Alcohol consumption over time and mortality in the Swedish Women’s Lifestyle and Health cohort

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ABSTRACT

Background: Alcohol consumption is steadily increasing in high-income countries but the harm and possible net benefits of light-to-moderate drinking remain controversial. We prospectively investigated the association between time-varying alcohol consumption and overall and cause-specific mortality among middle-aged women.

Methods: Among 48 249 women at baseline (33 404 at follow-up) in the prospective Swedish Women’s Lifestyle and Health cohort, age 30–49 years at baseline, we used repeated information on alcohol consumption and combined this method with multiple imputation in order to maximise the number of participants and deaths included in the analyses. Multivariable Cox regression models were used to calculate HRs for overall and cause-specific mortality.

Results: During >900 000 person/years, a total of 2100 deaths were recorded through Swedish registries. The median alcohol consumption increased from 2.3 g/day in 1991/1992 (baseline) to 4.7 g/day in 2004 (follow-up). Compared with light drinkers (0.1–1.5 g/day), a null association was observed for all categories of alcohol consumption with the exception of never drinkers. The HR comparing never with light drinkers was 1.46 (95% CI 1.22 to 1.74). There was a statistically significant negative trend between increasing alcohol consumption and cardiovascular and ischaemic heart diseases mortality. The results were similar when women with prevalent conditions were excluded.

Conclusions: In conclusion, in a cohort of young women, light alcohol consumption was protective for cardiovascular and ischaemic heart disease mortality but not for cancer and overall mortality.

INTRODUCTION

According to the WHO, alcohol consumption is steadily increasing in high-income countries and causally related to upper aerodigestive tract (UADT), liver, colorectal and female breast cancer.1 Worldwide, in 2012, 4% of all global female deaths were attributable to alcohol consumption. Alcohol-attributable deaths are highest in the European Region and particularly in high-income countries within Europe.2 In two recent studies, heavy alcohol consumption increased mortality from alcohol-related cancer (ARC), external causes and ‘other causes’ (external causes of deaths),3,4 while no association was observed for coronary heart disease (CHD) and other cardiovascular diseases (CVDs).5 A J-shaped association between alcohol and all-cause mortality was observed in two recent meta-analyses of prospective studies.5,6 Moderate alcohol drinking has been associated with a reduction in cardiovascular mortality7 but this is not consistent among studies. A recent meta-analysis found that low-volume alcohol consumption has no net mortality benefit compared with lifetime abstinence or occasional drinking.8 Some investigators argue that this proposed benefit depends on the...
choice of reference group. Studies on light-to-moderate alcohol consumption over time and risk of death in women are, however, scarce. Within the Swedish Women’s Lifestyle and Health (WLH) Study, an earlier analysis showed that a possible beneficial effect of light-to-moderate alcohol drinking was limited to CVD/CHD mortality, with no measurable increase in overall cancer mortality. In the current study, we quantify the associations between time-varying alcohol consumption and overall and cause-specific mortality, including cancer mortality—separating ARC and other cancers—death from CVDs, violence and injuries and other causes.

**METHODS**

**Study population**

The WLH cohort is a prospective study of women recruited between August 1991 and June 1992 in the Uppsala Healthcare Region, Sweden when 96 000 female residents aged 30–49 years were randomly selected and mailed a self-report questionnaire. Of these, 49 259 (51%) women gave their informed consent and were enrolled in the WLH study. A follow-up questionnaire, mailed between February 2003 and January 2004 to all cohort participants who were still alive, was completed and returned by 34 402 women. Both the baseline (1991/1992 questionnaire) and the follow-up questionnaire requested information regarding anthropometric measurements, personal history of diseases, smoking and drinking habits, diet and physical activity. The cohort profile has been previously described in detail. We excluded participants with implausible energy intake, outside the 1st and 99th centiles, and those who emigrated without re-immigration before enrolment (n=990). The final cohort comprised 48 249 women.

