Descriptive systematic review of sub-Saharan African studies on the association between alcohol use and HIV infection

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Abstract
The purpose of this review was to identify and assess studies that have quantified the association between alcohol consumption and HIV infection in sub-Saharan Africa. PubMed, CAB Abstracts and article references were searched to identify studies published in English between 2000 and 2008 that reported relative measures of the association between alcohol use and HIV prevalence and/or seroconversion rates. Twenty-one eligible studies were described in detail and information on study characteristics extracted. All of the identified studies were conducted either in east or southern Africa, and varied substantially regarding study population and alcohol use definitions. Overall, users of alcohol and especially problem drinkers were more likely to be HIV seropositive (HIV+) than non-users, frequency or quantity of alcohol use was positively associated with HIV prevalence, and the association varied by gender. The use of alcohol in sexual contexts was significantly associated with an increased risk of HIV acquisition and prevalence. The findings of this review of sub-Saharan African research strongly support an association between alcohol consumption and HIV infection. Although a causal relationship could not be established with certainty from the mainly cross-sectional studies, the negative consequences of such an association have profound implications for the burden of disease in this region. To confirm causality, future research should use prospective study designs, use clearly defined standardised measures of alcohol use (and problematic drinking) and an ‘event-specific’ approach to examine the situational links between alcohol use and HIV acquisition.

Keywords: Alcohol, HIV, sexual risk, Africa.

Résumé
L’objectif de cette revue consistait à identifier et à évaluer les études qui ont quantifié la relation entre la consommation d’alcool et l’infection par le VIH en Afrique subsaharienne. Des résumés de PubMed, de CAB et des références d’articles ont été recherchés afin d’identifier les études publiées en Anglais entre 2000 et 2008 qui se rapportaient aux mesures relatives de la relation entre la consommation d’alcool et les taux de prévalence du VIH et/ou de séroconversion. Vingt et une études étaient décrites en détail et des informations sur les caractéristiques de l’étude extraites. Toutes les études identifiées ont été réalisées en Afrique de l’Est ou australe et variaient de façon substantielle en termes de population de l’étude et de définitions de la consommation d’alcool. Dans l’ensemble, les consommateurs d’alcool et en particulier les buveurs présentaient davantage de probabilité d’être séropositifs que les non consommateurs, la fréquence ou la quantité de la consommation d’alcool était positivement associée à la prévalence du VIH et l’association variait selon le sexe. La consommation d’alcool dans des contextes sexuels était significativement associée à un risque plus élevé d’infection par le VIH et de séroprévalence. Les conclusions de cet examen de la recherche en Afrique subsaharienne étaient fortement l’association entre la consommation d’alcool et l’infection par le VIH. Bien qu’une relation causale n’ait pu être déterminée avec certitude à partir des études principalement transversales, les conséquences négatives d’une telle association ont des implications profondes sur le fardeau que constitue la maladie dans cette région. Pour confirmer la causalité, les futures études devraient utiliser des conceptions d’étude prospectives, des mesures normalisées clairement définies de la consommation d’alcool (et la consommation problématique d’alcool) et une approche ‘spécifique à l’événement’ pour examiner les liens situationnels entre consommation d’alcool et infection par le VIH.

Mots clés: Alcool, VIH, risque sexuel, Afrique.
Introduction
Towards the end of 2007 it was estimated that worldwide approximately 33.2 million people were living with HIV, approximately 2.1 million people died of AIDS-related illnesses, and some 2.5 million people contracted HIV during 2007 alone. In sub-Saharan Africa, the world’s most adversely affected region, it was estimated that approximately 22.5 million people were living with HIV, and in the past year, approximately 1.6 million AIDS-related deaths occurred, while approximately 1.7 million people were newly infected with HIV. Within sub-Saharan Africa, southern Africa is the worst affected region, with eight countries in 2005 having national adult HIV prevalence rates that exceeded 15% (UNAIDS, 2007).

Concurrent with the HIV/AIDS pandemic, many countries within sub-Saharan Africa exhibit very high levels of alcohol consumption, one of the most prevalent behavioural risk factors implicated in the transmission of HIV and other STDs (Cook & Clark, 2005; Kalichman, Simbayi, Kaufman, Cain & Jooste, 2007a). Of the 20 countries in Africa identified by the World Health Organization (WHO) with very high levels of child and adult mortality, it was estimated that for 2000 the total alcohol consumption per adult was 7.1 litres of absolute alcohol (Rehm et al., 2003a). However, when one takes into consideration that a relatively low percentage of adults in these countries consume alcohol (55% of men and 30% of women), the annual consumption per drinker increases to 16.6 litres of absolute alcohol, the highest level for any region of the world (Rehm et al., 2003a). In addition, the overall pattern of drinking in this region in 2000 was ranked as the second most detrimental in the world (indicative of high rates of binge drinking and alcohol dependence), with 1% of all deaths among women and 4% of all deaths among men attributable to alcohol (Rehm et al., 2003a; Rehm et al., 2003b). Corresponding figures from South Africa were 10.7% for men and 3.1% for women (Schneider et al., 2007). High-risk drinking patterns, especially binge drinking may play an intermediate role between alcohol use and sexual risk behaviour (Chersich et al., 2007).

Alcohol use and HIV sexual risk behaviours
Alcohol use has repeatedly been recognised as a key correlate of sexual risk behaviour in several African populations, including HIV+ individuals, and ‘heavy alcohol use’ in particular is thought to be associated with an increased likelihood of engaging in multiple risk behaviours (e.g. multiple sexual partners, unprotected vaginal and anal intercourse, inconsistent condom use, and paying for or selling sex) (Alem, Kebede, Mitike, Enquellase & Lemma, 2006; Lurie et al., 2008; Weiser et al., 2006). A number of theories have been proposed to explain the complex relationship between alcohol consumption and sexual risk behaviour, including the psychoactive effects of alcohol on sexual decision-making, expectations surrounding the effects of alcohol, high-risk settings and risk-taking personality characteristics (Bryant, 2006; Corte & Sommers, 2005; Kalichman, Simbayi, Jooste, Cain & Cherry, 2006; Morojele et al., 2006).

