



Perspective Paper

Prevention of Sexual Transmission of HIV

Alan Whiteside



First published 2011
Copenhagen Consensus Center
Copenhagen, Denmark
Rush Foundation,
Lausanne, Switzerland
© Copenhagen Consensus Center & Rush Foundation

ISBN: 978-87-92795-13-7
All rights reserved.

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise, without the prior written permission of the Copenhagen Consensus Center and the Rush Foundation

Perspective Paper

Prevention of Sexual Transmission of HIV

Alan Whiteside¹

¹ Professor and Director of the Health Economics and HIV/AIDS Research Division, University of KwaZulu-Natal, Durban South Africa

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

RethinkHIV: The Project	4
The Copenhagen Consensus Center	5
The Rush Foundation	5
The Papers	5
Background	8
The Assessment Paper	8
Male circumcision (MC)	9
HIV testing and counselling (HTC)	9
Information campaigns through mass media and peer groups (IC)	10
Findings	10
How Should We Assess Success: The Role of RCTs	11
The Underlying Assumptions for Critiquing the Paper	13
The Scale of the Epidemic	13
Modes of Transmission	14
Basics of Sexually Transmitted HIV Prevention	15
The Assessment Paper Critique	16
Male Circumcision	16
HIV Counselling and Testing and Treatment as Prevention	17
Information Campaigns and Mass Media	18
What is missing and what might come in the future	19
What policy recommendations can come out of this work	19
References	21

Background

This project tries to answer the question: if we raised an additional \$10 billion over the next five years to combat HIV and AIDS in sub-Saharan Africa how could it best be spent? What are the benefits and costs of the interventions? There are six assessment papers and twelve perspective papers. This perspective paper comments on the assessment paper focusing on prevention of sexual infections, (as received in August 2011). The assessment paper was asked to identify at least three of the most promising solutions and provide cost benefit analysis; the perspective paper is to provide an analysis of the assumptions and calculations used in the assessment paper as well as other viewpoints.

The work should be seen in the context of how HIV and AIDS is perceived and funded. The disease was first reported in 1981, the cause, a retro-virus, identified in 1983. By the early 1990s the epidemic was under control in the West, but prevalence was rising rapidly across much of sub-Saharan Africa (SSA). In 1996, the year UNAIDS was established, there was \$3 million available globally for HIV and AIDS. There was then an almost exponential increase until, by 2008, there was \$15.6 billion. The early years of the century saw the establishment of the Global Fund to Fight AIDS, TB, and Malaria (GFATM) and the US Presidential Emergency Plan for AIDS Relief (PEPFAR): both bringing significant additional resources to the table. (Smith and Whiteside 2010)

Since 2008 the situation has changed. AIDS is no longer at the top of the global health agenda, and indeed for most of the world this makes sense. The amount of money available rose slightly to \$15.9 billion in 2009 and dropped to \$15.3 billion in 2010. At best resources will be stable, at worst they may fall. The replenishment conference for the GFATM in October 2010 saw pledges fall below expectations. PEPFAR has indicated that its funding is unlikely to rise. A number of other donors have either not fulfilled their commitments or have cut back. The planned UN Non-Communicable Disease Summit in New York in September 2011 has the potential to further shift AIDS out of the spotlight. Unfortunately the nature of the disease (the long period between infection and illness) means needs are growing as more and more people become eligible for (comparatively) expensive treatment.

The RethinkHIV project comes at a critical juncture in the response to the epidemic. It is not enough to simply invest \$10 billion; the key is to get the best returns. This issue is increasingly important in the light of flat-lining of resources. Unfortunately, the question we may ultimately be faced with is not how to invest additional money, but rather how to make best use of what we have. This paper looks at prevention. There is Ugandan saying that 'we should not keep mopping the floor while the tap is running'. Prevention must be at the heart of the AIDS response.

The Assessment Paper

The authors, Behrman and Kohler (2011) describe how they arrive at possible solutions for prevention of sexual transmission of HIV infections in SSA. There are initially three criteria for interventions:

- Those for which there is reasonably strong empirical evidence from multiple countries about the efficacy—and possibly even effectiveness—of the intervention;
- Ones seen as important elements in HIV/AIDS prevention efforts by international organizations and local governments; and
- Interventions where reasonable estimates of benefits and costs could be obtained.

The question is what works? They recognise “considerable uncertainty about the efficacy and/or effectiveness of programme interventions to reduce the sexual transmission of HIV. Ultimately, under any of the criteria stated above, only programmes that reduce HIV risk behaviours, HIV infection risks and/or HIV incidence should be considered”. (Behrman and Kohler 2011) They recognise evidence - as to which interventions make a difference - is weak.

Three interventions are identified for further analysis. First biomedical: male circumcision (MC), which results in a long-term irreversible reduction in infection risk for men. Second: those HIV Testing and Counselling (HTC) campaigns which focus on individual’s information on their HIV status. Behrman and Kohler (2011) state theoretical and empirical arguments suggesting that if individuals know their HIV status (and that of their spouses and other sexual partners) they will make less risky decisions about sexual behaviours and relationships. The third intervention is information campaigns (IC) through mass media and peer groups, aiming to reduce risk behaviours by providing information about the disease and prevention. The commissioning brief to the authors was to pick ‘at least three of the most promising interventions’ – it is troubling that they struggled to come up with just these three, but this is a criticism of HIV responses, not their work.