**Measure of alcohol consumption**

In the baseline questionnaire, each woman was asked: ‘How much alcohol do you drink per week, month or year?’ for five different types of alcohol: class II beer (1 glass=2 dL), class III beer (1 glass=2 dL), wine (1 glass=1 dL), fortified wine (1 glass=4 cL) and spirits (1 glass=4 cL). Response categories were open, and included number of glasses per week, month and year, respectively. Furthermore, it was possible to answer that alcoholic beverages were consumed seldom or not at all. In the follow-up questionnaire, each woman was asked if she drank alcohol, and if the answer was affirmative, she was asked ‘How often on average do you usually drink the following kinds of alcohol?’ for seven different types of alcohol: low alcohol beer, beer, white wine, red wine, dessert wine and spirits. Apart from these questions, corresponding to the questions in the baseline questionnaire, each woman was asked about binge drinking and if alcohol was usually consumed with meals. These questions were not included in this study. The follow-up questionnaire contained similar corresponding questions regarding alcohol intake. The reported glasses of alcohol were converted to grams of alcohol using food composition data from the Swedish National Food Administration (http://www7.slv.se/SokNaringsinnehall/Home/ToggleLanguage) for both the baseline and follow-up questionnaires. This gives the grams of alcohol per glass for the aforementioned different categories of alcoholic beverages, and thus allows conversion of number of glasses to grams of alcohol.

**Follow-up and mortality**

Cohort members were followed from August 1991 through 31 December 2012 by linking the cohort to the national registers (Death Register, Cancer Register and Emigration Register) through their individually unique national registration number, making follow-up virtually complete.

All Swedish death certificates are issued by a physician and the quality of these has been found to be high. Causes of death were classified according to the International Classification of Diseases, 10th Revision, codes (ICD-10 codes or corresponding). In this study, the following seven causes of death were considered: ARC as defined by the International Agency for Cancer Research, (breast cancer C50; colorectal cancer C18–C20; UADT (including cancer of the mouth, C01–C15, larynx, C32, and excluding salivary gland, C08)), other cancers (all cancer mortality excluding ARC mortality), CVD mortality excluding ischaemic heart diseases mortality N=177 including (chronic rheumatic heart diseases I05–I09; hypertensive diseases I10–I15; pulmonary heart disease and diseases of pulmonary circulation I26–I28; other forms of heart disease I30–I52; cerebrovascular diseases I60–I69; diseases of arteries, arterioles and capillaries I70–I79; diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified I80–I89; other and unspecified disorders of the circulatory I95–I99), ischaemic heart diseases (IHD) I20–I25 which were studied separately, external causes of deaths directly or indirectly related to alcohol consumption including traffic injuries, poisoning, drowning and intentional self-harm (ICD-10 V01–99, W00–99, X00–99, Y00–36, Y85–87, and Y89) and other deaths (overall mortality minus all other previously defined cause of deaths i.e., excluding mortality from ARC, other cancer, CVD, IHD and external causes).

**Statistical analysis**

As proposed by Hu et al, we applied baseline information until follow-up information became available, until of death, or emigration, whichever occurred first. Thereafter, follow-up information was applied until age of death, emigration or the end of the study period, whichever occurred first. We used Cox proportional hazard regression models to calculate HRs with 95% CIs comparing abstainers with five categories of alcohol consumption (0.1–1.49 g/day (reference group), 1.5–4.9, 5–9.9, 10–14.9 and 15+ g/day). Age was used as the underlying time variable in all Cox regression analyses. The Breslow method was adopted for handling open access.
ties. Departures from proportional hazards assumption in the Cox models was tested through inclusion of an interaction variable between categories of alcohol intake and underlying time (age) (http://www.ats.ucla.edu/stat/examples/asa/test_proportionality.htm).