A descriptive systematic review of the literature on alcohol use and sexual risk behaviour in southern Africa found that any alcohol use and greater quantities of alcohol use were strongly associated with HIV transmission risks in this region (Kalichman et al., 2007a). In addition, a recent prospective cohort study conducted among 82 HIV+ women and men from five HIV service organisations in Cape Town, South Africa, has highlighted the importance of alcohol use and its implications for secondary HIV transmission (Kiene et al., 2008). Findings of this study, the first to examine event-level data over time in an HIV+ population in Africa, found that moderate or higher risk drinking before sex (>1.8 drinks for women and >3 drinks for men) was positively associated with an increased likelihood and number of subsequent unprotected sex acts.

Furthermore, studies have shown that individuals with alcohol use disorders have an increased risk of contracting HIV and similarly, alcohol-related problems are common among HIV+ individuals, both of which could have significant implications for the further expansion of the HIV epidemic (Braithwaite et al., 2007; Samet et al., 2007; Shaffer, Njeri, Justice, Odero & Tierney, 2004).

Alcohol use and HIV infection, disease progression and treatment
Chronic, and even acute, alcohol use results in impaired immunity and alcohol-induced malnutrition, increasing host susceptibility to infection by bacterial and viral pathogens (Brown et al., 2006; Waldschmidt, Cook & Kovacs, 2008). A growing body of literature suggests that alcohol directly increases biological and physiological susceptibility to HIV infection (Bagasra, Bachman & Jew, 1996; Wang et al., 2002; Liu, Zha, Nishitani, Chen & Zack, 2003). A thought-provoking study by Bagasra et al. (1996) found that a single dose of intravenous alcohol infusion not only impaired certain immune responses of white blood cells isolated from healthy volunteers, but also increased the cells susceptibility to HIV infection. Subsequent in vitro studies with human-derived macrophages and lymphocytes incubated with alcohol found significantly enhanced CCR5 and CXCR4 receptor expression, both significant co-receptors used by HIV-1 to gain entry into target cells (Liu et al., 2003; Wang et al., 2007).
et al., 2002). Increased availability of HIV-1 co-receptors would increase an individual's risk of HIV-1 infection.

Furthermore, evidence from clinical and laboratory studies has indicated that alcohol abuse may accelerate HIV disease progression (Bagby, Zhang, Purcell, Didier & Nelson, 2006; Hao rah et al., 2004; Miguez, Shor-Posner, Morales, Rodriguez & Burbano, 2003; Samet et al., 2007). In particular, proteasomes and immunoproteasomes, critical immune processes attenuated during progressive HIV-1 infection, are affected by alcohol abuse. Studies with human monocyte-derived macrophages support the notion that HIV-1 infection and alcohol may act synergistically to affect antigen presentation and in so doing, affect disease progression (Hao rah et al., 2004). Further evidence of the role of alcohol consumption as a cofactor in the immunopathogenesis of HIV disease comes from another in vitro study which found that alcohol inhibited natural killer (NK) cell-mediated innate immunity against HIV (Zhang et al., 2005).

In humans, conflicting findings have been obtained on the association between alcohol consumption and disease progression. Previous studies have shown that among HIV+ individuals with a history of alcohol problems and receiving antiretroviral therapy (ART), alcohol use was associated with lower CD4 counts and either higher or active undetectable HIV viral loads (Miguez et al., 2003; Samet, Horton, Traphagen, Lyon & Freedberg, 2003). In contrast, a recent prospective study found that among HIV+ individuals not receiving ART, heavy alcohol consumption was associated with lower CD4 counts, but no effect on HIV viral load was observed. Among HIV+ individuals who were on ART, heavy alcohol consumption was not associated with lower CD4 counts or higher HIV viral loads (Samet et al., 2007).

Among persons with HIV, alcohol consumption is the most prevalent risk factor for poor adherence to HIV medication, a factor known to lead to more rapid disease progression (Braithwaite et al., 2005; Chander, Lau & Moore, 2006). Recently, a temporal and dose-response relationship between alcohol use and poor medication adherence was demonstrated among veterans in care (Braithwaite et al., 2005). Additional analysis of the same cohort estimated that among HIV+ individuals, non-hazardous alcohol use (<5 standard drinks on drinking days) decreased survival by more than 1 year if the frequency of use was once per week or more, and by 3.3 years with daily use. Hazardous alcohol use (≥5 standard drinks on drinking days) decreased overall survival by more than 3 years if frequency of consumption was once per week or more, and by 6.4 years with daily use (Braithwaite et al., 2007). In addition, the effect of alcohol on liver function may affect its ability to metabolise certain HIV medication, thus reducing their therapeutic efficacy. This, together with non-compliance to ART, not only results in poorer HIV treatment outcomes, but can also lead to the development of drug-resistant HIV strains (Bekker, 2005; Bryant 2006).

In the light of the above evidence supporting alcohol use as both a risk factor for HIV infection and disease progression, and the significant contribution of both alcohol use and HIV infection to the burden of disease in sub-Saharan Africa, the following descriptive systematic review sought to identify and describe empirical studies that have analysed the association between alcohol use and HIV infection in this region. In addition we sought to expand the scope of a previous review of African literature by Fisher, Bang and Kapiga (2007) by including more recent studies and a few studies that were not included in their review, and by commenting on whether this association varied by study population, gender, drinking pattern or drinking context. The review was undertaken to generate knowledge that could be used to inform policy makers and practitioners, working in both the HIV/AIDS and substance abuse intervention areas, of the substantial amount of research conducted in Africa to date on the association between alcohol and HIV infection, to highlight commonalities and differences across studies conducted within different settings, and to identify areas where future research efforts need to be targeted.

