Published in final edited form as:

Alcohol Clin Exp Res. 2015 November ; 39(11): 2179–2188. doi:10.1111/acer.12890.

Targeting an alcohol intervention cost effectively to persons living with HIV/AIDS in East Africa

Jason KESSLER¹, Kelly RUGGLES¹, Anik PATEL^{1,2}, Kimberly NUCIFORA¹, Lifeng LI¹, Mark S ROBERTS³, Kendall BRYANT⁴, and R Scott BRAITHWAITE¹

¹Department of Population Health, NYU School of Medicine, New York, NY

²Department of Medicine, University of British Columbia, Vancouver, BC

³Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA

⁴National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda MD

Abstract

Objective—In the current report we ask if targeting a cognitive behavior therapy (CBT) based intervention aimed at reducing hazardous alcohol consumption to HIV infected persons in East Africa would have a favorable value at costs that are feasible for scale-up.

Design—Mathematical modeling utilized as clinical trial is not feasible

Methods—Using a computer simulation to inform HIV prevention decisions in East Africa we compared 4 different targeting strategies for a CBT intervention—(1) All HIV infected persons attending clinic; (2) Only those patients in the pre ART stages of care; (3) Only those patients receiving ART; (4) Only those patients with detectable viral loads regardless of disease stage. We compared these targeting strategies to a null strategy (no intervention) or a hypothetical scenario where an alcohol intervention was delivered to all adults regardless of HIV status.

Results—An intervention targeted to HIV infected patients could prevent 18,000 new infections and add 46,000 QALYs compared to the null scenario. Narrowing the prioritized population to only HIV infected patients in pre ART phases of care results in 15,000 infections averted, the addition of 21,000 QALYs, while prioritizing based on an unsuppressed HIV 1 viral load test results in 8,300 new infections averted and adds 6,000 additional QALYs.

Conclusions—Our results suggest that targeting a cognitive based treatment aimed at reducing hazardous alcohol consumption to subgroups of HIV infected patients provides favorable value in comparison with other beneficial strategies for HIV prevention and control in this region. It may even be cost saving under certain circumstances.

Keywords

HIV prevention; alcohol; cost effectiveness; mathematical modelling

Corresponding author: Jason Kessler, 227 E 30th St, Room 650, New York, NY 10016, jason.kessler@nyumc.org.

None of the authors have any conflicts of interest to report.

Introduction

HIV remains a major cause of preventable morbidity and mortality in Kenya and other East African nations, leading to estimated 100,000 new infections and nearly 60,000 deaths in Kenya during 2013 (UNAIDS 2014). At the same time, hazardous alcohol consumption (Reid et al. 1999), defined as a quantity or pattern of alcohol consumption that places individuals at risk for adverse health events, is an important risk factor for HIV acquisition and progression (Hahn et al. 2011; Shaffer et al. 2004; Saunders et al. 1993). East African nations have some of the highest rates of hazardous alcohol use worldwide (Shaffer et al. 2004; Acuda et al. 2011; Saunders et al. 1993) and previous modeling work suggests that 13% of new HIV infections in the region may be attributable to hazardous alcohol use (Braithwaite et al. 2014).

Randomized controlled trials of cognitive behavioral therapy based (CBT) interventions addressing hazardous alcohol consumption in Kenya have shown promising results, increasing abstinence by 45% and decreasing risky sex (Papas et al. 2011). However, alcohol mitigation remains an under-funded goal for preventing HIV related morbidity and mortality, especially in resource limited settings. The benefits of scaling up an effective intervention must be balanced against the opportunity costs of using those resources to scale up alternative interventions with potential benefit. Our previous published work estimated that population wide scale up of a CBT-based intervention in an East African nation for all individuals with HIV would have favorable value if the cost is less than \$1 per person (Braithwaite et al 2014). Because this cost threshold may be difficult to reach for a CBT-based intervention, even in resource limited settings, in the current report we ask if targeting a CBT-based intervention to a narrower group of HIV infected persons who may be more likely to benefit could enable the intervention to have favorable value at costs that are feasible for scale up (approximately \$5 per person).

Methods

We previously developed a computer simulation to inform HIV prevention decisions in East Africa across a wide range of possible interventions, including those directed at hazardous alcohol use. This simulation is composed of a disease progression module (e.g. hypothetical patients are followed over time, and depending on antiretroviral therapy [ART] adherence and other factors, may be more or less likely to die of AIDS vs. other causes) that provides data to inform a transmission module (e.g., hypothetical groups of persons interact with one another, and HIV-infected groups may transmit the infection to non-HIV-infected groups). The simulation projects the course of the HIV epidemic over varying time horizons, and tracks the benefits of potential interventions using a variety of outcome measures, including (i) number of infections averted, (ii) number of AIDS-related deaths averted, and (iii) quality adjusted life years (QALYs) gained. More complete details describing the simulation structure, parameterization, and calibration are described in the supplementary materials.

HIV Progression Module

Disease progression was modeled by evaluating mortality rates and trajectories of CD4 counts and HIV-1 viral load within a previously described HIV progression simulation

calibrated and validated on East African populations. This model explicitly represents the main cause of ART failure, non-adherence leading to the accumulation of genotypic resistance, and has been well-validated in East African populations (Braithwaite et al. 2011). The HIV-infected population in the transmission simulation at baseline was divided into compartments based on CD4 and viral load strata. Five CD4 strata were represented (<50, 50 to 200, 200 to 350, 350 to 500, >500 cells/mm³) and 5 log viral load logarithmic strata were represented (<2.5, 2.5 to 3.5, 3.5 to 4.5, 4.5 to 5.5, >5.5 log units/ml).

