Impact of Interventions Targeting Unhealthy Alcohol Use in Kenya on HIV Transmission and AIDS-Related Deaths

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Background: HIV remains a major cause of preventable morbidity and mortality in Kenya. The effects of behaviors that accompany unhealthy alcohol consumption are a pervasive risk factor for HIV transmission and progression. Our objective was to estimate the portion of HIV infections attributable to unhealthy alcohol use and to evaluate the impact of hypothetical interventions directed at unhealthy alcohol use on HIV infections and deaths.

Methods: We estimated outcomes over a time horizon of 20 years using a computer simulation of the Kenyan population. This computer simulation integrates a compartmental model of HIV transmission with a mechanistic model of HIV progression that was previously validated in sub-Saharan Africa. Integration of the transmission and progression models allows simultaneous consideration of alcohol's effects on HIV transmission and progression (e.g., lowering antiretroviral adherence may increase transmission risk by elevating viral load, and may simultaneously increase progression by increasing the likelihood of AIDS). The simulation considers important aspects of heterogeneous sexual mixing patterns, including assortativeness of partners by age and activity level, age-discordant relationships, and high activity subgroups. Outcomes included number of new HIV infections, number of AIDS deaths, and infectivity (number of new infections per infected person per year).

Results: Our model estimated that the effects of behaviors accompanying unhealthy alcohol consumption are responsible for 13.0% of new HIV infections in Kenya. An alcohol intervention with effectiveness similar to that observed in a published randomized controlled trial of a cognitive-behavioral therapy-based intervention in Kenya (45% reduction in unhealthy alcohol consumption) could prevent nearly half of these infections, reducing their number by 69,858 and reducing AIDS deaths by 17,824 over 20 years. Estimates were sensitive to assumptions with respect to the magnitude of alcohol's underlying effects on condom use, antiretroviral therapy adherence, and sexually transmitted infection prevalence.

Conclusions: A substantial number of new HIV infections in Kenya are attributable to unhealthy alcohol use. An alcohol intervention with the effectiveness observed in a published randomized controlled trial has the potential to reduce infections over 20 years by nearly 5% and avert nearly 18,000 deaths related to HIV.

Key Words: Unhealthy Alcohol Use, HIV Prevention, HIV/AIDS, Sub-Saharan Africa.

HIV REMAINS A major cause of preventable morbidity and mortality in Kenya, with an estimated 110,000 new infections and an estimated 80,000 deaths in 2009 (UNAIDS, 2010). At the same time, the effects of behaviors that accompany unhealthy alcohol consumption are an important risk factor for HIV acquisition (Pithey and Parry, 2009) and progression (Jaquet et al., 2010). Kenya in particular and sub-Saharan Africa in general have some of the worldwide highest rates of heavy episodic drinking and other types of unhealthy alcohol use (Hahn et al., 2011), leading to a confluence of HIV-related and alcohol-related diseases (Chersich and Rees, 2010). Indeed, a substantial portion of the burden of the HIV epidemic in Kenya and elsewhere in sub-Saharan Africa may be attributable to unhealthy alcohol use.

Randomized controlled trials of interventions that address unhealthy alcohol consumption in sub-Saharan Africa show promising results, increasing abstinence from alcohol (Papas et al., 2010, 2011) and decreasing sexual risk behaviors (Kalichman et al., 2008). However, even though experimental data are beginning to suggest that unhealthy alcohol use is modifiable in a sub-Saharan African context, alcohol treatment remains conspicuously absent from intervention

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programs in HIV and substance use (Fritz et al., 2010; Hahn et al., 2011).

We developed a computer simulation of HIV progression and transmission to estimate the burden of HIV infection in Kenya that is attributable to unhealthy alcohol consumption. In addition, we evaluated the potential impact of a hypothetical alcohol intervention on HIV transmission and AIDS-related deaths in Kenya. Because research on alcohol interventions in Kenya is at a nascent stage and magnitude and duration of effects are not known with certainty, our analyses explore widely varying scenarios regarding the effect of hypothetical interventions.

