Original article

Self-reported alcohol consumption and its association with adherence and outcome of antiretroviral therapy in the Swiss HIV Cohort Study

Anna Conen[1], Jan Fehr[1], Tracy R Glass[2], Hansjakob Furrer[3], Rainer Weber[4], Pietro Vernazza[5], Bernard Hirschel[6], Matthias Cavassini[7], Enos Bernasconi[8], Heiner C Bucher[1,2], Manuel Battegay[1] and the Swiss HIV Cohort Study[†]*

[1]Divison of Infectious Diseases and Hospital Epidemiology, University Hospital, Basel, Switzerland
[2]Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital, Basel, Switzerland
[3]Department of Infectious Diseases, University Hospital Bern and University of Bern, Bern, Switzerland
[4]Division of Infectious Diseases and Hospital Epidemiology, University Hospital, Zurich, Switzerland
[5]Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital, St Gallen, Switzerland
[6]Division of Infectious Diseases and Hospital Epidemiology, University Hospital, Geneva, Switzerland
[7]Division of Infectious Diseases and Hospital Epidemiology, University Hospital, Lausanne, Switzerland
[8]Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital, Lugano, Switzerland

*Corresponding author: E-mail: mbattegay@uhbs.ch
[†]See additional file for a list of study group participants

Background: Alcohol consumption leading to morbidity and mortality affects HIV-infected individuals. Here, we aimed to study self-reported alcohol consumption and to determine its association with adherence to antiretroviral therapy (ART) and HIV surrogate markers.
Methods: Cross-sectional data on daily alcohol consumption from August 2005 to August 2007 were analysed and categorized according to the World Health Organization definition (light, moderate or severe health risk). Multivariate logistic regression models and Pearson's χ^2 statistics were used to test the influence of alcohol use on endpoints.
Results: Of 6,323 individuals, 52.3% consumed alcohol less than once a week in the past 6 months. Alcohol intake was deemed light in 39.9%, moderate in 5.0% and severe in 2.8%. Higher alcohol consumption was significantly associated with older age, less education, injection drug use, being in a drug maintenance programme, psychiatric treatment, hepatitis C virus coinfection and with a longer time since diagnosis of HIV. Lower alcohol consumption was found in males, non-Caucasians, individuals currently on ART and those with more ART experience. In patients on ART (n=4,519), missed doses and alcohol consumption were positively correlated (P<0.001). Severe alcohol consumers, who were pretreated with ART, were more often off treatment despite having CD4$^+$ T-cell count <200 cells/μl; however, severe alcohol consumption *per se* did not delay starting ART. In treated individuals, alcohol consumption was not associated with worse HIV surrogate markers.
Conclusions: Higher alcohol consumption in HIV-infected individuals was associated with several psychosocial and demographic factors, non-adherence to ART and, in pretreated individuals, being off treatment despite low CD4$^+$ T-cell counts.

Introduction

Alcohol consumption leading to health risks is the third leading cause of morbidity and mortality in developed countries and also affects HIV-infected individuals [1]. The World Health Organization (WHO) categorizes daily alcohol consumption into drinking with a light, moderate or severe health risk [2]. Broad ranges of prevalence of both any and severe alcohol consumption in HIV-infected individuals have been described, ranging 46–82% and 8–35%, respectively [3–9].

As a result of the dramatic success of combination antiretroviral therapy (ART) and therefore longer survival of HIV-infected individuals [10–13], comorbidities, such as alcohol-related liver diseases, are of increasing concern. End-stage liver disease, mainly caused by

chronic hepatitis C virus (HCV) infection, has been shown to be an important cause of death in the era of ART [14] and alcohol consumption might accelerate this disease in HIV–HCV-coinfected individuals. With its cytotoxic and immunomodulatory effects, alcohol might lead to the deterioration of immunological and viral responses in HIV-infected individuals [15–18]. In addition, alcohol abuse is associated with reduced adherence to ART, possibly leading to virological failure and progression of HIV [5,19,20]. Results from animal studies of alcohol consuming macaques infected with the simian immunodeficiency virus support such assumptions [21–24]; however, studies in human beings show conflicting results [3,9,25–28].

