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How inexpensive does an alcohol intervention in Kenya need to be in order to deliver favorable value by reducing HIV-related morbidity and mortality?

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Introduction

HIV remains a major cause of preventable morbidity and mortality in Kenya, with 100,000 new infections and an estimated 62,000 deaths in 2011.¹ At the same time, unhealthy alcohol consumption is an important risk factor for HIV acquisition^{2–7} and progression.⁸ Kenya has one of the highest rates of unhealthy alcohol use worldwide,^{9,10} and as many as 13% of new HIV infections in Kenya may be attributable to unhealthy alcohol use.¹¹

Randomized controlled trials (RCTs) of cognitive behavioral therapy (CBT)-based interventions addressing unhealthy alcohol consumption in Kenya show promising results, increasing abstinence by 45%,^{12, 13} and decreasing risky sex.^{14, 15} However, alcohol remains conspicuously absent from programming in HIV and substance use.^{9, 16} In low-resource settings, the benefits of scaling up an effective intervention must be balanced against the opportunity costs of using those resources to scale up alternatives intervention with potential benefit (for example, increasing eligibility for first-line ART). Accordingly, we used a published validated computer simulation of the HIV epidemic in Kenya, incorporating HIV transmission as well as disease progression, to evaluate the cost-effectiveness of the alcohol

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intervention reported by Papas et al.¹² Given the uncertainty surrounding costs of scale-up, we varied costing assumptions over a wide range (\$1 to \$50 per person), to identify the threshold at which its incremental cost-effectiveness ratio (ICER) descended below those of alternative resource uses (e.g., when an alcohol intervention bought more “health” than alternative resource uses).

Methods

We developed a computer simulation to inform HIV prevention decisions in East Africa across a wide range of possible interventions, including those directed at unhealthy alcohol use. This simulation is composed of a within-host progression module (e.g. hypothetical patients are followed over time, and depending on ART adherence and other factors, may be more or less likely to die of AIDS versus other causes) that provides data to inform a population-level 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). For example, an alcohol intervention may improve ART adherence, which lowers viral load and extends life expectancy in the progression model. The reduced viral load then decreases the risk of transmitting HIV in the transmission model. Additionally, an alcohol intervention may decrease risky sex. The design of the simulation, as well as its calibration and validation, is described in more detail elsewhere.^{11, 17}

Representation of alcohol interventions

Based on a systematic review of pathways through which alcohol may impact HIV transmission risk,¹⁸ unhealthy alcohol use was modeled as having three main effects: (1) increasing the risk of condom nonuse (RR 1.29 for unsafe sex, based on two sub-Saharan studies),^{19, 20} (2) increasing the risk of ART nonadherence (RR 2.33 of missing doses based on pooled estimate from 4 studies),²¹⁻²⁴ and (3) increasing STI prevalence. The effect size of unhealthy alcohol use on increasing condom nonuse was assumed to be 1.72, based on two sub-Saharan studies.^{6,25} Other inputs to the simulation (e.g. costs, utilities) are described elsewhere.^{17, 29} In base case analyses, an alcohol intervention was assumed to decrease unhealthy alcohol consumption by 45%, based on the RCT of Papas et al,¹² which used a CBT-based intervention adapted for Kenya.

Cost-effectiveness analysis

Outcomes included total life years, total quality-adjusted life years, incremental cost per quality-adjusted life year, and incremental cost per infection averted. Costs and effects were discounted at 3% per WHO guidelines²⁶ over a time horizon of 20 years, and costs were assessed from a societal perspective, in 2012 US\$. Cost inputs were based on expenditure data from a large healthcare system in Western Kenya (AMPATH – The Academic Model Providing Access to Healthcare),²⁷ and analyses followed recommendations by the Panel on Cost-Effectiveness in Health and Medicine,²⁸ except we chose a 20-year rather than infinite time horizon to make the analysis more useful for stakeholders.

Cost-effectiveness was considered favorable with reference to two thresholds, the first based on the cost-effectiveness of a simultaneously resource-constrained intervention advocated

for scale-up (initiating ART at 350 cells/ul rather than 200 cells/ul) (\$2,600/LY),²⁹ and the second based on the WHO standard of 3× GDP per capita (\$2,400/LY).^{30, 31}

Sensitivity analyses

We performed sensitivity analyses incorporating estimates of the alcohol intervention's effect that were higher (85% reduction) and lower (5% reduction). Similarly, we varied estimates of alcohol's impact on transmission mediators - condom nonuse, ART nonadherence, and STI prevalence based on our systematic review,¹⁸ to 1.00-1.52 for unsafe sex (condom non-use), 1.00-6.66 for ART nonadherence, and 1.00-10.71 for untreated STI prevalence.

Results

A scaled-up CBT alcohol intervention could reduce alcohol-related infections from 13% to 9% of total new infections, thereby adding 137,728 life-years (169,457 quality-adjusted life-years) in Kenya over 20-years.