MATERIALS AND 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 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). A novel methodological feature of this simulation is that the 2 models work in tandem, with the progression model projecting the disease progression for each compartment in the transmission model. For example, an alcohol intervention may lead to improved ART adherence, which lowers viral load and extends life expectancy in the progression module. The lowered viral load then decreases the risk of transmitting HIV in the transmission module.

The simulation projects the course of the HIV epidemic in Kenya 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) reduction in infectivity, where "infectivity" is defined as the number of new HIV transmissions transmitted annually per infected person. The reason we measure infectivity in addition to number of infections averted is because changes in infectivity can be easier to interpret than changes in number of infections averted. Some interventions may simultaneously reduce the probability of HIV transmission per risk event and also prolong life expectancy, and, therefore, the duration of time over which HIV can be transmitted. Thus, a reduction in probability of transmission per event may result in more overall new infections. Number of infections averted may increase or decrease, whereas infectivity will always decrease.

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, nonadherence leading to the accumulation of genotypic resistance, and has been well-validated in multiple 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/μl) 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). Details of this module are described elsewhere (Braithwaite et al., 2011).

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.

HIV Transmission Module

A dynamic 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 1 among a set of mutually exclusive and collectively exhaustive compartments (Fig. 1). 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, nonmonogamous with a low number of concurrent partners, or may occupy an even higher risk group (community sex workers [CSW] if women, and migrant workers if men), with greater numbers of concurrent partners and correspondingly greater chances of contracting or spreading HIV. Women in any of the nonabstinent states may "mix" (have sexual contact) with men in any of the nonabstinent 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 nonmonogamous men because likelihood of initiating contact is high, condom use is low, and duration of the relationship may be high.

Other assumptions include

1. All sexually active persons may have sexually transmitted infections (STIs), and this increases HIV transmission risk. Risk of having STIs, like HIV itself, will increase with greater numbers of sexual contacts, and will decrease with protection.
2. Men may or may not be circumcised. Men who are circumcised have a decreased chance of becoming infected with HIV.
3. Likelihood of transmission per sexual encounter will vary with viral load (greater with higher viral load). For this reason, those who are receiving antiretroviral treatment will have a lower risk of transmission than those who are not receiving antiretroviral treatment, whereas people with primary HIV infection (and a correspondingly high viral load) or AIDS will be especially likely to transmit the virus.
4. Likelihood of transmission may vary depending on whether the HIV virus is drug resistant. Drug-resistant viruses have lower replication capacity and less viral "fitness" and for this reason may not be as easy to transmit as "wild-type" viruses.

