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Global burden of HIV/AIDS in 2004 resulting from non-adherence to medication regimes and alcohol-attributable non-adherence to medication regimes

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Abstract

Aims: Using novel methodology, this article aims to quantify the number of HIV/AIDS-related deaths and the potential years of life lost (PYLL) in 2004 resulting from non-adherence to antiretroviral treatment (ART) and non-adherence to ART due to alcohol consumption.

Design: HIV/AIDS-related deaths and PYLL attributable to non-adherence to ART and attributable specifically to non-adherence due to alcohol consumption were calculated using attributable fractions. These fractions were based on new risk modeling methodology, which combines estimates of the mortality of those people currently adhering to ART, the mortality attributable to non-adherence to ART, and the proportion of those people not adhering to ART because of alcohol consumption.

Measurements: Data on alcohol indicators were obtained from the Comparative Risk Assessment study, data on deaths and PYLL were obtained from the World Health Organization, and ART indicators were obtained from UNAIDS.

Findings: In 2004, for people 15 years of age and older, 67,000 (95% CI: 62,000–72,000) deaths and 1,608,000 (95% CI: 1,491,000–1,725,000) PYLL were caused by non-adherence to ART, of which 8,000 (95% CI: 3,000–13,000) HIV/AIDS-related deaths and 187,000 (95% CI: 70,000–304,000) HIV/AIDS-related PYLL were attributable to alcohol consumption.

Conclusions: As the burden of disease for HIV/AIDS-related deaths attributable to non-adherence to ART and attributable to alcohol consumption is non-trivial, additional research is required to examine the effectiveness of different interventions aimed at reducing alcohol consumption among people with HIV/AIDS and at increasing adherence to ART among both drinkers and non-drinkers.

The global burden of HIV/AIDS is substantial, with an estimated 2.8 million new HIV infections, 2.0 million HIV-attributable deaths, and 58.5 million disability-adjusted years of life lost (a combination of years of life lost due to premature mortality and years lived with disability) due to HIV/AIDS in 2004 (World Health Organization [WHO], 2008). During the 2004 Global Burden of Disease (GBD) study, evidence was not available for a causal relationship between alcohol consumption and the probability of becoming infected by HIV and worsening of disease course for people with HIV/AIDS, so previous iterations of the Comparative Risk Assessment (CRA) study (a study that compares the impact of various modifiable risk factors on death and disability) did not include HIV/AIDS in the estimates of the alcohol-attributable burden of disease (Rehm et al., 2010; WHO, 2009).

This lack of causal evidence was in part attributable to the lack of research on how personality factors confound and/or mediate the relationship between alcohol consumption and the probability of HIV/AIDS (Dingle & Oei, 1997; Shuper et al., 2010; Stall & Leigh, 1994). To control for these personality factors Rehm, Shield, Joharchi, and Shuper (2012) performed a meta-analysis, combining results from different randomized controlled studies. This study found a causal relationship between alcohol consumption and unsafe sex, which leads to an increased probability of acquiring HIV through sexual transmission (see Rehm et al., 2012, for the causal relationship between alcohol consumption and unsafe sex, and Baliunas, Rehm, Irving, & Shuper, 2010, and Fisher, Bang, & Kapiga, 2007, for the magnitude of the association). In addition to this causal association, alcohol consumption has

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been shown to affect susceptibility to HIV infection by weakening the immune system (Baliunas et al., 2010; Braithwaite et al., 2005; Hahn & Samet, 2010; Neuman, Monteiro, & Rehm, 2006; Shuper, Joharchi, Irving, & Rehm, 2009; Shuper et al., 2010). Although a causal association exists between alcohol consumption and acquiring HIV/AIDs through sexual transmission, estimation of the burden of HIV/AIDS due to alcohol-attributable acquired HIV infections is currently not possible as the methodology to calculate this burden does not exist.

In addition to a causal relationship between alcohol consumption and acquiring HIV though sexual transmission, there is sufficient causal evidence that alcohol worsens the disease course of HIV/AIDS and can subsequently increase the likelihood of mortality, especially by impacting adherence to antiretroviral treatment (ART) (Azar, Springer, Meyer, & Altice, 2010; Braithwaite et al., 2007; Gmel, Shield, & Rehm, 2010; Hendershot, Stoner, Pantalone, & Simoni, 2009). Specifically in a meta-analysis of alcohol and ART adherence, individuals who indicated that they had consumed alcohol within the past year were approximately 60% (*OR* = 0.60, CI: 0.53–0.69) as likely to be adherent to ART as were non-drinkers. Drinkers whose alcohol consumption patterns were problematic were approximately 47% (*OR* = 0.47, CI: 0.41–0.55) as likely to be adherent to ART as were non-problematic drinkers or abstainers (Hendershot et al., 2009). This association is also supported by previous research, which has found that ART doses were missed most frequently among binge drinkers and that the relative frequency of these missed doses occurred on binge drinking days (Braithwaite et al., 2005).

Given the association between alcohol consumption and non-adherence to ART, and given the significant impact of ART non-adherence on mortality (e.g., Garcia de Olalla et al., 2002; Lima et al., 2008; Lima et al., 2009; Nachega et al., 2006) it is the objective of this paper to estimate the deaths and potential years of life lost (PYLL) caused by HIV/AIDS due to non-adherence to ART and non-adherence to ART attributable to alcohol consumption.

Method

The methodology employed in this investigation consisted of the following two main steps: (1) calculation of non-adherence attributable fractions (NAdAFs) and alcohol-attributable fractions (AAFs) by age, sex, and region; and (2) application of the NAdAFs and AAFs to region-, age-, and sex-specific mortality, and to region-, age-, and sex-specific PYLL.

Definition of regions and population data

The GBD regions (2005) are based on geography, child and adult mortality, and major causes of death (Institute for Health Metrics and Evaluation [IHME], 2010; see http://www.globalburden.org/gbdops.html for the countries included in each region). Population estimates by country for 2004 were based on data obtained from the 2008 revisions of the United Nations Population Division (2010).

Definition of age categories

Three age categories were used in the CRA study: 15–34, 35–64, and 65 years of age or older. Ages were clustered so as to be comparable to the 2005 GBD study (IHME, 2010).

Measures of alcohol consumption

Data on alcohol use for 2005 were compiled for the GBD regions based on drinking status. Current drinkers were defined as people who had consumed at least one drink in the past year, and current abstainers were defined as people who had not consumed alcohol within the past year. Data on drinking status were obtained from large representative population surveys taken in the 2000s (WHO, 2011). The prevalence of heavy drinkers, defined as those consuming on average 40 or more grams of alcohol per day for women (3.33 standard drinks or more per day) and 60 or more grams of alcohol per day for men (5 standard drinks or more) was calculated based on methods developed by Kehoe and colleagues, whereby the distribution of average daily consumption of alcohol is estimated based on 80% of the mean alcohol consumption for men and women (allowing 20% for alcohol not consumed due to spillage, breakage, and waste, and to account for the underreporting of alcohol consumption commonly seen in surveys (Kehoe et al., 2012; Shield & Rehm, 2012).

Measures of the prevalence of antiretroviral therapy

Country data on the proportion of people who were in need of ART and who were also receiving ART were obtained for 2005 from the 2006 Report on the Global AIDS Epidemic (UNAIDS, 2006). Regional data were then estimated based on a population-weighted average. The prevalence of those in need of antiretroviral treatment who were also receiving treatment, by region, is outlined in Appendix Table 1.

The prevalence of people adhering to antiretroviral therapy was estimated to be 40.1% (95% CI: 36.9%–43.3%), provided by Lima and colleagues (2008). This estimate was similar to two other estimates of 47.6% and 31.8% for adherence rates of less than 80% and less than 90% respectively (Garcia de Olalla et al., 2002; Nachega et al., 2006).

Measures of risk

Multiple risk measures were used in calculating the association between alcohol consumption and HIV/AIDS-related mortality from non-adherence to ART. To characterize the association between alcohol consumption and ART adherence, the odds ratio (*OR*) of 0.60 (95% CI: 0.53–0.69), comparing the odds of adherence by drinkers versus non-drinkers, was based on results from a meta-analysis performed by Hendershot and colleagues (2009). To calculate the AAF of HIV/AIDS-related mortality due

to heavy consumption of alcohol, we performed a sensitivity analysis where people who were considered heavy consumers of alcohol had an *OR* of 0.47 (95% CI: 0.41–0.55) (in this sensitivity analysis, as no alternative existed, the above-noted *OR* of 0.60 was used for non-heavy drinkers (Hendershot et al., 2009)). Since no meta-analyses exist of the association between non-adherence and mortality, we used a hazards ratio (HR) for mortality of 3.13 (95% CI: 1.95–5.05) for people not adhering to ART compared to people who adhere to their ART regime (where non-adherence is defined as adhering to ART less than 95% of the time (Lima et al., 2009)). This HR was similar to findings from two other studies, which observed HRs of 3.2 and 3.9 for adherence rates of less than 80% and less than 90% respectively (Garcia de Olalla et al., 2002; Nachega et al., 2006) for the mortality of people on ART compared to those who were not on ART.

Step 1: Calculation of the NAdAFs and AAFs by sex and by alcohol consumption

The AAF for mortality due to non-adherence to ART was calculated using three composite measures: (1) the adherence attributable fraction (AdAF), (2) the non-adherence due to alcohol attributable fraction (NAAAF), and (3) the proportion of deaths of people undergoing treatment (PDT).