Data regarding rates of transition between CD4 and viral load strata given treatment and adherence level were captured from the progression model and interfaced with the transmission simulation in the form of rate multipliers. The spectrum of infection and care was modeled as a stepwise progression from (i) HIV acquisition/primary infection to (ii) chronic infection, (iii) HIV detection through testing or symptomatic presentation, followed by (iv) linkage to care, and finally initiation of (v) treatment with ART. We assume that all patients will initiate ART if their CD4 count is ≥ 350 cells/mm³. Although this does not reflect the current WHO recommendation (World Health Organisation 2013), it does reflect a common situation in under-resourced programs (World Health Organization 2013). There is no explicit representation of attrition from care, though the model is calibrated to account for this.

HIV Transmission Module

A compartmental model of HIV transmission was developed, specified by sets of differential equations. The model includes heterosexual transmission but does not include homosexual transmission or transmission from needle-sharing during injection drug use. At any particular time, hypothetical people in the module must occupy one among a set of mutually exclusive and collectively exhaustive compartments. These compartments describe health characteristics as well as behavioral risk characteristics. As time proceeds, hypothetical people may change the compartment that they occupy, for example, proceeding from being uninfected to having a primary HIV infection to having a chronic HIV infection to death. (Alternatively, they may die without ever contracting HIV). In addition, people in the model may alternatively be abstinent (in which case they will not contract HIV), monogamous, non-monogamous with a low number of concurrent partners, or may occupy an even higher risk group (community sex workers [CSW] if women, and clients of such if men), with greater numbers of concurrent partners and correspondingly greater chances of contracting or spreading HIV. Women in any of the non-abstinent states may “mix” (have sexual contact) with men in any of the non-abstinent states. Probability of transmission is a function of multiple factors, including rate of acquiring new partners, duration of partnership, frequency of sexual contact within a partnership, and likelihood of condom use. For example, members of the CSW group are especially likely to transmit HIV to non-monogamous men because likelihood of initiating contact is high, condom use is low, and duration of the relationship may be high. Other key assumptions, descriptions and prior calibration of the model are included in the supplementary materials.

Mixing Patterns—Whereas many transmission models assume “homogenous mixing” (i.e., each hypothetical individual has an equal chance of transmitting the infection to each

other hypothetical individual) or homogenous mixing stratified by age (i.e., each hypothetical individual within a particular age stratum has an equal chance of transmitting the infection to each other hypothetical individual within that age stratum), our transmission module assumes heterogeneous mixing patterns that are informed by sub-Saharan African data (Garnett & Anderson 1993). Therefore, it represents the common phenomenon of assortative mixing, for example, people who engage in risky sex may be more likely to partner with other people who have risky sex than with people who do not engage in risky sex, even after controlling for the increase in partnering opportunities that may be available. Additionally, because older men may be more likely to have sexual contact with younger women than vice versa, the model includes a parameter that can be varied to include this age-asymmetry of mixing.

Decomposition of Risk Per Partnership—Transmission models typically assume a single, aggregate risk that accumulates from all contacts that occur over the duration of a partnership. However, this approach has the disadvantage of implicitly assuming that the number of acts per partnership is static, and is independent of the number of concurrent partnerships. In other words, if a person has 10 times as many simultaneously sexual partners as the average person, conventional model approaches may implicitly assume that each person has 10 times as many sexual encounters in a particular time period. However, data suggest that people with many simultaneous partners do not have a proportionate increase in frequency of sexual encounters per unit time, and therefore this implicit assumption may exaggerate the impact of concurrency on transmission risk (Sawers et al. 2011).

To avoid incorporating this bias in our model, we chose not to represent the composite risk that accumulates from all events over the duration of a partnership, but instead represented the underlying determinates of this composite risk: frequency of sexual contacts, concurrency of sexual partnerships, and duration of sexual partnerships. Each characteristic is a separate “dial” that can be increased or decreased without directly affecting the other “dials.” Decomposing risk per partnership into its constituent characteristics is particularly important for modeling the sub-Saharan HIV pandemic because non monogamous contacts (e.g., CSWs) may be persistent (Voeten et al. 2002).

Representation of alcohol’s interaction with HIV

Based on a systematic review of pathways through which alcohol may impact HIV transmission risk (Mentor et al. 2013) hazardous alcohol use was modeled as having three main effects: (1) increasing the risk of condom nonuse (RR 1.29 for unsafe sex based on 2 sub-Saharan studies) (Weiser et al. 2007; Weiser et al. 2006) (2) increasing the risk of ART non-adherence (RR 2.33 of missing doses based on pooled estimate from 4 studies) (Byakika-Tusiime et al. 2009; Nakimuli-Mpungu et al. 2012; Nduna et al. 2010; Tadios & Davey 2006) and (3) increasing sexually transmitted infection (STI) prevalence (RR 1.72 based on 2 sub-Saharan African studies) (Fisher et al. 2008; Chersich et al. 2007). We assumed that the prevalence of hazardous alcohol consumption was 20% in men and 10% in women (NACADA 2010; WHO 2011). Other inputs to the simulation are described in Table

1, the supplementary materials, or elsewhere (Scott Braithwaite et al. 2014; Braithwaite et al. 2011).