The goal of this study is twofold. First, we aim to assess the prevalence, sociodemographic and HIV disease associated correlates of self-reported alcohol consumption in relation to health risk categories defined by the WHO in the Swiss HIV Cohort Study (SHCS). Second, we aim to describe the relation between alcohol consumption and both adherence to ART and surrogate markers of HIV infection.

Methods

Study population

Study participants were followed within the SHCS [29], a large prospective cohort study with continuing enrolment of HIV-infected individuals aged ≥16 years. Enrolment in the SHCS is independent from the stage of disease, the degree of immunosuppression or whether the individual is receiving ART. Over 15,000 HIV-infected individuals have been included in the SHCS so far, corresponding to approximately 70% of all HIV-infected individuals in Switzerland. Informed consent is obtained from all participants. Participants of the SHCS are followed every 6 months in outpatient clinics and asked to provide information on sociodemographics, treatment, adherence, comorbidities and medication currently taken. Laboratory tests, including liver parameters, $CD4^+$ T-cell counts and HIV viral load, are collected at each visit.

Assessment of self-reported alcohol consumption

Self-reported alcohol consumption is a well established method to measure the amount of alcohol consumed [30]. A questionnaire on alcohol consumption was introduced into the SHCS in August 2005 asking the following questions: did you drink alcohol at least once a week during the last 6 months? (yes, no or refuse to answer) and if 'yes', how much did you drink on a daily basis? The questionnaire was administered by clinicians or study nurses. Average daily alcohol consumption was estimated with the help of a predefined list of different alcoholic beverages with their alcohol content in g. Daily alcohol intake was translated into health risk categories developed by the WHO [2]: light (<20 g for women and <40 g for men), moderate (20–40 g for women and 40–60 g for men) and severe health risk (>40 g for women and >60 g for men). Patients were classified as 'at risk drinkers' if their alcohol consumption met the criteria for moderate or severe health risk. For simplicity, patients who indicated that they did not consume ≥1 alcoholic beverage a week in the previous 6 months are referred to as 'non-drinkers' throughout the manuscript. Binge drinking (excessive consumption on one occasion) was not assessed [31].

All patients in the SHCS answering their first questionnaire about alcohol consumption during a regular cohort visit between August 2005 and August 2007 were included, irrespective of their treatment status.

Covariate factors

Self-reported adherence to antiretroviral medication was assessed by asking individuals how often a dose of medication was missed in the previous 4 weeks (never, more than once a week, once a week, once every 2 weeks or once a month) and if ≥2 consecutive doses were missed (yes or no). Non-adherence was defined according to missed doses (0, 1, 2 or >2). This definition of non-adherence has been validated within the SHCS for predicting virological failure [32] and subtle differences in adherence were found to have an effect on viral load [33]. Social factors used for analyses were ethnicity, education level (completed 9 years of mandatory schooling or less versus more), relationship status (involved in a stable partnership versus not) and living status (living alone versus not). Patient factors were age, gender, current injection drug use (IDU), being in a drug maintenance programme, psychiatric treatment and legal problems. HIV-related disease factors were time living with the diagnosis of HIV infection, mode of transmission and CDC disease stage. Comorbidity factors were chronic hepatitis B (positive hepatitis B surface antigen test or detection of hepatitis B virus DNA) and chronic hepatitis C (detection of HCV viral load or currently on treatment for HCV). ART-related factors were time on current ART, total time on ART, number of previous ART regimens, drug class of current regimen (nucleoside reverse transcriptase inhibitors [NRTIs], non-NRTIs, boosted or unboosted protease inhibitors), reasons for stopping ART and medication for opportunistic infections currently taken. Laboratory factors were HIV surrogate markers ($CD4^+$ T-cell count and HIV viral load).

Statistical methods

Baseline characteristics were summarized according to health risk categories on the basis of daily alcohol consumption (none, light, moderate and severe health risk).

For the first aim of the study, a logistic regression model was used to compare moderate and severe drinkers to those with light alcohol intake in a cross-sectional analysis of individuals reporting alcohol intake at least on a weekly basis in the past 6 months. For the multivariate analyses, when variables had correlation coefficients >0.60, one variable was excluded.