Methodology
The primary search strategy involved automated searches of PubMed and CAB Abstracts (on 15 September 2008) for all journal articles published between 2000 and 2008 using the terms ‘alcohol,’ ‘HIV,’ ‘Africa,’ and ‘risk.’ Exclusion criteria included: (i) studies where there was no definition of alcohol use or drinking behaviour; (ii) studies where HIV status or HIV prevalence or incidence rates were not reported; (iii) studies not conducted in Africa; (iv) studies that did not consider alcohol use as a risk factor for HIV infection; (v) studies that did not include a relative measure of the association between alcohol use and HIV infection; and (vi) studies that did not involve the conducting of original, empirical research. Manual searches of articles cited in reference sections of papers (particularly the review articles) identified through the automated search were also conducted. In addition, relevant literature was obtained from colleagues working in the field. In all, 156 articles published in English were sourced and of these, 21 studies that reported relative measures of the association between alcohol use and HIV prevalence and/or seroconversion rates were identified and reviewed in detail. Information on the country of study, alcohol use definition (e.g. general measure/frequency/quantity/drinking context),
study population characteristics (e.g. community or group, study setting, age, gender and number of participants), HIV prevalence and relative measures were extracted from each of the 21 identified articles. The findings were primarily categorised and analysed according to three study populations: clinic/health facility attendees, community/population-based, and high-risk groups. This was followed by a secondary analysis to examine whether any differences between gender, drinking pattern (e.g. ever use/never use, frequency, quantity, standardised measure of problem drinking), or drinking context were apparent.

Results
All of the identified studies were conducted either in east or southern Africa, with the majority conducted in northern Tanzania. Since almost all of the studies were observational in design and varied substantially regarding study population and alcohol use definition, a descriptive approach was selected rather than a more quantitative approach (e.g. using meta-analysis) (Dickersin, 2002). Furthermore, the time frames measured were also not consistent, with some studies reporting current use, for example last week, while others used last month or lifetime use. Regarding study population, five studies were conducted among clinic/health facility attendees, eleven studies involved representative samples from community/population-based surveys and five studies involved high-risk groups (e.g. beer hall patrons, bar and hotel workers). When grouped according to drinking pattern or drinking context, six studies used an ever use/never use dichotomy, four studies assessed frequency/quantity, five studies used a standardised self-report screening instrument for problem drinking (e.g. AUDIT and CAGE), five studies investigated alcohol use either before or during sex, and one study collected data on number of visits to beer halls in the last month. Details of the 21 studies follow and are summarised according to study population in Tables 1, 2 and 3.

Clinic/health facility attendees
In the context of an ongoing study to determine the effect of placental malaria on mother-to-child transmission of HIV, risk factors for HIV infection among asymptomatic women attending an antenatal clinic in Kisumu, western Kenya, were identified between June 1996 and November 1997 (Ayisi et al., 2000). HIV prevalence was 26.1% among the 2 844 women included in the final analysis, and a multivariate analysis found that reported alcohol consumption was independently associated with being HIV+ (adjusted RR 1.6, 95% CI: 1.1-2.5).

A study conducted from June 2002 to March 2004 sought to determine the social, behavioural and biological risk factors among 2 654 pregnant women (14 - 43 years) in Moshi, Tanzania (Msuya et al., 2006). Overall HIV prevalence was 6.9%, and women who consumed alcohol either occasionally/weekly (9.2% HIV+; OR 1.66, 95% CI: 1.21-2.26) or daily (13.7% HIV+; OR 2.59, 95% CI: 1.14-5.89) were significantly more likely to be HIV+ than those who did not (5.8% HIV+). Among pregnant women the daily use of alcohol by their male partner significantly increased the women’s risk of HIV infection (adjusted odds ratio (AOR) 1.70, 95% CI: 1.06-2.67).

To identify risk factors associated with HIV, an unmatched case-control study in Gaborone, Botswana, was conducted between 1 May and 1 December 1999 among 135 tuberculosis (TB) patients whose HIV status was known (Talbot et al., 2002). HIV prevalence among men (N=82) was 62.2%, and among women (N=53) this figure was 79.2%. In the univariate analysis a positive HIV status was not significantly associated with those who had ‘enjoyed alcohol’ before becoming ill with TB or with those who consumed ≥3 drinks per day, but was significantly associated with those respondents who reported that they or their sex partner had used alcohol before sex. This association remained positively and independently associated with a positive HIV status in the multivariate analysis (77% v. 55%; adjusted prevalence odds ratio (aPOR) 6.8, 95% CI: 1.9-24.1).

The association between alcohol use and sexual risks for HIV infection was examined over a 3-month period among a group of adults (149 men and 78 women) receiving services from a STI clinic in Cape Town, South Africa (Simbayi et al., 2004). Global use of alcohol was assessed by the use of the AUDIT (Babor, De la Fuente, Saunders & Grant, 1992). Seventy-two per cent of men and 38% of women reported current use of alcohol, 52% of men and 17% women indicated likely problem drinking (AUDIT score ≥9), and 36% of men and 10% of women indicated probable alcohol-related problems (AUDIT score ≥13). In the past month the use of alcohol in sexual contexts by men was common (42%), but less so by women (12%). The use of alcohol in the context of sex in the previous month was reported by 61% of those with likely problem drinking patterns (AUDIT score≥9), and by 69% of the heavy drinkers (AUDIT score ≥13). Alcohol use in sexual contexts in the past month was associated with indicators of higher risk for HIV infection (e.g. more sex partners and unprotected vaginal intercourse). In spite of this, 13% of those who had used alcohol in sexual contexts were HIV+, compared with 15% for those who had not (AOR 0.7).

An unmatched case-control study investigated the association between substance abuse and HIV infection among 953 people visiting HIV counselling and testing centres in Addis Ababa, Ethiopia (Seme, Mariam & Worku, 2005). The overall HIV
### Table 1. Characteristics of the 5 clinic/health facility-based studies

| Reference with | Country       | Alcohol use definition | Study population                                      | # Men | % HIV | # Women | % HIV | Relative measure |
|----------------|---------------|------------------------|-------------------------------------------------------|-------|-------|---------|-------|------------------|
| Ayisi et al., 2000 | Kenya         | Current use - Yes/No   | Asymptomatic antenatal clinic attendees, Kisumu        | 2,844 | 26.1  |         |       | adj RR 1.6 (1.1 - 2.5) |
| Msuya et al., 2006 | Tanzania      | Current use            | Pregnant women (14 - 43 years), Moshi                 | 2,654 | 6.9   |         |       | OR 1.66 (1.21 - 2.26) |
| Talbot et al., 2002 | Botswana      | Before ill with TB, ≥3 drinks per day & * when the subject or their partner used alcohol before sex | Moshi | 82 | 62.2 | 53 | 79.2 |     | Not significant |
| Simbayi et al., 2004 | South Africa  | In sexual contexts in past month & AUDIT | Men & women receiving STI clinics services, Cape Town | 149 | 78 | | | AOR 0.7 (N/A) |
| Seme et al., 2005 | Ethiopia      | Ever drink alcohol     | Men and women HIV counselling & testing centres, Addis Ababa | 336 | 25.1 | 617 | 25.1 | AOR 2.48 (1.65 - 3.72) |