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

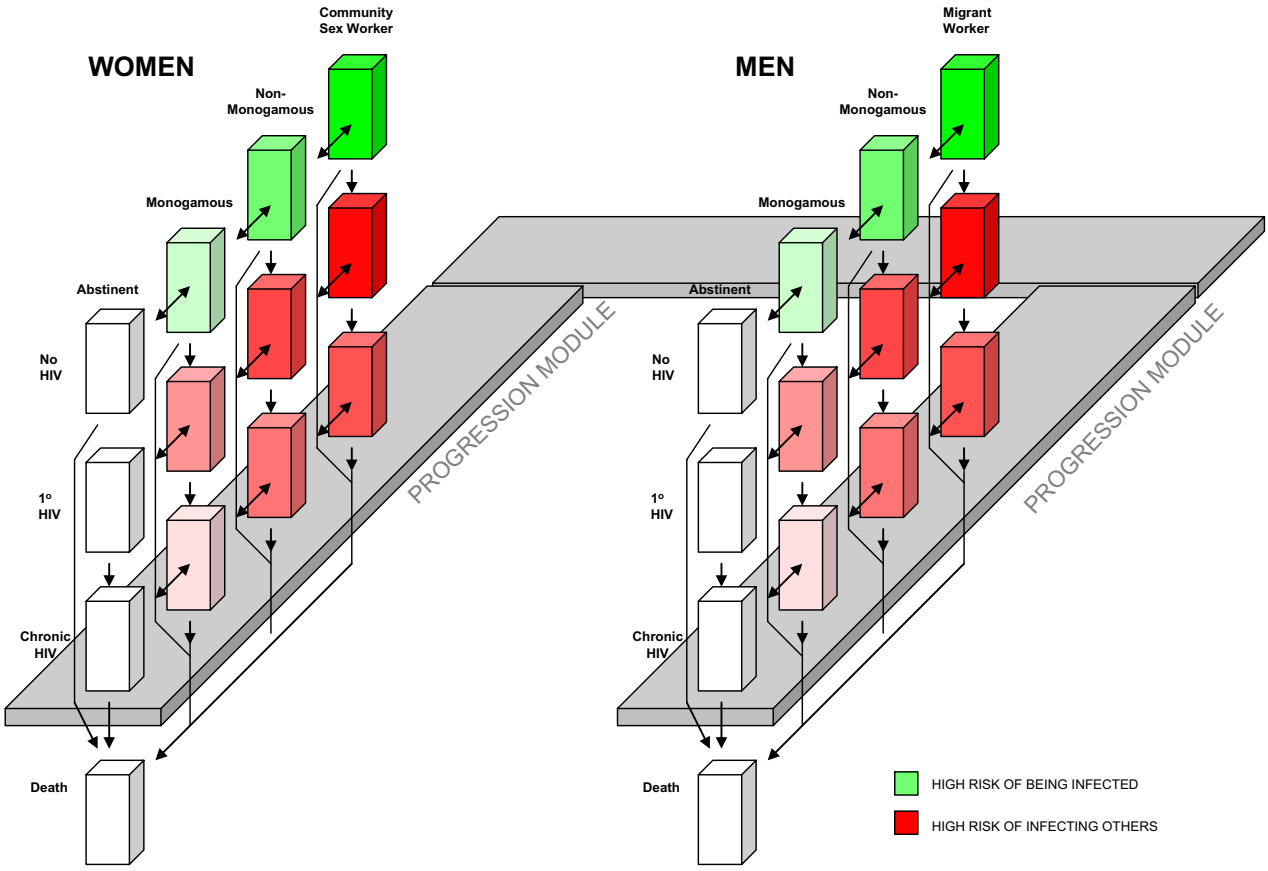

Fig. 1. Schematic of HIV computer simulation. The transmission module and the progression module pass information back and forth, so that interventions that directly impact transmission risk may indirectly impact progression risk, and interventions that directly impact progression risk may indirectly impact transmission risk. Additionally, there are important simulation features that are not depicted in the diagram. The probability of transmission is higher from men to women, and lower from women to men. Additionally, mixing may be asymmetric by age (greater from older men to younger women; lower from younger men to older women). Although similarly sized cubes are used to designate different states of the simulation, this is not meant to suggest that the number of individuals in each state is similar: the proportion may vary from state to state, and may also vary between corresponding states of men and women.

heterogeneous mixing patterns that are informed by sub-Saharan African data (Garnett and 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." For example, increasing the frequency of sexual encounters without changing the concurrency or duration of partnerships will increase the transmission risk per partnership without altering the partner change rate. In another example, increasing the concurrence of sexual relationships without increasing their frequency or the duration will reduce the transmission risk per partnership, but may increase the transmission risk per unit time because the number of simultaneous partnerships increase. Decomposing risk per partnership into its constituent characteristics is particularly important for modeling the sub-Saharan HIV pandemic because nonmonogamous contacts (e.g., CSWs) may be persistent (Voeten et al., 2002).

Representation of Alcohol Interventions

We performed a systematic review of the peer-reviewed literature based on pathways through which alcohol may impact HIV transmission risk. Our systematic literature review aimed to identify all scientific papers that examined potential risk factors and protective

factors related to HIV transmission in sub-Saharan Africa, to characterize their level of evidence, and to pool estimates when appropriate (e.g., not too heterogeneous, as assessed by visual inspection of Forest plots and evaluation of Q statistics ($p > 0.10$) and I^2 statistics (> 0.25). Our search identified 68,971 unique records of which 208 articles were selected for full-text review. The majority of excluded articles were omitted because of undefined effect sizes, link was not of interest, or article only included prevalence data. A total of 135 articles were included in the systematic review. Studies came from 24 countries and were conducted in both urban and rural settings. Based on these results, unhealthy alcohol use was modeled as having 3 main effects: (i) increasing the risk of condom nonuse (risk ratio [RR] = 1.29), (ii) increasing the risk of ART nonadherence (RR = 2.33), and (iii) increasing the STI prevalence (RR = 1.72). Other inputs into the simulation are shown in Table 1.