The limitations and assumptions are clearly stated by Behrman and Kohler (2011). The analysis is grounded 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”. (Emphasis mine). They say, somewhat touchingly: “One could therefore conclude that the 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.” The three solutions are summarised below.

Male circumcision (MC)

Medical male circumcision programmes are in place in many African countries. Behrman and Kohler (2011) view MC as the policy intervention with the strongest empirical evidence. This is based on randomized controlled trials in SSA with extensive studies to assess the costs and challenges of implementing and scaling-up. These suggest scale-up is cost-effective. MC has the added advantage of being high on the UNAIDS agenda as well as that of many governments, donors and NGOs. Early work (pre-1990) showed that high HIV prevalence coincided with low rates of circumcision (ecological evidence). It should be noted that the campaign is for **medical male** circumcision. In settings where this is done as part of coming of age rituals the circumcision may be effective, but if not enough of foreskin is removed it will not work.

HIV testing and counselling (HTC)

HTC is considered although empirical evidence is mixed. The reason for its continued inclusion is it remains “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 VCT programmes were evaluated, thereby improving access to HTC as well as potential frequency and convenience of testing and the possible expansion of couple-based HTC.” This inclusion of HCT is partly based on the recent finding on the role of treatment in reducing

infection, this is critiqued below. The authors note benefit-cost calculations for HTC are more speculative than those for MC because programme effects and costs are uncertain. It is not clear from the paper as to exactly what we should be funding in HCTs as they are many and varied. What is the mix?

Information campaigns through mass media and peer groups (IC)

The third solution is information campaigns through mass media and peer groups. It is included because, although there is little clear evidence on their effects, they “constitute an important component of HIV prevention strategies.” Behrman and Kohler (2011) state “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 programme 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 programmes that rely on cell phones and related technologies—are effective in reducing HIV infections among young adults”. The benefit-cost calculations for IC are speculative, and implicit is that they are even more uncertain than for HTC programmes.

Findings

The conclusions of the paper are presented in two tables. Both look at the three solutions with alternative estimates for: a \$1,000 DALY economy and a \$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. The authors exclude, correctly in my view, low prevalence countries from the analysis. This is a good decision because the HIV epidemic is not high on the agenda, nor should it be, in these settings.

The first table presents benefit-cost estimates. Overall these are high. The lowest ratio is in the case of the high-cost information campaign in a \$1,000 DALY economy with a 5% discount rate where the benefit-cost ratio is 1.0. In all other scenarios it is above this, at the peak it is 82.9 for low cost circumcision at a 3% discount rate in \$5 000 DALY, high prevalence economy.

This means there are ‘substantial possibilities for interventions that reduce the transmission of sexually-transmitted HIV/AIDS’. Benefit-cost ratios remain high even if benefits are overestimated or costs underestimated. These ratios are about 2.5 times as large for the \$5,000 DALY economy than the \$1,000 DALY economy; they are 40% larger for the 3% discount rate than for a 5% discount rate; are twice as large for a high (25%) initial HIV prevalence than for a medium (11%) initial HIV prevalence; and low-cost intervention estimates are higher for each solution than the higher-cost intervention estimates.

A plain language conclusion is: the less the intervention costs, the higher the prevalence, and the higher the value of a life, the greater the benefits against the cost. For the low-cost alternatives, MC has the highest benefit-cost ratios, with HTCs second, and IC third. But for the high-cost intervention assumptions, HTCs tend to have the highest benefit-cost ratios with MC second and IC third.

The second table presents the costs per HIV infection averted (HIA) and the costs per DALY that are implied by calculations of the benefit-cost ratios. MC is the most cost-effective intervention, both in terms of costs per infection averted and cost per DALY averted, in high- and medium-prevalence

scenarios. HTC is cost-effective if the programme is sufficiently comprehensive and well-designed to result in the reductions of HIV infection risks that are assumed in the author's calculations. Information campaigns are the least cost-effective intervention based on the calculations, with considerable uncertainty about the costs per DALY and HIA.

There are important differences between the benefit-cost approach and the cost-effectiveness approach. Based on cost-effectiveness calculations, MC always dominates HTC, and MC is between 1.5–2 times more cost-effective than HTC (the costs per DALY and HIA for MC are between 50%–66% those for HTC). In the benefit-cost analyses for the high-cost scenario and high initial prevalence HTC is the intervention with the higher benefit-cost ratio than MC. This is because benefits are discounted, and circumcision is for life while the other interventions fade over time.

The plain language conclusion is benefit-cost analysis is more relevant for policy analysis. On this basis if we had an extra \$10 billion and the cost of the intervention is high we should invest in HTC otherwise MC will produce the best return. This is interesting but not terribly helpful to policy and decision makers as will be discussed. It illustrates the complexity of the epidemic and the limitations of this approach.

How Should We Assess Success: The Role of RCTs

Behrman and Kohler write “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”. It is on the basis of this analysis they put forward their three solutions for the prevention of sexually transmitted HIV infections (with cost-benefit and cost-effectiveness estimates). It is worth noting I am not aware of any other work at this point.

In science the gold standard to assess if something works is a randomised controlled trial (RCT). This is a scientific experiment where subjects are randomly allocated to receive one or other of alternative treatments. Usually one group is the intervention arm, the other the control. Ideally the trial is blind – the participants do not know which intervention they are receiving. There may be additional levels of ‘blinding’: those administering the intervention, collecting results, and carrying out first stage of analysis should not know what the participants are getting – double and triple blinding. What is crucial is if the outcome of the intervention can be measured. In the case of HIV prevention the outcome should be biologically measurable, and reduced HIV incidence is the best result but proxies such as pregnancy rates may be used. There is an entire corpus of work devoted to RCTs.