*Results not stratified by gender.*

**Community/population-based studies**

During 1996, as part of a study on factors influencing the differential spread of HIV infection in four African cities a large cross-sectional population-based survey was conducted using the 27 cases (HIV-seropositive) and 270 controls (HIV-seronegative) from the interview. Fifty-five per cent (558) of cases (HIV+) had consumed alcohol in the past year, while only 41.9% (545) of controls (HIV-) had done so. Persons who had used alcohol were twice as likely to be HIV+ than those who had never drunk, 10% versus 5%. The association remained after adjusting for potential confounders, including ever using a condom and number of sexual partners in the past 12 months (AOR 1.8, 95% CI: 1.2 - 2.7). However, no gender difference for the risk of HIV infection was found.
Table 2. Characteristics of the 11 population-based studies

| Reference          | Country      | Alcohol use definition | Study population                                                                 | # Men | % HIV | # Women | % HIV | Relative measure with 95% CI |
|--------------------|--------------|------------------------|-----------------------------------------------------------------------------------|-------|-------|---------|-------|-------------------------------|
| Mbuya et al., 2000 | Uganda       | Ever drink alcohol     | Adults from 15 neighbouring villages, Masaka district                               | 1,072 | 7.8   | 1,267   | 8.7   | AOR 1.8 (1.2 - 2.7) – men     |
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Hargreaves et al., 2002 | Kenya     | Last month             | Adults (25 - 49 years), Kisumu                                                     | 306   | 31    | 466     | 30    | AOR 1.9 (1.1 - 3.2) – men     |
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Zuma et al., 2003  | South Africa | Last month             | Women (13 - 60 years), Khutsong, Carletonville                                    | 701   | 37.1  | 458     | 33.0  | AOR 1.58 (1.05 - 2.38) – men  |
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Sebit et al., 2003 | Zimbabwe     | Current use (AUDIT)    | Men and women (18 - 55 years), Epworth                                            | 47    | 53.2  | 147     | 61.2  | AOR 1.98 (0.52 - 7.8) – men   |
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Lewis et al., 2005 | Zimbabwe     | Self-reported visits to | Household survey of adults, Manicaland province                                   | 3,317 | 23.1  | 3,840   | 30.8  | AOR 1.4 (1.2 - 1.7) – men     |
|                    |              | bear halls in last month|                                                                                   |       |       |         |       |                               |
| Kapiga et al., 2006| Tanzania     | Current use            | Women (20 - 44 years) & their regular male partners, Moshi                        | 566   | 7     | 1,418   | 10.3  | AOR 1.42 (0.62 - 3.27) – women|
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Sa & Larsen, 2008  | Tanzania     | Last 12 months         | Women (20 - 44 years), Moshi                                                       | 1,418 | 10.3  | 475     | 13.8  | AOR 1.44 (1.0 - 2.08) – men   |
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Mitsunaga & Larsen, 2008 | Tanzania | Current use (CAGE score 2 - 4) | Women (20 - 44 years) & their regular male partners, Moshi | 1,200 | 10.1  |         |       | AOR 1.42 (0.62 - 3.27) – women|
|                    |              |                        |                                                                                   |       |       |         |       |                               |
| Mimbaga et al., 2007| Tanzania   | Current use at least    |                                                                                   | 1,200 | 10.1  |         |       | AOR 1.42 (0.62 - 3.27) – men   |
|                    |              | once a week             |                                                                                   |       |       |         |       |                               |
|                    |              | Local brew - No        |                                                                                   | 601   | 3.2   | 890     | 8     | AOR 1.42 (0.62 - 3.27) – men   |
|                    |              | Bottled alcohol - No    |                                                                                   | 502   | 2.2   | 779     | 7.7   | AOR 1.42 (0.62 - 3.27) – men   |
|                    |              | Bottled alcohol - Yes   |                                                                                   | 99    | 10.1  | 111     | 13.6  | AOR 1.42 (0.62 - 3.27) – men   |
|                    |              | Bottled alcohol - No    |                                                                                   | 581   | 2.9   | 864     | 8.4   | AOR 1.42 (0.62 - 3.27) – men   |
|                    |              | Bottled alcohol - Yes   |                                                                                   | 20    | 20.2  | 26      | 8.7   | AOR 1.42 (0.62 - 3.27) – men   |
conducted in Kisumu, western Kenya (Hargreaves et al., 2002). For both males and females aged 25 - 49 years, the consumption of alcohol in the last month was significantly associated with HIV infection. Among males aged 25 - 49 years ($N=306$), for those who drank alcohol in the last month HIV prevalence was 37.6%, compared with 26% for those who had not (AOR 1.9, 95% CI: 1.1-3.2). Among females ($N=466$) aged 25 - 49 years, HIV prevalence was 42.3% among those who drank alcohol in the last month, compared with 28.5% for those who had not (AOR 1.9, 95% CI: 1.0-3.3).

To investigate the prevalence of and risk factors for HIV infection, a community cross-sectional study was conducted in August 1998 among 834 women in Carletonville, South Africa (Zuma, Gouws, Williams & Lurie, 2003). The overall HIV prevalence was 37.1% ($N=701$). Alcohol use in the past 4 weeks was shown to be independently associated with HIV infection. For those who had used alcohol less than once a day in the past 4 weeks, 43.9% were HIV+ (AOR 1.58, 95% CI: 1.05-2.38), and for those that had used alcohol at least once a day in the past 4 weeks, 48.6% were HIV+ (AOR 1.88, 95% CI: 1.07-3.33), compared with non-users of alcohol. HIV prevalence among those who had not used alcohol in the past 4 weeks was 33%. However, a different study among the same sample population only found a significant difference in HIV prevalence between those who had consumed alcohol and those who had never consumed alcohol, regardless of frequency of drinking (daily, weekly or monthly) (Campbell, Williams & Gilgen, 2002).