Representation of alcohol focused intervention

An alcohol-intervention was assumed to decrease hazardous alcohol consumption by 45%, based on the results of the randomized controlled trial of Papas et al (Papas et al. 2011), which uses a cognitive behavior therapy based screening and intervention adapted for Kenya. The intervention's cost was estimated to be \$5 per person/year based on costing analysis of a screening and brief intervention alcohol intervention in the developed world (Zarkin GA Davis KL, et al 2003) as we could find no information for studies in Africa. For this analysis we compared 4 different targeting strategies for the CBT intervention which was assumed to be a part of the care and treatment delivered at facilities providing ART for HIV positive clients—(1) All HIV infected persons attending clinic (2) Only those patients in the pre ART stages of care (3) Only those patients receiving ART (4) Only those patients with detectable viral loads regardless of disease stage (i.e. those patients at higher risk of transmission of HIV to their partners). We compared these targeting strategies to a hypothetical scenario where an alcohol intervention was delivered to all adults regardless of HIV status.

Cost-effectiveness analysis

Outcomes included total life years, total number of new HIV infections averted, total quality adjusted life years (QALYs), incremental cost per QALY gained and incremental cost per infection averted. Costs and effects were discounted at 3% per WHO guidelines (Edejer TT et al 2003) over a time horizon of 20 years, and costs were assessed from a healthcare payer perspective, in 2014 US\$. Cost inputs were based on expenditure data from a large health care system in Western Kenya (AMPATH-Academic Model Providing Access to Healthcare) (Braithwaite et al. 2011) unless otherwise noted and analyses followed recommendations by the Panel on Cost Effectiveness in Health and Medicine (Weinstein et al. 1996), except we chose a 20 year rather than an infinite time horizon to make the analyses more useful for stakeholders.

Cost-effectiveness was considered with reference to 2 thresholds, the first based on our simulation model derived estimate of the cost-effectiveness of a simultaneously resource-constrained intervention advocated for scale-up (initiating ART at 500 cells/mm³ rather than 350 cells/mm³) and the second based on the WHO standard of 3x gross domestic product (GDP) per capita (\$2800/QALY).

Sensitivity analyses

We performed sensitivity analyses incorporating estimates of the alcohol intervention's cost that were both higher (as high as \$50) and lower (as low as \$1), as well as its effectiveness (higher [90% reduction] and lower [20% reduction]). Additionally, we conducted a multivariate sensitivity analysis considering higher estimates (as high as RR 10) and lower (as low as RR 1.1) of alcohol's impact on transmission mediators—condom nonuse, ART non adherence, and STI prevalence as well as clinically plausible estimates of intervention cost and effectiveness as above.

Results

Impact of a scaled-up CBT intervention within HIV treatment programs

A CBT alcohol intervention scaled up across a national population could prevent nearly 70,000 new HIV infections (5% of all new infections over 20 years), and add 104,000 additional QALYs compared to the counterfactual scenario where no intervention exists. A similar intervention targeted to only HIV infected patients seeking care and treatment could prevent 18,000 new infections (1% of all new infections over 20 years) and add 46,000 QALYs, compared to the counterfactual scenario where no intervention exists (Figure 1). When compared to the hypothetical scenario of a generalized CBT intervention across the entire population, focusing only on HIV infected persons retains 26% of the preventative benefit (18,000/70,000 infections averted).

Further targeting of the CBT intervention to only the pre-ART HIV infected patients results in 15,000 infections averted, and the addition of 21,000 QALYs. This strategy would retain 21% of the benefit of the generalized scale up scenario. Targeting CBT to only those HIV infected patients on ART would reduce the number of infections averted to 10,000, thereby adding 9,000 QALYs. When compared to the generalized CBT scenario this represents 14% of the preventative benefits. Finally, targeting HIV infected patients treated with ART and who have detectable HIV-1 viral loads (VL) would result in 8,000 new HIV infections being averted, and the addition of 6,000 QALYs. The VL targeting strategy would retain 11% of the benefit of the generalized scale-up strategy.

Cost effectiveness of scaled up CBT intervention in HIV treatment programs

A CBT intervention targeted at all HIV infected persons enrolled in care would cost an additional \$10 million (M) in comparison to the counterfactual scenario (no intervention). This would result in an ICER of \$600 which would be considered cost effective ($< 3 \times$ GDP per capita) according to WHO standards. Expanding ART access to all HIV infected individuals with a CD4 > 500 cells/mm³ in line with the most recent WHO treatment guidelines results in the prevention of 100,000 new HIV infections, the addition of 250,000 QALYs with an incremental cost of \$400M USD, yielding an ICER of \$1,600 (Figure 1). Targeting only those individuals who are receiving ART with the CBT intervention would cost an additional \$5M and results in an ICER of \$400. However, targeting the CBT intervention to only those HIV infected persons who are in the pre-ART stages of care would be cost saving, adding \$5M. Further tailoring of the intervention targeting strategy to include only those patients on ART who have detectable viral loads would result in even more cost savings: \$10M in comparison to the base case scenario (Figure 1).