We decided a priori to adjust for age at recruitment, smoking status (never, former, current, nmissing=0) and duration of smoking (continuous nmissing=0), body mass index (BMI; ≤18.49, 18.5-24.9, 25-29.9, and ≥30 kg/m² nmissing=1813) and height (continuous nmissing=911), educational attainment (≤9, 10-12, 13-16, ≥17 years nmissing=944), physical activity score derived from self-assessment scale of 1 through 5 and considering both working and leisure time (low (1-2), middle (3) and high (4-5), total energy intake not from alcohol consumption (continuous, in kJ/day), number of children (0, 1-2, ≥3, nmissing=0), age at first birth (<20, 20-24, 25-29, and ≥30 years, nmissing=6782), oral contraceptive (yes/no nmissing=96) use and duration (<3, 3-7, ≥8, nmissing=96), menopausal status and age at menopause (premenopausal, postmenopausal at <51 years of age, and postmenopausal at ≥51 years of age nmissing=1985), and history of breast cancer in mother or sister (yes/no nmissing=6782)

We have used follow-up information on smoking exposure and BMI, in addition to alcohol consumption, for both complete-case analyses and analyses performed in multiple imputed data sets.

The test for trend across categories of alcohol consumption was based on the median alcohol intake (g/day) in each category. We tested for interaction between alcohol consumption and smoking status, BMI or physical activity levels. For overall mortality, we estimated the HRs of different categories of alcohol consumption in never-smokers. For overall mortality, the effect of age was further investigated by stratifying according to age at enrolment (before (<) or after (≥) 40 years of age) and age at exit (before (<) or after (≥) 60 years of age). To reduce the risk of reverse causality, sensitivity analyses were run excluding women with prevalent conditions at cohort entry (n=7316; cancer n=2952, stroke n=138, heart attack n=98 and hypertension n=4514, with 366 women experiencing more than one of the conditions).

In a complementary set of analyses, we started following the women for mortality from 2004 instead of 1991/1992. We classified them according to the change in alcohol consumption between 1991/1992 and 2004. We created seven mutually exclusive categories: stop drinking; start drinking; continue as never consumer; maintain a low level of alcohol consumption (<5 g/day); maintain a high level (≥5 g/day); increased alcohol consumption (from <5 to ≥5 g/day); and decreased alcohol consumption (from ≥5 to <5 g/day). We estimated the HRs and their 95% CI between the ‘change’ variable and overall and cause-specific mortality. None of the cofactors were considered as time-varying but all models were adjusted for alcohol consumption in 1991/1992. For this analysis, models were adjusted for baseline (1991/1992) or follow-up (2004) characteristics when we had the information (ie, smoking, physical activity and BMI).

**RESULTS**

During >900 000 person/years, in 48 249 women at baseline (33 845 women at follow-up), a total of 2100 deaths were recorded (table 1). The median alcohol consumption increased from 2.3 g/day in 1991/1992 to 4.7 g/day in 2004. Simultaneously, the proportion of abstainers decreased from 13.6% to 10.3% (10.8% including women who dropped out of the study at follow-up). On average, between baseline and follow-up, the majority (89.6%) of WLH women were drinking <10 g/day (table 1).

Comparing point estimates (mean and percentages), abstainers had more children, were younger at the time of first birth, and were more likely to have prevalent health conditions at baseline (table 1). Women drinking more than 15 g/day were more often current smokers, had a longer history of smoking, were more often nulliparous, and underlying time (age) (http://www.ats.ucla.edu/stat/examples/asa/test_proportionality.htm).

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**Dropping out of the study and multiple imputation**

The women who dropped out of the study at follow-up (n=14 404 (29.8%)) have been described elsewhere. Briefly, compared with women who did not drop out, the women who dropped out had lower education (35.9% vs 27.1%), were more often abstainers (17.0% vs 12.2%) and reported lower levels of daily alcohol consumption (1.9 g/day vs 2.4 g/day). In order to deal with the dropouts of the study, we used multiple imputation models, and compared the results with complete case Cox regression analyses. Multiple imputation models were used under the assumption of data missing at random. To reduce sampling variability, we created 20 replicate data sets from the imputation simulation. Separate imputation models were created for overall death and cause-specific death. We used the Nelson-Aalen cumulative hazard estimator as a predictor in all the imputation models. We separately imputed information from women who died or emigrated before the follow-up questionnaire (age at exit < age at follow-up questionnaire: 1351 women of whom 715 died) and those who died or emigrated after follow-up (age at exit ≥ age at follow-up: 46 898 women of whom 1385 died).