For the second aim of the study, we considered the subset of individuals on ART who reported drinking at least once a week in the past 6 months (n=2,117). Linear regression models were used to test for significant differences in HIV viral load and CD4$^+$ T-cell count according to the WHO alcohol consumption categories calculated from the raw data. Both HIV viral load and immune function variables were transformed ($\log_{10}$ [HIV viral load] and $\sqrt{}$[CD4$^+$ T-cell count]) to ensure that the assumption of linearity was met. In these models, we adjusted for non-adherence to ART (0, 1, 2 or >2 missed doses in the previous 4 weeks).

As a hypothesis-generating analysis, we looked for suggestions that alcohol consumption interfered with ART treatment. In treatment-naive individuals with a delayed start of ART or treated patients who stopped or interrupted treatment, proportions of individuals with CD4$^+$ T-cell counts <200 cells/μl were informally compared across alcohol consumption categories. In addition, reasons for stopping treatment were presented.

We conducted exploratory analyses of the association between alcohol consumption and non-adherence (0, 1, 2 or >2 missed doses in the previous 4 weeks) using Pearson's χ^2 test. Multinomial regression models were performed to test for the likelihood of reporting missed doses across the alcohol consumption categories. All statistical analyses were done with SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Study population

Between August 2005 and August 2007, 6,323 of 7,091 (89.2%) eligible individuals filled in ≥1 questionnaire on alcohol consumption, 220 (3.1%) refused to answer the questions and 548 (7.7%) had missing data. Compared with responders, individuals refusing to answer the questions more often had received psychiatric treatment, had CD4$^+$ T-cell count ≥500 cells/μl, had HIV viral load ≥400 copies/ml, were not on ART, were more likely to have acquired HIV by homosexual contact and were less likely to be in a stable partnership (data not shown).

Health risk categories according to daily alcohol consumption

From the 6,323 responders, 3,306 individuals (52.3%) indicated that they consumed alcohol less than once a week in the past 6 months, 2,523 (39.9%) were categorized as having a light health risk, 317 (5.0%) a moderate health risk and 177 (2.8%) a severe health risk according to the WHO classification. Table 1 provides baseline variables for all individuals according to the four different drinking categories. Individuals with a severe health risk compared with those with a light health risk drinking behaviour more often had only a basic education level, were IDU, received psychiatric treatment and had legal problems. Furthermore, they more often lived alone, were coinfected with HCV, had CD4$^+$ T-cell counts <200 cells/μl with detectable viral load, more often missed doses of ART and had a longer time since HIV diagnosis.

Correlates of moderate or severe drinking

In the 3,017 individuals who reported drinking alcohol at least once a week in the past 6 months, we investigated correlates of alcohol drinking that were associated with a moderate or severe health risk compared with a light health risk (Table 2). The likelihood of being in the moderate or severe health risk drinking category was significantly higher for older individuals, those with basic education, those with current IDU or in a drug maintenance programme, those receiving psychiatric treatment, individuals with positive HCV antibodies and with a longer time since diagnosis of HIV. A lower likelihood of being in the moderate or severe health risk drinking category was found for males, non-Caucasians, individuals currently on ART and those with more ART experience.

Relationship between alcohol consumption, adherence and HIV surrogates

There was a significant positive association between missed doses of ART and alcohol consumption categorized as either none, light, moderate or severe health risk in patients on ART (n=4,519; Pearson's χ^2 test P<0.001). In a multinomial model with individuals in the severe health risk category as a comparison group, individuals in all other alcohol consumption categories were less likely to report missed doses of ART in the 4 weeks prior to answering the questionnaire (non-drinkers odds ratio [OR] 0.33, 95% confidence interval [CI] 0.22–0.49; P<0.001; light health risk OR 0.40, 95% CI 0.27–0.59; P<0.001; and moderate health risk OR 0.56, 95% CI 0.34–0.91; P=0.02). When comparing adjacent categories (that is, non-drinkers to light, light to moderate and moderate to severe drinkers), the results remained significant.

