



Perspective Paper

Prevention of Non-Sexual Transmission of HIV

Rob Baltussen and Jan Hontelez



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

ISBN: 978-87-92795-07-6
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 Non-Sexual Transmission of HIV

Rob Baltussen¹, Jan Hontelez^{1,2}

¹ Nijmegen International Center for Health Systems Research and Education (NICHE), Radboud University Nijmegen Medical Center, The Netherlands

² Department of Public Health, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, Netherlands

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
Introduction	8
Options and limitations of multi-country analyses	8
Methods of analysis	9
Preventive versus treatment interventions	10
Equity in resource allocation	11
Conclusion	12
References	13

Introduction

The contribution by Bollinger (Bollinger 2011) on the costs, effect and cost-effectiveness of prevention of non-sexual HIV infections in Sub-Saharan Africa is an ambitious undertaking. This perspective paper qualifies the merits of the analysis, and puts forward a number of important issues to consider when interpreting its results. We first reflect on the options and limitations of detailed continent-wide analysis in the absence of comprehensive data and then identify a number of analytical shortcomings. We proceed by presenting results from other studies based on country-level analysis, and finally draw a number of conclusions.

Options and limitations of multi-country analyses

The study provides cost, effects and cost-effectiveness estimates at the continent-level, on the basis of individual analyses for each of 44 countries in Sub-Saharan Africa. Compared to previous similar analysis by e.g. Floyd et al (Floyd et al. 2002) that provided single cost-effectiveness estimates for Sub-Saharan Africa as a whole, and Hogan et al. (Hogan et al. 2005) that provided estimates for several African sub-regions, the study has the potential to bring more detail and therefore credibility to its estimates. At the same time, the question is whether the study can actually live up to these standards – does it really provide estimates that are sufficiently transparent, valid and reliable at the country level? Unfortunately, we do have doubts on this, and we identify four key issues.

Firstly, at the analytical level, the study relies on a range of models under the name of SPECTRUM to make country-specific models and subsequently projections of the HIV/AIDS epidemic – it is not clear to what extent these models reflect the actual epidemiology in the country of analyses. Estimates are said to be based on a number of country-level workshops, but no indication is given of the goodness of fit of the resulting models. Second, in these kinds of analyses, where subgroups of the HIV epidemic are investigated, it is important to have adequate estimates of the relative contribution of each transmission route to the overall epidemic. Although the Modes of Transmission (MoT) initiative (Colvin M et al. 2011) aims at mapping the attributable fraction of different transmission routes in individual countries, the methodology is questionable and ultimately depends on local data, which is often unreliable or missing. The assumed number of infections caused by unsafe medical injections, IDU use, or blood transfusions is therefore subject to high levels of uncertainty. Third, and closely related, the impact of the interventions is estimated on the basis of an impact matrix, that reflects the reported evidence of almost 200 preventive interventions - however, it is not known to what extent these reflect the intervention effectiveness of the countries under study. Average effectiveness estimates are not necessarily locally meaningful, as they are subject to a wide range of local practices (e.g. needles exchange programs are culturally very sensitive). Fourth, the study often relies on costing data that is extrapolated from a small number of other countries, or are based on international prices (e.g. that of ARV drug) and its accuracy can only be guessed. Having said this, it should be noted that the above limitations are inherent to the task at hand and therefore virtually inevitable – any detailed country analysis in the absence of comprehensive data is fraught with difficulties. At the same time, this places question marks on the usefulness of studies of this nature, and whether series of high-quality country level studies may not be more relevant.

Methods of analysis

The study also suffers from a number of shortcomings related to (analytical) choices made by the author. Firstly, the study falls short in its presentation – most importantly, it only presents summary information for Sub-Saharan Africa as a whole, and not for the individual countries. A more detailed documentation of the analysis, country by country, would add the necessary transparency to the study. Also, sources of data are not always presented, or are presented without argumentation. For example, the HIV transmission probability of contaminated blood is assumed to be 90%, but the reader cannot make a judgement on the strength of the evidence behind this assumption. Tables listing all variables and their values, including sources and strengths of evidence would have been most useful. More generally, the author presents some overview of the cost-effectiveness of preventive interventions to reduce non-sexual transmission – it is not clear whether this is a literature review (if so, what are the sources?) or a summary of the present study (if so, how did the authors come to the conclusion that opioid substitution therapy may not be cost-effective?).