There are concerns with using RCTs as a measure of effectiveness of HIV prevention – they are better suited to assessing treatment. They are complex, expensive and take time. An example is the microbicide trials, a prevention method not prioritised here, for good reason, as it is not yet available.

The idea of a female controlled prevention method was first mooted in 1990 by Professor Zena Stein (Stein 1990). The Centre for the AIDS Programme of Research in South Africa (CAPRISA), based in Durban completed the most recent study on microbicides. They looked at whether a gel containing the anti-retroviral drug tenofovir, applied vaginally by women would reduce the risk of infection. Following years of design work and preparation, the trial began in May 2007 in an area outside Pietermaritzburg in South Africa, finished in December 2009, and data were first published in March 2010. The trial had 1800 participants half the women were given the gel with tenofovir and others the gel with no drug. They were asked to use the first dose 12 hours prior to and 12 hours after having sex. All were given HIV risk reduction counselling and received condoms.

The headline result was: a microbicide containing 1% tenofovir was 39% effective in reducing risk of contracting HIV during sex and 51% effective in preventing genital herpes infections.(Mbadi, N and CAPRISA 2010) (Fox, M 2010). Further trials will need to be done (and are in process) before the gel is approved by the regulatory agencies – the Food and Drug Administration in the USA and Medicines Control Council in South Africa, this probably won't happen before 2015. This is 25 years after the idea was first mooted.

The situation is further complicated because a number of prevention RCTs have been halted early as they were shown to be effective and it was considered unethical to withhold the intervention. It is worth noting that this unfortunately does not mean that the interventions are either sustained or scaled up.

Some interventions do not lend themselves to RCTs. For example how can a national media programme be tested in a control population? All and sundry would be exposed to billboards, and radio messages are available to everyone with a receiver.

Finally while results from a RCT are considered the gold standard they can be wrong. Again an HIV prevention intervention illustrates this. It was thought in the 1990s that the presence of sexually transmitted infections (STIs) was an important cofactor for HIV infection and pre-emptive treating of STIs might be a way of bringing down HIV incidence. Indeed the belief was so strong that trials went into the field to find out what impact STI prevention and control might have on HIV infection rates. The two landmark trials were in Mwanza, Tanzania and across the border in Rakai in Uganda. The full details of the studies can be found in the references.

In 1995, the first results of the Mwanza study showed 40% of HIV infections had been prevented in the communities receiving the intervention. At this point there was nothing else with such promising outcomes, and it was greeted with great excitement by the AIDS community. The Rakai study, which reported in 1999 showed no HIV infections were prevented in the intervention communities. Subsequent studies have not been able to replicate the Mwanza work. (Hitchcock, P and Fransen, L 1999) (Crosskurth H, et al 2000).

The gold standard then is to have a number of RCTs which can then be subjected to a systematic review. "A systematic review is a literature review focused on a research question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question. Systematic reviews of high-quality randomized controlled trials are crucial to evidence-based medicine." (Wikipedia Cochrane 2011) The best way to do such reviews in medicine is by using the well-known Cochrane methodology.¹

¹ See <http://www.cochrane.org/cochrane-reviews>

Returning to the example of STI control there is a current Cochrane review on the impact of population-based biomedical STI interventions on the incidence of HIV infection. This states: “We failed to confirm the hypothesis that STI control is an effective HIV prevention strategy. Improved STI treatment services were shown in one study to reduce HIV incidence in an environment characterised by an emerging HIV epidemic (low and slowly rising prevalence), where STI treatment services were poor and where STIs were highly prevalent; Incidence was not reduced in two other settings. There is no evidence for substantial benefit from a presumptive treatment intervention for all community members. There are, however, other compelling reasons why STI treatment services should be strengthened, and the available evidence suggests that when an intervention is accepted it can substantially improve quality of services provided.” (Ng, BE 2011)

Social science has its own systematic review body, the Campbell Collaboration, which “helps people make well-informed decisions by preparing, maintaining and disseminating systematic reviews in education, crime and justice, and social welfare.” (Campbell Collaboration 2011) This may be of help moving forward but it is still in its early stages.

Differences in philosophy between social sciences, natural science and humanities are beyond the scope of this paper but are nonetheless important. Kagan (2009) puts forward three components to intellectual efforts: the unquestioned premises that create preferences for particular questions and hence particular answers – in the case of this project that economic analysis works; the analytical tools used – here monetary costs and benefits; and a preferred set of concepts that are the core of explanations – for RethinkHIV that is cost benefit analysis.

The Underlying Assumptions for Critiquing the Paper

The Scale of the Epidemic

There are three major epidemics in the subcontinent. This is well illustrated on the map in Behrman and Kohler’s paper (2011). First and easiest to deal with are those areas where prevalence is low. This predominantly encompasses the Muslim countries of North and West Africa. The main modes of transmission are probably drug use, men having sex with men and commercial sex work. This should partly be the topic of the non-sexual transmission paper. One question that is relevant but beyond the scope of this paper is: why are infection rates so low? Levels of male circumcision may be a critical reason. The Behrman and Kohler (2011) assessment paper does not consider these countries further, a correct decision.