For our base case analyses, a hypothetical alcohol intervention was assumed to decrease unhealthy alcohol consumption by 45%. This effect size was based on the randomized controlled trial of Papas and colleagues (2011), which employed a cognitive-behavioral therapy (CBT)-based intervention adapted for Kenya on individuals with unhealthy alcohol use, and found that abstinence rates increased by 45% at the end of the trial.

Sensitivity Analyses

In addition to performing analyses that estimated the effect of an alcohol intervention based on the findings of Papas and colleagues (2011), we also performed sensitivity analyses incorporating widely varying estimates that are higher (90% reduction in unhealthy alcohol use) and lower (0% reduction in unhealthy alcohol use). We incorporate widely varying ranges to increase the usefulness of this analysis, as it is good modeling practice to use widely plausible ranges in modeling studies when there is substantial uncertainty regarding input parameters.

RESULTS

Calibration

We prespecified 3 calibration criteria in order to evaluate whether the model's predictions were compatible with observed results: HIV prevalence, people living with HIV, and AIDS-related mortality (Fig. 2). We compared data from the most recent year available (2007), as well as time trends over the longest period of time (1997 to 2007) over which East Africa data were available for all 3 criteria (WHO, 2008). We selected Uganda rather than Kenya as the target country for calibration because it had particularly complete and accessible epidemiological data, and is a neighboring country. Accordingly, during the calibration, we used Ugandan rather than Kenyan input data.

Table 1. Key Model Input Parameters

Description of parameter input	Value	References
Alcohol use and SBIRT		
Prevalence of unhealthy alcohol use (Male/Female)	20%/10%	WHO (2011), NACADA (2010)
Relative risk of unhealthy alcohol use on unsafe sex	1.29	Unpublished systematic review and meta-analysis
Relative risk of unhealthy alcohol use on non-HIV STIs	1.72	Unpublished systematic review and meta-analysis
Relative risk of unhealthy alcohol use on nonadherence to ART	2.33	Unpublished systematic review and meta-analysis
SBIRT intervention effect size[a]	45%	Papas and colleagues (2011)
Sexual risk behaviors		
Proportion abstinent (M/F)—Class 1	5%/10%	Kapiga and colleagues (2002, 2006), Ao and colleagues (2006), Mbizvo and colleagues (1996), Quigley and colleagues (1997)
Proportion in stable, monogamous relationship (M/F)—Class 2	31%/69%	Quigley and colleagues (1997), Mishra (2009), Volle and colleagues (2009)
Proportion in multiple, concurrent relationships (if nonmonogamous) (M/F)—Class 3	56%/17%	Assumption
Proportion in multiple, concurrent relationships (if nonmonogamous) (M/F)—Class 4	8%/4%	Mmbaga and colleagues (2008), Vandepitte and colleagues (2006)
Frequency of sex acts (per year)	104	Assumption
Duration of relationship[b]	0.5 to 30 years	Assumption
Median number of concurrent partners (Class 3)	3	Volle and colleagues (2009)
Median number of concurrent partners (Class 4)	10	Volle and colleagues (2009)
Probability of consistent condom use	34%	Westercamp and colleagues (2010)
Relative risk of unsafe sex (condom nonuse most or all of the time) if aware of HIV status	0.47	Marks and colleagues (2005)
HIV epidemiology and transmission		
Adult HIV prevalence (1997)	10.60%	WHO (2008)
Probability of transmission per sex act[c]	0.00011 to 0.01243	Boily and colleagues (2009), Attia and colleagues (2009)
Untreated non-HIV STI prevalence	6%	WHO (2001)
Probability of HIV testing (per annum)	16%	Anonymous (2000), Irungu and colleagues (2008), Mossdorf and colleagues (2010)
Probability of linkage to HIV care and treatment	68%	Rosen and Fox (2011)
Probability of adherence to ART regimen	85%	Bajunirwe and colleagues (2009)

ART, antiretroviral therapy; STI, sexually transmitted infection; SBIRT, Screening, Brief Intervention, and Referral to Treatment.