AAFs were calculated as follows:

$$AAF = AdAF * NAAAF * PDT$$

NAdAFs were calculated using two of the above-noted composite measures as follows:

$$NAdAFs = AdAF * PDT$$

The AdAF, defined as the fraction of HIV/AIDS-related deaths attributable to non-adherence to antiretroviral therapy, using a definition of non-adherence as adherence to ART less than 95% of the time, was calculated as follows:

$$AdAF = \frac{P_{adher} + P_{na} RR_{na} - 1}{P_{adher} + P_{na} RR_{na}}$$

where P_{adher} is the proportion of people adhering to ART more than 95% of the time, P_{na} is the proportion of people adhering to treatment less than 95% of the time, and RR_{na} is the relative risk of mortality for those people not adhering to medication compared to those people who follow a treatment regime.

The NAAAF, defined as the proportion of non-adherence due to alcohol consumption, was calculated as follows for all HIV/AIDS-related deaths due to alcohol consumption:

$$NAAAF = \frac{P_{abs} + P_{drink}\, RR_{drink} - 1}{P_{abs} + P_{drink}\, RR_{drink}}$$

and as follows for all HIV/AIDS-related deaths due to heavy alcohol consumption:

$$NAAAF = \frac{P_{abs} + P_{H\_drinker}\, RR_{H\_drinker} + P_{NH\_drinker} - 1}{P_{abs} + P_{H\_drinker}\, RR_{H\_drinker} + P_{NH\_drinker}\, RR_{drinker}}$$

where P_{drink} is the proportion of current drinkers, P_{abs} represents the current abstainers among the antiretroviral-treated HIV population, $P_{H\_drinker}$ represents the prevalence of heavy drinkers in the population, $P_{NH\_drinker}$ represents the prevalence of heavy drinkers, and RR_{drink} represents the relative risk of not adhering to ART for a current drinker compared to a current abstainer.

Defined as PDT, the proportion of HIV/AIDS-related deaths of those people currently under treatment compared to those who are under treatment was calculated as follows:

$$PDT = \frac{P_{treat}}{P_{treat} + HR_{nontreat} P_{nontreat}}$$

where P_{treat} is the proportion of HIV-infected people who are in need of ART and who are receiving it, $P_{nontreat}$ is the proportion of HIV-infected people who are in need of ART and who are not receiving it, and $HR_{nontreat}$ is the hazards ratio for mortality of those people not adhering to ART compared to those who are adhering to ART.

Estimation of the variances of the NAdAFs and AAFs

The variances of the NAdAFs and AAFs were estimated by using the variance of each parameter making up the final expression. Specifically, the variances of AdAF, NAAAF, and PDT were first estimated using the variances of the parameters used in calculating each of these measures. Next, the variance estimates of AdAF and PDT were used to estimate the variances of NAdAFs, and the variance estimates AdAF, NAAAF, and PDT were used to estimate the variances of the AAFs for each region by age and by sex. For the formulas used to calculate the variance of the AAFs, see Gmel et al., 2010.

Step 2: Application of the NAdAFs and AAFs to region-, age-, and sex-specific mortality data, and to region-, age-, and sex-specific PYLL data

This step required multiplying the sex-, age-, and region-specific NAdAFs and AAFs by mortality data and by PYLL data, respectively.

Estimates of mortality and morbidity

To quantify the burden of disease attributable to alcohol consumption we used an event-based measure (mortality) and time-based measures (PYLL). Comprehensive revision estimates of mortality and PYLL for 2004 were provided by WHO (2008) for the 160 GBD disease and injury

Table 1a

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 (Men)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	12	11	14	32	28	36	3	3	3
Asia, Central	6	5	7	6	5	7	0	0	0
Asia, East	304	266	342	488	425	551	6	6	7
Asia, South	485	464	505	419	394	444	4	4	5
Asia, Southeast	1,686	1,567	1,805	2,318	2,179	2,457	31	29	32
Australasia	4	3	4	13	11	14	2	2	2
Caribbean	417	368	466	801	709	892	28	25	30
Europe, Central	31	28	35	37	32	41	2	2	3
Europe, Eastern	103	89	117	138	119	157	2	2	2
Europe, Western	247	216	278	702	610	794	65	58	73
Latin America, Andean	207	183	231	265	232	299	4	4	4
Latin America, Central	1,042	943	1,141	1,412	1,258	1,566	45	41	49
Latin America, Southern	155	135	175	298	261	335	18	16	20
Latin America, Tropical	1,127	1,007	1,248	2,012	1,831	2,194	84	79	89
Northern Africa / Middle East	51	49	52	57	55	60	1	1	1
North America [High Income]	411	362	460	1,656	1,465	1,847	117	106	128
Oceania	7	6	8	13	12	15	0	0	0
Sub-Saharan Africa, Central	84	75	94	165	146	183	4	4	4
Sub-Saharan Africa, East	1,974	1,852	2,097	4,490	4,106	4,873	162	148	175
Sub-Saharan Africa, Southern	2,912	2,672	3,152	6,556	6,015	7,096	163	152	174
Sub-Saharan Africa, Western	902	829	976	2,019	1,810	2,227	68	62	74
World	12,167	11,127	13,207	23,896	21,703	26,089	809	742	875

categories. Methods to estimate the mortality and the PYLL in the GBD project are described elsewhere (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006a, 2006b). Estimates of mortality and of PYLL were available for each country by age and sex and were used to calculate region estimates. This meant that for each region, sex-, injury-, and consumption-specific AAFs were applied to sex- and injury-specific outcome data.

We used the 2004 estimate as it is the last estimate from the GBD study, and thus has been processed for coherence with other causes of death and consistency, and corrected for comparability between regions (WHO, 2008; see also Lopez et al., 2006b, for a general description of GBD methodology).

All statistics and analyses were performed using R version 2.11.1.

Results

The mortality and PYLL caused by non-adherence to ART are outlined in Tables 1a and 1b, and Tables 2a and 2b respectively. In 2004 an estimated 67,386 (95% CI: 62,391–72,380) deaths and 1,680,155 (95% CI: 1,491,000–1,725,000) PYLL were caused by HIV/AIDS-related mortality due to non-adherence to ART for people 15 years of age and older, representing 3.30% (95% CI: 3.06%–3.55%) of all deaths and 3.07% (95% CI: 2.84%–3.29%) of all PYLL caused by HIV/AIDS. Men had a slightly higher rate of HIV/AIDS-related deaths and PYLL due to non-adherence to ART, with the age groups of 15-34 and 35–64

Table 1b

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 (Women)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	3	3	4	4	3	4	1	1	1
Asia, Central	1	1	1	1	1	1	0	0	0
Asia, East	87	80	94	107	99	116	3	2	3
Asia, South	174	172	177	107	105	109	3	3	3
Asia, Southeast	533	518	547	565	554	577	16	16	17
Australasia	1	1	1	1	1	1	0	0	0
Caribbean	278	253	304	357	334	379	12	12	13
Europe, Central	19	17	21	11	10	12	0	0	0
Europe, Eastern	29	26	32	32	28	35	1	1	1
Europe, Western	80	70	90	171	149	192	14	13	15
Latin America, Andean	63	57	68	62	56	68	2	2	2
Latin America, Central	320	296	343	333	309	357	11	10	12
Latin America, Southern	54	47	60	75	67	82	4	3	4
Latin America, Tropical	625	570	680	997	925	1,068	47	45	49
Northern Africa / Middle East	15	14	15	13	13	13	0	0	0
North America [High Income]	194	172	216	578	517	639	37	35	40
Oceania	4	3	4	5	4	5	0	0	0
Sub-Saharan Africa, Central	154	141	166	206	191	221	5	5	6
Sub-Saharan Africa, East	3,615	3,447	3,782	5,367	5,031	5,703	114	107	120
Sub-Saharan Africa, Southern	4,478	4,303	4,653	6,599	6,302	6,897	157	152	163
Sub-Saharan Africa, Western	1,524	1,439	1,609	2,196	2,035	2,358	49	46	52
World	12,250	11,631	12,869	17,787	16,735	18,840	477	454	500

having the greatest burden. The deaths and PYLL attributable to HIV/AIDS from not adhering to antiretroviral therapy by GBD region for 2004 per 10,000,000 people are outlined in Appendix Tables 2a and 2b. The Sub-Saharan Africa Southern, region had the highest number of HIV/AIDS-related deaths and PYLL per 10,000,000 people due to non-adherence to ART, with an estimated 3,530.92 (95% CI: 3,311.90–3,749.94) deaths per 10,000,000 people and 81,949 (95% CI: 76,948–86,949) PYLL per 10,000,000 people. In contrast, the Asia South region had the lowest number of HIV/AIDS-related deaths and PYLL per 10,000,000 people due to non-adherence to ART, with an estimated 1.95 (95% CI: 1.71–2.18) deaths per 10,000,000 people and 50 (95% CI: 44–56) PYLL per 10,000,000 people.

The prevalence of current abstainers and current drinkers designated by levels of alcohol consumption, age, and sex is outlined in Tables 3a and 3b. The prevalence of current drinkers and current abstainers varied greatly by region, age, and sex, with men having the largest prevalence of current drinkers in all regions. Overall, for both men and women, the age groups of 15 to 34 and of 35 to 64 years had the highest prevalence of current drinkers and heavy drinkers in all regions.