The second cohort consists of countries where HIV rates are stable or falling, but high – 5-15% among adults. These include East African nations where the epidemic first emerged: Kenya, Tanzania and Uganda, and some West African countries. It should be noted here that the big unknown in terms of prevalence is Nigeria; both because the data are unreliable and the size of the population means the numbers could be huge. These are dealt with as medium prevalence in the paper.

Worst affected are the hyper-endemic countries of Southern Africa: Zambia, Malawi, Zimbabwe, Mozambique, South Africa, Swaziland, Botswana and Lesotho, (but not, interestingly, Angola, a country where males are circumcised early). Here prevalence is shockingly high. There are two important points about prevalence. The first is the rate and the second is the numbers. It is appalling that 50% of women aged between 25 and 29 in Swaziland are infected; this translates into a lifetime risk of probably close to 80%. It is also worth noting that while South Africa does not appear to have the same infection rates as Botswana, Lesotho and Swaziland, this is because

some provinces have diluted overall prevalence. It is estimated that 5 million South Africans may be infected. There are more people with HIV in the province of KwaZulu-Natal than in Botswana, Lesotho and Swaziland combined. In these situations HIV has to be an overriding priority. These countries are identified as high prevalence in the paper.

Modes of Transmission

The main modes of transmission among adults are sex; injecting drug use; blood transfusions; and contaminated medical equipment (nosocomial infection). In sub-Saharan Africa sexual contact accounts for the largest proportion of infections although other modes of transmission are present and important in some settings. It must be remembered that sexual contact can be sex between men and women, heterosexual sex; and sex between men, known as men who have sex with men (MSM).

The probability of sexual transmission can be expressed as

$$I = S [1 - \{ pB[1-\beta']\alpha(1-v) + p(1-B)[1-\beta]\alpha(1-v) + (1-p) \}n]$$

S = number susceptible

p = HIV prevalence in partners

B = prevalence of Sexually Transmitted Infections (STIs) in partners

β = probability of transmission (with STI (β'), without STI (β))

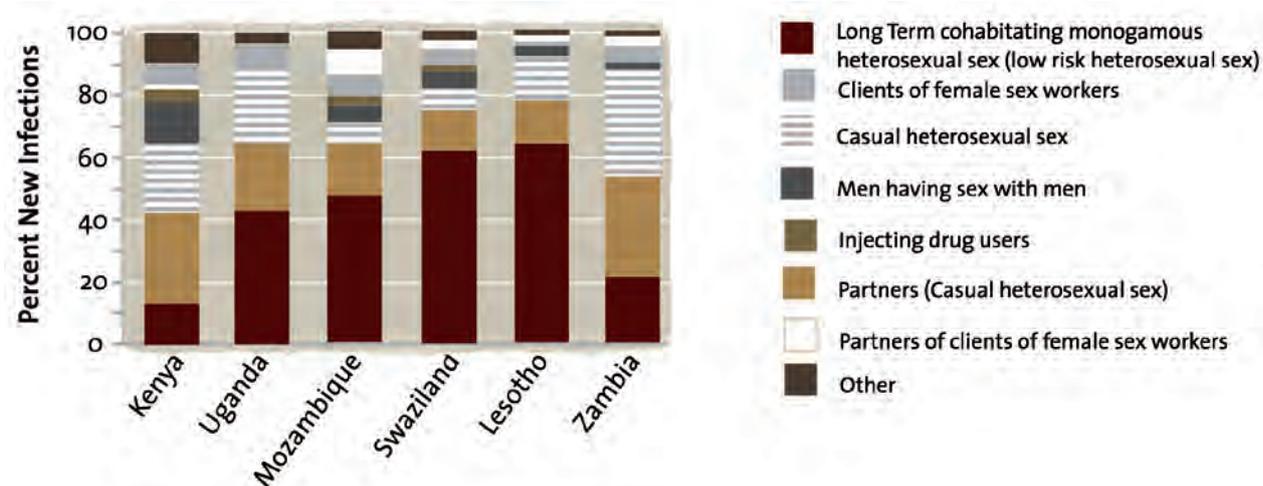
α = contacts per partner

v = proportion acts protected by condom use

n = number of partners (UNAIDS 2011)

There are a number of important studies from UNAIDS on modes of transmission. These are well described on the UNAIDS website, which also has tools, guidelines and gives access to country reports. (UNAIDS 2011a) The chance of infection for heterosexual intercourse is 0.006 per risky exposure act with an STI present and 0.002 with no STI, no matter if the person is a sex worker or in a long-term relationship. It is higher for men who have sex with men (MSM): the probability per risky act is 0.030 if there is an STI and 0.010 with no STI. If, in a population many men, (S) visit

Figure 1: Incidence by modes of HIV transmission (sexual)



Sources: Results from Know your Epidemic project in Southern and Eastern Africa. Reports available from <http://www.unaidsrستا.org/hiv-prevention-modes-of-transmission>

commercial sex workers (CSW) frequently (α), who in turn have high levels of infections and STIs (p) and (B), and these sex acts are unprotected (v) then chance of transmission increases.

What therefore drives the epidemic (in the absence of interventions) is the underlying prevalence, frequency of sex, multiple partners, levels of STIs and condom usage. These determine the chance of exposure and the number of exposures. The very different epidemics in Africa are illustrated in Figure 1.