[a]Effect size represents relative risk reduction for unhealthy alcohol users in population.

[b]Duration dependent on class of sexual risk behavior with stable, monogamous relationships having the longest duration and multiple, concurrent relationships having the shortest.

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

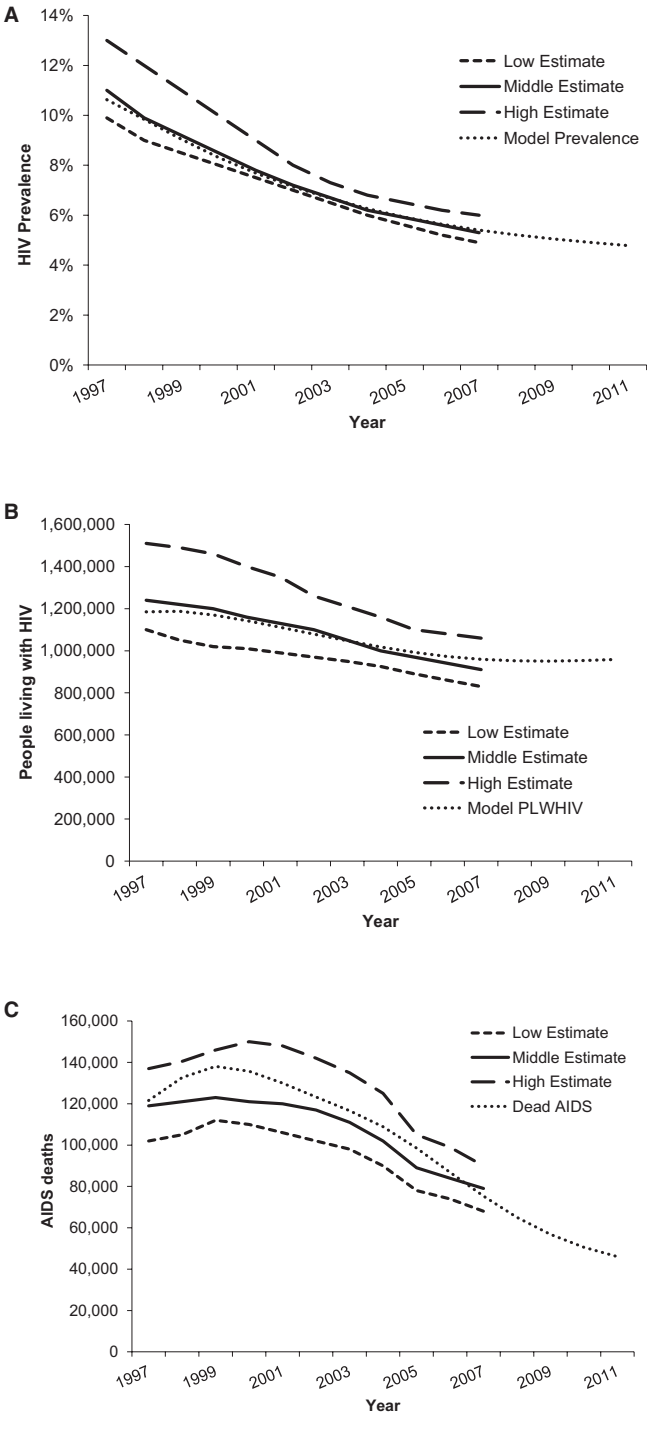

Fig. 2. Calibration of East Africa HIV simulation model. **(A)** Model calibration of HIV prevalence over time. The dotted line shows model projections and the solid line shows the HIV middle estimate from published literature (WHO, 2008). The long dashed line shows a high estimate and the short dashed line shows a low estimate from the literature (WHO, 2008). **(B)** Model calibration of people living with HIV (PLWHIV) over time. The dotted line shows model projections and the solid line shows the middle estimated number of PLWHIV from published literature (WHO, 2008). The long dashed line shows a high estimate and the short dashed line shows a low estimate from the literature (WHO, 2008). **(C)** Model calibration of AIDS-related deaths over time. The dotted line shows model projections and the solid line shows the middle estimated AIDS-related deaths from published literature (WHO, 2008). The long dashed line shows a high estimate and the short dashed line shows a low estimate from the literature (WHO, 2008).

Proportions of HIV Infections Attributable to Alcohol

Our analysis revealed that a substantial number of new infections were attributable to unhealthy alcohol use, and could potentially be prevented by alcohol interventions with high effectiveness. With conservative assumptions regarding the magnitude of the impact of unhealthy alcohol use on condom nonuse, ART nonadherence, and STI prevalence, we estimated that 13.0% of new HIV infections in Kenya are attributable to unhealthy alcohol use (Table 2). With less conservative assumptions, we estimated that as many as 16.5% of new HIV infections may be attributable to unhealthy alcohol use.