HIV/AIDS-related deaths due to non-adherence to ART because of alcohol consumption by GBD region, age, and sex are presented in Tables 4a and 4b. Overall, 8,000 (95% CI: 3,000–13,000) HIV/AIDS deaths from non-adherence to ART were attributable to alcohol consumption. This can

Table 2a

Potential years of life lost to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 (Men)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	340	296	384	619	541	697	23	21	26
Asia, Central	178	158	197	131	113	148	1	0	1
Asia, East	8,801	7,704	9,898	10,453	9,108	11,798	55	49	62
Asia, South	14,813	14,184	15,441	9,262	8,704	9,820	36	35	38
Asia, Southeast	49,621	46,110	53,132	49,548	46,576	52,519	256	243	270
Australasia	92	80	104	250	217	284	13	12	15
Caribbean	11,694	10,326	13,062	16,753	14,835	18,672	221	205	238
Europe, Central	980	865	1,094	785	688	881	17	15	19
Europe, Eastern	3,071	2,641	3,501	2,900	2,506	3,295	18	16	20
Europe, Western	6,337	5,536	7,138	14,482	12,582	16,382	450	396	504
Latin America, Andean	6,117	5,412	6,823	5,686	4,970	6,402	32	30	34
Latin America, Central	30,686	27,757	33,614	30,210	26,910	33,510	352	322	383
Latin America, Southern	4,335	3,777	4,892	6,371	5,586	7,156	144	128	160
Latin America, Tropical	31,822	28,411	35,232	43,022	39,140	46,904	637	600	675
Northern Africa / Middle East	1,523	1,481	1,564	1,242	1,195	1,289	5	5	6
North America [High Income]	10,491	9,238	11,745	31,507	27,877	35,138	898	813	984
Oceania	187	161	212	289	251	327	2	2	2
Sub-Saharan Africa, Central	2,387	2,117	2,657	3,455	3,060	3,850	37	34	39
Sub-Saharan Africa, East	54,459	51,073	57,846	92,700	84,781	100,619	1,416	1,299	1,534
Sub-Saharan Africa, Southern	79,375	72,831	85,920	136,938	125,648	148,228	1,475	1,373	1,577
Sub-Saharan Africa, Western	25,042	22,998	27,086	41,622	37,318	45,926	615	560	669
World	342,350	313,157	371,543	498,226	452,606	543,847	6,705	6,158	7,253

be broken down into 5,600 (95% CI: 2,300–8,900) HIV/AIDS-related deaths in men and 2,400 (95% CI: 800–4,100) HIV/AIDS-related deaths in women from non-adherence to ART attributable to alcohol consumption. This represents 0.39% (95% CI: 0.15%–0.64%) of all HIV/AIDS-related deaths, 0.54% (95%CI: 0.22%–0.86%) of all HIV/AIDS-related deaths for men, and 0.24% (95% CI: 0.07%–0.41%) of all HIV/AIDS-related deaths for women. Of these totals, 2,646 (1,898 for men and 748 for women) HIV/AIDS-related deaths were attributable to heavy alcohol consumption. Thus an estimated 11.9% (15.1% for men and 8.0% for women) of all HIV/AIDS-related deaths from non-adherence to ART were attributable to alcohol consumption and 3.93% (5.15% for men and 2.45% for women) of all HIV/AIDS-related deaths from non-adherence to ART were attributable to heavy alcohol consumption. The alcohol-attributable fractions for HIV from not adhering to ART because of alcohol consumption by GBD region for 2004 are outlined in Appendix Tables 3a and 3b. The deaths attributable to HIV/AIDS from not adhering to ART because of heavy alcohol consumption by GBD isease region for 2004 is outlined in Appendix Tables 4a and 4b.

The number of HIV/AIDS-related deaths per 10,000,000 people attributable to non-adherence to ART due to alcohol consumption and to heavy alcohol consumption are presented in Figures 1 and 2 respectively. The Sub-Saharan Africa, Southern, region had the highest rate of HIV/AIDS-related deaths from non-adherence to ART because of alcohol consumption, with 320.39 (95% CI: 101.37–539.40) deaths per 10,000,000 people, of which

Table 2b

Potential years of life lost to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 (Women)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	101	88	114	84	74	94	3	3	3
Asia, Central	39	36	42	24	21	27	0	0	0
Asia, East	2,599	2,384	2,813	2,414	2,215	2,613	23	21	24
Asia, South	5,458	5,376	5,540	2,487	2,443	2,532	24	24	24
Asia, Southeast	16,116	15,676	16,556	12,685	12,422	12,949	144	142	146
Australasia	22	19	25	25	22	28	1	1	2
Caribbean	8,195	7,452	8,938	8,130	7,616	8,643	106	102	109
Europe, Central	619	547	690	264	235	292	0	0	0
Europe, Eastern	885	782	987	679	602	755	12	11	13
Europe, Western	2,192	1,920	2,464	3,776	3,302	4,251	104	95	114
Latin America, Andean	1,903	1,727	2,079	1,399	1,267	1,531	16	15	17
Latin America, Central	9,692	8,971	10,412	7,479	6,945	8,014	99	93	105
Latin America, Southern	1,581	1,397	1,765	1,674	1,505	1,842	34	30	37
Latin America, Tropical	18,153	16,558	19,749	21,861	20,298	23,424	379	361	397
Northern Africa / Middle East	446	438	454	292	289	294	3	3	3
North America [High Income]	5,235	4,646	5,824	11,813	10,561	13,064	278	260	297
Oceania	110	101	119	110	100	121	1	1	1
Sub-Saharan Africa, Central	4,529	4,160	4,899	4,660	4,314	5,006	52	49	54
Sub-Saharan Africa, East	104,754	99,889	109,619	121,551	113,937	129,165	1,062	1,002	1,122
Sub-Saharan Africa, Southern	129,312	124,259	134,365	149,326	142,597	156,055	1,493	1,443	1,542
Sub-Saharan Africa, Western	44,327	41,866	46,788	49,574	45,927	53,221	467	436	498
World	356,268	338,294	374,243	400,307	376,691	423,923	4,298	4,091	4,505

154.54 (95% CI: 59.46–249.63) were caused by heavy alcohol consumption. The Northern Africa/Middle East region had the lowest rate of HIV/AIDS-related deaths from non-adherence to ART because of alcohol consumption, with 0.11 (95% CI: 0.01–0.22) deaths per 10,000,000 people, of which 0.03 (95% CI: 0.01–0.05) were attributable to heavy alcohol consumption.

PYLL caused by non-adherence to ART because of alcohol consumption for both men and women by GBD region are outlined in Tables 5a and 5b. In 2004 there were an estimated 187,000 (95% CI: 70,000–304,000) PYLL from not adhering to ART because of alcohol consumption. This indicates that 0.36% (95% CI: 0.13%–0.58%) of all PYLL are caused by non-adherence to ART due to alcohol consumption. This can be broken down into 127,000 (95% CI: 51,000–202,000) PYLL, representing 0.31% (95% CI: 0.03%–0.69%) of all PYLL caused by HIV/AIDS for men, and 60,000 (95% CI: 18,000 to 102,000) PYLL, representing 0.22% (95% CI: 0.07%–0.38%) of all PYLL caused by HIV/AIDS for women. Thus, an estimated 11.6% (15.0% for men and 7.9% for women) of all HIV/AIDS-related PYLL from non-adherence to ART were attributable to alcohol consumption and 3.80% (5.06% for men and 2.41% for women) of all HIV/AIDS-related PYLL from non-adherence to ART were attributable to heavy alcohol consumption. The PYLL attributable to HIV/AIDS from not adhering to ART because of heavy alcohol consumption by GBD region for 2004 is outlined in Appendix Tables 5a and 5b.

Table 3a

Drinking indicators by Global Burden of Disease region for 2005 (Men)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Current drinkers		Current abstainers	Current drinkers		Current abstainers	Current drinkers		Current abstainers
	0 to < 60 grams	60+ grams		0 to < 60 grams	60+ grams		0 to < 60 grams	60+ grams	
Asia, Pacific [High Income]	84.9%	8.0%	7.2%	73.4%	16.2%	10.4%	64.4%	6.1%	29.5%
Asia, Central	48.0%	8.1%	43.9%	67.5%	9.1%	23.4%	49.0%	4.0%	47.0%
Asia, East	69.5%	1.1%	29.4%	62.4%	11.7%	25.9%	57.7%	6.5%	35.8%
Asia, South	11.1%	2.1%	86.8%	17.2%	4.8%	78.1%	10.4%	2.5%	87.0%
Asia, Southeast	28.5%	2.2%	69.3%	18.1%	6.0%	75.9%	17.0%	2.9%	80.1%
Australasia	78.0%	9.4%	12.6%	77.1%	12.9%	10.1%	68.5%	8.2%	23.3%
Caribbean	63.8%	5.8%	30.4%	59.3%	8.0%	32.6%	32.0%	3.6%	64.4%
Europe, Central	60.1%	14.7%	25.2%	60.2%	21.4%	18.4%	54.8%	15.4%	29.8%
Europe, Eastern	53.4%	21.7%	24.8%	52.1%	19.7%	28.1%	46.6%	13.1%	40.3%
Europe, Western	73.5%	12.8%	13.6%	74.8%	17.1%	8.2%	68.9%	10.0%	21.1%
Latin America, Andean	60.3%	7.2%	32.6%	65.2%	12.2%	22.6%	21.1%	1.1%	77.8%
Latin America, Central	44.8%	8.6%	46.6%	54.1%	11.6%	34.2%	38.2%	7.3%	54.5%
Latin America, Southern	81.0%	10.7%	8.3%	74.2%	11.1%	14.7%	62.4%	7.2%	30.4%
Latin America, Tropical	55.2%	13.6%	31.2%	40.8%	11.5%	47.7%	24.5%	2.6%	72.9%
Northern Africa / Middle East	5.3%	1.9%	92.8%	10.5%	1.5%	88.0%	5.5%	0.0%	94.5%
North America [High Income]	62.6%	15.4%	21.9%	62.9%	10.8%	26.3%	49.5%	5.1%	45.5%
Oceania	81.2%	0.9%	17.9%	75.5%	1.7%	22.8%	68.5%	0.3%	31.2%
Sub-Saharan Africa, Central	47.9%	3.1%	49.0%	47.9%	4.0%	48.1%	19.9%	0.6%	79.5%
Sub-Saharan Africa, East	20.3%	4.3%	75.4%	29.1%	9.7%	61.2%	31.9%	5.3%	62.8%
Sub-Saharan Africa, Southern	26.8%	11.2%	62.0%	26.8%	11.2%	62.0%	24.8%	4.7%	70.5%
Sub-Saharan Africa, Western	29.6%	6.6%	63.8%	38.9%	12.0%	49.1%	36.6%	3.9%	59.5%
World	39.8%	5.1%	55.0%	45.4%	10.2%	44.4%	43.3%	6.1%	50.7%