A cross-sectional study was conducted in Epworth, Zimbabwe, to determine the overall prevalence of HIV and psychiatric disorders and their related risk factors among 194 adults in this less affluent community (Sebit et al., 2003). Two sample populations and two sampling methods for subject recruitment were used. The first sample comprised of 101 subjects who claimed to be HIV+, and the second sample comprised of 93 subjects who were unaware of their HIV status and were recruited by systematic random sampling from a population of houses. Overall the HIV prevalence was 59.3% ($N=194$). Alcohol consumption, dependence symptoms, personal and social harm reflective of drinking were measured using the AUDIT (Babor et al., 1992). No significant differences were found between alcohol users and non-users and socio-demographic factors with regards to HIV prevalence. AUDIT scores were not significantly different between those with and without HIV infection when comparisons were made between users and non-users or even between hazardous and harmful drinkers. The overall prevalence of alcohol use/misuse was 21.1% ($N=41$), with higher prevalence among HIV+ subjects (24.3%; $N=28$) than those who were HIV- (16.5%; $N=13$). Among those that
Table 3. Characteristics of the 5 studies of high-risk groups

| Reference         | Country     | Alcohol use definition                  | Study population                                           | # Men | % HIV | # Women | % HIV | Relative measure with 95% CI                           |
|-------------------|-------------|----------------------------------------|------------------------------------------------------------|-------|-------|---------|-------|-------------------------------------------------------|
| Fritz et al., 2002| Zimbabwe    | Frequency in last 30 days & at least 1 episode of sex while intoxicated in last 6 months? | Male beerhall patrons, Harare                              | 324   | 29.6  | 225     | 26.2  | OR 1.7 (1.0 - 2.8) – prevalent HIV                     |
|                   |             |                                        |                                                            |       |       | 99      | 37.4  | OR 4.5 (1.0-19.4) – recent HIV seroconversion          |
| Kapiga et al., 2002| Tanzania   | Current use                            | Female bar & hotel workers, Moshi                          | 312   | 6.3   | 93      | 17.2  |                                                      |
|                   |             |                                        |                                                            |       |       | 129     | 24    | AOR 1.73 (0.82 - 3.68)                                 |
|                   |             |                                        |                                                            |       |       | 90      | 38.9  | AOR 2.56 (1.12 - 5.88)                                 |
| Ao et al., 2006   | Tanzania    | Current use (CAGE)                     | Female bar & hotel workers, Moshi                          | 1 042 | 19    | 274     | 9.5   |                                                      |
|                   |             |                                        |                                                            |       |       | 408     | 19.1  | AOR 1.37 (0.82 - 2.35)                                 |
|                   |             |                                        |                                                            |       |       | 179     | 22.9  | AOR 1.3 (0.7 - 2.42)                                   |
|                   |             |                                        |                                                            |       |       | 181     | 29.3  | AOR 1.92 (1.06 - 3.47)                                 |
| Watson-Jones et al., 2007 | Tanzania | Current use, alcoholic drinks per week | Female facility workers (16-24 years), northwest | 1 143 | 21    | 103     | 15    |                                                      |
|                   |             |                                        |                                                            |       |       | 51      | 24    | AOR 1.27 (0.9 - 1.9)                                  |
|                   |             |                                        |                                                            |       |       | 29      | 37    | AOR 2.37 (1.4 - 4.1)                                  |
|                   |             |                                        |                                                            |       |       | 19      | 28    | AOR 1.46 (0.8 - 2.7)                                  |
|                   |             |                                        |                                                            |       |       | 35      | 38    | AOR 1.99 (1.2 - 3.4)                                  |
| Fisher et al., 2008| Tanzania   | Ever drink alcohol                     | Female bar & hotel workers, Moshi                          | 1 044 | 19    | 273     | 9.5   |                                                      |
|                   |             |                                        |                                                            |       |       | 771     | 22.4  | AOR 2.1 (1.29 - 3.42)                                 |
|                   |             |                                        |                                                            |       |       | 193     | 13    | AOR 2.2 (1.33 - 3.62)                                 |
|                   |             |                                        |                                                            |       |       | 578     | 25.6  | AOR 2.5 (1.52 - 4.11)                                 |
|                   |             |                                        |                                                            |       |       | 410     | 19    | AOR 1.79 (1.06 - 3.04)                                 |
|                   |             |                                        |                                                            |       |       | 361     | 26.3  | AOR 2.43 (1.45 - 4.6)                                 |
were HIV+ and used/misused alcohol, a significant difference was found between those who had two or more sexual partners versus only one sexual partner (64.3% v. 35.7%; OR 3.0, 95% CI: 1.13-8.28).

As part of an ongoing study to identify risky places for targeting HIV prevention activities, the role of beer halls in the HIV epidemic was assessed in rural Zimbabwe (Lewis et al., 2005). The stratified population-based survey collected data between July 1998 and January 2000 on the self-reported number of visits to beer halls in the last month, together with socio-demographic characteristics, sexual risk behaviours and HIV infection levels. Fifty-two per cent of men had visited a beer hall in the last month, but only 3.7% of women had done so. Overall HIV prevalence among males (N=3,317) was 23.1% and among females (N=3,840) it was 30.8%. HIV prevalence among sexually active men who had visited a beer hall in the last month was 27.8%, in comparison to 16.9% for those who had not, and for women these figures were 52.2% versus 29.9%, respectively. The associations remained significant in the multivariate analysis which controlled for age, marital status and both short-term and long-term sexual behaviour (men: AOR 1.4, 95% CI: 1.2-1.7; women: AOR 1.4, 95% CI: 1.0-2.1).