HIV Infections Averted

With conservative assumptions regarding alcohol's impact on HIV transmission risk factors, an alcohol intervention with the effectiveness of Papas' CBT-based intervention in Kenya (45% reduction in unhealthy alcohol use) could reduce new HIV infections attributable to unhealthy alcohol use from 13.0 to 7.2%, which corresponds to a reduction of 69,858 infections over 20 years (Tables 2 and 3). With less conservative assumptions regarding alcohol's impact on HIV transmission risk factors, we estimated that an alcohol

Table 2. Proportion of New HIV Infections Over 20 Years Due to Alcohol Consumption Under Various Model Assumptions

Efficacy of alcohol intervention (% reduction in proportion of individuals with unhealthy alcohol use)	Effect of unhealthy alcohol use on condom nonuse (RR)	Effect of unhealthy alcohol use on ART nonadherence (RR)	Effect of unhealthy alcohol use on STI prevalence (RR)	Proportion of new HIV infections due to alcohol (%)
No effect	1.29	2.33	1.72	13.0
No effect	1.29	2.33	10	15.2
No effect	1.29	10	1.72	13.0
No effect	1.29	10	10	15.2
No effect	10	2.33	1.72	14.3
No effect	10	2.33	10	16.5
No effect	10	10	1.72	14.4
No effect	10	10	10	16.5
45	1.29	2.33	1.72	7.2
45	1.29	2.33	10	8.7
45	1.29	10	1.72	7.2
45	1.29	10	10	8.7
45	10	2.33	1.72	8.0
45	10	2.33	10	9.5
45	10	10	1.72	8.0
45	10	10	10	9.5
90	1.29	2.33	1.72	1.3
90	1.29	2.33	10	1.6
90	1.29	10	1.72	1.3
90	1.29	10	10	1.6
90	10	2.33	1.72	1.5
90	10	2.33	10	1.8
90	10	10	1.72	1.5
90	10	10	10	1.8

RR, risk ratio; ART, antiretroviral therapy; STI, sexually transmitted infection.

Table 3. Number of HIV Infections Averted Over 20 Years by Various Effectiveness Characteristics of an Alcohol Intervention