In Swaziland and Lesotho over 60% of infections are between people engaged in so called 'long term cohabiting monogamous heterosexual sex'. Of considerable significance are those having 'casual heterosexual sex' and their partners. The figure is also telling because it shows a small but significant contribution from MSM in Kenya, Mozambique and Swaziland, numbers are smaller in Lesotho and Zambia. There appear to be no transmissions via this route in Uganda but MSM activities are illegal and highly stigmatized there. Indeed MSM is illegal in a number of countries and stigmatized in most – in Malawi two gay men were jailed in the past six months. This impacts on reporting and makes interventions problematic. Also significant are infections between commercial sex workers and their clients. Again in some settings this may be illegal which causes problems for identifying and addressing the problem.

Basics of Sexually Transmitted HIV Prevention

Preventing HIV transmission through sexual intercourse is not rocket science! There are behavioural interventions which involve abstinence, delaying sexual debut, sticking to one partner, having fewer partners, and not having concurrent partners. In the equation above this is intervening in the α (contacts per partner) and n (number of partners) to reduce the S (number susceptible) and hence the incidence. In terms of the Schwartländer et al (2011) investment approach this is reducing risk. The second set of options are about making the chance of transmission in an act of sexual intercourse less likely. Interventions available at the moment focus on the B (prevalence of STIs in partners) and the v = proportion acts protected by condom use. Not in the equation is circumcision which is a biomedical intervention. When microbicides and vaccines become available they will fall into the category of interventions that make sex less risky.

Of course in getting prevention programmes that work, the devil is in the detail, as with benefit cost analysis. Obviously not engaging in sex is a sure way to avoid infection. The abstinence option was pushed in the PEPFAR funding where one third of prevention money had to be earmarked for this. There is little evidence that this works. My unit undertook an evaluation of a project in Durban where a faith based organisation was providing an intervention in schools. We found the project had mixed results. Qualitative analysis showed the community valued the intervention and it created a safe space for adolescents to discuss HIV and abstinence, life skills and socio-economic challenges. Quantitative analyses showed that participation was associated with higher scores on a number of resilience dimensions, including hope, mastery and optimism. Participation was statistically related to a lower likelihood of reporting ever having had sex, (42.1% of learners reported having had sex, compared to 52.8% of those who had not received the intervention). This effect was stronger in boys, 20% of male learners exposed to the intervention reported having had sex in the past year compared to 35.3% of those who were not. However those exposed to this intervention had less favourable attitudes towards using condoms as the most reliable form of HIV prevention. (Casale et al 2010; Nixon 2009). The good news is participants delayed sexual debut; the bad news was they were less likely to use condoms. I think the problem with faith-based abstinence programmes is that to have sex is a 'sin'; to use a condom is a worse 'sin' because it

implies premeditation and a willingness to 'sin'. Therefore to have sex and use a condom is not a 'sin + sin = 2 sins' equation but rather 'sin + sin + premeditation = sin³'.

If a person cannot abstain, they can avoid infection by not being exposed to infected partners. Having one uninfected life time partner will achieve this. Other ways of decreasing risk include delaying sexual debut, this is particularly important for younger women for physiological reasons; having fewer partners; not having concurrent partners; and choosing partners from pools where infection levels are lower. This last option is cited by Behrman and Kohler (2011) who cite a study showing sexual behaviours of female teenagers are responsive to HIV risk information. When girls were informed of the HIV prevalence rates in men of various ages they choose their sexual partners from those with lower infection rates. This randomised study documented a 28% decrease in teen pregnancy. (Dupas, P 2011) These are the HCT and IC options. They are social interventions.

If a person is exposed through sex to someone who is infected then the likelihood of transmission can be reduced. If they do not have STIs (B = prevalence of Sexually Transmitted Infections (STIs) in partners) then transmission is reduced, but as the RCTs show that STI interventions as currently designed do not work Behrman and Kohler (2011) correctly do not pursue this option. To repeat the quote, "There is no evidence for substantial benefit from a presumptive treatment intervention for all community members. **There are, however, other compelling reasons why STI treatment services should be strengthened**" (Emphasis mine). For both men and women using condoms – male or female will reduce the chance of exposure; and men who are engaged in heterosexual sex are at lower risk if they are circumcised.

The Assessment Paper Critique

The assessment paper identifies three possible solutions for lessening sexual transmission of HIV: male circumcision; HIV counselling and testing; and information campaigns. This is essentially one biomedical intervention and two social interventions. Before commenting on these solutions it is worth noting that in all cases the assessment paper discusses this as a decrease in infection among young men. This is of concern, as the bulk of infections are in young women.

The paper assumes that male circumcision will reduce the probability of infection by 30%. The data suggests that the reduction is about 60% so this is a conservative estimate. Voluntary counselling and testing is assumed to reduce infection by 25%. Information through mass media and peer groups is assumed to reduce the rate of infection by 25%. The data for these interventions are rather a guesstimate.

Male Circumcision

Medical male circumcision is the prevention intervention for which there is the most evidence and there are RCTs. It is a straightforward binary option: circumcised/not circumcised and works for life. However it is protective for uninfected men, not women. If enough men in a population are circumcised then it will impact transmission in the population.

There can be no doubt that this is a good option. In 2006 following the publication of the second edition of *AIDS in the Twenty-first Century: Disease and Globalisation*. (Barnett, T and Whiteside A 2006) My co-author Tony Barnett and I felt that we lacked solutions and convened a meeting of senior people, from a range of organisations to talk about what was needed. All were invited in their personal capacity. The meeting was attended by the AIDS ambassadors, senior donor agency

staff, a representative of a pharmaceutical company and people from hyper-endemic countries. The conversation, which took place over two days on a sailing boat in the IJsselmeer, was private, but at the end we agreed an *Informal Aide Memoire of the Silos to Windmill Meeting* which was to be realistic, advocating and discussing limited issues to see if they were feasible.