We repeated the imputation procedure after excluding women with prevalent conditions at baseline (n=7316) and ran the time-varying Cox models for overall and cause-specific mortality. The estimates from 20 imputed data sets were combined using Rubin’s rules in order to obtain HRs and corresponding 95% CI. Finally, we compared the complete-case analysis with the results of Cox models after imputation.

All the analyses and the multiple imputations were done in SAS-V.9.4/STATA-V.13.1 (SAS Institute, USA/ Stata Corp, USA).
Table 1: Women's characteristics by baseline levels of alcohol consumption, the Women's Lifestyle and Health cohort, 1991–2012 (N=48,249, N_{2004}=33,845)

| Baseline (1991/92) alcohol consumption in g/day | 0 | 0.1–1.4 | 1.5–4.9 | 5.0–9.9 | 10.0–14.9 | 15+ | Total |
|-----------------------------------------------|---|----------|----------|---------|-----------|-----|-------|
| Characteristics                               | 0 Abstainers (N=6587) | ‘Light’ intake (N=12,357) | 1.5–4.9 (N=17,272) | 5.0–9.9 (N=8,853) | 10.0–14.9 (N=2176) | 15+ (N=1,004) | Total (N=48,249) |
| Missing at follow-up (%)                      | 37.1 | 30.3 | 28.5 | 27.5 | 28.3 | 28.6 | 29.8 |
| Mean (SD) age at baseline                     | 40.2 (6.0) | 40.1 (5.9) | 40.1 (5.7) | 40.8 (5.6) | 41.4 (5.6) | 41.7 (5.5) | 40.8 (5.8) |
| All death (n)                                 | 369 | 515 | 641 | 398 | 116 | 61 | 2,100 |
| ARC mortality (n)                             | 61 | 115 | 129 | 89 | 27 | 9 | 430 |
| Other cancers mortality (n)                   | 139 | 209 | 283 | 161 | 47 | 22 | 861 |
| CVD mortality (n)                              | 41 | 40 | 50 | 35 | 6 | 5 | 177 |
| IHD mortality (n)                              | 34 | 35 | 29 | 25 | 4 | 1 | 128 |
| External causes of deaths (n)                  | 27 | 38 | 58 | 37 | 14 | 9 | 183 |
| Other deaths (n)                               | 70 | 87 | 100 | 56 | 22 | 17 | 352 |
| Smoking status at baseline (%)                | 51.0 | 47.6 | 41.1 | 32.5 | 26.4 | 17.6 | 41.4 |
| Never                                         | 29.7 | 33.3 | 38.8 | 43.2 | 43.4 | 44.1 | 37.3 |
| Former                                        | 19.3 | 19.2 | 20.1 | 24.3 | 30.2 | 38.3 | 21.4 |
| Smoking status at follow-up (%)               | 51.6 | 48.0 | 41.5 | 32.9 | 26.6 | 16.2 | 41.5 |
| Never                                         | 28.5 | 32.2 | 38.3 | 43.4 | 45.6 | 46.9 | 37.0 |
| Former                                        | 19.9 | 19.8 | 20.2 | 23.7 | 27.8 | 37.0 | 21.4 |
| Mean (SD) smoking duration in years at baseline | 9.9 (11.9) | 10.2 (11.5) | 11.3 (11.5) | 13.7 (11.8) | 16.1 (12.2) | 19.1 (11.8) | 11.7 (11.8) |
| Menopause status and age at menopause (%)     | 89.6 | 91.2 | 92.0 | 91.4 | 91.0 | 90.8 | 91.3 |
| Premenopausal                                 | 3.5 | 3.4 | 3.1 | 3.0 | 3.4 | 3.0 | 3.2 |
| Postmenopausal at <51 years of age            | 1.8 | 1.3 | 1.2 | 1.5 | 1.5 | 1.3 | 1.4 |
| Postmenopausal at ≥51 years of age            | 5.1 | 4.1 | 3.7 | 4.1 | 4.1 | 4.9 | 4.1 |
| Mean (SD) baseline educational attainment (years) | 11.4 (3.0) | 12.0 (3.0) | 12.3 (2.9) | 12.7 (3.1) | 12.8 (3.2) | 12.9 (3.3) | 12.2 (3.0) |
| Mean (SD) BMI (kg/m²) at baseline             | 24.2 (4.3) | 23.7 (3.9) | 24.2 (4.3) | 23.3 (3.4) | 23.1 (3.3) | 23.3 (3.3) | 23.5 (3.7) |
| Mean (SD) BMI (kg/m²) at follow-up            | 26.1 (4.9) | 25.7 (4.5) | 25.1 (4.0) | 24.9 (3.9) | 24.9 (4.1) | 25.2 (4.2) | 25.3 (4.3) |
| Mean (SD) physical activity score at baseline (5 categories) | 3.0 (0.9) | 3.1 (0.9) | 3.2 (0.9) | 3.2 (0.9) | 3.0 (0.9) | 3.0 (0.9) |
| Number of children (%)                        | 15.6 | 12.4 | 12.9 | 15.2 | 19.5 | 22.1 | 14.1 |
| None                                          | 51.5 | 58.16 | 60.93 | 60.3 | 57.86 | 54.48 | 58.55 |
| 1–2                                          | 32.9 | 29.43 | 26.15 | 24.56 | 22.65 | 23.4 | 27.4 |
| Mean (SD) age at first birth (years)          | 23.6 (4.5) | 24.2 (4.4) | 24.3 (4.4) | 24.5 (4.6) | 23.4 (4.6) | 24.3 (4.8) | 24.2 (4.6) |
| Ever use of OC (%)                            | 72.7 | 80.6 | 86.5 | 88.0 | 88.9 | 90.1 | 83.6 |
| Mean (SD) duration of OC use (years)          | 6.0 (5.2) | 6.4 (5.2) | 6.8 (5.3) | 7.1 (5.5) | 7.3 (5.6) | 7.6 (5.7) | 6.7 (5.3) |
| Mean (SD) energy except from alcoholic beverages (kJ/day) | 6315 (2048) | 6443 (1913) | 6427 (1828) | 6397 (1842) | 6396 (1856) | 6250 (1854) | 6405 (1866) |
| Prevalent conditions (%)†                     | 16.2 | 14.9 | 14.8 | 14.9 | 17.1 | 16.8 | 15.2 |