In the subset of patients who were currently on ART and reported drinking at least once a week over the past 6 months (n=2,117), the association between alcohol consumption and HIV surrogate markers was explored. In univariate linear regression models of the association between alcohol consumption and HIV

Table 1. Comparison of baseline characteristics by WHO categorization for health risk on the basis of daily alcohol consumption[a]

Baseline variable	All patients	No alcohol consumption[a]	Health risk[a]		
			Light	Moderate	Severe
Total, *n* (%)	6,323 (100)	3,306 (52.3)	2,523 (39.9)	317 (5.0)	177 (2.8)
Median age, years (IQR)	42 (37–48)	42 (36–47)	43 (38–49)	44 (38–50)	43 (38–48)
Male gender, %	69.3	60.7	80.6	66.9	71.8
Non-Caucasian ethnicity, %	17.4	22.7	12.3	10.1	7.3
Basic education, %[b]	26.2	31.1	19.5	23.6	36.1
Transmission risk category					
Homosexual, %	37.8	30.3	49.7	28.1	25.4
Heterosexual, %	38.5	42.8	32.7	43.2	33.3
IDU, %	19.5	21.9	14.1	27.4	38.4
Other, %	4.2	5.0	3.5	1.3	2.8
Psychiatric treatment, %[c]	9.3	10.0	7.3	11.7	19.8
Legal problems, %[c]	2.2	2.3	1.7	2.8	6.8
Stable partnership, %[c]	58.8	57.0	61.7	60.7	46.3
Living alone, %[c]	44.6	41.8	47.3	44.8	56.8
CDC stage C, %	23.6	25.0	22.3	19.4	24.4
Coinfection					
Hepatitis B virus, %[d]	2.1	2.2	1.8	2.8	1.1
Hepatitis C virus, %[e]	6.7	7.8	4.7	7.9	11.3
Currently taking medication for OI, %[f]	10.0	10.8	8.8	8.8	11.9
$CD4^+$ T-cell count					
Median $CD4^+$ T-cell count, cells/μl (IQR)	438 (295–615)	428.5 (286–605)	447 (308–632)	454 (291–641)	390 (263–581)
<200 cells/μl, %	11.1	12.1	9.1	15.1	15.3
200–<500 cells/μl, %	48.9	48.8	49.7	42.9	50.3
≥500 cells/μl, %	25.1	39.1	41.2	42.0	34.5
HIV RNA viral load					
Median HIV RNA viral load, $\log_{10}$ copies/ml (IQR)	0 (0–3.4)	0 (0–3.3)	0 (0–3.5)	0 (0–3.8)	1.8 (0–4.1)
<400 copies/ml, %	68.2	69.4	67.8	62.5	59.9
≥400 copies/ml, %	31.8	30.6	32.2	37.5	40.1
Treatment status					
Naive, %	17.8	16.2	18.9	24.3	22.0
Off treatment, %	10.7	11.2	9.5	13.6	14.1
Currently treated overall, %	71.5	72.7	71.6	62.2	63.8
Currently treated with NNRTIs, %	33.9	32.1	35.3	38.1	41.6
Currently treated with PIs (non-boosted), %	10.7	11.5	9.6	11.7	9.7
Currently treated with PIs (boosted), %	43.4	44.8	42.7	35.5	39.8
Currently treated with triple-NRTI and others, %	12.0	11.6	12.3	14.7	8.9
Missed doses of ART[g]					
0, %	77.0	79.3	75.8	69.8	58.7
1, %	13.7	12.4	15.2	15.3	14.4
2, %	5.1	4.8	4.7	7.4	14.4
>2, %	4.2	3.5	4.3	7.4	12.5
Median number of previous ART regimens (IQR)	2 (1–5)	3 (2–6)	3 (2–5)	3 (1–5)	3 (1–5)
Median time on current ART, years (IQR)	1.02 (0.2–2.5)	1.5 (0.6–3.0)	1.6 (0.7–3.0)	1.5 (0.5–3.2)	1.6 (0.7–3.3)
Median cumulative time on ART, years (IQR)	4.2 (0.5–7.8)	5.4 (2.3–8.3)	5.6 (2.6–8.5)	5.3 (2.5–8.3)	5.5 (2.7–8.3)
Median time since HIV diagnosis, years (IQR)	8.8 (3.6–14.8)	8.8 (3.7–14.9)	8.5 (3.3–14.4)	9.0 (3.5–15.1)	11.5 (5.2–16.9)