Efficacy of alcohol intervention (% reduction in proportion of individuals with unhealthy alcohol use)	Effect of unhealthy alcohol use on condom nonuse (RR)	Effect of unhealthy alcohol use on ART nonadherence (RR)	Effect of unhealthy alcohol use on STI prevalence (RR)	Mean number new infections per infected per year	Number of HIV infections averted
No effect	1.29	2.33	1.72	0.081	0
No effect	1.29	2.33	10	0.092	0
No effect	1.29	10	1.72	0.083	0
No effect	1.29	10	10	0.094	0
No effect	10	2.33	1.72	0.090	0
No effect	10	2.33	10	0.104	0
No effect	10	10	1.72	0.092	0
No effect	10	10	10	0.107	0
45	1.29	2.33	1.72	0.079	69,858
45	1.29	2.33	10	0.085	264,515
45	1.29	10	1.72	0.080	62,899
45	1.29	10	10	0.086	257,365
45	10	2.33	1.72	0.084	224,920
45	10	2.33	10	0.093	567,861
45	10	10	1.72	0.085	216,357
45	10	10	10	0.094	561,019
90	1.29	2.33	1.72	0.077	138,288
90	1.29	2.33	10	0.078	515,842
90	1.29	10	1.72	0.077	124,032
90	1.29	10	10	0.078	499,743
90	10	2.33	1.72	0.078	430,994
90	10	2.33	10	0.080	1,064,171
90	10	10	1.72	0.078	412,411
90	10	10	10	0.080	1,045,427

RR, risk ratio; ART, antiretroviral therapy; STI, sexually transmitted infection.

Table 4. Number of AIDS-Related Deaths Averted Over 20 Years by Various Effectiveness Characteristics of an Alcohol Intervention

Efficacy of alcohol intervention (% reduction in proportion of individuals with unhealthy alcohol use)	Effect of unhealthy alcohol use on condom nonuse (RR)	Effect of unhealthy alcohol use on ART nonadherence (RR)	Effect of unhealthy alcohol use on STI prevalence (RR)	Number of AIDS-related deaths averted
No effect	1.29	2.33	1.72	0
No effect	1.29	2.33	10	0
No effect	1.29	10	1.72	0
No effect	1.29	10	10	0
No effect	10	2.33	1.72	0
No effect	10	2.33	10	0
No effect	10	10	1.72	0
No effect	10	10	10	0
45	1.29	2.33	1.72	17,824
45	1.29	2.33	10	67,482
45	1.29	10	1.72	53,887
45	1.29	10	10	111,751
45	10	2.33	1.72	58,524
45	10	2.33	10	144,997
45	10	10	1.72	99,525
45	10	10	10	198,559
90	1.29	2.33	1.72	35,386
90	1.29	2.33	10	132,686
90	1.29	10	1.72	106,452
90	1.29	10	10	217,348
90	10	2.33	1.72	112,871
90	10	2.33	10	274,082
90	10	10	1.72	191,466
90	10	10	10	372,372

RR, risk ratio; ART, antiretroviral therapy; STI, sexually transmitted infection.

intervention with the effectiveness of Papas' CBT-based intervention could avert as many as 561,019 infections over 20 years (Table 3) by effectively reducing new infections attributable to unhealthy alcohol consumption from 16.5 to 9.5%.

AIDS Deaths Averted

With conservative assumptions regarding alcohol's impact on HIV transmission risk factors, an alcohol intervention with the effectiveness of Papas' CBT-based intervention could reduce AIDS-related deaths attributable to unhealthy alcohol use by 17,824 over 20 years (Table 4), corresponding to a reduction in new HIV infections attributable to unhealthy alcohol use from 13.0 to 7.2%. With less conservative assumptions regarding alcohol's impact on HIV transmission risk factors, the simulation estimated that an alcohol intervention with the effect of Papas' CBT-based intervention could avert as many as 198,559 AIDS-related deaths over 20 years.

DISCUSSION

Our results suggest that the effects of behaviors that accompany unhealthy alcohol consumption are responsible for approximately one-eighth of new HIV infections in Kenya. Nearly half of these alcohol-attributable infections could be averted by an alcohol intervention program with the same effectiveness as CBT-based interventions (Papas et al., 2011), assuming that the effect persists. Such an alcohol intervention would also reduce the mortality by 2.3%. Interestingly, the fraction of HIV infections attributable to alcohol (13.0%) is substantially greater than the proportion of deaths attributable to alcohol (3.8% worldwide, 2.4% in sub-Saharan Africa; Rehm et al., 2009).