We agreed on four key issues. In order of priority they were:

1. We advocated routine opt-out male infant circumcision. Evidence so far is substantial enough to make this case. Opt-in circumcision should be available for older males.
2. We perceived a disconnect between those who (desperately) need funding and their potential donors, due to communication problems, bureaucracy and different perceptions and expectations. The donor community needs to get to know its 'customers' better.
3. We argued for investigating the need for and possibilities of establishing health insurance funds.
4. We felt the need to find a system for accountability on all levels.

Why is medical male infant circumcision not advocated for? One answer might be that it would take too long to be effective. However boys become sexually active in their late teens or early twenties so, at worst, it would take 25 years to show an impact. This is the same period from conceptualisation to delivery of the microbicide!

In general HIV/ AIDS scholars and activists are reactive and have tended to focus on immediate quick fixes and conceptualise "impacts" as sequential and short-term effects resulting from the virus, rather than considering the complexities and inter-generational dimensions of epidemics and their consequences. I worked with colleagues in thinking about key conceptual limitations through a novel comparative analysis of historical trends and contemporary debates within HIV/ AIDS and climate change scholarship. These share certain similarities. Scholars in both areas are struggling to understand phenomena that are unprecedented, complex and highly dynamic, and that have different impacts on different people and places. However in climate change people look forward, in AIDS we don't. (Chazan, Brklacich, and Whiteside 2009)

Ignored in this paper is the issue of MSM. Is medical male circumcision effective at reducing transmission between men who have sex with men? These numbers may be significant. A recently published Cochrane systematic review (Wiysonge et al 2011) designed to answer this question found there is no conclusive evidence suggesting a protective role of medical male circumcision (MMC) between men who have sex with men (MSM), although there may be some protection for men who practice primarily insertive anal sex. At present there is no completed randomised controlled trial (RCT) that has assessed the effects of male circumcision on acquisition of HIV and other sexually transmitted infections among MSM. It will be important to watch for the results of an RCT currently being conducted in China among MSM. (Wiysonge et al 2011)

HIV Counselling and Testing and Treatment as Prevention

The HCT solution is conditional on it "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 counselling." (Behrman and Kohler 2011) It is not entirely clear what these solutions will look like, but they do advocate for early treatment of those found to be infected, and the critique needs to spend a few paragraphs on this.

The idea of AIDS treatment as prevention has been around for some time. Montaner of the British Columbia Center for Excellence on HIV AIDS suggested that, by getting many of the small cohort of HIV-infected people on treatment in his province, HIV transmission would be greatly reduced. (Montaner JSG et al 2006) He further argued, albeit on the basis of very poor data, that this was cost effective. The publication of a model by Ruben Granich and others in 2009 (Granich RM 2009) suggested that if people were tested regularly and those infected were immediately put on therapy, this would, over time, eliminate HIV transmission. This was a mathematical model. Nonetheless there was a great deal of interest in operationalizing it. Swiss authorities released guidance in which discordant couples, on antiretroviral therapy, were advised they had no need for other prevention techniques. Most recently a study: HPTN-052 showed that there were 96% fewer HIV transmission events in couples who began treatment immediately, than in couples who started later.

There are a number of important questions that need to be raised before this is adopted as a gold standard policy, with the expectation that it will bring an end to the HIV epidemic. These are particularly important in resource poor settings.

What is the meaning of immediately? Recent work shows a significant number of HIV transmissions take place in the early stages of a person being infected. (Powers KA et al 2011) A comment in the Lancet (Cohen T et al 2011) notes “if individuals within the first 6 months of their HIV infection are indeed responsible for a high proportion of all transmission events, a substantial proportion needs to be rapidly identified and treated during this stage to have any prospect of the large decreases in HIV prevalence”. This adds to logistical challenges and costs especially since HIV is still stigmatizing. It also means that the idea of population wide safe sex could work, in conjunction with treatment see below. (Parkhurst J and Whiteside A 2010)

What will the costs be? The early detection needs more expensive kits. People will be on treatment for longer, adding to the price of therapy. Cost benefit analysis from the treatment papers of RethinkHIV may be of value in addressing these questions.

What are the population effects? Will this accelerate the emergence of antiviral resistance?

What are the individual effects? Will there be risk compensation (more risky sexual behaviours when an individual feels protected). Does it make sense for an individual to go on early treatment in resource constrained environments where, should they develop resistance and side effects; they have a shorter period of access to ART, and earlier death?

Information Campaigns and Mass Media

This is the third and weakest part of the proposal. There are numerous such programmes but trying to evaluate them is extremely difficult and there are no RCTs or robust cost analyses. Two examples spring to mind: LoveLife and Swaziland’s *Makhwapheni* Campaign, both from hyper-endemic Southern Africa.

LoveLife was a campaign in South Africa supported primarily by the Kaiser Family Foundation.² Millions of dollars were mobilized in support of its programmes from 1999. I, along with many other South Africans, found the messaging impenetrable. The most visible were billboards that left us confused. One giant lime-green billboard featured the words, “Score” and “Red Card,” with

² See <http://www.lovelife.org.za/>

corresponding check boxes beside them. Other posters featured cryptic word pairs: “Your Body/ Anybody,” “Climax/Anticlimax,” or “Drop Dead Gorgeous/The Drop.”