[a]Health risk was on the basis of daily alcohol intake (light <20 g for women and <40 g for men, moderate 20–40 g for women and 40–60 g for men and severe >40 g for women and >60 g for men). Daily alcohol consumption was only estimated in those who consumed alcohol at least once a week over the previous 6 months with all others being characterized as having no alcohol consumption. [b]Completed ≤9 years of mandatory schooling. [c]In the 6 months prior to answering the questions on alcohol consumption. [d]Positive hepatitis B surface antigen test or positive hepatitis B virus DNA test. [e]Detection of hepatitis C viral load or currently receiving treatment for hepatitis C infection. [f]Medication for opportunistic infection (OI) currently taken at the time of answering the questions on alcohol consumption. [g]Individuals currently on combination antiretroviral therapy (ART; *n*=4,519) who reported missed doses in the previous 28 days. IDU, injection drug use; IQR, interquartile range; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; WHO, World Health Organization.

Table 2. Logistic regression model of correlates of moderate or severe drinking in those reporting alcohol intake at least weekly in the previous 6 months[a,b]

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*P*-value
Age per 5-year increase	1.02 (0.98–1.08)	1.11 (1.04–1.17)	<0.001
Male gender	0.53 (0.42–0.65)	0.51 (0.40–0.65)	<0.001
Non-Caucasian ethnicity	0.72 (0.52–1.00)	0.66 (0.45–0.96)	0.03
Basic education[c]	1.60 (1.28–2.01)	1.35 (1.05–1.74)	0.02
Current IDU or in drug maintenance programme[d]	3.51 (2.69–4.58)	2.42 (1.73–3.39)	<0.001
Receiving psychiatric treatment[d]	2.18 (1.63–2.92)	1.51 (1.09–2.10)	0.01
Legal problems[d]	2.62 (1.54–4.47)	1.34 (0.72–2.51)	0.36
Stable partnership[d]	0.78 (0.64–0.94)	0.90 (0.73–1.11)	0.36
Living alone[d]	1.07 (0.88–1.31)	–	–
AIDS	0.94 (0.74–1.19)	0.99 (0.76–1.29)	0.93
Hepatitis B virus coinfection[e]	1.25 (0.64–2.44)	1.56 (0.79–3.10)	0.20
Hepatitis C status			
None	Reference	Reference	–
Positive for HCV antibodies	2.90 (1.28–6.56)	3.75 (1.52–9.23)	0.004
Chronic/active[f]	1.04 (0.51–2.12)	2.10 (0.94–4.70)	0.07
Currently taking medication for OI[g]	0.96 (0.77–1.21)	1.01 (0.78–1.32)	0.91
Treatment status			
Naive	Reference	Reference	–
Off treatment	1.16 (0.93–1.63)	0.97 (0.66–1.43)	0.87
Currently treated	0.70 (0.56–0.89)	0.64 (0.47–0.88)	0.005
Number of previous ART regimens	0.96 (0.93–0.99)	0.95 (0.90–0.99)	0.03
Cumulative time on ART per 5-year increase	0.86 (0.76–0.98)	–	–
Time since HIV diagnosis per 5-year increase	1.12 (1.04–1.20)	1.12 (1.01–1.23)	0.03

[a]*n*=3,017. [b]Model shows the odds ratio (OR) of moderate or severe drinking (compared with light drinking) in males, for example, compared with females. [c]Completed ≤9 years of mandatory schooling. [d]In the 6 months prior to answering the questions on alcohol consumption. [e]Positive hepatitis B surface antigen test or positive hepatitis B virus DNA test. [f]Detection of hepatitis C viral load or currently receiving treatment for hepatitis C infection. [g]Medication currently taken at the time of answering the questions on alcohol consumption. ART, combined antiretroviral therapy; CI, confidence interval; HCV, hepatitis C virus; IDU, injection drug use; OI, opportunistic infection.

viral load, individuals with light or moderate alcohol consumption had a significantly lower viral load than those with severe alcohol consumption (Table 3). However, this significant association did not remain in models adjusted for non-adherence. By contrast, individuals with light alcohol consumption had a significantly higher CD4$^+$ T-cell count than those with severe alcohol consumption in univariate models, but not in multivariate models (Table 3).