ARC as defined by the International Agency for Cancer Research (breast cancer C50; colorectal cancer C18–C20; UADT (including cancer of the mouth, C01 -C15, larynx, C32, and excluding salivary gland, C08), other cancers (all cancer mortality excluding ARC mortality)).‡

†Hypertension, stroke, heart attack, cancer before enrolment.

ARC, alcohol-related cancers; BMI, body mass index; CVD, cardiovascular disease; IHD, ischaemic heart diseases; UADT, upper aerodigestive tract.
and were better educated compared with women in other alcohol consumption categories (table 1).

Abstainers at both baseline and follow-up had higher BMI and lower education and were less physically active (table 2). The proportion of those who quit both smoking and drinking (from ≥5 g/day to never) was 1.3% of those who reduced alcohol consumption.

**Alcohol intake (time-varying) and mortality**
Compared with light drinkers (0.1–1.5 g/day), a statistical null association with overall mortality was observed for all categories of alcohol consumption with the exception of never drinkers. The HR comparing never with light drinkers was 1.46 (95% CI 1.22 to 1.74) in the smoking-adjusted model, but was reduced to HR=1.22 (95% CI 1.02 to 1.46) in the fully adjusted model (table 3). The results were similar when women with prevalent conditions were excluded and among never-smokers only, with the exception that abstainers did not experience a statistically significantly higher risk when compared with light drinkers (data not shown).