There was an evaluation planned. It began successfully but as the research began to suggest that this programme was not having the impact claimed, the two researchers found their work blocked. Various odd happenings occurred around them including the theft of their computers and data. So with regard to the biggest IC campaign we have no clear data on its impact. (Halperin, D and Williams, B 2001)

In Swaziland a bold initiative was instigated, the *Makhwapheni* Campaign. Literally this means something hidden in the armpit, but in Swaziland it was known to mean “secret lover.” It was bold and explicit. In Swaziland most people have cell phones and they were at the centre of the campaign. This began in July 2006 and lasted just a few weeks. It was based on billboards showing the screen of a cell phone with invitations in cell-phone talk. One said, “i’m all alone. cum 4 a quicky.” Another said, “she’s working late, cum work on me.” Beside these invitations were strong punch lines, in siSwati. One example, “why kill your family”, another, “and more orphans were left behind.” The slogan for the entire campaign was ‘*makhwapheni uyabulala*’: ‘your secret lover can kill you.’

The campaign got the country talking. But it resulted in a backlash from some AIDS activists. They felt they were singled out, accused of spreading HIV and being stigmatised. Others read it as focussing on the women’s sexuality. There were demonstrations, the billboards came down and one of the most successful campaigns (at least in terms of getting people to talk) ended.

On the basis of available evidence IC campaigns cannot be evaluated. However they are important and to understand this we should look at the Schwartländer et al (2011) paper. Many interventions fall into the category of critical enablers. Necessary but not sufficient!

What is missing and what might come in the future

The assessment paper identifies the interventions for which there is cost and benefit information. We are left asking, with them, is that all! Microbicides are not available, but may be important in the future. Condoms seem not to be evaluated. It would, on the basis of this work, seem that resource allocation decisions are not being made on good data and analysis.

One wild idea is to explore the concept of a ‘sexual abstinence month’ to reduce HIV incidence, a behavioural intervention where a population-wide ‘safe sex/no sex’ effort for a set period of time could make a significant contribution to global prevention efforts. This is based on the idea that people have higher viral loads immediately after they are infected and if they could avoid infecting others then the population viral load and infectivity would be reduced. This idea is a *hypothesis* which requires further exploration and testing. A month of ‘safe sex/no sex’ would produce easily verifiable data with regards to adherence, evidenced in the number of births occurring nine months after the campaign. (Parkhurst JO and Whiteside, A 2010)

What policy recommendations can come out of this work

The Copenhagen Consensus is known for taking difficult issues and applying rigorous analysis to them. For those of us working in the field of AIDS, and especially coming from a southern Africa, which is where the epidemic is at its worst, this project offered the opportunity to grapple with

critical issues. From an economic point of view it suggests where resources should be allocated. At this stage I have to say it does not yet provide the answers.

On the basis of the paper I have critiqued male circumcision takes priority, but note that this is something available only for young men, while the worst epidemic is located among women. If we do succeed in circumcising enough young men, it will make a difference to the epidemic, but not for years to come. Beyond circumcision the answers remain unclear. It may be that the investment framework put forward by Schwartländer et al (2011) needs to be looked at in conjunction with this process. Ultimately it may also be that it is only through equitable development that is gender sensitive or through restrictive regimes and religions that we can hope to bring the epidemic under control. This is all rather depressing.