The number of PYLL per 10,000,000 people for alcohol consumption and heavy alcohol consumption are presented in Figures 3 and 4 respectively. The Sub-Saharan Africa, Southern, region had the highest rate of HIV/AIDS-related PYLL from non-adherence to ART because of alcohol consumption, with 7,279 (95% CI: 2,279–12,279) PYLL per 10,000,000 people, of which 3,542 (95% CI: 1,364–5,721) were attributable to heavy alcohol consumption. The Northern Africa/Middle East region had the lowest rate of HIV/AIDS-related PYLL from non-adherence to ART because of alcohol consumption, with 3 (95% CI: 0–6) PYLL per 10,000,000 people, of which 1 (95% CI: 0–1) was attributable to heavy alcohol consumption.

Discussion

Previous evidence has shown that alcohol consumption has a large impact on adherence to ART; however, due to methodological limitations the overall mortality caused by not adhering to ART and the mortality caused by not adhering to ART because of alcohol consumption have previously not been quantified. Our findings indicate that this burden of mortality is non-trivial, and additional research is required concerning the effectiveness of different interventions aimed at reducing alcohol consumption among people with HIV/AIDS. These interventions may also have beneficial effects on other diseases to which

Table 3b

Drinking indicators by Global Burden of Disease region for 2005 (Women)

	15–34 years			35–64 years			65+ years		
	Current drinkers		Current abstainers	Current drinkers		Current abstainers	Current drinkers		Current abstainers
Global Burden of Disease region	0 to < 40 grams	40+ grams		0 to < 40 grams	40+ grams		0 to < 40 grams	40+ grams	
Asia, Pacific [High Income]	85.8%	2.4%	11.8%	74.2%	5.4%	20.5%	49.8%	0.4%	49.8%
Asia, Central	32.7%	1.8%	65.4%	61.0%	4.4%	34.5%	32.9%	0.3%	66.8%
Asia, East	38.3%	0.0%	61.7%	35.6%	2.8%	61.7%	29.9%	0.7%	69.5%
Asia, South	2.4%	0.1%	97.6%	2.7%	0.6%	96.7%	0.4%	0.0%	99.6%
Asia, Southeast	6.9%	0.3%	92.8%	3.8%	0.8%	95.5%	1.9%	0.0%	98.1%
Australasia	77.4%	5.6%	17.0%	80.5%	5.8%	13.7%	54.7%	2.2%	43.1%
Caribbean	42.0%	5.2%	52.8%	26.7%	1.0%	72.4%	8.7%	0.1%	91.3%
Europe, Central	63.0%	10.2%	26.8%	55.4%	10.7%	33.9%	16.9%	0.8%	82.4%
Europe, Eastern	42.4%	14.4%	43.2%	42.5%	12.5%	45.0%	29.3%	2.5%	68.1%
Europe, Western	78.3%	5.6%	16.1%	74.3%	11.2%	14.5%	49.8%	3.6%	46.6%
Latin America, Andean	44.3%	4.0%	51.6%	47.8%	2.1%	50.1%	26.4%	1.2%	72.4%
Latin America, Central	31.8%	4.7%	63.4%	31.5%	3.0%	65.5%	26.3%	0.3%	73.4%
Latin America, Southern	74.1%	3.4%	22.5%	53.8%	7.9%	38.3%	49.3%	2.3%	48.4%
Latin America, Tropical	45.0%	5.2%	49.8%	29.9%	6.6%	63.5%	18.6%	0.5%	80.8%
Northern Africa / Middle East	3.1%	0.5%	96.5%	0.9%	0.2%	98.9%	0.3%	0.0%	99.6%
North America [High Income]	63.7%	7.2%	29.0%	59.2%	5.3%	35.6%	31.2%	1.0%	67.8%
Oceania	47.6%	0.0%	52.4%	48.0%	0.1%	52.0%	43.5%	0.0%	56.5%
Sub-Saharan Africa, Central	30.6%	1.8%	67.6%	25.9%	2.5%	71.5%	11.6%	0.3%	88.1%
Sub-Saharan Africa, East	14.1%	1.9%	83.9%	20.3%	4.5%	75.1%	19.7%	1.7%	78.6%
Sub-Saharan Africa, Southern	8.5%	4.1%	87.4%	11.3%	4.4%	84.3%	8.5%	1.2%	90.2%
Sub-Saharan Africa, Western	17.6%	3.2%	79.2%	24.0%	7.2%	68.8%	24.8%	2.3%	72.9%
World	26.5%	2.1%	71.3%	31.1%	4.0%	64.9%	26.6%	1.2%	72.2%

alcohol consumption is causally related (Rehm et al., 2010).

There are limitations in the methodology used to estimate the HIV/AIDS-related mortality from non-adherence to ART due to alcohol consumption. The very broad categories used in this method for alcohol consumption and adherence to ART do not allow us to take into account different types of drinking patterns (e.g., moderate versus heavy drinking patterns) or to account for different percentages of non-adherence. This is especially important for regions with high variations in drinking patterns and for comparisons across regions. For example, in Africa many people abstain from alcohol, but those who do drink tend to do so heavily (WHO, 2011). Since we expect heavier drinking patterns to have a greater impact on ART adherence, and adherence to medication regimes to have a continuous effect on the rate of HIV/AIDS-related mortality (Hendershot et al., 2009; Marcellin et al., 2008), future research will be necessary to obtain more accurate estimates of the burden of HIV/AIDS-related mortality caused by non-adherence to ART because of alcohol consumption.

There are also limitations in our alcohol exposure and mortality data. The alcohol exposure data used to calculate the estimates presented in this study came from large population surveys, which have limitations with respect to

Table 4a

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 (Men)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	3	2	5	8	4	12	1	0	1
Asia, Central	1	0	2	1	1	2	0	0	0
Asia, East	66	28	104	110	47	173	1	1	2
Asia, South	24	3	45	33	8	58	0	0	0
Asia, Southeast	181	62	301	201	62	340	2	1	4
Australasia	1	0	1	3	2	5	0	0	1
Caribbean	89	41	138	168	76	259	3	1	5
Europe, Central	7	3	11	9	4	13	1	0	1
Europe, Eastern	23	9	38	30	12	49	0	0	1
Europe, Western	63	31	94	186	94	278	15	8	23
Latin America, Andean	43	19	67	62	28	95	0	0	1
Latin America, Central	181	81	280	290	136	444	7	3	11
Latin America, Southern	41	21	61	75	38	112	4	2	6
Latin America, Tropical	240	119	361	343	162	525	8	3	13
Northern Africa / Middle East	1	0	3	3	0	5	0	0	0
North America [High Income]	96	47	145	372	181	563	21	9	32
Oceania	2	1	3	3	1	5	0	0	0
Sub-Saharan Africa, Central	14	5	24	28	9	47	0	0	1
Sub-Saharan Africa, East	174	51	297	594	210	977	21	7	34
Sub-Saharan Africa, Southern	378	138	618	851	310	1,391	17	6	28
Sub-Saharan Africa, Western	112	39	186	336	128	545	9	3	15
World	1,742	702	2,782	3,705	1,513	5,898	111	45	178

population coverage (Shield & Rehm, 2012). The survey instruments commonly have inherent biases, leading to underestimation of the prevalence of current drinkers which, in turn, leads to an underestimation of the HIV/AIDS mortality caused by non-adherence to ART because of alcohol consumption (Shield & Rehm, 2012). In addition, the mortality data used in our study are limited and have variations (Lopez et al., 2006b). For example, some countries, such as Ethiopia, do not have available information on numerous causes of death. In these instances, data on the missing causes of death are provided by WHO, which statistically estimates the number of deaths from these causes using information such as mortality profiles of other countries that are in the same geographic region (Lopez et al., 2006b).

Our main analysis is also limited by the fact that it does not include people younger than 15 years of age, because they tend not to consume alcohol. Although this is not a problem for the estimates of the alcohol-attributable burden of HIV/AIDS-related mortality, there may be people younger than 15 years who take ART. If our analysis is extended to include individuals of all ages, we estimate that 76,500 (95% CI: 71,100–81,800) deaths and 1,922,000 (95% CI: 1,791,000–2,054,000) PYLL were attributable to non-adherence to ART.