To explore the possibility that alcohol consumption could lead to a delayed start of ART, we looked at the percentage of treatment-naive individuals with CD4$^+$ T-cell counts <200 cells/μl across alcohol consumption categories, but did not find strong evidence to suggest an association between delayed start of ART and alcohol consumption (non-drinkers 14.1%, light 10.9%, moderate 18.2% and severe risk drinkers 12.8%). However, as alcohol consumption increased according to the health risk drinking categories, there was an increasing percentage of pretreated individuals who were currently not on ART despite CD4$^+$ T-cell counts <200 cells/μl (light 8.3%, moderate 20.9% and severe risk drinkers 48%); one explanation found was that severe drinkers were more likely to cite 'patient wish' as the reason for stopping ART (58.0% versus 42.1% of light risk and 46.3% of moderate risk drinkers). There was no indication that patients with high liver parameters (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]) were more likely to stop ART regimens because of patient wish. Severe drinkers were more likely to have high AST or high ALT regardless of whether they stopped ART because of patient wish or not.

Discussion

In this large cross-sectional study of self-reported alcohol consumption in 6,323 participants of the SHCS, more than half reported drinking at least once a week in the previous 6 months and 2.8% reported drinking behaviour associated with a severe health risk according to the WHO. These prevalences were rather low compared with the literature, where broad ranges of any alcohol consumption (46–82%) and severe drinking (8–35%) have been reported [3,6,7]. However, these studies primarily included at-risk populations, such as those with known alcohol problems, homeless, IDU or predominately males. Our data consists of a nationwide-based cohort including a large number of

Table 3. Linear regression model of correlates of HIV surrogate markers in those on ART reporting alcohol intake at least weekly in the previous 6 months[a]

Variable	Unadjusted change (95% CI)	Adjusted change (95% CI)	*P*-value
Outcome: HIV RNA, copies/ml[b]			
Alcohol consumption[c]			
Light	-0.25 (-0.47–-0.03)	-0.10 (-0.32–0.12)	0.39
Moderate	-0.28 (-0.55–-0.02)	-0.17 (-0.44–0.09)	0.20
Severe	Reference	Reference	–
Missed doses of ART[d]			
0	Reference	Reference	–
1	0.07 (-0.06–0.21)	0.07 (-0.06–0.21)	0.30
2	0.56 (0.34–0.77)	0.55 (0.34–0.77)	<0.001
>2	0.82 (0.59–1.04)	0.81 (0.59–1.04)	<0.001
Outcome: CD4$^+$ T-cell count, cells/μl[e]			
Alcohol consumption[c]			
Light	1.16 (0.01–2.31)	0.81 (-0.39–2.02)	0.19
Moderate	0.84 (-0.56–2.25)	0.65 (-0.80–2.11)	0.38
Severe	Reference	Reference	–
Missed doses of ART[d]			
0	Reference	Reference	–
1	-0.72 (-1.46–0.02)	-0.72 (-1.46–0.02)	0.06
2	0.09 (-1.08–1.26)	0.17 (-1.00–1.34)	0.78
>2	-0.66 (-1.87–0.56)	-0.56 (-1.80–0.64)	0.35

