



ORIGINAL ARTICLE

## A 32-year longitudinal study of alcohol consumption in Swedish women: Reduced risk of myocardial infarction but increased risk of cancer

DOMINIQUE HANGE<sup>1</sup>, JÓHANN A. SIGURDSSON<sup>2,3</sup>, CECILIA BJÖRKELUND<sup>1</sup>, VALTER SUNDH<sup>1</sup> & CALLE BENGTSSON<sup>1,†</sup>

<sup>1</sup>Department of Public Health and Community Medicine/Primary Health Care, Sahlgrenska Academy, University of Gothenburg, Sweden, <sup>2</sup>Department of Public Health and General Practice and the Research Unit in General Practice, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, <sup>3</sup>Department of Family Medicine, University of Iceland, Reykjavik, Iceland

### Abstract

**Objective.** To assess associations between the intake of different types of alcoholic beverages and the 32-year incidence of myocardial infarction, stroke, diabetes, and cancer, as well as mortality, in a middle-aged female population. **Design.** Prospective study. **Setting.** Gothenburg, Sweden, population about 430 000. **Subjects.** Representative sample of a general population of women (1462 in total) aged 38 to 60 years in 1968–1969, followed up to the ages of 70 to 92 years in 2000–2001. **Main outcome measures.** Associations between alcohol intake and later risk of mortality and morbidity from myocardial infarction, stroke, diabetes, and cancer, studied longitudinally. **Results.** During the follow-up period, 185 women developed myocardial infarction, 162 developed stroke, 160 women became diabetic, and 345 developed cancer. Women who drank beer had a 30% lower risk (hazards ratio (HR) 0.70, 95% confidence interval (CI) 0.50–0.95) of developing myocardial infarction and almost half the risk (HR 0.51 CI 0.33–0.80). A significant association between increased risk of death from cancer and high spirits consumption was also shown (hazards ratio [HR] 1.47, CI 1.06–2.05). **Conclusions.** Women with moderate consumption of beer had a reduced risk of developing myocardial infarction. High spirits consumption was associated with increased risk of cancer mortality.

**Key Words:** Alcohol, diabetes mellitus, general practice, longitudinal studies, myocardial infarction, neoplasms, Sweden, women

### Introduction

The association between alcohol consumption and health has been an issue of much debate during recent decades [1]. The relationship between alcohol intake and cardiovascular health is complex, involving both protective and harmful effects [2]. Results from ecological studies have shown reduced mortality from cardiovascular diseases (CVD) in countries with high alcohol consumption per capita compared with countries with low alcohol consumption [3]. These results have been confirmed by large cohort

studies, which show a J-shaped risk consumption curve, such that those who consumed one to two drinks (beer, wine, or spirit) a day showed the lowest risk of death from all causes as well as mortality in cardiovascular diseases [4].

As alcohol consumption is closely related to social habits, religion, culture, and personal life stories, the meaning of and definitions of light, moderate, and heavy alcohol intake may differ across countries and studies [5]. Therefore, comparisons between studies concerning the relationship between alcohol

<sup>†</sup>Calle Bengtsson passed away on 23 March 2013

Correspondence: Dominique Hange, Department of Public Health and Community Medicine/Primary Health Care, PO Box 454, SE-405 30 Gothenburg, Sweden. Tel: +46-31-773 68 49. Fax: +46-31-778 17 04. E-mail: dominique.hange@vgregion.se

© 2015 The Author(s). Published by Taylor & Francis. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

(Received 29 August 2014; accepted 30 May 2015)

The effect of alcohol intake upon health remains a key issue.

- Regular consumption of, e.g., one glass of wine seems to prevent various diseases while excessive consumption may give rise to serious disease.
- In this study, women with moderate consumption of beer had a reduced risk of myocardial infarction over 32 years.
- Women who often drank spirits had an increased risk of death from cancer.

consumption and mortality, as well as morbidity, can be difficult to interpret. Most of the cohort studies have originated from countries where daily consumption of alcohol is part of the social culture and where one to two drinks a day are called “moderate” drinking. However, in most of the Nordic countries, binge drinking or drinking during weekends was the traditional way to consume alcoholic beverages in the late 1960s, and daily drinking was unusual or exceptional [6]. The alcohol habits in the Nordic countries today remind of those in the rest of Europe. Some studies among males have shown a higher morbidity and all-cause mortality among abstainers and high consumers of alcohol, compared with light and moderate drinkers [7]. Similar studies among women are fewer in number and have not confirmed an association between high alcohol consumption and a higher risk of mortality. However, studies by Rimm [8] and Fuchs [9] also showed a protective effect of moderate alcohol intake on overall mortality in women, even if this survival benefit appeared largely confined to women at greater risk for coronary heart disease [10].

Approximately 60% excess risk of stroke was observed among heavy drinkers compared with occasional drinkers after adjustment for cardiovascular risk factors, but adjustment for hypertension attenuated the relationship among middle-aged men [11]. Some results indicated that heavy alcohol consumption increased the relative risk of any stroke while light or moderate alcohol consumption seemed to be protective against ischaemic stroke [12,13]. It has also been observed that moderate alcohol consumption was associated with a decreased incidence of diabetes mellitus in both men and women [14]. A higher consumption of alcohol has been associated with an increased risk of breast cancer [15,16].

The multidisciplinary Population Study of Women in Gothenburg, Sweden has been collecting information on women’s drinking habits since 1968–1969, and the participants, aged 38–60 years upon entering the study, have now been followed up for 32 years [17]. The purpose of this paper was to investigate

alcohol habits as reported in 1968–1969 (at baseline) in relation to 32-year overall mortality and to the incidence of myocardial infarction, stroke, diabetes, and cancer.