Although the association between alcohol consumption and adherence to ART is replicable and reliable, there is a lack of research on the interpersonal and situational moderators of the effect of alcohol consumption on adherence to ART,

Table 4b

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 (Women)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	1	0	1	1	0	1	0	0	0
Asia, Central	0	0	0	0	0	0	0	0	0
Asia, East	11	4	19	14	5	23	0	0	0
Asia, South	2	0	4	1	0	3	0	0	0
Asia, Southeast	15	0	29	10	0	22	0	0	0
Australasia	0	0	0	0	0	0	0	0	0
Caribbean	44	18	69	35	12	57	0	0	1
Europe, Central	4	2	6	2	1	4	0	0	0
Europe, Eastern	5	2	9	6	2	9	0	0	0
Europe, Western	20	10	30	43	21	64	2	1	4
Latin America, Andean	10	4	16	10	4	16	0	0	0
Latin America, Central	40	16	64	40	16	63	1	0	2
Latin America, Southern	13	6	19	15	7	22	1	0	1
Latin America, Tropical	103	48	158	125	54	196	3	1	6
Northern Africa / Middle East	0	0	0	0	0	0	0	0	0
North America [High Income]	42	20	64	117	56	178	4	2	7
Oceania	0	0	1	1	0	1	0	0	0
Sub-Saharan Africa, Central	17	5	30	21	5	36	0	0	0
Sub-Saharan Africa, East	215	47	383	478	141	814	9	2	15
Sub-Saharan Africa, Southern	212	37	387	383	86	681	6	1	11
Sub-Saharan Africa, Western	115	31	200	240	78	401	5	1	8
World	870	252	1,489	1,541	491	2,594	33	9	56

with alcohol consumption decreasing cognitive capacity, thereby decreasing the ability to remember to take medication and impairing judgment (Braithwaite et al., 2008; Hendershot et al., 2009; Parsons, Rosof, & Mustanski, 2008). In addition the magnitude of the effect of alcohol on adherence to ART may be affected by alcohol users having misconceptions of the possible detrimental interactions between alcohol and medications (Brigido et al., 2001; Kalichman et al., 2009; Sankar, Wunderlich, Neufeld, & Luborsky, 2007), and the use of alcohol to reduce the impact of the negative effects of HIV/AIDS (McKirnan, Ostrow, & Hope, 1996; Nemeroff, Hoyt, Huebner, & Proescholdbell, 2008). Despite the limitations in methodology used to estimate the burden of HIV/AIDS due to non-adherence to ART attributable to alcohol consumption, the finding is still valid that alcohol has a large impact on HIV/AIDS mortality due to people not adhering to ART.

Conclusions

Our results demonstrate that in 2004 alcohol was attributable for 8,000 (95% CI: 3,000–13,000) HIV/AIDS-related deaths and 187,000 (95% CI: 70,000–304,000) HIV/AIDS-related PYLL caused by non-adherence to ART because of alcohol consumption. This represents a portion of the HIV/AIDS-related deaths and PYLL that are attributable to alcohol. Additional research is needed to quantify the HIV/AIDS-related deaths caused by unsafe sex and by the worsening of the disease course other than by non-adherence to ART, such as a weakening of the immune system (Braithwaite et al., 2005; Hahn & Samet, 2010; Neuman et al., 2006). Our research indicates that alcohol has a non-trivial impact on mortality for both men and women from HIV/AIDS-related deaths due to non-adherence to ART.

Figure 1

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older

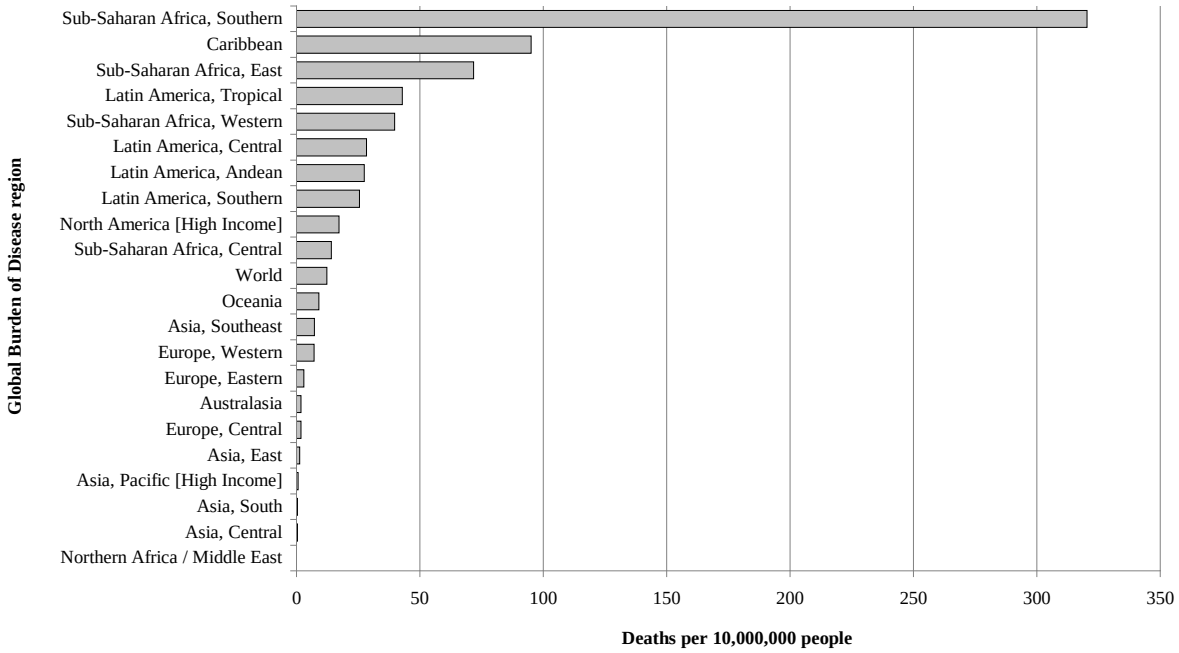

Figure 2

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older

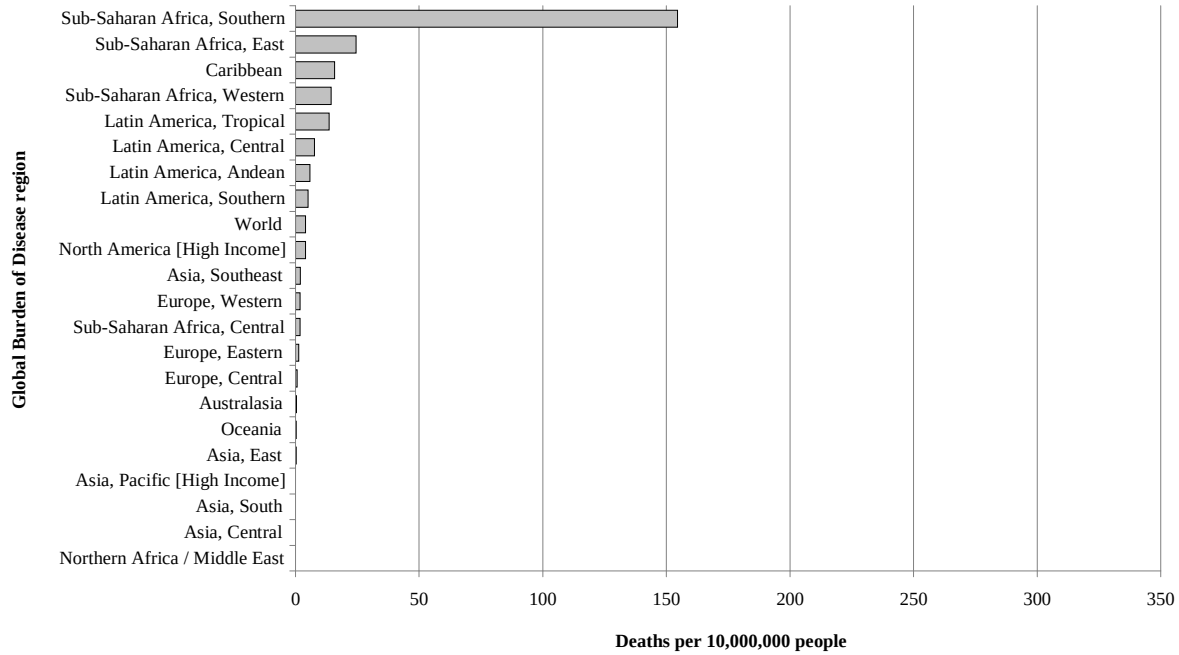

Figure 3

Potential years of life lost attributable to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older

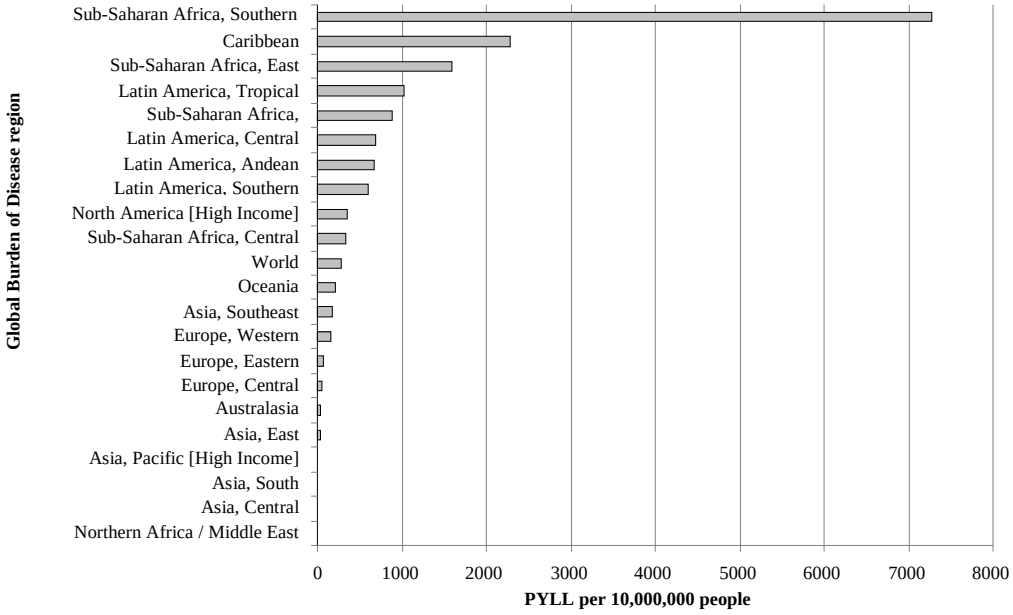

Figure 4

Potential years of life lost attributable to HIV/AIDS from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older