A community-based study was conducted between November 2002 and March 2003 to determine the predictors of HIV-1 infection among women aged 20 - 44 years (N=1,418) and their regular male partners (N=566) in Moshi, northern Tanzania (Kapiga et al., 2006). HIV prevalence was 10.3% among women and 7% among their long-term male partners. Univariate analysis found that during the previous year physical violence (26.9%) and sexual violence/sexual coercion in the past and HIV prevalence was examined in a sample of young women from a population-based cohort in Rakai, Uganda (Zablotska et al., 2006). Interviews took place during 2001 - 2003 and the sample comprised of 3,422 women aged 15 - 24 years. Results indicated that during the previous year physical violence (26.9%) and sexual coercion (13.4%) were common, and that the use of alcohol by at least one partner before sex was associated with a
higher risk of physical violence/sexual coercion. HIV prevalence was 7% overall and 4.5% among those who reported no prior sexual coercion or alcohol use before sex. In the multivariate analysis, HIV prevalence was found to be significantly higher among women who reported alcohol use before sex (8.9% HIV+; AOR 1.45, 95% CI: 1.06-1.98), and in particular when women reported both prior sexual coercion and alcohol use before sex (12.2% HIV+; AOR 1.79, 95% CI: 1.25-2.56). Although HIV incidence was also higher among women who reported the use of alcohol before sex or sexual coercion in the previous year, the results were not significant due to the small size of these groups.

Studies of high-risk groups
From April to August 2000 alcohol use as the primary risk factor for HIV infection was examined among a cross-sectional sample of male beer hall patrons in the high-density localities surrounding Harare, Zimbabwe (Fritz et al., 2002). Among the 324 men recruited, HIV prevalence was 29.6% and increased with increasing frequency of alcohol use. The prevalence of HIV was 11.1% among men reporting no alcohol use in the last 30 days, 22% among men drinking 1 - 5 days, 23.8% among men drinking 6 - 10 days, 37.7% among men drinking 11 - 15 days, and 40.7% among men drinking on more than 15 days of the last 30 days. Men who reported drinking to intoxication on at least one day in the last month were more likely to be HIV+ than those who had not (34% v. 18%, p=0.054). Having at least one episode of sex while intoxicated in the previous 6 months was reported by 31% of men, and was significantly associated with recent HIV seroconversion (7.5% v. 1.8%, p=0.047). After adjustment for the cluster sampling design, having sex while intoxicated was significantly associated with prevalent HIV infection (OR 1.7, 95% CI: 1.0-2.8, p=0.048) and with recent HIV seroconversion (OR 4.5, 95% CI: 1.0-19.4, p =0.046).

From June to October 2000, a pilot study to determine the prevalence and risk factors for HIV-1 infection among female bar and hotel workers in Moshi, northern Tanzania, was conducted (Kapiga et al., 2002). Of the 312 study participants with complete data, 26.3% were HIV-1 seropositive, and 70.2% reported that they currently drank alcohol. The risk of HIV-1 was positively associated with increasing frequency of alcohol intake in both the univariate and multivariate analysis. HIV prevalence for those who did not drink was 17.2%, and among those who reported drinking alcohol about once a week it was 24% (AOR 1.73, 95% CI: 0.82-3.68). Drinking alcohol at least twice a week was a significant risk factor for HIV-1 infection among the women working in the bars and hotels, with 38.9% testing positive for HIV-1 (AOR 2.56, 95% CI: 1.12-5.88).

In continuation of the pilot study by Kapiga et al., (2002), 1 050 female bar/hotel workers were enrolled in an ongoing prospective cohort study between December 2002 and November 2003 in Moshi, northern Tanzania (Ao, Sam, Masenga, Seage & Kapiga, 2006). Data collected at baseline for 1 042 women was analysed to assess the associations between alcohol, sexual behaviour, STDs, and HIV-1 infection. In this study women were classified as having a probable drinking problem if they had a CAGE score (Ewing, 1984) of 2 and were considered to have a strong indication of problem drinking if their CAGE score was 3 - 4. HIV-1 prevalence in this cohort was 19%, and 34.6% were classified as having a probable or strong indication of problem drinking. Among the 26.3% of women who reported to have never used alcohol, 9.5% were HIV+. In comparison, among those who did not have a problem with alcohol use, 19.1% were HIV+ (AOR 1.37; 95% CI: 0.8-2.35), while among the 17.2% who were classified as having a probable drinking problem, 22.9% were HIV+ (AOR 1.3; 95% CI: 0.7-2.42). HIV prevalence was 29.3% among the 17.4% of women with a strong indication of problem drinking. The latter was shown to be an independent risk factor for HIV-1 in this population (AOR 1.92, 95% CI: 1.06-3.47).

From November 2003 to December 2005, the prevalence of and risk factors for herpes simplex virus type 2 (HSV-2) and HIV were determined among female facility workers being screened for a randomised controlled trial of HSV suppressive therapy in north-western Tanzania (Watson-Jones et al., 2007). HIV prevalence among female facility workers aged 16 - 24 years (N=1 143) was 21%, and was associated with increasing alcohol use. Interestingly, in comparison to those who did not drink (15% HIV+) the association was not significant among those women who reported drinking 1 - 4 (24% HIV+; AOR 1.27, 95% CI: 0.9-1.9) or 10 to 19 (28% HIV+; AOR 1.46,95% CI: 0.8-2.7) alcoholic drinks per week, but was significant among those women who reported drinking 5 - 9 (37% HIV+; AOR 2.37, 95% CI: 1.4-4.1) or ≥20 (38% HIV+; AOR 1.99, 95% CI: 1.2-3.4) alcoholic drinks per week.