Sensitivity analyses

Cost of the CBT intervention had a substantial impact on the value of the different targeting strategies. If the cost per person is \$5 under nearly all targeting strategies and strengths of association between hazardous alcohol consumption and HIV risk that were considered, implementation of a CBT intervention given our modeling assumptions, may be highly favorable from an economic perspective (i.e. have an ICER $<$ scale up of ART in line with 2013 WHO guidelines or is cost saving) (Figure 2a). However, if we consider that

effectiveness of the CBT intervention diminishes with scale up (i.e. reduction in hazardous alcohol consumption is only 20%) the same findings hold only under the pre-ART targeting strategy or detectable VL strategy (Strategy C or E; Figure 2b). Under conditions where risks associated with hazardous alcohol consumption are attenuated from our baseline assumptions, other targeting strategies other than pre-ART patients may not be cost effective by either standard we used (Strategies B,D, and E; Figure 2b).

If cost = \$50, and all other modeling assumptions hold, a CBT intervention would only be considered highly favorable if it were targeted to HIV infected patients with a detectable VL or those in the pre-ART phase of care and the risks on HIV disease progression and transmission associated with hazardous alcohol consumption were greater than what we initially estimated (specifically if the risk of non-adherence to ART is greater than a relative risk of 5). However, if we consider that effectiveness of the CBT intervention diminishes with scale up no targeting strategy would be considered cost effective at that cost unless unrealistically high assumptions were made about the risks hazardous alcohol consumption have on HIV disease progression or transmission.

Finally, if we assume the cost of the intervention were between \$10–\$20 per person per annum, and effectiveness was at least 45% scale up of CBT would remain highly favorable among all targeted groups if the relative risk of non-adherence among hazardous alcohol users was at least 5 times that of non-users (Figure 2a,c). If we considered that effectiveness of the CBT intervention diminishes with scale up, it may only be considered highly favorable if it were targeted to HIV infected patients with a detectable VL or those in the pre ART phase of care and only under the assumptions that the risks on HIV disease progression and transmission associated with hazardous alcohol consumption were greater than what we initially estimated (specifically if the risk of non-adherence to ART is greater than a relative risk of 5) (Figure 2b).

Discussion

Our prior results have suggested that approximately one-third of the alcohol-attributable new HIV infections in East Africa could be averted by a population-wide implementation of a CBT intervention (Braithwaite et al. 2014) modeled on the one studied in Western Kenya by Papas, et al (Papas et al. 2011). In addition, such an implementation strategy would be cost effective and offer favorable value in relation to other highly valued interventions aimed at ameliorating the HIV epidemic in this region if costs could be kept under \$1 per person (Braithwaite & Nucifora 2014). This may be an overly optimistic cost threshold even in resource limited settings. Furthermore, it is unclear what additional costs would be necessary to reach large segments of the population in such settings where primary healthcare is extremely limited and many persons are not directly engaged with a health care provider or facility (Bigogo et al. 2010; Chuma et al. 2007).

Our current results highlight how alcohol interventions may be able to achieve favorable value and cost-effectiveness if they are targeted to different subgroups of HIV-infected persons. Our results suggest that targeting this intervention to subgroups of HIV-infected patients provides favorable value in comparison with other beneficial strategies for HIV

prevention and control in this region. It may even be cost saving under certain circumstances. In particular, targeting Papas' CBT-based intervention to individuals not yet receiving ART provides cost savings as compared to a counterfactual scenario where no intervention is implemented.

Implementation of similar alcohol interventions among HIV infected persons provide health benefits at a cost per unit increase less than that provided by other key interventions and policies such as expanding ART access to patients with a CD4 < 500 cells/mm³. However, as is true with any targeting strategy, this increase in efficiency (\$ spent per unit of health benefit gained) decreases the overall population level impact. These results highlight the importance of accounting for budgetary impact and economic feasibility when advancing recommendations for implementation strategies. Furthermore, our findings suggest that investments in alcohol interventions aimed at persons living with HIV enrolled in care would retain favorable value even if costs were significantly greater than \$1 per person if the intervention is targeted, though the overall population health benefit returned would be diminished in comparison to a population wide scale up.

Interestingly, we found that alcohol interventions aimed at those patients in the pre-ART period resulted in greater health benefits than targeting only those patients who have begun on ART. This is likely explained by the fact that treatment with ART has dramatic individual level benefits reducing both morbidity and mortality related to HIV (Slaymaker et al. 2014). Furthermore, the associated decreases in viral load even if complete viral suppression is not achieved (as may be the case among hazardous alcohol users who are assumed to have poorer adherence) provide impactful reductions in transmission risk (Attia et al. 2009; Cohen et al. 2011) thereby limiting additional secondary effects attributable to alcohol mitigation. Given our assumptions regarding treatment access and the cascade of care (i.e. mean CD4 of population and ART eligibility criteria) we would expect the relative value of this targeting strategy to decrease; however, as compared to increasing access to ART through its provision at earlier stages of disease as HIV testing and linkage to care is strengthened (resulting in increases in mean CD4 at presentation) across the region. These results strengthen the idea that the pre-ART period is a key moment when patients presumably at high risk of HIV transmission (given relative lack of symptoms and absence of treatment) can be assessed and provided services for co-morbid conditions that may impact on their own disease as well as their risks of transmitting the disease to their partners (Bastard et al. 2013).