References

- Barnett, T & Whiteside, A 2006, *AIDS in the Twenty-first century: disease and globalization*, 2nd ed., Basingstoke: Palgrave.
- Behrman, Jere R & Kohler, H-P 2011, 'RethinkHIV: assessment paper on the prevention of sexual infection.'
- Campbell Collaboration 2011 http://www.campbellcollaboration.org/about_us/index.php
- Casale, M Dawad, S Flicker, S Hynie, M Jenney, A Jobson, G Nixon, S O'Brien, K Rogan, M Rubincam, C Cele, P Magadla, O Mhlongo, W Phakathi, P Radebe, S Zwane, T 2010, 'They made us who we are today: a retrospective evaluation of the 1st 5-Year cohort of the iThembaLethu HIV Prevention Programme (2002-2006).' Final evaluation report available on the HEARD website at: <http://www.heard.org.za/heard-resources/2010#reports>
- Chazan M, Brklacich M, & Whiteside A 2009, 'Rethinking the conceptual terrain of AIDS scholarship: lessons from comparing 27 years of AIDS and climate change research', *Globalization and Health* 5:12 doi:10.1186/1744-8603-5-12.
- Cohen, T & Corbett, EL 2011, 'Test and treat in HIV: success could depend on rapid detection.' *Lancet* 378 (9787): 204–206. doi:10.1016/S0140-6736(11)60896-9.
- Dupas, P 2011, 'Do teenagers respond to HIV risk information? Evidence from a field experiment in Kenya.' *American Economic Journal: Applied Economics* 3(34): 1–34. doi:10.1257/app.3.1.1.
- Fox, M 2010 'AIDS gel with Gilead drug protects women in study.' 19 July. Reuters. <http://www.reuters.com/article/2010/07/19/aids-gel-idUSN1920562920100719> Retrieved 28 March 2011
- Granich, RM Gilks, CF Dye, C De Cock, KM and Williams BG 2009, 'Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model.', *Lancet* 373: 48–57.
- Grosskurth, H Gray, R Hayes, R Mabey, D Wawer, M 2000, 'Control of sexually transmitted diseases for HIV-1 prevention: understanding the implications of the Mwanza and Rakai trials.', *Lancet* 355(9219):1981–7.
- Halperin, D and Williams, B 2001, 'This is no way to fight AIDS in Africa.' *Washington Post* 26th August.
- Hitchcock, P & Fransen, L 1999, 'Preventing HIV infection: lessons from Mwanza and Rakai'. *The Lancet*, 353(9152) 513 - 515, 13 February.
- Kagan, J 2009, *The Three cultures natural sciences, social sciences and the humanities in the 21st century*, New York: Cambridge University Press.
- Mbadi, N & CAPRISA 2010, 'Study of microbicide gel shows reduced risk of HIV and herpes infections in women' 2011 www.caprisa.org/joomla/Micro/CAPRISA%20004%20Press%20Release%20for%2020%20July%202010 Retrieved 23 January 2011.
- Ng, BE Butler, LM Horvath, T & Rutherford, GW 2011, 'Population-based biomedical sexually transmitted infection control interventions for reducing HIV infection.' *Cochrane Database of Systematic Reviews* 2011, Issue 3. Art. No.: CD001220. DOI: 10.1002/14651858.CD001220. pub3.
- Nixon, S Flicker, S Hynie, M Casale, M Rogan, M Rubincam, C O'Brien, K & Jenney, A 2009, 'Destiny, disease and desire: unpacking the results of a school-faith-based HIV intervention.' Fourth Southern African AIDS Conference, 31 March to 3 April 2009.
- Padian, NS, McCoy, SI, Balkus, JE & Wasserheit, JN 2010, 'Weighing the gold in the gold standard: challenges in HIV prevention research.' *AIDS* 24(5), 621–635. doi:10.1097/QAD.ob013e328337798a.
- Parkhurst, JO & Whiteside, A 2010, 'Innovative responses for preventing HIV transmission: the protective value of population-wide interruptions of risk activity.' *South African Journal of HIV Medicine*, 3, April.
- Powers, KA Ghani, AC Miller, WC, Hoffman, IF Pettifor, AE Kamanga, G Martinson, FE & Cohen, MS. 2011 'The role of acute and early HIV infection in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: A modelling study.' *Lancet* 378(9787): 256–268. doi:10.1016/S0140-6736(11)60842-8.
- Ross, DA 2010, 'Behavioural interventions to reduce HIV risk: What works?' *AIDS* 24(Supplement 4): S4–S14. doi:10.1097/01.aids.0000390703.35642.89.
- Schwartländer, B Stover, J Hallett, T Atun, R Avila, C Gouws, E Bartos, M Ghys, P D Opuni, M Barr, D Alsallaq, R Bollinger, L de Freitas, M Garnett, G Holmes, C Legins, K Pillay, Y Stanciole, A E McClure, C Hirnschall, G Laga, M & Padian, N 2011, 'Towards an improved investment approach for an effective response to HIV/AIDS.' *Lancet* –.doi:10.1016/S0140-6736(11)60702-2. Published online June 3.
- Smith J & Whiteside A 2010, 'The History of AIDS exceptionalism', *Journal of the International AIDS Society* 13:47. 2010.
- Stein, ZA 1990, 'HIV prevention: the need for methods women can use' *American Journal of Public Health*, 80, (4), 460–462.
- UNAIDS 2011, 'Modelling the expected distribution of new HIV infections by exposure group' slide presentation from UNAIDS accessed 11th July 2011 at http://www.unaids.org/en/media/unaids/contentassets/restored/mot_gen_2007_pres_en.pdf
- UNAIDS 2011a, Know your epidemic and modes of transmission. <http://www.unaidsrsta.org/thematic-areas/hiv-prevention/know-your-epidemic-modes-transmission> accessed 11th July 2011
- Wikipedia 2011 http://en.wikipedia.org/wiki/Systematic_review#Cochrane_Collaboration, accessed 31st August.
- Wiysonge, CS, Kongnyuy, EJ Shey, M Muula, AS Navti, OB Akl, EA Lo, YR 2011, 'Male circumcision for prevention of homosexual acquisition of HIV in men.' *Cochrane Database of Systematic Reviews*, Issue 6.

RethinkHIV RESEARCH PAPERS

Prevention of Sexual Transmission

Assessment Paper: Jere Behrman, Hans-Peter Kohler

Perspective Paper: Damien de Walque

Perspective Paper: Alan Whiteside

Prevention of Non-sexual Transmission

Assessment Paper: Lori Bollinger

Perspective Paper: Rob Baltussen, Jan Hontelez

Perspective Paper: Mira Johri

Treatment

Assessment Paper: Mead Over, Geoffrey Garnett

Perspective Paper: Robert J Brent

Perspective Paper: John Stover

Vaccine Research and Development

Assessment Paper: Dean Jamison, Robert Hecht, with Jared Augenstein, Gabrielle Partridge, and Kira Thorien

Perspective Paper: Steven S. Forsythe

Perspective Paper: Joshua Salomon

Social Policy

Assessment Paper: Anna Vassall, Michelle Remme and Charlotte Watts

Perspective Paper: Tony Barnett

Perspective Paper: Harounan Kazianga

Strengthening Health Systems

Assessment Paper: William McGreevey, with Carlos Avila, Mary Punchak

Perspective Paper: Till Bärnighausen, David E. Bloom, and Salal Humair

Perspective Paper: Nicoli Nattrass