We observed a statistically significant inverse trend between alcohol consumption and both CVD and IHD mortality (p value for trend=0.04 and 0.02, respectively). Compared with light drinkers (0.1–1.5 g/day), none of the categories of consumption reached a statistically significant level for CVD mortality. Alcohol consumption above 10 g/day was associated with a reduction of IHD mortality. Overall and cause-specific mortality was similar to the complete-case analysis (see online supplementary table S1). Overall mortality was similar for women enrolled in the cohort at age <40 and those enrolled after ≥40, and also between women who exited from the cohort at age <60 and those who exited at ≥60 years of age (see online supplementary table S2).

**Change in alcohol consumption and mortality**
On the basis of a reduced number of deaths, alcohol abstinence at 1991/1992 and follow-up in 2004, and those who declared that they had stopped had an increased overall mortality risk when compared with women who maintained a low (<5 g/day) alcohol consumption (table 4).

None of the interactions tested between alcohol intake and age smoking status, BMI and physical activity level were statistically significant in any of the outcomes investigated.

**DISCUSSION**
Using the WLH cohort of young and light alcohol drinking women, we observed a null association between all levels of alcohol consumption and overall and cause-specific mortality while alcohol abstainers appeared at greater risk of overall mortality compared with light consumers. We observed a consistent negative association with cardiovascular and ischaemic heart disease mortality. The results were similar when women with prevalent conditions at cohort entry were excluded. Compared with maintaining a low alcohol consumption, abstinence and stop drinking between baseline (1991/1992) and follow-up (2003/2004) were associated with an increased overall mortality risk.

Study strengths included the prospective design, detailed updated assessment of alcohol consumption (reducing the within-person variation) and virtually complete long-term follow-up. We used repeated measurements of alcohol consumption, smoking and BMI in order to take into account changes in these variables over time and to attenuate the risk of measurement errors. Measurements errors such as change in the serving size may have occurred between baseline and follow-up, partly explaining the increase in alcohol consumption that we observed during this period. However, they would most likely lead to a non-differential bias and a potential underestimation of the true effect. Analyses excluding participants with morbid condition at cohort entry, and a small proportion of women who quit both smoking and alcohol drinking between baseline and follow-up suggest that reverse causality is unlikely to have driven our results. Main limitations included the small number of cases for specific causes of death, especially among women drinking ≥15 g/day. Other limitations were the self-reported alcohol consumption and that we had no information on excessive alcohol consumption in the WLH cohort. However, in Sweden, until 2004 occasional consumption of large amounts of alcohol was more often related to the behaviour of younger men, rather than middle-aged women. Following the International Agency for Cancer Research (IARC) and the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) suggestions,12 23 we chose not to separately study the effects of different alcohol beverages.

Compared with other similar studies, our cohort comprised younger women who drank smaller quantities of alcohol,1 24 which has not been sufficiently described earlier. Our findings are in agreement with two recent multicentre prospective studies from the European Prospective Investigation into Cancer and Nutrition (EPIC), which found that overall mortality did not differ between light drinkers (0.1–4.9 g/day or ≤1 g/day) and those who consumed up to 30 g/day of alcohol.5 4 We found a similar increased risk of overall mortality among abstainers (HR=1.22) as the above-referenced EPIC studies (HR=1.26 and HR=1.19, respectively). In contrast, when comparing different amounts of alcohol intake to abstinence, two meta-analyses found a j-shaped dose–response relationship between alcohol and all-cause mortality. Consumption of up to 2 drinks per day (equivalent to 20–25 g/day of alcohol) was inversely associated with total mortality.5 6 The protective effect observed in some epidemiological prospective studies may be explained by the choice of the reference group.5 6 In order to minimise the reverse causality problem, the reference group should control for the so-called ‘sick