A limitation of any simulation is that results may be affected by statistically uncertain or biased inputs, and or incorrect specification of model structure. Although hazardous alcohol consumption has reproducible and significant associations with greater condom nonuse, ART non-adherence, and STI prevalence, these associations do not demonstrate causality. Our simulation does not incorporate the possible effects of alcohol on HIV progression independent from ART adherence nor does it incorporate effects of alcohol unrelated to HIV such as increased risk of trauma and alcohol related organ damage (e.g. cirrhosis) and therefore the simulation's estimates are likely conservative.

Additional limitations stem from inadequate data available to inform our simulation. Notably, we assumed that weighted utility scores (which are needed to calculate QALYs) developed from HIV infected persons' preferences in a developed world setting were a reasonable approximation of preferences in the population under study in this analysis, as there are no studies we are aware of that provide similar information for HIV infected persons in East Africa. Furthermore, there was insufficient data to operationalize our simulation to one specific national jurisdiction. Where possible we tried to incorporate accessible East African sources of data and where gaps existed chose to use other available data sources from sub Saharan Africa.

Alcohol interventions are one of many approaches for reducing new HIV infections in East Africa. In particular, earlier detection and ART treatment, promoting male circumcision and the provision of pre-exposure prophylaxis for serodiscordant couples may have substantial potential to avert HIV infections (Cohen et al. 2011; Okwundu et al. 2012; Mills et al. 2008; Kunutsor et al. 2012). To determine the optimal share and targeting of HIV prevention resources that should be allocated to alcohol interventions future research should evaluate and compare alternative portfolios of interventions, including strategies aimed at strengthening the HIV care cascade, as well as account for the additional impacts of hazardous alcohol use on the population in this region, such as its impact on non-HIV related causes of morbidity and mortality (e.g. liver disease, motor vehicle accidents).

In conclusion our results suggest that a CBT-based intervention evaluated in a RCT may be a cost-effective or even cost saving measure if targeted appropriately among HIV positive patients enrolling in care and treatment programs in East Africa. Such a targeted intervention could potentially offer favorable value compared with other resource-constrained decisions under several optimistic assumptions and or conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work has used computing resources at the High Performance Computing Facility of the Center for Health Informatics and Bioinformatics at the New York University Langone Medical Center.

Funding source: Supported by the National Institutes of Alcohol Abuse and Alcoholism award R01 AA017385.

References

- Acuda W, et al. The epidemiology of addiction in Sub Saharan Africa: a synthesis of reports, reviews, and original articles. *Am J Addict*. 2011; 20(2):87–99. Available at: <http://onlinelibrary.wiley.com/store/10.1111/j.15210391.2010.00111.x/asset/j.1521-0391.2010.00111.x.pdf?v=1&t=hnq6y03v&s=cb572e0543931c8f0ebb6f6646f50f02bc229e09>. [PubMed: 21314750]
- Adazu K, et al. Health and demographic surveillance in rural western Kenya: a platform for evaluating interventions to reduce morbidity and mortality from infectious diseases. *The American journal of tropical medicine and hygiene*. 2005; 73(6):1151–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16354829> [Accessed January 7, 2015]. [PubMed: 16354829]
- Ao TT, et al. Human immunodeficiency virus type 1 among bar and hotel workers in northern Tanzania: the role of alcohol, sexual behavior, and herpes simplex virus type 2. Sexually transmitted

diseases. 2006; 33(3):163–169. Available at: <http://graphics.tx.ovid.com/ovftpdfs/FPDDNCIBDAMOBJ00/fs047/ovft/live/gv031/00007435/0000743520060300000008.pdf>. [PubMed: 16505740]

- Attia S, et al. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS*. 2009; 23(11):1397–1404. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19381076>. [PubMed: 19381076]
- Bajunirwe F, et al. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government hospital in Southwestern Uganda. *Journal of the International Association of Physicians in AIDS Care*. 2009; 8(2):139–147. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19258526>. [PubMed: 19258526]
- Bastard M, et al. Adults receiving HIV care before the start of antiretroviral therapy in sub Saharan Africa: patient outcomes and associated risk factors. *Journal of acquired immune deficiency syndromes* 1999. 2013; 64(5):455–63. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23892242>. [Accessed February 9, 2015]. [PubMed: 23892242]
- Bigogo G, et al. Health-seeking patterns among participants of population-based morbidity surveillance in rural western Kenya: implications for calculating disease rates. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases*. 2010; 14(11):e967–73. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20800525> [Accessed January 7, 2015]. [PubMed: 20800525]
- Boily MC, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. *The Lancet infectious diseases*. 2009; 9(2):118–29. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19179227> [Accessed June 17, 2014]. [PubMed: 19179227]
- Braithwaite R, Nucifora K. How Inexpensive Does an Alcohol Intervention in Kenya Need to be in Order to Deliver Favorable Value by Reducing HIV-Related Morbidity and Mortality? *JAIDS*. 2014; 66(2):54–58. Available at: http://journals.lww.com/jaids/Abstract/2014/06010/How_Inexpensive_Does_an_Alcohol_Intervention_in.23.aspx [Accessed October 17, 2014].
- Braithwaite RS, et al. Alternative antiretroviral monitoring strategies for HIV-infected patients in east Africa: opportunities to save more lives? *Journal of the International AIDS Society*. 2011; 14(1): 38. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3163507&tool=pmcentrez&rendertype=abstract> [Accessed March 7, 2014]. [PubMed: 21801434]
- Braithwaite RS, et al. How do different eligibility guidelines for antiretroviral therapy affect the cost-effectiveness of routine viral load testing in sub-Saharan Africa? *AIDS (London, England)*. 2014; 28(Suppl 1):S73–83. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24468949> [Accessed February 23, 2014].
- Braithwaite, RS., et al. Impact of Interventions Targeting Unhealthy Alcohol Use in Kenya on HIV Transmission and AIDS Related Deaths. *Alcoholism, clinical and experimental research*. 2014. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24428236> [Accessed February 24 2014]
- Byakika Tusiime J, et al. Longitudinal antiretroviral adherence in HIV+ Ugandan parents and their children initiating HAART in the MTCT-Plus family treatment model: role of depression in declining adherence over time. *AIDS and behavior*. 2009; 13(Suppl 1):82–91. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/19301113> [Accessed July 14, 2014]. [PubMed: 19301113]
- Chersich MF, et al. Heavy episodic drinking among Kenyan female sex workers is associated with unsafe sex, sexual violence and sexually transmitted infections. *International journal of STD & AIDS*. 2007; 18(11):764–9. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18005511> [Accessed January 7, 2015]. [PubMed: 18005511]
- Chuma J, Gilson L, Molyneux C. Treatment-seeking behaviour, cost burdens and coping strategies among rural and urban households in Coastal Kenya: an equity analysis. *Tropical medicine & international health : TM & IH*. 2007; 12(5):673–86. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17445135> [Accessed January 7, 2015]. [PubMed: 17445135]
- Cohen MS, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011; 365(6):493–505. [PubMed: 21767103]
- Edejer, TT.Adam, T.Hutubessy, R.Acharya, A.Evans, DB.Murray, CLJ., B, R., editors. Making choices in health: WHO guide to cost-effectiveness analysis. Geneva: WHO; 2003.