Second, cost estimates are not optimal. For example, the author assumes linear cost function whereas evidence is available that, with increasing coverage, costs increase or diminish depending on the programme under study (Johns and Tan Torres Edejer 2005). Detailed estimates are also available (WHO-CHOICE 2011). Also, in estimating costs of averted infections, the author assumes all patients receive antiretroviral treatment – this is of course a gross overestimate and not realistic. Furthermore, in extrapolating cost estimates from country to country, proper analysis distinguishes prices and quantities and adapts the former to price levels of the country under study, and where possible the latter to local resource utilization patterns. The author follows this methodology to calculate unit costs of the prevention of mother-to-child transmission (pMTCT) but fails to do this for safe medical injections and safe blood transfusions – the unit costs of the latter are based on median costs as reported in a limited number of studies, and one can only guess whether this reflects real costs.

Third, effectiveness and benefit estimates have important shortcomings resulting in a gross overestimation of the number of life-years gained and net financial gains of the evaluated prevention interventions. The direct effectiveness outcomes - that result from the modelling exercise - are the number of infections prevented, which are then used to calculate the number of life-years saved by multiplying the number with a certain standard. This approach ignores the dynamics of an HIV infection and antiretroviral therapy such as the natural history, time till treatment eligibility (i.e. when CD4 cell counts drop below 350 cells/ μ L), health seeking behaviour of individuals, treatment coverage, etc. This introduces important biases into the analysis. Most importantly, it seems like the author simply subtracts the age of infection from the life-expectancy at birth to calculate the number of life years gained per averted infection (e.g. an averted infection due to reduced unsafe drug injections at, on average, age 22 would lead to $65-22 = 42$ life years gained). This implies that a person with an HIV infection dies at age 22, which is an unrealistic assumption, resulting in a gross overestimation of the number of life-years gained of preventing an infection. The average survival of an untreated HIV infection is about 11 years, while ART will further increase life expectancy by about 20 years. Thus, a person would not die at age 22 (age of infection), but at age 50 resulting in 15 life-years gained, almost three times lower compared to the 42 years calculated by the author. This overestimation becomes especially apparent in the calculations regarding pMTCT, where the number of life-years gained of one prevented infection is 65. Also, estimates of life years gained are based on a standardized average African life-expectancy of 65 years – the rational must be that the use of realistic but lower life-expectancies in some countries (like in Sierra Leone, life-

expectancy is 37 years) would render interventions in these countries less cost-effective. However, this rationale is only valid in case countries would be compared in terms of economic attractiveness of interventions, which is not the purpose in the present study. Hence, the use of an artificial life-expectancy of 65 years is misleading and overestimates the economic attractiveness.

Further, financial benefits of an averted infection are assumed to consist of - among others - averted costs of 20 years of ART (which in itself is rather optimistic since it is based on the survival in one of the most successful ART cohorts in Sub-Saharan Africa - average survival while on treatment in the whole of Sub-Saharan Africa is likely to be considerably lower). It is unclear how this matches with the above mentioned mechanism of calculating the number of life-years saved of an intervention. It seems that saved ART costs are always based on number of infections averted, not life-years gained. The simple assumption of 20 years of ART saved per averted infection is thus in mismatch with the 42 life-years saved. Finally, future ART costs and saved costs due to life-years gained are discounted, however, this seems to start only when treatment costs start to be saved. This ignores the fact that patients with a new infection in the period 2011-2015 that is now prevented due to the intervention will start treatment only after about 7-8 years after they got infected (2018 - 2022). This pre-treatment period is not taken into account into the discounting, resulting in a further overestimation of saved costs.

Fourth, the author presents cost-effectiveness estimates in terms of cost per infection averted, and compares these to international benchmarks as put forward by the Commission of Macroeconomics and Health (CMH). CMH states that interventions that cost, per DALY averted, less than one time gross national income (GNI) per capita can be considered cost-effective. The author makes a clear mistake by comparing *cost per infection* averted to the CMH benchmark, that is - as said - expressed as *cost per DALY* averted. Since the number of DALYs saved from (preventive) interventions is 10-15 higher than the number of averted infections, the resulting conclusions are seriously flawed, and the economic attractiveness of intervention - when compared to CMH benchmarks - is much better than presented. Also, the author used the PPP-adjusted GNI in the calculations whereas the cost estimates are in ordinary US\$: the result is that the benchmark - already wrongly interpreted - is also wrongly valued. In addition, it is rather confusing and theoretically incorrect to employ two different monetary benchmarks for a life year saved, i.e. that of the CMH (US\$1,125) and the value as put forward by RethinkHIV (US\$1,000 - 5,000). These values have the same conceptual underpinning, and either one of them should be used throughout the analysis.