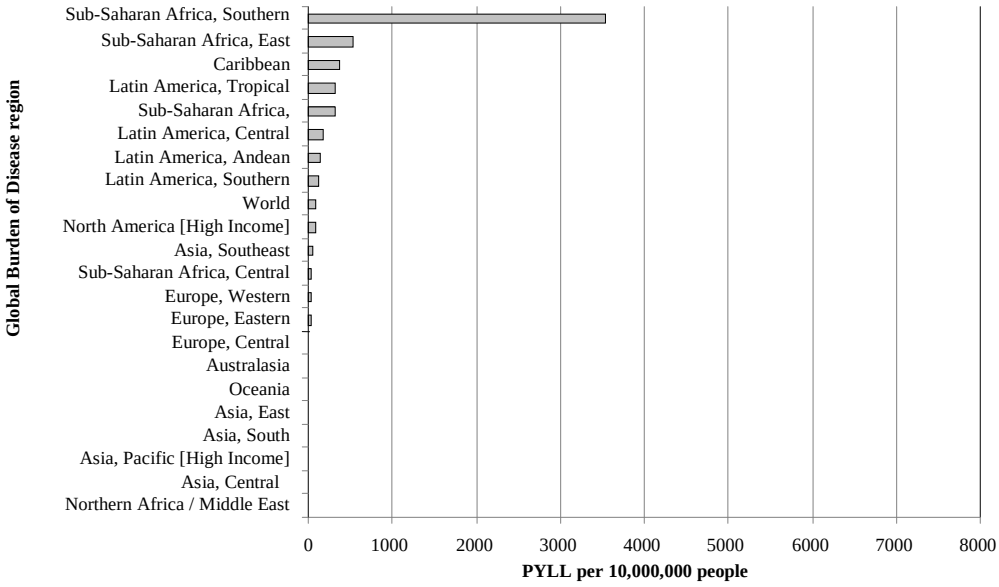

Table 5a

Potential years of life lost to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 (Men)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	91	47	135	161	83	239	5	3	8
Asia, Central	32	12	52	30	12	48	0	0	0
Asia, East	1,911	814	3,008	2,357	1,012	3,702	11	5	18
Asia, South	732	104	1,361	735	177	1,293	2	0	3
Asia, Southeast	5,338	1,827	8,849	4,290	1,318	7,261	19	5	32
Australasia	23	11	36	65	32	99	3	1	5
Caribbean	2,511	1,143	3,878	3,505	1,587	5,423	27	11	44
Europe, Central	222	108	337	190	94	287	4	2	6
Europe, Eastern	700	270	1,130	639	244	1,033	3	1	5
Europe, Western	1,605	804	2,406	3,840	1,939	5,740	107	53	160
Latin America, Andean	1,281	576	1,986	1,326	610	2,041	3	1	4
Latin America, Central	5,318	2,390	8,246	6,203	2,903	9,503	53	23	84
Latin America, Southern	1,148	591	1,706	1,599	815	2,384	31	15	47
Latin America, Tropical	6,767	3,356	10,177	7,336	3,455	11,218	61	24	99
Northern Africa / Middle East	42	0	83	56	9	103	0	0	0
North America [High Income]	2,462	1,209	3,716	7,071	3,441	10,702	158	73	244
Oceania	46	20	71	67	29	105	0	0	1
Sub-Saharan Africa, Central	399	129	669	585	189	980	3	1	5
Sub-Saharan Africa, East	4,801	1,414	8,187	12,258	4,340	20,177	180	63	298
Sub-Saharan Africa, Southern	10,299	3,755	16,844	17,769	6,478	29,059	153	51	255
Sub-Saharan Africa, Western	3,118	1,074	5,163	6,934	2,630	11,239	84	30	139
World	48,847	19,654	78,039	77,016	31,396	122,637	908	361	1,455

Table 5b

Potential years of life lost to HIV/AIDS from not adhering to antiretroviral therapy because of alcohol consumption by Global Burden of Disease region for 2004 (Women)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	26	13	39	20	10	30	0	0	1
Asia, Central	5	2	8	5	2	8	0	0	0
Asia, East	340	126	554	316	117	515	2	1	4
Asia, South	52	0	134	32	0	76	0	0	0
Asia, Southeast	443	3	883	222	0	486	1	0	3
Australasia	5	3	8	6	3	10	0	0	0
Caribbean	1,282	540	2,025	795	282	1,309	4	0	7
Europe, Central	138	67	209	54	26	83	0	0	0
Europe, Eastern	161	59	264	121	44	197	1	0	2
Europe, Western	543	271	816	949	475	1,424	18	8	28
Latin America, Andean	304	128	480	229	97	362	2	1	3
Latin America, Central	1,217	497	1,938	892	357	1,426	9	3	15
Latin America, Southern	369	185	553	326	158	495	6	3	9
Latin America, Tropical	2,992	1,397	4,588	2,742	1,179	4,305	27	9	44
Northern Africa / Middle East	6	0	14	1	0	4	0	0	0
North America [High Income]	1,141	552	1,731	2,386	1,135	3,637	31	13	50
Oceania	14	5	23	18	7	28	0	0	0
Sub-Saharan Africa, Central	511	142	881	469	122	815	2	0	4
Sub-Saharan Africa, East	6,221	1,356	11,085	10,818	3,204	18,433	82	22	142
Sub-Saharan Africa, Southern	6,118	1,065	11,171	8,673	1,944	15,402	55	6	105
Sub-Saharan Africa, Western	3,351	890	5,812	5,414	1,767	9,061	45	14	76
World	25,241	7,298	43,216	34,489	10,927	58,105	286	80	493

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Appendices

Appendix Table 1

Prevalence of people who are receiving antiretroviral therapy out of those who are also in need of antiretroviral therapy by region

	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	80.00%	77.52%	82.48%
Asia, Central	14.29%	12.12%	16.46%
Asia, East	24.56%	21.89%	27.23%
Asia, South	5.63%	4.20%	7.06%
Asia, Southeast	24.55%	21.88%	27.22%
Australasia	60.38%	57.35%	63.42%
Caribbean	49.19%	46.09%	52.29%
Europe, Central	68.45%	65.57%	71.33%
Europe, Eastern	7.49%	5.86%	9.12%
Europe, Western	71.85%	69.07%	74.64%
Latin America, Andean	46.58%	43.49%	49.67%
Latin America, Central	62.98%	59.99%	65.97%
Latin America, Southern	78.64%	76.10%	81.18%
Latin America, Tropical	81.35%	78.93%	83.76%
Northern Africa / Middle East	17.36%	15.01%	19.71%
North America [High Income]	70.10%	67.26%	72.94%
Oceania	26.75%	24.01%	29.49%
Sub-Saharan Africa, Central	4.25%	3.00%	5.50%
Sub-Saharan Africa, East	14.24%	12.07%	16.41%
Sub-Saharan Africa, Southern	21.67%	19.11%	24.22%
Sub-Saharan Africa, Western	13.47%	11.36%	15.59%
World	30.87%	28.56%	33.18%

Appendix Table 2a

Alcohol-attributable fractions for HIV from not adhering to antiretroviral therapy because of alcohol consumption, and heavy alcohol consumption, by Global Burden of Disease region for 2004 (Men)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	7.42%	3.84%	11.01%	7.23%	3.72%	10.74%	6.02%	2.99%	9.06%
Asia, Central	0.50%	0.19%	0.80%	0.63%	0.26%	1.01%	0.47%	0.18%	0.76%
Asia, East	1.10%	0.47%	1.73%	1.14%	0.49%	1.80%	1.02%	0.43%	1.61%
Asia, South	0.05%	0.01%	0.09%	0.08%	0.02%	0.14%	0.05%	0.01%	0.09%
Asia, Southeast	0.55%	0.19%	0.90%	0.44%	0.13%	0.74%	0.37%	0.10%	0.63%
Australasia	4.32%	2.10%	6.53%	4.41%	2.15%	6.67%	3.91%	1.87%	5.96%
Caribbean	2.66%	1.21%	4.11%	2.59%	1.17%	4.01%	1.52%	0.59%	2.45%
Europe, Central	4.73%	2.30%	7.16%	5.05%	2.49%	7.62%	4.50%	2.16%	6.84%
Europe, Eastern	0.31%	0.12%	0.51%	0.30%	0.12%	0.49%	0.26%	0.10%	0.43%
Europe, Western	5.74%	2.88%	8.61%	6.01%	3.04%	8.99%	5.37%	2.65%	8.08%
Latin America, Andean	2.40%	1.08%	3.72%	2.67%	1.23%	4.12%	0.92%	0.29%	1.55%
Latin America, Central	3.13%	1.41%	4.86%	3.71%	1.74%	5.69%	2.74%	1.19%	4.30%
Latin America, Southern	7.11%	3.66%	10.57%	6.74%	3.43%	10.05%	5.76%	2.84%	8.68%
Latin America, Tropical	6.11%	3.03%	9.19%	4.90%	2.31%	7.49%	2.76%	1.07%	4.45%
Northern Africa / Middle East	0.09%	0.00%	0.19%	0.15%	0.02%	0.28%	0.07%	0.00%	0.15%
North America [High Income]	5.09%	2.50%	7.69%	4.87%	2.37%	7.37%	3.83%	1.76%	5.89%
Oceania	1.37%	0.60%	2.14%	1.31%	0.57%	2.04%	1.19%	0.51%	1.88%
Sub-Saharan Africa, Central	0.13%	0.04%	0.21%	0.13%	0.04%	0.22%	0.06%	0.01%	0.10%
Sub-Saharan Africa, East	0.24%	0.07%	0.41%	0.36%	0.13%	0.60%	0.35%	0.12%	0.57%
Sub-Saharan Africa, Southern	0.57%	0.21%	0.93%	0.57%	0.21%	0.93%	0.45%	0.15%	0.76%
Sub-Saharan Africa, Western	0.32%	0.11%	0.53%	0.43%	0.16%	0.69%	0.35%	0.13%	0.58%