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### Table 2 Women’s Lifestyle and Health cohort characteristics by change in alcohol consumption between baseline (1991) and follow-up (2004)

| Characteristics                                      | Stop 2614 | Start 3924 |
|------------------------------------------------------|-----------|------------|
| **Change in alcohol consumption between baseline (1991/92) and follow-up (2004) period** |           |            |
| Abstainers at baseline and follow-up                 | 2465      | 14 941     |
| Maintain low <5 g/day                                | 9337      | 9.3 (5.4)  |
| Maintain high ≥5 g/day                               | 11 660    | 2.6 (1.3)  |
| Increase                                             | 2165      | 7.9 (6.0)  |
| Decrease                                             | 1143      | 4.8 (6.8)  |
| Exit before follow-up (death or emigration)         |           |            |
| **Mean (SD) baseline alcohol consumption* (g/day)**  | 1.8 (3.5) | –          |
| Baseline abstainers (%)                              | –         | 60 (10.8)  |
| Mean (SD) follow-up alcohol consumption* (g/day)     | –         | 4.0 (10.8) |
| Follow-up abstainers (%)                             | 51.5      | 48.5       |
| Prevalent conditions at baseline (%)                 | 5.6       | 39.4 (5.8) |
| Mean (SD) age at baseline (years)                    | 41.3 (5.7)| 39.4 (5.8) |
| Smoking status at baseline (%)                       | 5.6       | 39.4 (5.8) |
| Never                                                | 51.9      | 43.7       |
| Former                                               | 27.6      | 34.4       |
| Current                                              | 20.5      | 21.9       |
| Smoking status at follow-up (%)                      | 51.0      | 42.1       |
| Never                                                | 51.0      | 42.1       |
| Former                                               | 27.7      | 33.3       |
| Current                                              | 21.3      | 24.6       |
| Mean (SD) baseline educational attainment (years)    | 11.5 (3.1)| 11.4 (2.9) |
| Mean (SD) physical activity score (5 categories)     | 3.0 (0.9) | 3.0 (0.9)  |
| Mean (SD) BMI (kg/m²) at baseline                    | 24.3 (4.5)| 23.9 (4.1) |
| Mean (SD) BMI (kg/m²) at follow-up                   | 26.3 (5.2)| 26.0 (4.8) |
| All death (n)                                        | 100       | 132        |
| ARC mortality (n)                                    | 21        | 25         |
| Other cancers mortality (n)                          | 39        | 47         |
| CVD mortality (n)                                    | 9         | 20         |
| IHD mortality (n)                                    | 7         | 14         |
| External causes of deaths (n)                        | 3         | 3          |
| Other deaths (n)                                     | 23        | 24         |

**Mean (SD)** and **(%)** are shown for continuous and categorical variables, respectively.

**ARC** as defined by the International Agency for Cancer Research (breast cancer C50; colorectal cancer C18–C20; UADT (including cancer of the mouth, C01 -C15, larynx, C32, and excluding salivary gland, C08). (all cancer mortality excluding ARC mortality)).

*Among alcohol consumers at baseline.

**ARC,** alcohol-related cancers; **BMI,** body mass index; **CVD,** cardiovascular disease; **IHD,** ischaemic heart diseases; **OC,** oral contraceptive; **UADT,** upper aerodigestive tract.
We observed a higher overall mortality in abstainers and women who stop drinking. However, alcohol drinkers may differ from abstainers in unmeasured ways that influence mortality, and so uncontrolled confounding cannot be ruled out in our study. The risk of death of women who abstained decreased when finer socio-economic characteristics such as income, employment status, ethnicity and social isolation were controlled for. We observed a decrease in abstainer’s risk of overall mortality from the smoking-adjusted model to the fully adjusted model. Our results were similar when women with prevalent conditions at cohort entry were excluded; nevertheless, residual confounding for ‘sick quitters’ in the abstainers group could have contributed to the increased risk association for abstainers with all-cause mortality. Alcohol consumption was self-reported in our study and misclassification of the amount of alcohol intake, as well as lack of accuracy in reporting prevalent morbid conditions at baseline in the group of abstainers, could explain the excess risks observed.