A recent systematic review and meta-analysis of African studies of the reported risks associated with alcohol use and HIV found that alcohol users were 70% more likely to be HIV+ than non-users in the bivariate case, and 57% more likely when potential confounders were controlled for in the multivariate analysis. Men and women had comparable risk estimates, while studies among high-risk groups tended to report greater ORs than studies of the general population. In addition, a crude dose-response relationship was observed, with non-problem drinkers 57% and problem drinkers 104% more likely to be HIV+ than non-drinkers (Fisher et al., 2007). As a consequence
of the inherent limitations encountered during the review and meta-analysis, such as inconsistent measures of alcohol use across studies, Fisher, Cook, Sam and Kapiga, (2008) recently conducted an in-depth analysis of the baseline data collected during the aforementioned prospective cohort study of female bar/hotel workers in Moshi, northern Tanzania (see Ao et al., 2006). In the study by Fisher et al. (2008), drinkers were significantly more likely to be HIV+ when compared with non-drinkers (22.4% HIV+ v. 9.5% HIV+; AOR 2.1; 95% CI: 1.29-3.42). Drinkers who had consumed alcohol in the past month (recent drinkers) (25.6% HIV+; AOR 2.5, 95% CI: 1.52-4.11) and less recent drinkers (13% HIV+; AOR 2.2, 95% CI: 1.33-3.62) were also significantly more likely to be HIV+ than non-drinkers. The risk of HIV infection was found to be positively correlated with both the quantity (p<0.0001, test for linear trend) and frequency of alcohol consumed (p=0.0001, test for linear trend), as well as the number of affirmative responses to the CAGE questionnaire (p<0.0002, test for linear trend). Furthermore, problem drinkers were significantly more likely to be HIV+ than non-problem drinkers when compared with non-drinkers (26.3% HIV+; AOR 2.43, 95% CI: 1.45-4.6 v. 19% HIV+; AOR 1.79, 95% CI: 1.06-3.04). In this particular study problem drinkers were defined as those with a CAGE score of 2-4. The greatest risk of being HIV+ was among those women with a CAGE score of 4 (50% HIV+; AOR 6.8, 95% CI: 2.59-17.88).

In addition to the above, the following studies also conducted in sub-Saharan Africa since 2000 provided evidence of a positive relationship between alcohol use and HIV status. Clift et al. (2003) found that female food and recreational facility workers (FRFWs) from communities surrounding gold mines near Lake Victoria in Tanzania were, in comparison to other women in the community, significantly more likely to be HIV+ (41.8% v. 17.6%, p<0.001). Among the FRFWs, being HIV+ was independently associated (36.1% HIV+ v. 13.3% HIV+; AOR 2.5, 95% CI: 1.1-5.5) with high alcohol consumption (≥15 units per week). Findings from a study conducted among female sex workers in Mombasa, Kenya, found that women who had ever drunk were 1.99 times more likely to be HIV+ than lifetime abstainers (39.9% v. 23.2%; 95% CI: 1.31-3.03; p<0.001). However, no association was found between HIV prevalence and drinking patterns (Chersich et al., 2007). These findings corroborate those of the study conducted in Uganda by Mbuliatelye et al. (2000).

**Discussion**

Many regions in Africa, in particular sub-Saharan Africa, carry the double burden of high levels of HIV and alcohol-related morbidity and mortality (Rehm et al., 2003a; 2003b; UNAIDS, 2007). With increasingly more evidence that alcohol consumption plays a pivotal role in HIV infection and disease progression in sub-Saharan Africa, an improved understanding of alcohol use as a behavioural risk factor related to HIV in different sub-populations is critical, in order to reduce the further spread of the epidemic. Since both heavy alcohol consumption and HIV infection compromise the immune system, it is likely that in combination they may also increase the risk of subsequent opportunistic infections, thereby accelerating the progression of HIV to AIDS (Parry, Rehm, Poznyak & Room, 2009).

The relationship between alcohol use and HIV risk behaviours is complex, and is context- and community-specific. Outcomes are likely to vary depending on the situation, gender and age of the individual, cultural norms and practices, and individual physiological responses to alcohol (Kalichman et al., 2007a; Morojele et al., 2006; WHO, 2005). Many of these factors are subjective and difficult to quantify, and makes the comparative analysis between different countries or even within a given country a particularly challenging task (Heath, 2000). In addition, the effects of alcohol depend on the total cumulative quantities consumed, drinking patterns and drinking contexts, and lifestyles that are characterised especially by ‘heavy alcohol use’ can compound HIV risk through multiple channels (Chersich et al., 2007; Kalichman et al., 2007a; Morojele et al., 2004). Unfortunately, the distinction between alcohol use, abuse and dependence is often difficult, even though this is fundamental in the understanding of HIV risk behaviour (Kalichman et al., 2007a).

The purpose of this descriptive systematic review was to identify and describe studies that have analysed the association between alcohol consumption and HIV infection in sub-Saharan Africa. Twenty-one studies published between 2000 and 2008 that reported relative measures of the association between alcohol use and HIV prevalence and/or seroconversion rates were identified. As almost all of the studies were observational in design and used disparate definitions of alcohol use across various study populations, a descriptive analysis was selected to elicit any common themes emerging from the studies. The findings were primarily categorised and analysed according to three types of study population followed by a secondary analysis relating to gender, drinking pattern or drinking context.

Five studies were conducted among clinic/health facility attendees, and of these two studies conducted among pregnant women found that women who currently consumed alcohol were significantly more likely to be HIV+ than those who did not (Ayisi et al., 2000; Msuya et al., 2006). In addition, one of the studies found that women whose male partners consumed...
alcohol on a daily basis were significantly more at risk of HIV infection (Msuya et al., 2006). A study among TB patients found the use of alcohol before sex by either the respondent or their sex partner was significantly associated with being HIV+ (Talbot et al., 2002). In contrast, another study conducted among men and women receiving STI clinic services found no significant difference in HIV prevalence between those who had or had not used alcohol in sexual contexts in the previous month (Simbayi et al., 2004). An unmatched case control study among men and women visiting HIV testing and counselling centres found that persons who had used alcohol at some stage in their life were significantly more likely to be HIV+ than those who had never used alcohol (Seme et al., 2005).

Two of the community/population-based studies involving both men and women that used an ever use/never use dichotomy (last month or lifetime use) found that persons who had used alcohol were significantly more likely to be HIV+ than persons who had not used alcohol over the specified time period (Hargreaves et al., 2002; Mbalaiye et al., 2000). These findings conflict with those of another study that found no significant difference between current users and non-users of alcohol with regards to HIV prevalence (Sebit et al., 2003). The last study in this group found that the consumption of local brew or bottled alcohol at least once per week was significantly associated with HIV-1 infection among men, but not among women (Mmbaga et al., 2007). A different type of study found that men and women who had frequented a beer hall in the previous month were significantly more likely to be HIV+ than those who had not (Lewis et al., 2005).