Appendix Table 2b

Alcohol-attributable fractions for HIV from not adhering to antiretroviral therapy because of alcohol consumption, and heavy alcohol consumption, by Global Burden of Disease region for 2004 (Women)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	7.15%	3.67%	10.62%	6.61%	3.35%	9.88%	4.58%	2.13%	7.02%
Asia, Central	0.33%	0.11%	0.54%	0.56%	0.23%	0.90%	0.32%	0.11%	0.53%
Asia, East	0.66%	0.25%	1.08%	0.66%	0.25%	1.08%	0.54%	0.19%	0.90%
Asia, South	0.01%	0.00%	0.03%	0.01%	0.00%	0.03%	0.00%	0.00%	0.01%
Asia, Southeast	0.14%	0.00%	0.28%	0.09%	0.00%	0.19%	0.04%	0.00%	0.10%
Australasia	4.15%	2.00%	6.30%	4.28%	2.08%	6.48%	3.09%	1.39%	4.78%
Caribbean	1.94%	0.82%	3.06%	1.21%	0.43%	1.99%	0.41%	0.04%	0.78%
Europe, Central	4.65%	2.25%	7.05%	4.29%	2.04%	6.54%	1.35%	0.40%	2.30%
Europe, Eastern	0.25%	0.09%	0.41%	0.24%	0.09%	0.40%	0.15%	0.05%	0.26%
Europe, Western	5.62%	2.80%	8.44%	5.70%	2.85%	8.55%	3.93%	1.81%	6.05%
Latin America, Andean	1.83%	0.77%	2.89%	1.88%	0.79%	2.96%	1.12%	0.39%	1.85%
Latin America, Central	2.27%	0.93%	3.62%	2.16%	0.86%	3.45%	1.71%	0.62%	2.80%
Latin America, Southern	6.27%	3.15%	9.39%	5.24%	2.53%	7.95%	4.53%	2.11%	6.95%
Latin America, Tropical	4.73%	2.21%	7.26%	3.60%	1.55%	5.66%	2.01%	0.66%	3.37%
Northern Africa / Middle East	0.05%	0.00%	0.11%	0.01%	0.00%	0.05%	0.01%	0.00%	0.02%
North America [High Income]	4.73%	2.29%	7.17%	4.38%	2.08%	6.68%	2.44%	0.98%	3.90%
Oceania	0.70%	0.26%	1.15%	0.89%	0.35%	1.43%	0.82%	0.32%	1.32%
Sub-Saharan Africa, Central	0.09%	0.02%	0.15%	0.08%	0.02%	0.13%	0.03%	0.00%	0.06%
Sub-Saharan Africa, East	0.16%	0.04%	0.29%	0.24%	0.07%	0.41%	0.21%	0.06%	0.37%
Sub-Saharan Africa, Southern	0.21%	0.04%	0.38%	0.25%	0.06%	0.45%	0.16%	0.02%	0.31%
Sub-Saharan Africa, Western	0.19%	0.05%	0.34%	0.28%	0.09%	0.47%	0.25%	0.08%	0.42%

Appendix Table 3a

Alcohol-attributable fractions for HIV from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Men)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	1.07%	0.38%	1.75%	2.14%	0.85%	3.43%	0.87%	0.28%	1.45%
Asia, Central	0.12%	0.04%	0.20%	0.13%	0.05%	0.20%	0.06%	0.02%	0.10%
Asia, East	0.03%	0.01%	0.05%	0.30%	0.10%	0.49%	0.17%	0.06%	0.29%
Asia, South	0.01%	0.01%	0.02%	0.03%	0.01%	0.05%	0.02%	0.01%	0.03%
Asia, Southeast	0.07%	0.03%	0.10%	0.18%	0.08%	0.29%	0.09%	0.05%	0.14%
Australasia	0.77%	0.27%	1.27%	1.04%	0.39%	1.69%	0.70%	0.26%	1.14%
Caribbean	0.37%	0.16%	0.58%	0.51%	0.21%	0.81%	0.26%	0.07%	0.44%
Europe, Central	1.52%	0.56%	2.48%	2.15%	0.85%	3.44%	1.62%	0.64%	2.59%
Europe, Eastern	0.15%	0.04%	0.25%	0.14%	0.04%	0.23%	0.09%	0.03%	0.16%
Europe, Western	1.41%	0.51%	2.31%	1.83%	0.72%	2.94%	1.13%	0.42%	1.84%
Latin America, Andean	0.43%	0.13%	0.72%	0.70%	0.25%	1.15%	0.08%	0.00%	0.18%
Latin America, Central	0.84%	0.33%	1.35%	1.09%	0.47%	1.70%	0.74%	0.29%	1.18%
Latin America, Southern	1.38%	0.51%	2.25%	1.45%	0.53%	2.38%	0.99%	0.33%	1.66%
Latin America, Tropical	1.98%	0.89%	3.08%	1.78%	0.68%	2.89%	0.44%	0.11%	0.77%
Northern Africa / Middle East	0.04%	0.02%	0.06%	0.03%	0.02%	0.05%	0.00%	0.00%	0.00%
North America [High Income]	1.65%	0.68%	2.62%	1.18%	0.48%	1.88%	0.59%	0.22%	0.97%
Oceania	0.03%	0.00%	0.05%	0.05%	0.01%	0.09%	0.01%	0.00%	0.02%
Sub-Saharan Africa, Central	0.01%	0.00%	0.02%	0.02%	0.01%	0.03%	0.00%	0.00%	0.01%
Sub-Saharan Africa, East	0.07%	0.03%	0.11%	0.15%	0.06%	0.24%	0.08%	0.04%	0.13%
Sub-Saharan Africa, Southern	0.28%	0.10%	0.46%	0.28%	0.10%	0.45%	0.12%	0.05%	0.19%
Sub-Saharan Africa, Western	0.10%	0.04%	0.16%	0.17%	0.07%	0.27%	0.06%	0.03%	0.09%

Appendix Table 3b

Alcohol-attributable fractions for HIV from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Women)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	0.33%	0.04%	0.62%	0.75%	0.19%	1.31%	0.06%	0.00%	0.14%
Asia, Central	0.03%	0.00%	0.06%	0.06%	0.02%	0.11%	0.00%	0.00%	0.01%
Asia, East	0.00%	0.00%	0.00%	0.08%	0.03%	0.13%	0.02%	0.01%	0.03%
Asia, South	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%
Asia, Southeast	0.01%	0.01%	0.02%	0.03%	0.01%	0.04%	0.00%	0.00%	0.00%
Australasia	0.47%	0.13%	0.81%	0.48%	0.15%	0.81%	0.20%	0.04%	0.36%
Caribbean	0.36%	0.18%	0.54%	0.07%	0.04%	0.11%	0.01%	0.00%	0.01%
Europe, Central	1.07%	0.34%	1.81%	1.15%	0.36%	1.94%	0.10%	0.00%	0.25%
Europe, Eastern	0.10%	0.02%	0.19%	0.09%	0.02%	0.16%	0.02%	0.00%	0.04%
Europe, Western	0.63%	0.13%	1.13%	1.24%	0.39%	2.08%	0.44%	0.08%	0.80%
Latin America, Andean	0.26%	0.05%	0.47%	0.14%	0.03%	0.24%	0.08%	0.00%	0.16%
Latin America, Central	0.49%	0.21%	0.78%	0.32%	0.15%	0.48%	0.04%	0.02%	0.05%
Latin America, Southern	0.47%	0.13%	0.80%	1.12%	0.31%	1.92%	0.34%	0.09%	0.59%
Latin America, Tropical	0.83%	0.38%	1.28%	1.08%	0.35%	1.81%	0.09%	0.04%	0.15%
Northern Africa / Middle East	0.01%	0.01%	0.02%	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%
North America [High Income]	0.80%	0.30%	1.31%	0.60%	0.21%	0.98%	0.13%	0.02%	0.24%
Oceania	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Sub-Saharan Africa, Central	0.01%	0.00%	0.01%	0.01%	0.00%	0.02%	0.00%	0.00%	0.00%
Sub-Saharan Africa, East	0.03%	0.02%	0.05%	0.07%	0.03%	0.11%	0.03%	0.01%	0.04%
Sub-Saharan Africa, Southern	0.11%	0.05%	0.18%	0.12%	0.06%	0.18%	0.03%	0.02%	0.05%
Sub-Saharan Africa, Western	0.05%	0.02%	0.08%	0.11%	0.05%	0.17%	0.03%	0.02%	0.05%