For light-to-moderate alcohol consumption (up to 30 g/day), our results were similar to the EPIC study conducted by Ferrari et al., which showed no association in any of the cause-specific mortalities studied (CVD, ARC, external causes of deaths) compared with 0.1–4.9 g/day of alcohol intake. In contrast with this EPIC study, we did not observe a statistically increased risk in any of the cause-specific mortalities studied among abstainers. Like previous studies, another EPIC study showed a lower effect on CVD mortality (excluding IHD mortality) when light-to-moderate (up to 30 g/day) intake was compared with light (≤1 g/day) alcohol intake. The two studies from EPIC had only one measurement of alcohol consumption and their reference group; ‘light’ alcohol consumption was different (0.1–4.9 g/day and ≤1 g/day). Cardiovascular benefits of alcohol have not been confirmed by a recent Mendelian randomisation project, and were limited to older women ≥60 years in pooled analyses of all-cause mortality associated with alcohol consumption. In addition, even if low-dose alcohol consumption reduces CVD and IHD mortality, the increased incidence of cancer, traffic accidents and risk for alcohol dependence weaken any possible benefits. The biological explanation most often proposed for the potential ‘cardioprotective’ effect of alcohol is an increase in high-density lipoprotein cholesterol.

Most cohort studies only have information on alcohol consumption at cohort entry, but alcohol consumption is likely to vary over time. In our prospective cohort study, we observed a considerable increase in alcohol consumption between 1991/1992 and 2004. In Sweden, among both men and women, over a similar period from 1990 to 2003, annual consumption based on sales increased from 7.8 to 10.3 L of pure alcohol per person.
| Changes in alcohol consumption between baseline 1991 and follow-up 2004 | Causes of deaths |ARC N=599| CVD N=120| IHD N=85| External causes of deaths N=72| Other deaths N=259 |
|---|---|---|---|---|---|
| Maintain low, <5 g/day | All death N=1389 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Stop drinking | 1.49 (1.10 to 2.02) | 1.17 (0.92 to 1.48) | 1.12 (0.91 to 1.36) | 1.29 (0.86 to 1.93) | 1.01 (0.66 to 1.59) | 1.29 (0.86 to 1.93) | 1.00 | 1.00 |
| Start drinking | 1.71 (0.88 to 3.33) | 1.19 (0.71 to 1.99) | 1.01 (0.71 to 1.43) | 1.68 (0.70 to 4.00) | 1.70 (0.66 to 4.38) | 0.81 (0.17 to 3.83) | 1.90 (1.00 to 3.61) |
| Never at both times | 1.53 (1.20 to 1.96) | 1.30 (0.74 to 2.27) | 1.41 (0.99 to 2.00) | 1.82 (0.70 to 4.72) | 2.13 (1.03 to 4.42) | 1.44 (0.64 to 3.26) | 1.63 (0.90 to 2.95) |
| Maintain high, ≥5 g/day | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Increased from <5 to ≥5 g/day | 0.82 (0.68 to 1.00) | 0.92 (0.58 to 1.44) | 0.82 (0.62 to 1.08) | 0.91 (0.72 to 1.16) | 0.95 (0.52 to 1.76) | 0.57 (0.23 to 1.40) | 1.27 (0.63 to 2.56) | 1.09 (0.75 to 1.58) |
| Decreased from ≥5 to <5 g/day | 1.17 (0.89 to 1.54) | 1.30 (0.70 to 2.43) | 1.00 (0.66 to 1.53) | 1.54 (0.64 to 3.70) | 2.14 (0.91 to 5.06) | 1.80 (0.67 to 4.89) | 1.05 (0.51 to 1.98) |

ARC as defined by the International Agency for Cancer Research (breast cancer C50; colorectal cancer C18–C20; UADT (including cancer of the mouth, C01–C15, larynx, C32, and excluding salivary gland, C08), other cancers (all cancer mortality excluding ARC mortality)).

*Age at follow-up was considered as age at start.
†A priori systematic adjustment was undertaken for age at follow-up, smoking status (follow-up) and duration of smoking, BMI (follow-up) and height, education attainment, physical activity score, energy intake not from alcohol consumption, number of children, age at first birth, oral contraceptive use and duration, menopausal status at baseline and history of breast cancer in mother or sister.

ARC, alcohol-related cancers; BMI, body mass index; CVD, cardiovascular disease; IHD, ischaemic heart diseases; UADT, upper aerodigestive tract.
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