[a]*n*=2,117. [b]Both HIV RNA and CD4$^+$ T-cell count have been transformed ($\log_{10}$ and square root, respectively) because of non-linearity. The multivariate model of viral load shows the change in $\log_{10}$ viral load in, for example, light drinkers compared with severe drinkers, after adjusting for adherence. [c]Health risk on the basis of daily alcohol intake (light <20 g for women and <40 g for men, moderate 20–40 g for women and 40–60 g for men and severe >40 g for women and >60 g for men). Daily alcohol consumption was only estimated in those who consumed alcohol at least once a week over the previous 6 months with all others being characterized as having no alcohol consumption. [d]Individuals currently on combined antiretroviral therapy (ART) who reported missed doses in the previous 28 days. [e]Model of CD4$^+$ T-cell counts shows the change in the square root of CD4$^+$ T-cell count in, for example, light drinkers compared with severe drinkers, after adjusting for adherence. CI, confidence interval.

individuals and a significant representation of different HIV transmission risk categories and social classes. Two other population-based cohorts of HIV-infected individuals found alcohol drinking in 46–53% and drinking associated with a severe health risk in 8–11% [4,8]. These two studies used quantity and frequency questions to assess alcohol consumption. The heterogeneous tools used to screen for alcohol consumption might additionally explain different prevalence rates in literature. We assessed the quantity and frequency of alcohol consumption by a two-item questionnaire that has not been validated. Others used standardized screening questions, questions about quantity and frequency of alcohol consumption or predefined questionnaires (for example, CAGE, Michigan Alcoholism Screening Test and Alcohol Use Disorders Identification Test [AUDIT]) [3,5–7]. CAGE and AUDIT are reliable screening methods in detecting alcohol problems with sensitivity rates ≤97% [34].

Published factors associated with a moderate or severe health risk alcohol drinking behaviour, such as older age, lower educational attainment, lower incomes, concomitant drug use, receiving psychiatric treatment or having a psychiatric illness are similar to the ones we found and rather point to lower social classes [4–6,35]. This is relevant as multiple substance dependence syndrome and psychiatric comorbidities, especially depressive symptoms, are often found in HIV-infected adults (≤12.5% and 40%, respectively) [36–39]. We also found coinfection with hepatitis C to be associated with moderate and severe alcohol consumption. In fact, HCV infection is common in IDU, which is also a risk factor for multiple substance dependence syndrome, including alcohol [37,40].

Although females were less likely to consume alcohol than males, women who did consume alcohol were more likely to report moderate to severe drinking habits than males. Other studies do not support this finding, instead homosexual men and male individuals were overall found to be associated with a higher risk for severe alcohol consumption [4,28,41,42]. A differential underreporting according to gender could be a reason for this finding with women feeling more comfortable than men admitting their true alcohol consumption.

Interestingly, for individuals on ART, we found a decreased likelihood of being in the moderate or severe health risk drinking category. Large studies on this issue are lacking and, although causal connections cannot be drawn, one might speculate that the patient's belief of incompatibility between ART and alcohol, doctor's information about aggravated hepatotoxicity or concerns about adherence might

have led to this result. The latter perception can be a reason for occasionally withholding ART from very severe alcohol drinking individuals, even when indicated, as evidenced with IDU [35,43,44]. We found that as alcohol consumption increased to the moderate and severe health risk, there was an increased percentage of ART-pretreated individuals who were currently not on ART despite CD4+ T-cell counts <200 cells/μl. We found that 'patient wish' was the main reason for stopping ART, which again, could be explained by the patient's belief of incompatibility between ART and alcohol [35].

Severe alcohol intake is a major concern with respect to decreased adherence to medication, including timing of intake [5,8,19,20]. We found a significant correlation between non-adherence and severe alcohol consumption. In addition, there was a dose–response relationship between alcohol use and medication non-adherence as shown in other studies [8,19]. Our results add to the validity of these findings because our data were determined from a large population-based cohort. Risk factors for non-adherence, such as homelessness, IDU and depressive symptoms were highly prevalent in others, but not in our study [19]. These findings strongly suggest that alcohol use prior to the start of ART should be assessed. Short interventions that aim to cut down alcohol consumption are useful and effective [45]; however, severe drinkers are likely to be alcohol-dependant and will require more extensive support to diminish alcohol intake. Support strategies, such as directly observed therapy (DOT), to enhance adherence could be used as they are likely to affect HIV outcomes [46].