Appendix Table 4a

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Men)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	0	0	1	2	1	4	0	0	0
Asia, Central	0	0	0	0	0	0	0	0	0
Asia, East	2	1	3	29	10	47	0	0	0
Asia, South	6	3	10	12	5	19	0	0	0
Asia, Southeast	22	11	32	84	37	130	1	0	1
Australasia	0	0	0	1	0	1	0	0	0
Caribbean	12	5	20	33	14	53	1	0	1
Europe, Central	2	1	4	4	2	6	0	0	0
Europe, Eastern	11	3	19	14	4	23	0	0	0
Europe, Western	15	6	25	57	22	91	3	1	5
Latin America, Andean	8	2	13	16	6	27	0	0	0
Latin America, Central	48	19	78	85	37	133	2	1	3
Latin America, Southern	8	3	13	16	6	26	1	0	1
Latin America, Tropical	78	35	121	125	47	202	1	0	2
Northern Africa / Middle East	1	0	1	1	0	1	0	0	0
North America [High Income]	31	13	50	90	37	144	3	1	5
Oceania	0	0	0	0	0	0	0	0	0
Sub-Saharan Africa, Central	1	1	2	4	1	6	0	0	0
Sub-Saharan Africa, East	51	22	80	245	104	387	5	2	7
Sub-Saharan Africa, Southern	183	64	303	412	145	680	5	2	7
Sub-Saharan Africa, Western	34	13	55	131	52	209	2	1	2
World	515	202	829	1,360	530	2,190	23	9	37

Appendix Table 4b

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Women)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	0	0	0	0	0	0	0	0	0
Asia, Central	0	0	0	0	0	0	0	0	0
Asia, East	0	0	0	2	1	3	0	0	0
Asia, South	0	0	0	0	0	1	0	0	0
Asia, Southeast	1	1	2	3	1	4	0	0	0
Australasia	0	0	0	0	0	0	0	0	0
Caribbean	8	4	12	2	1	3	0	0	0
Europe, Central	1	0	2	1	0	1	0	0	0
Europe, Eastern	2	0	4	2	0	4	0	0	0
Europe, Western	2	0	4	9	3	16	0	0	1
Latin America, Andean	1	0	3	1	0	1	0	0	0
Latin America, Central	9	4	14	6	3	9	0	0	0
Latin America, Southern	1	0	2	3	1	5	0	0	0
Latin America, Tropical	18	8	28	37	12	63	0	0	0
Northern Africa / Middle East	0	0	0	0	0	0	0	0	0
North America [High Income]	7	3	12	16	6	26	0	0	0
Oceania	0	0	0	0	0	0	0	0	0
Sub-Saharan Africa, Central	2	1	3	3	1	5	0	0	0
Sub-Saharan Africa, East	43	20	66	145	68	223	1	1	2
Sub-Saharan Africa, Southern	116	47	185	180	87	273	1	1	2
Sub-Saharan Africa, Western	30	13	46	92	40	144	1	0	1
World	242	102	381	502	224	781	4	2	6

Appendix Table 5a

Potential years of life lost attributable to HIV from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Men)

	15–34 years			35–64 years			65+ years		
Global Burden of Disease region	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**	**Point estimate**	**Lower estimate**	**Upper estimate**
Asia, Pacific [High Income]	13	5	21	48	19	76	1	0	1
Asia, Central	8	2	13	6	2	10	0	0	0
Asia, East	51	15	87	613	208	1,017	2	1	3
Asia, South	195	86	304	266	117	416	1	0	1
Asia, Southeast	642	328	955	1,786	785	2,787	5	2	7
Australasia	4	1	7	15	6	25	1	0	1
Caribbean	348	147	548	694	287	1,101	5	1	8
Europe, Central	72	27	117	81	32	130	1	1	2
Europe, Eastern	328	98	557	285	84	485	1	0	2
Europe, Western	393	141	645	1,169	461	1,878	22	8	37
Latin America, Andean	227	69	384	346	123	569	0	0	0
Latin America, Central	1,423	556	2,290	1,814	786	2,841	14	6	23
Latin America, Southern	223	83	363	345	126	564	5	2	9
Latin America, Tropical	2,199	987	3,410	2,670	1,013	4,327	10	3	17
Northern Africa / Middle East	18	9	28	12	6	17	0	0	0
North America [High Income]	799	329	1,269	1,715	695	2,734	25	9	40
Oceania	1	0	2	2	0	5	0	0	0
Sub-Saharan Africa, Central	41	15	66	75	28	123	0	0	0
Sub-Saharan Africa, East	1,406	612	2,199	5,065	2,149	7,982	43	20	65
Sub-Saharan Africa, Southern	4,994	1,737	8,251	8,616	3,032	14,199	41	18	63
Sub-Saharan Africa, Western	949	364	1,534	2,695	1,073	4,317	14	6	21
World	14,331	5,612	23,050	28,318	11,032	45,603	190	78	301

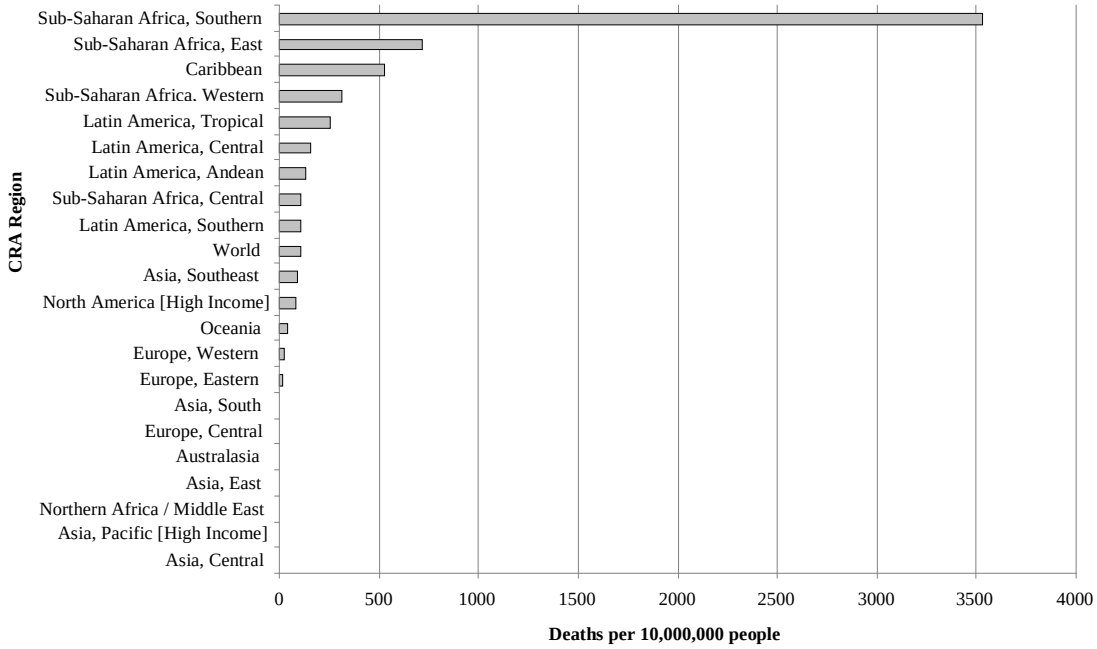
Appendix Table 5b

Potential years of life lost attributable to HIV from not adhering to antiretroviral therapy because of heavy alcohol consumption by Global Burden of Disease region for 2004 (Women)

Global Burden of Disease region	15–34 years			35–64 years			65+ years		
	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate	Point estimate	Lower estimate	Upper estimate
Asia, Pacific [High Income]	1	0	2	2	1	4	0	0	0
Asia, Central	0	0	1	1	0	1	0	0	0
Asia, East	1	0	1	38	14	62	0	0	0
Asia, South	2	1	3	10	4	16	0	0	0
Asia, Southeast	34	17	50	63	32	94	0	0	0
Australasia	1	0	1	1	0	1	0	0	0
Caribbean	236	117	355	47	24	69	0	0	0
Europe, Central	32	10	54	15	5	25	0	0	0
Europe, Eastern	67	13	121	45	9	81	0	0	0
Europe, Western	61	12	109	206	65	347	2	0	4
Latin America, Andean	43	8	78	17	4	30	0	0	0
Latin America, Central	264	112	416	131	61	200	0	0	0
Latin America, Southern	27	8	47	70	20	119	0	0	1
Latin America, Tropical	522	237	807	822	268	1,375	1	0	2
Northern Africa / Middle East	1	1	2	0	0	1	0	0	0
North America [High Income]	194	73	316	325	117	534	2	0	3
Oceania	0	0	0	0	0	0	0	0	0
Sub-Saharan Africa, Central	47	19	75	70	27	113	0	0	0
Sub-Saharan Africa, East	1,259	594	1,925	3,294	1,534	5,053	11	5	17
Sub-Saharan Africa, Southern	3,353	1,362	5,345	4,069	1,960	6,178	12	6	17
Sub-Saharan Africa, Western	862	378	1,346	2,070	892	3,249	6	3	10
World	7,008	2,962	11,054	11,294	5,037	17,552	35	16	54

Appendix Figure 1

Deaths attributable to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older



Appendix Figure 2

Potential years of life lost attributable to HIV/AIDS from not adhering to antiretroviral therapy by Global Burden of Disease region for 2004 per 10,000,000 people 15 years or older