Fifth, and more specifically, in the analysis on IDU-related infections, the author combines costs and effectiveness of three different interventions - (i) outreach/information and education campaigns; (ii) needle and syringe exchange programs; and (iii) opioid substitution therapy. This very much limits the interpretation of results. Together, the interventions are said to be moderately economically attractive - but it is not clear whether there is large variation in the cost-effectiveness of the individual interventions and e.g. one, highly cost-ineffective, intervention dominates the others.

Preventive versus treatment interventions

A more general observation relates to the role of this study in the broader RethinkHIV project. We applaud the use of a fairly consistent methodological approach in the present paper to evaluate sets of interventions. This is definitely a virtue, and allows a direct comparison of the relative economic attractiveness of these interventions and the identification of 'best buys'. The 'science' of

cost-effectiveness analyses typically focuses on a single intervention only and employs different methodological approaches, and as a consequence their results are difficult to compare. The present study design overcomes this problem. However, important caveat is that present results may be difficult to compare to other studies in the same series of the RethinkHIV project. Most important is the choice to express health effects of interventions in terms of infections averted – this provides an uneven playing level for the comparison of economic attractiveness of preventive and treatment interventions as it is not the sole aim of the latter to prevent infections. In other words, by defining outcomes in averted infections, preventive interventions are advantaged over treatment interventions. The use of life years gained as a common outcome measure would have provided a more equal playing ground.

Given the above mentioned important limitations, the added value of the presented analyses should be considered carefully. The cost-effectiveness of preventing non-sexually transmitted HIV - especially mother-to-child transmission - in Sub-Saharan Africa has been extensively studied by others (Wilkinson, Floyd et al. 2000; Sweat, O'Reilly et al. 2004; Maclean and Stringer 2005; Soorapanth, Sansom et al. 2006; Robberstad and Evjen-Olsen 2010; van Hulst, Smit Sibinga et al. 2010; Alistar, Owens et al. 2011; Johri and Ako-Arey 2011; Shah, Johns et al. 2011). Although these studies are usually country-based rather than continent-based, they do provide more comprehensive data and analyses on the likely impact of interventions that prevent the non-sexual transmission of HIV. Robberstad et al found that the incremental cost of preventing one child infection of HIV in Tanzania is 4,062 US\$, while the cost per DALY averted is 162 US\$ (Robberstad and Evjen-Olsen 2010). These results are in line with Shah et al, who modeled the cost-effectiveness of the new WHO recommendations on pMTCT in Nigeria, showing that new WHO treatment guidelines cost 113 US\$ per DALY averted (Shah, Johns et al. 2011). Although the comparison with the results of Bollinger is difficult since the author only presents continent-wide results and gives costs per averted infection, the cost estimates and thus cost-effectiveness ratios in the analyses by Robberstad et al and Shah et al are considerably higher than the 520 US\$ per infection averted calculated by Bollinger (nearly 8 times lower than estimated by Robberstad et al), indicating that the results presented by Bollinger might be overly optimistic.

In addition, others have shown that needle exchange programs and opiate substitute therapies can be highly cost-effective (Alistar, Owens et al. 2011), which is in contrast to Bollinger, who concludes that these interventions are not cost-effective. However, the cost-effectiveness of HIV prevention interventions in IDUs is largely determined by the HIV prevalence in the IDU population (Cohen, Wu et al. 2004). Here, Bollinger highlights an important gap in knowledge: some information regarding injecting drug use was available in only 4 of the 44 countries in the analyses. For most Sub-Saharan African countries, data on the size of the injecting drug use population and HIV prevalence among these drug users are absent (Strathdee and Stockman 2010), leaving us guessing as to the real size of the problem and the likely cost-effectiveness of interventions. Finally, current knowledge regarding the cost-effectiveness of preventing HIV through providing safe medical injections or screening of donor blood is considerably less. Nevertheless, these interventions are relatively cheap and easy to implement, and are therefore likely highly economically attractive (van Hulst, Smit Sibinga et al. 2010).

Equity in resource allocation

A general critique on cost-effectiveness and cost-benefit analysis is that it ignores the question; who benefits from interventions. For purposes of equity, policy makers may well want to give

priority to certain disadvantaged groups in society to give them as much of a fair chance to live a healthy life. However, interventions that target disadvantaged groups in society may well be more costly and/or yield less health effects, and will not necessarily be most cost-effective or cost-beneficial. For example, mobile clinics are more costly than central distribution of ARVs but much improves service coverage among remote areas. Policy makers thus need to strike a balance between efficiency and equity objectives in health when setting priorities. Unfortunately, as in the present study, these equity aspects are seldom reported, and it is not clear at what (extra) costs disadvantaged groups can be reached.