A community-based study conducted among women and their regular male partners in Moshi, Tanzania, found that HIV prevalence was positively associated with increasing frequency of use among the women, but not among their regular male partners (Kapiga et al., 2006). Two further studies among women, one by Sa and Larsen, (2008) on the same data set, and another by Zuma et al. (2003) conducted in Carletonville, South Africa corroborated these findings. A later study among the aforementioned community in Moshi, Tanzania, found no significant relationship between HIV infection and alcohol abuse (CAGE score of 2 - 4) by women or men (Mitsunaga & Larsen, 2008).

Three of the five studies that were conducted among high-risk groups (e.g. male beer hall patrons, bar and hotel workers) found that HIV prevalence was positively associated with increasing frequency or quantity of alcohol use (Fritz et al., 2002; Kapiga et al., 2002; Watson-Jones et al., 2007). Another study conducted among a cohort of female bar and hotel workers found that problem drinking (as defined by CAGE) was an independent risk factor for HIV infection (Ao et al., 2006). A subsequent study using the same cohort revealed that both the quantity and frequency of alcohol consumed, as well as the number of affirmative responses to the CAGE questionnaire were related to HIV infection in a dose response manner (Fisher et al., 2008).

Five studies examined the use of alcohol either before or during sex. Of these, one study conducted among TB patients found that alcohol use before sex was significantly associated with being HIV+, whereas another study conducted among STI clinic patients found no significant difference between those who had or had not used alcohol in sexual contexts in the previous month and HIV prevalence (Simbayi et al., 2004; Talbot et al., 2002). One study conducted among beer hall patrons found that having sex while intoxicated in the previous 6 months was significantly associated with HIV prevalence and recent seroconversion (Fritz et al., 2002). These findings lend support to an earlier population-based study conducted in Tanzania that found that women who had engaged in sex under the influence of alcohol were more than twice as likely to be infected with HIV than those who did not (AOR 2.58, 95% CI: 1.17-5.69) (Mnyika, Klepp, Kvale & Ole-Kingori, 1996). Two recent studies examined the use of alcohol before sex among a large population-based cohort in Rakai, Uganda (Zablotska et al., 2006; 2009). One of these studies examined the association between alcohol use before sex (by at least one partner) and lifetime sexual coercion with prevalent HIV among young women (aged 15 - 24 years). The authors found that alcohol use before sex, and especially prior sexual coercion and alcohol use before sex, was significantly associated with prevalent HIV (Zablotska et al., 2009). In the other study the use of alcohol before sex was significantly associated with an increased risk of HIV acquisition among both women and men (Zablotska et al., 2006). Of relevance to the aforementioned theme is the finding from a recent study conducted among men and women receiving STI clinic services in Cape Town, South Africa, that the use of alcohol in sexual contexts was more likely to predict sexual risk behaviour (unprotected sex and number of sex partners) than either quantity or frequency of use. To complicate matters further, the pattern of association varied by sexual risk behaviour and gender suggesting that alcohol contributes differently to men and women's sexual risks for HIV (Kalichman, Simbayi, Jooste & Cain, 2007b).

To date, only a few studies with contradictory findings have investigated the effect of alcohol use on ART adherence in Africa. Preliminary evidence from South Africa has found that among a sample of HIV+ adults on ART, 32% were alcohol dependent (as evaluated by CAGE), with males significantly more likely to
have a lifetime history of alcohol abuse than women. A history of alcohol abuse was associated with increased odds of poor adherence (Selin, Mills & Nachega, 2007). An unmatched case control study conducted in Jimma, Ethiopia among ART users found that using alcohol ‘most of the time’ was independently associated with defaulting from ART when compared with controls (AOR 3.57, 95% CI: 1.78-7.14) (Deribe, Hailekiros, Biadgilign, Amberbir & Beyene, 2008). In this study, a control was an individual who had been on ART for at least 1 year and considered to be an excellent adherer by the providers, while a default case was defined as an HIV+ individual who had been on ART treatment and had missed two or more monthly clinical appointments during the period of register review. In contrast, an earlier cross-sectional study conducted in Kampala, Uganda among 304 HIV+ individuals on ART, found that the use of alcohol was not associated with ART adherence (Byakika-Tusime et al., 2005).

The findings of the above literature should be interpreted with caution due to the number of limitations in the various studies. Most of the studies were cross-sectional, relied on self-reported alcohol use, used a variety of alcohol measures over different time frames or in specific situations, making it difficult to determine causality or to know which pattern of alcohol consumption poses the greatest risk. The studies were also limited by sampling constraints that relied on small convenience samples, or were part of larger studies that were not focussed on the association between alcohol use and HIV. To confirm causality, future research should use prospective study designs, use clearly defined standardised measures of alcohol use and an ‘event-specific’ approach to examine the situational links between alcohol use and HIV acquisition. For example, a greater understanding of the role drinking venues play in exacerbating gender-based sexual violence/coercion and subsequent heightened risk of HIV acquisition would significantly contribute to the research base in sub-Saharan Africa.

Conclusion

Although the above studies provide strong evidence of the association between alcohol consumption and HIV infection, a causal relationship is problematic to establish in view of the fact that almost all of the studies were cross-sectional in design. As stated by Fisher et al. (2007, p. 860), ‘an equally plausible explanation for some or all of the observed associations is that people living with HIV drink more to cope with their circumstance’. Another hypothesis is that both the misuse of alcohol and sexual risk behaviour are coupled to a common third factor (e.g. risk-taking personality) that predisposes a particular individual to a variety of risk behaviours. Nonetheless, the overall consistency of results across all three broad study populations, the crude dose-response relationship between alcohol use and HIV infection, the biological plausibility, and especially the finding that alcohol use before sex is an important risk factor for HIV acquisition, all indicate that alcohol use is more likely to be a cause than a consequence of HIV infection. In the event that causality cannot be determined with certainty, their observed association still dramatically compounds the negative consequences than if either were present alone.

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