Interventions that decrease transmissibility of an infection may paradoxically increase the number of new infections if they simultaneously increase the life expectancy of infected persons, therefore extending the duration of time over which they may infect others. Similarly, interventions that increase transmissibility of an infection may paradoxically decrease the number of new infections. Accordingly, our results showed that assuming greater effects of unhealthy alcohol consumption on ART nonadherence (at the same time it was assumed to have a large effect on condom nonuse) increased the infectiousness of individuals from 0.093 new infections annually per infected person annually to 0.094 new infections annually per infected person, yet decreased the number of infections averted over 20 years from 567,861 to 561,019.

Alcohol interventions are one among a multiplicity of pathways for reducing new HIV infections in Kenya. In particular, interventions directed at early detection and treatment with ART, enhancing retention in care, increasing ART adherence, promoting male circumcision, providing chemoprophylaxis for high-risk couples, and condom promotion have great potential to reduce numbers of new HIV infections (Kunutsor et al., 2012; Losina et al., 2009; Mills et al., 2008; Okwundu et al., 2012; Sandoy et al., 2012). For these reasons, future research is needed to quantify the cost-effectiveness of alcohol interventions. To determine the relative effectiveness of alcohol interventions compared to alternative approaches for reducing new HIV infections in Kenya, future research should evaluate and compare alternative portfolios of HIV interventions, seeking to determine the share of HIV prevention resources that should be allocated to alcohol interventions in order to achieve optimal efficiency of an HIV prevention program (e.g., number of HIV infections averted is maximized given a particular resource constraint).

Limitations

Our analyses have multiple limitations. Even though we subjected our simulation to prespecified calibration procedures, the results of any simulation may be affected by statistically uncertain or biased inputs, and/or incorrect specification of model structure. Indeed, the majority of model inputs were based on low quality evidence, and it can be argued that even though we based our inputs on a systematic review of the literature, many of the estimates identified by this systematic review were based on nonrepresentative samples (e.g., the effect of alcohol use on STI prevalence is based on one study that studied sex workers in Ethiopia and on another study of bar and hotel workers in Northern Tanzania. A sizable portion of the latter sample is sex workers, alcohol is abundant in their workplace, and about half have another STI, most often HSV-2, hardly representative of the overall population). Many of the source studies used criteria for alcohol consumption that do not correspond closely to the National Institute of Alcohol Abuse and Alcoholism (NIAAA) criterion for unhealthy alcohol consumption; however, when a particular study incorporated alternative thresholds of alcohol consumption, we based our effect size estimate on the threshold that corresponded most closely with the NIAAA definition. Major subgroups are not represented in the analysis (men who have sex with men, injection drug users), although it can be argued that they encompass a small proportion of HIV transmission in East Africa, and therefore this is unlikely to be a critical limitation of our study. Furthermore, it could be argued that it is unreasonable to base population projections on 1 test program that showed such an optimistic effect size (45%). However, this program remains the only experimentally studied alcohol intervention in our population of interest, and therefore is arguably the most reasonable base case assumption. Additionally, a wide range of alternative effects of alcohol interventions were tested in sensitivity analyses in accord with standard modeling practice, including far more pessimistic estimates.

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 transmission independent from its effects on viral load, likelihood of untreated STIs, and condom nonuse, and 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. Finally, our analyses assume that a hypothetical alcohol intervention could be scaled-up across Kenya without attenuating the magnitude of the intervention's effect. However, infrastructure to provide alcohol interventions is lacking in most of Kenya. Accordingly, scaling up alcohol interventions would require large infrastructure investments, and likely would involve attenuation of intervention fidelity and effect size. Indeed, some might argue that it is unrealistic to believe that any alcohol intervention would ever be implemented so broadly in Kenya.

Conclusion

In summary, a substantial number of new HIV infections in Kenya may be attributable to the effects of behaviors that accompany unhealthy alcohol consumption, subject to the data limitations described above. At the same time, interventions to reduce unhealthy alcohol consumption in Kenya are being developed, adapted, and demonstrated to be effective using experimental study designs. Widespread adaptation of interventions to reduce alcohol consumption has the potential to reduce HIV infections by nearly 5% and avert nearly 18,000 deaths to HIV.

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