Conclusion

To conclude, the effort of the author to conduct an economic analysis of the prevention of non-sexual infection of HIV in not less than 44 Sub-Saharan African countries is an ambitious undertaking. The study suffers from the inherent limitations of such a continent-wide analysis, and a number of other, avoidable, methodological shortcomings which hamper the interpretation of the results. On the other hand, the results from this and other studies regarding the cost-effectiveness of the presented interventions - either because the intervention is easy and cheap (providing clean needles for medical injections and screening donated blood) or because a large number of infections can be prevented (prevention of mother-to-child transmission) - are so overwhelming that we tend to agree with the authors conclusions that interventions to reduce non-sexual transmission of HIV are generally economically attractive.

References

- Alistar, S. S., D. K. Owens, et al. (2011). "Effectiveness and cost effectiveness of expanding harm reduction and antiretroviral therapy in a mixed HIV epidemic: a modeling analysis for Ukraine." *PLoS Med* 8(3): e1000423.
- Bollinger L. Prevention of non-sexual transmission of HIV. Assessment paper for RethinkHIV. 2011 (forthcoming).
- Cohen, D. A., S. Y. Wu, et al. (2004). "Comparing the cost-effectiveness of HIV prevention interventions." *J Acquir Immune Defic Syndr* 37(3): 1404-1414.
- Colvin M, Gorgens-Albino M, Kasedde S. Analysis of HIV Prevention Response and Modes of HIV Transmission: The UNAIDS-GAMET Supported Synthesis Process (available at http://www.unaidsrstea.org/sites/default/files/modesoftransmission/analysis_hiv_prevention_response_and_mot.pdf. Accessed August 15, 2011.
- Creese A, Floyd K, Alban A, Guinness L. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *Lancet*. 2002 May 11;359(9318):1635-43.
- Hogan DR, Baltussen R, Hayashi C, Lauer JA, Salomon JA. Cost effectiveness analysis of strategies to combat HIV/AIDS in developing countries. *BMJ*. 2005 Dec 17;331(7530):1431-7. Epub 2005 Nov 10. Johns B, Torres TT; WHO-CHOICE. Costs of scaling up health interventions: a systematic review. *Health Policy Plan*. 2005 Jan;20(1):1-13.
- Johri, M. and D. Ako-Arrey (2011). "The cost-effectiveness of preventing mother-to-child transmission of HIV in low- and middle-income countries: systematic review." *Cost Eff Resour Alloc* 9: 3.
- Maclean, C. C. and J. S. Stringer (2005). "Potential cost-effectiveness of maternal and infant antiretroviral interventions to prevent mother-to-child transmission during breast-feeding." *J Acquir Immune Defic Syndr* 38(5): 570-577.
- Robberstad, B. and B. Evjen-Olsen (2010). "Preventing mother to child transmission of HIV with highly active antiretroviral treatment in Tanzania--a prospective cost-effectiveness study." *J Acquir Immune Defic Syndr* 55(3): 397-403.
- Shah, M., B. Johns, et al. (2011). "Cost-effectiveness of new WHO recommendations for prevention of mother-to-child transmission of HIV in a resource-limited setting." *AIDS* 25(8): 1093-1102.
- Soorapanth, S., S. Sansom, et al. (2006). "Cost-effectiveness of HIV rescreening during late pregnancy to prevent mother-to-child HIV transmission in South Africa and other resource-limited settings." *J Acquir Immune Defic Syndr* 42(2): 213-221.
- Strathdee, S. A. and J. K. Stockman (2010). "Epidemiology of HIV among injecting and non-injecting drug users: current trends and implications for interventions." *Curr HIV/AIDS Rep* 7(2): 99-106.
- Sweat, M. D., K. R. O'Reilly, et al. (2004). "Cost-effectiveness of nevirapine to prevent mother-to-child HIV transmission in eight African countries." *AIDS* 18(12): 1661-1671.
- van Hulst, M., C. T. Smit Sibinga, et al. (2010). "Health economics of blood transfusion safety--focus on sub-Saharan Africa." *Biologicals* 38(1): 53-58.
- Wilkinson, D., K. Floyd, et al. (2000). "National and provincial estimated costs and cost effectiveness of a programme to reduce mother-to-child HIV transmission in South Africa." *S Afr Med J* 90(8): 794-798.
- WHO-CHOICE website available at www.who.int/choice. Accessed August 15, 2011.

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