- Fisher JC, et al. Patterns of alcohol use, problem drinking, and HIV infection among high risk African women. Sexually transmitted diseases. 2008; 35(6):537–44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18418292> [Accessed July 14, 2014]. [PubMed: 18418292]
- Garnett GP, Anderson RM. Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes. Philos Trans R Soc Lond B Biol Sci. 1993; 342(1300):137–159. [PubMed: 7904355]
- Hahn JA, Woolf-King SE, Muyindike W. Adding fuel to the fire: alcohol's effect on the HIV epidemic in Sub-Saharan Africa. Curr HIV/AIDS Rep. 2011; 8(3):172–180. Available at: http://download.springer.com/static/pdf/582/art%253A10.1007%252Fs11904-011-0088-2.pdf?auth66=1384013376_b338ab256bac4288557065ab44d5fd8d&ext=.pdf. [PubMed: 21713433]
- Irungu TK, et al. HIV voluntary counselling and testing in Nakuru, Kenya: findings from a community survey. HIV medicine. 2008; 9(2):111–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18257773> [Accessed July 14, 2014]. [PubMed: 18257773]
- Kapiga SH, et al. The epidemiology of HIV-1 infection in northern Tanzania: results from a community based study. AIDS care. 2006; 18(4):379–387. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16809117>. [PubMed: 16809117]
- Kunutsor S, et al. Improving adherence to antiretroviral therapy in sub-Saharan African HIV-positive populations: an enhanced adherence package. AIDS care. 2012; 24(10):1308–15. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22621288> [Accessed January 7, 2015]. [PubMed: 22621288]
- Marks G, Senterfitt W, Janssen RS, C N. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for prevention programs. JAIDS. 2005; 39(4):446–453. [PubMed: 16010168]
- Mentor, S., Uyei, J., Braithwaite, R. A systematic literature review and meta-analysis for potential causal linkages between interventions and HIV transmission in sub-Saharan Africa. 2013. at <<http://torchresearch.org>>
- Mills E, et al. Male circumcision for the prevention of heterosexually acquired HIV infection: a meta-analysis of randomized trials involving 11,050 men. HIV medicine. 2008; 9(6):332–5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18705758> [Accessed January 7, 2015]. [PubMed: 18705758]
- Mishra, V., B, VAS. Concurrent sexual partnerships and HIV infection:evidence from 462 national population-based surveys. Calverton, MD: 2009. Available at: <http://www.measuredhs.com/pubs/pdf/WP62.pdf> [Accessed January 7, 2015]
- Mmbaga EJ, et al. Sexually transmitted infections knowledge and its impact in the practice of risky sexual behaviours and HIV serostatus: results from rural Kilimanjaro, Tanzania. Sexually transmitted infections. 2008; 84(3):224–6. [PubMed: 18283095]
- Mossdorf E, et al. Impact of a national HIV voluntary counselling and testing (VCT) campaign on VCT in a rural hospital in Tanzania. Tropical medicine & international health : TM & IH. 2010; 15(5):567–573. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20345555>. [PubMed: 20345555]
- NACADA. , editor. Alcohol use in central province of Kenya: a baseline survey on magnitude, causes and effects from the perspective of community members and individual users. NACADA; 2010. Available at: <http://www.nacada.go.ke/wp-content/uploads/2011/02/centralservey.pdf>. [Accessed July 14 2014]
- Nakimuli-Mpungu E, et al. Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: a systematic review. AIDS and behavior. 2012; 16(8):2101–18. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22116638> [Accessed August 10 2014]. [PubMed: 22116638]
- Nduna M, et al. Associations between depressive symptoms, sexual behaviour and relationship characteristics: a prospective cohort study of young women and men in the Eastern Cape, South Africa. Journal of the International AIDS Society. 2010; 13:44. Available at:<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2992477&tool=pmcentrez&rendertype=abstract> [Accessed July 14, 2014]. [PubMed: 21078150]

