estimating benefits and costs within an appropriate dynamic life-cycle framework are considerable. This paper has proceeded, nevertheless, while trying to make as explicit as possible the various necessary assumptions. The estimated benefit-cost ratios obtained are shown to be sensitive to critical assumptions related to the value of averting mortality, the discount rate, the HIV prevalence rate and the costs of interventions. Nevertheless the benefit-cost estimates suggest that under most plausible conditions the benefit-cost ratios for these interventions in high-prevalence and (somewhat less so) medium-prevalence countries are likely to be large, particularly for MC and probably for HTCs, though the smaller estimates for information campaigns in part reflect the greater fuzziness in the underlying information available for the estimates. Therefore interventions to reduce the spread of HIV/AIDS in SSA through reducing sexual infection rates indeed seem to have considerable promise – and greater promise where prevalence rates DALYs are higher and resource costs of interventions and discount rates are lower. The estimates also show that cost-effectiveness estimates per HIV infection averted and per DALY in a broad general sense reveal similar patterns, but also differ importantly from benefit-cost estimates in specific respects because they do not incorporate some critical factors that are incorporated in the benefit-cost estimates such as intertemporal trade-offs that require discounting, life-cycle considerations, and impacts on production and consumption.

Because the benefits–including the values of DALYs and lives saved–in the benefit-cost calculations performed in this paper (and the RethinkHIV project more generally) increase more strongly with income levels than do the costs, benefit-cost ratios tend to be highest in relatively rich high-prevalence countries. Relatively rich high-prevalence countries would therefore receive priority if interventions were allocated based on benefit-cost criteria alone.

But, as generally is the case with public programs and policies, other criteria also may be important - most importantly poverty reduction and reductions in inequality. The utilization of such criteria in addition to benefit-cost ratios is likely to lead to increases in the relative priorities for investing in poorer countries.

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