Data on the correlation between alcohol consumption, outcome of HIV surrogate markers and clinical endpoints are scarce and show contradictory results. Earlier studies showed no effect of alcohol consumption on HIV disease progression [9,25,26]. Compared with our cohort, the sample sizes were considerably smaller by a factor of 4 to 67 and less details about study duration and the exact amount of daily alcohol consumption were available. Also, only selected groups of patients (for example, homosexual men) were included and some data originate from the pre-ART era in those studies [9,26]. The more recent Veterans Aging Cohort Study found an association between alcohol consumption, AIDS-defining diseases and other comorbidities [6]. In our cohort, AIDS-defining diseases were equally distributed between all drinking categories. In the subset of individuals currently treated with ART and consuming alcohol at least once a week over the past 6 months, the association between severe alcohol consumption and worse HIV surrogate markers showed significant results only in the univariate, but not in the multivariate analyses. Similar results were also shown in literature, where severe alcohol consumption was not associated with lower CD4+ T-cell counts in individuals treated with ART [3]. One might speculate that being on ART counterbalances potentially harmful effects of alcohol, especially alcohol-induced immunosuppression. Two other studies of individuals receiving ART indicated that severe alcohol drinking was associated with significantly lower CD4+ T-cell counts and higher viral loads [27,28]; however, in one of these studies, only individuals with IDU were included and data on adherence to ART were not available [28]. The second cross-sectional study included individuals with alcohol problems of whom two-thirds belonged to ethnic minorities with 29% being homeless. Hence, risk factors for non-adherence possibly confounded the results [27]. Taken together, alcohol might influence HIV disease in many aspects, for example, cytotoxic and immunomodulatory effects [15–18] or decreased adherence to ART [5,8,19,20]. Alcohol might interact in liver metabolism with ART and might cause diarrhoea and malabsorption of ART. Also, alcohol might increase the proportion of individuals not on ART despite the need for it, as shown with our results for selected individuals. In the subset of ART-pretreated individuals, increasing alcohol consumption was associated with being off treatment despite CD4+ T-cell counts <200 cells/μl. It is possible that longitudinal long-term data will clarify whether a relevant correlation between alcohol and HIV-related disease progression exists. According to our results, no significant effect of alcohol on HIV surrogate markers in ART-treated individuals can be demonstrated in multivariate analysis.

Our study has several strengths. In addition to the large representative population, there was only a small percentage of missing data (7.7%). To assess alcohol use, we used a simple two-item questionnaire, including quantity and frequency questions. Psychosocial, clinical and laboratory data were available for all individuals at the time when the questionnaire was completed. This study also has several limitations. The analysis was on the basis of cross-sectional data. Therefore, no causal conclusions can be drawn regarding the long-term influence. Data were on the basis of self-reported alcohol consumption (some over- and underreporting might influence interpretation of data), although studies have shown the reliability of self-reported alcohol consumption. Furthermore, data on binge drinking were not assessed within the SHCS. Binge drinking is known to be a risky drinking behaviour with the likelihood that it influences the relationship of alcohol intake, adherence, treatment start and interruption. We recognize that the omission of binge drinking data can be associated with the underestimation of the degree of hazardous drinking in this population because binge drinking is the most common form of hazardous drinking – especially among a working population. Nevertheless, despite highlighting

this limitation, we believe that the main results over the years were not significantly influenced by this omission.

In summary, this is the first large representative study on self-reported alcohol consumption of a nationwide-based HIV cohort. Investigating psychosocial factors, HIV surrogate markers, ART use, adherence to ART and outcome, allowed us to comprehensively address the prevalence and associations of alcohol consumption with high external validity. Our results, namely that higher alcohol consumption is associated with increasing non-adherence, should guide clinicians to evaluate alcohol problems before the initiation of ART. Strategies to identify at risk drinkers, consecutive short intervention programmes and possibly DOT might help to reduce alcohol consumption and ameliorate adherence to ART. A longitudinal study with long-term follow-up is warranted to determine the potential causal association between higher alcohol consumption, HIV surrogate markers and clinical outcomes.

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Disclosure statement

The authors declare no competing interests.

Additional file

An additional file listing the members of the Swiss HIV Cohort Study can be accessed at www.intmedpress.com

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