- Okwundu CI, Uthman OA, Okoromah CA. Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals. The Cochrane database of systematic reviews. 2012; 7:CD007189. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22786505> [Accessed January 3, 2015].
- Papas RK, et al. Treatment outcomes of a stage 1 cognitive-behavioral trial to reduce alcohol use among human immunodeficiency virus-infected out-patients in western Kenya. *Addiction*. 2011; 106(12):2156–2166. Available at: <http://onlinelibrary.wiley.com/store/10.1111/j.1360-0443.2011.03518.x/asset/j.1360-0443.2011.03518.x.pdf?v=1&t=hmq83bda&s=633518fb1bdcfc3fa99406655768cd4927f61994>. [PubMed: 21631622]
- Quigley M, et al. Sexual behaviour patterns and other risk factors for HIV infection in rural Tanzania: a case-control study. *AIDS*. 1997; 11(2):237–248. Available at: <http://graphics.tx.ovid.com/ovftpdfs/FPDDNCIBDAMOBJ00/fs047/ovft/live/gv024/00002030/00002030-199702000-00015.pdf>. [PubMed: 9030372]
- Reid MC, Fiellin DA, O'Connor PG. Hazardous and Harmful Alcohol Consumption in Primary Care. *Archives of Internal Medicine*. 1999; 159(15):1681. Available at: <http://archinte.jamanetwork.com/article.aspx?articleid=1105638> [Accessed March 3, 2014]. [PubMed: 10448769]
- Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoS medicine*. 2011; 8(7):e1001056. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3139665&tool=pmcentrez&rendertype=abstract> [Accessed February 20, 2014]. [PubMed: 21811403]
- Saunders JB, et al. Alcohol consumption and related problems among primary health care patients: WHO collaborative project on early detection of persons with harmful alcohol consumption-I. *Addiction* (Abingdon, England). 1993; 88(3):349–62. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8461852> [Accessed July 18, 2014].
- Sawers L, Isaac AG, Stillwaggon E. HIV and concurrent sexual partnerships: modelling the role of coital dilution. *Journal of the International AIDS Society*. 2011; 14:44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21914208>. [PubMed: 21914208]
- Shaffer DN, et al. Alcohol abuse among patients with and without HIV infection attending public clinics in western Kenya. *East African medical journal*. 2004; 81(11):594–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15868970> [Accessed July 18, 2014]. [PubMed: 15868970]
- Slaymaker E, et al. How have ART treatment programmes changed the patterns of excess mortality in people living with HIV? Estimates from four countries in East and Southern Africa. *Global health action*. 2014; 7:22789. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3999950&tool=pmcentrez&rendertype=abstract> [Accessed February 9, 2015].
- Tadios Y, Davey G. Antiretroviral treatment adherence and its correlates in Addis Ababa, Ethiopia. *Ethiopian medical journal*. 2006; 44(3):237–44. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17447389> [Accessed July 14, 2014]. [PubMed: 17447389]
- UNAIDS. Kenya AIDS Response Progress Report Progress towards Zero. 2014. Available at http://www.unaids.org/sites/default/files/country/documents/KEN_narrative_report_2014.pdf. [Accessed July 14, 2014]
- Vandepitte J, et al. Estimates of the number of female sex workers in different regions of the world. *Sex Transm Infect*. 2006; 82(Suppl 3):iii18–iii25. [PubMed: 16735288]
- Voeten HACM, et al. Clients of female sex workers in Nyanza province, Kenya: a core group in STD/HIV transmission. *Sexually transmitted diseases*. 2002; 29(8):444–52. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12172528> [Accessed April 6, 2015]. [PubMed: 12172528]
- Volle, J., Letsatsi, T., Tan, A., F, J. A baseline survey of multiple and concurrent sexual partnerships among Basotho men in Lesotho. Washington DC: C Change/AED; 2009. Available at: http://pdf.usaid.gov/pdf_docs/PNADY234.pdf
- Weinstein MC, et al. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. *JAMA : the journal of the American Medical Association*. 1996; 276(15):1253–8. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8849754> [Accessed June 6, 2014]. [PubMed: 8849754]
- Weiser SD, et al. A population based study on alcohol and high-risk sexual behaviors in Botswana. *PLoS medicine*. 2006; 3(10):e392. Available at: <http://www.pubmedcentral.nih.gov/>

articerender.fcgi?artid=1592342&tool=pmcentrez&rendertype=abstract [Accessed September 22, 2014]. [PubMed: 17032060]

Weiser SD, et al. Food insufficiency is associated with high-risk sexual behavior among women in Botswana and Swaziland. *PLoS medicine*. 2007; 4(10):1589–97. discussion 1598. Available at: <http://www.pubmedcentral.nih.gov/articerender.fcgi?artid=2039764&tool=pmcentrez&rendertype=abstract> [Accessed October 2, 2014]. [PubMed: 17958460]

Westercamp N, et al. Determinants of consistent condom use vary by partner type among young men in Kisumu, Kenya: a multi-level data analysis. *AIDS and behavior*. 2010; 14(4):949–959. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18791819>. [Accessed on July 14, 2014]. [PubMed: 18791819]