Assuming an alcohol intervention costs \$50 per person

When we assumed an annual cost of \$50 per person for the alcohol intervention (Figure 1A), its incremental cost-effectiveness ratio (ICER) far exceeded favorable thresholds in resource-constrained environments, approximating \$100,000 per quality-adjusted-life-year (QALY) saved. Even under the most optimistic assumptions regarding the intervention's effect size and dramatic assumptions regarding alcohol's impact on mediators of HIV transmission, its cost-effectiveness still exceeded acceptable thresholds.

Assuming an alcohol intervention costs \$10 per person

When we assumed an annual cost of \$10 per person for the alcohol intervention (Figure 1B), its cost-effectiveness fell to approximately \$30,000 per QALY. Optimistic assumptions regarding the intervention's effect size and dramatic assumptions regarding alcohol's impact on mediators of HIV transmission lowered the ICER to around \$2,450/QALY, falling below the cost-effectiveness of initiating ART at 350 cells/ul rather than 200 cells/ul (\$2,600/QALY), and approximating 3× GDP per capita (\$2,400/QALY).

Assuming an alcohol intervention cost \$1 per person

When we assumed an annual cost of \$1 per person (Figure 1C), the cost-effectiveness ratio was \$2,445/QALY, similar to earlier ART initiation and three times the GDP per capita for Kenya. Optimistic assumptions regarding effect size resulted in the alcohol intervention becoming cost-saving.

The cost-effectiveness ratio of the alcohol intervention became more favorable than that of earlier ART initiation when the alcohol intervention cost \$0.98 per person or less. An alcohol intervention that cost \$1.04 per person or less met the WHO criteria for “cost-effective” interventions.

Considering the possibility that effectiveness of intervention diminishes with scale-up

While a clinical trial of a CBT-based alcohol intervention has been shown to reduce unsafe alcohol consumption by 45%, this result was based on a one-site study. It can be challenging to replicate effect sizes beyond original sites because their effect was partly due to site-specific characteristics. Nonetheless, even assuming that replication halved the effectiveness of Papas' intervention, it would still offer favorable value compared to other resource-constrained Kenyan interventions if its cost did not exceed approximately \$1 per person.

Discussion

Our results suggest approximately one-third of the alcohol-related new HIV infections in Kenya could be averted by a CBT-based intervention.^{11, 12} Additionally, life-years and QALYs could be increased substantially. Our results highlight the potentially favorable cost-effectiveness for alcohol interventions in Kenya. Even if scale-up halved its effectiveness, it would still offer good value at costs $\leq$ \$1 per person, approximating the value of initiating ART at 350 cells/ul rather than 200 cells/ul, and offering greater value than routine viral load monitoring of known infecteds.²⁹

Alcohol interventions are one of many approaches for reducing Kenyan HIV infections. In particular, early detection and ART treatment, enhancing retention in care, increasing ART adherence, promoting male circumcision, providing chemoprophylaxis for high-risk couples, and condom promotion may have great potential to avert HIV infections.³²⁻³⁷ To determine the optimal share of HIV prevention resources that should be allocated to alcohol interventions, future research should evaluate and compare alternative portfolios of interventions to reduce HIV infections in Kenya.

A limitation of any simulation is that results may be affected by statistically uncertain or biased inputs, and/or incorrect specification of model structure. While unhealthy alcohol consumption has reproducible and significant associations with greater condom nonuse, ART nonadherence, 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 (e.g. impaired immune response). It does not incorporate effects of alcohol unrelated to HIV, such as increased risk of trauma and alcohol-related organ disease such as cirrhosis, and therefore the simulation's estimates are likely conservative. Finally, infrastructure to provide alcohol interventions is lacking in most of Kenya. Accordingly, scaling up alcohol interventions would require infrastructure investments, which could impact the cost-effectiveness and could involve attenuation of intervention fidelity and effect size.

In conclusion, a substantial minority of new HIV infections in Kenya is likely to be attributable to unhealthy alcohol consumption, and a CBT-based intervention evaluated in a RCT would be cost-effective at costs below \$1 per person, offering favorable value compared to other resource constrained decisions.

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Figure 1. Cost-effectiveness of an alcohol intervention, assuming varying costs of the intervention Cost-effectiveness ratios in cost per quality-adjusted life year (QALY) are shown for varying relative risk multipliers (of unhealthy alcohol use on condom nonuse, non-adherence, and having an untreated STI), and by intervention effect size. All three effects were varied simultaneously from no effect to certain effect. The effect size of the intervention on reducing unhealthy alcohol use is shown along the depth axis. A low effect size (e.g. 0.15, meaning that the intervention reduces the proportion of people with unhealthy alcohol use by 85%) corresponds to the most efficacious intervention.

- A. Assuming an alcohol intervention cost of \$50 per person
- B. Assuming an alcohol intervention cost of \$10 per person
- C. Assuming an alcohol intervention cost of \$1 per person