World Health Organization. Global prevalence and incidence of selected curable sexually transmitted infections. 2001. Available at http://www.who.int/hiv/pub/sti/who_hiv_aids_2001.02.pdf. [Accessed on October 10, 2014]

World Health Organization. Global update on HIV treatment 2013: results, impact and opportunities. Geneva: World Health Organization; 2013. Available at: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2013/20130630_treatment_report_en.pdf. [Accessed on October 2, 2014]

World Health Organisation. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. 2010. Available at <http://www.who.int/hiv/pub/guidelines/arv2013/download/en/>

WHO/UNAIDS. Epidemiological fact sheet on HIV and AIDS: Uganda. p. 2008 Available at <http://www.who.int/hiv/pub/epidemiology/pubfacts/en/>

World Health Organization. Global status report on alcohol and health. Geneva: 2011. Available at http://www.who.int/substance_abuse/publications/global_alcohol_report/en/

Zarkin GA, Davis KL, et al. B.J.W. The costs of screening and brief intervention for risky alcohol use. *J Stud Alcohol*. 2003; 64:849–857. [PubMed: 14743949]

Figure 1. Comparison of incremental health benefits and costs associated with alcohol focused CBT intervention as compared with expansion of ART access to all HIV infected persons with CD4 500 cells/mm³

Health benefits (QALYs) and costs for each intervention scenario compared to counterfactual scenario where no additional interventions are implemented. Costs are calculated in 2014 US\$.

Figure 2a–c. Multivariate sensitivity analysis of the cost effectiveness of targeted, alcohol focused CBT

The three figures represent three different assumptions regarding CBT intervention efficacy (a-Efficacy assumed to be 45%; b-20%; c-90%). Within each figure the cost of intervention is varied running from top (least expensive) to bottom (most expensive). Assumptions regarding the associations between hazardous alcohol use and HIV risk factors vary along the horizontal portion of each figure. The base line assumptions for these associations were as follows: effect of alcohol use on condom nonuse (RR 1.29); effect of hazardous alcohol use on ART non-adherence (RR 2.33); effect of hazardous alcohol use on STI prevalence (RR 1.72). Within each cell the cost effectiveness (ICER) is categorized as either a) having **favorable value** (i.e. ICER of CBT is < ICER associated with scale up of ART in line with 2013 WHO guidelines or is cost saving); b) **cost –effective** (i.e. ICER of CBT > ICER associated with scale up of ART in line with 2013 WHO guidelines but <3x GNP per capita of Kenya); or c) **not cost effective** (i.e. ICER of CBT is > 3x GNP per capita of Kenya).

Table 1

Key model input parameters

Description of parameter input	Value	References
Alcohol use and CBT intervention *		
Prevalence of hazardous alcohol use (Male/Female)	20%/10%	(Anon 2011; NACADA 2010)
Relative risk of hazardous alcohol use on unsafe sex	1.29	(Mentor et al. 2013)
Relative risk of hazardous alcohol use on non-HIV STIs	1.72	(Mentor et al. 2013)
Relative risk of hazardous alcohol use on non-adherence to ART	2.33	(Mentor et al. 2013)
CBT intervention effect size **	45%	(Papas et al. 2011)
Cost of CBT intervention (per person)	\$5	(Zarkin GA Davis KL, et al 2003)
Sexual risk behaviors		
Proportion abstinent (M/F) - Class 1	5%/10%	(Kapiga et al. 2006; Ao et al. 2006; Quigley et al. 1997)
Proportion in stable, monogamous relationship - (M/F) Class 2	31%/69%	(Quigley et al. 1997; Mishra V 2009; Volle J Letsatsi T, Tan A 2009)
Proportion in multiple, concurrent relationships (if non-monogamous) (M/F) - Class 3	56%/17%	Assumption
Proportion in multiple, concurrent relationships (if non-monogamous) (M/F) - Class 4	8%/4%	(Mmbaga et al. 2008; Vandepitte et al. 2006)
Frequency of sex acts (per year)	104	Assumption
Duration of relationship †	1y–30y	Assumption
Median number of concurrent partners (Class 3)	3	(Volle J Letsatsi T, Tan A 2009)
Median number of concurrent partners (Class 4)	10	(Volle J Letsatsi T, Tan A 2009)
Probability of consistent condom use	34%	(Westercamp et al. 2010)
Relative risk of unsafe sex (condom nonuse most or all of the time) if aware of HIV status	0.47	(Marks G Senterfitt W, Janssen RS 2005)
HIV epidemiology and transmission		
Adult HIV prevalence (1997)	10.60%	(STI 2008)
Probability of transmission per sex act §	0.00011–0.01243	(Boily et al. 2009; Attia et al. 2009)
Untreated non-HIV STI prevalence	6%	(Organization 2001)
Probability of HIV testing (per annum)	16%	(Irungu et al. 2008; Mossdorf et al. 2010)
Probability of linkage to HIV care and treatment	68%	(Rosen & Fox 2011)
Probability of adherence to ART regimen	85%	(Bajunirwe et al. 2009)

* CBT= cognitive behavior therapys

** Effect size represents relative risk reduction for unhealthy alcohol users in population.

† Duration dependent upon class of sexual risk behavior with stable, monogamous relationships having the longest duration and multiple, concurrent relationships having the shortest.

§ Transmission probability varies according to both sex (M/F) and HIV viral load of the infected person.