## Material and methods

The study took place in Gothenburg, the second largest city in Sweden, with about 430 000 inhabitants in 1968 and situated on the south-west coast of Sweden. The initial examination of the population sample described in this paper was carried out in 1968–1969 in Gothenburg, when a total of 1462 women in five age strata between 38 and 60 participated [18]. Table I shows number of participants in different age cohorts and some basic demographic data on the women in 1968–1969.

The sampling was based on date of birth, which together with the high participation rate (90.1%), ensured that the participants were a representative cross-section of women from the community in the age groups studied [18]. Women who reported having CVD (myocardial infarction or stroke), cancer, or diabetes at start of the examinations in 1968–1969 were excluded. The participants were re-examined in 1974–1975, in 1980–1981, in 1992–93 and, after 32 years, in 2000–2001. At the follow-up examinations the participation rates were 91%, 83%, 70%, and 71%, respectively, among those still alive [19].

### *Alcohol consumption by women in 1968–1969*

Information regarding alcohol habits was obtained at baseline using a standardized structured interview conducted by a physician. All participants were asked to report their intake frequency (not in grams/day or drinks/week) of three different types of alcoholic drinks, namely, beer, wine, and spirits. Women were asked to report the frequency of alcohol intake according to the following answer alternatives:

Table I. Number of participants in different age cohorts and some basic demographic data of the women in 1968–1969.

Year of birth	Age	n	Smokers n	LPA* n	High triglycerides (> 1.5 mmol/L)
1930	38	372	173	63	49
1922	46	431	189	82	85
1918	50	398	147	71	85
1914	54	180	69	23	55
1908	60	81	16	26	20
Total		1462	594	265	294

Note: \*LPA = low physical activity; less than 4 hours/week.

- 0 Never.
1. Earlier, but not during the last 10 years.
2. Earlier, but not during the last year.
3. Monthly.
4. Weekly.
5. Several times a week.
6. Daily.

For the purpose of this study we derived three separate categories of consumption of alcohol, based on the various levels (frequency) where:

- (i) "Never" included levels 0, 1 and 2.
- (ii) "Sometimes" included levels 3 and 4.
- (iii) "Regularly" included levels 5 and 6.

The relative validity of the questions about alcohol was assessed by comparing these data recorded in 1968–1969 with alcohol intake as reported in a 24-hour dietary recall interview conducted in 1968–1969 [18]. The Spearman correlation coefficient between the information concerning total alcohol intake acquired using the two methods was 0.44. This indicated that these questions successfully ranked the subjects.

#### *Assessment of potential confounders*

Information on hypertension, body mass index (BMI), serum triglycerides and cholesterol, medication, medical history, diet, smoking, and leisure-time physical activity was obtained at every examination. Hypertension was defined as systolic blood pressure  $\geq 160$  mmHg and/or diastolic blood pressure  $\geq 95$  mmHg at the time of the examination (1968–1969) or taking antihypertensive medication. Body weight was measured to the nearest 0.1 kg using a balance scale. Body height without shoes was measured to the nearest 0.5 cm. BMI was calculated as weight/height<sup>2</sup> (kg/m<sup>2</sup>). Blood samples were drawn in the fasting state. Lipids were measured in units of millimoles per litre. Chemical analyses were done at the Department of Clinical Chemistry at Sahlgrenska University Hospital in Gothenburg using standard routine clinical laboratory procedures.

Smoking was defined as present or recent smoking versus never smoking or giving up smoking more than 10 years ago. Leisure-time physical activity was defined as: "usually spending more than four hours a week gardening, running, dancing, playing golf, tennis or similar activities, during the last year" versus "less than this level of activity". The measure "leisure-time exercise" compared physical activity of at least four hours/week with less activity.

Information on marital status, children, total income status, and education was obtained by means of a questionnaire completed in the initial study in

1968–1969 to assess socioeconomic status (SES). SES was defined according to a five-point scale [20]. High SES as defined in the present paper designated large-scale employers and officials of high or intermediate rank, intermediate SES to small-scale employers, officials of lower rank, and foremen, while low SES designated skilled and unskilled workers. Higher education was defined as education beyond elementary school (elementary schooling was usually for six or seven years).

#### *Definition of myocardial infarction and stroke*

A woman was defined as having myocardial infarction, other CVD and/or stroke if the diagnosis had been made by a doctor and was classified according to the International Classification of Diseases, Ninth and Tenth Revisions (ICD 9 and 10), diagnostic codes ICD 391–448B or I01.0–I79.2, respectively (myocardial infarction, heart failure, other cardiovascular diseases, stroke). Women with a diagnosed CVD before study began in 1968 were excluded.

#### *Verification of diabetes diagnosis*

A woman was defined as having diabetes if she was on anti-diabetic therapy or if the diagnosis had been made by a physician, as well as a fasting blood sample of glucose concentration  $> 7$  mmol/l at the time of examination. Women with diagnosed diabetes before the study began in 1968 were excluded.

#### *Verification of cancer diagnosis*

Data from the Swedish Cancer Registry and from regional cancer registries from the total 32-year period 1968–1969 to 2000–2001 were obtained. Each participant was also asked if she had any history of neoplastic disease and, if so, she was asked to provide details concerning type, localization, and treatment. Women with a diagnosed cancer before the study began in 1968 were excluded.

A comparison between the 1988 Cancer Registry and the observations made in the Prospective Population Study of Women showed that all but one of 103 cases (99%) were registered in the Cancer Registry and all but one (99%) in the Prospective Population Study of Women [17].

#### *Verification of morbidity and mortality*

Information concerning morbidity and mortality was continuously obtained from local parish registers and

supplemented by information from the National Central Bureau of Statistics as well as the Swedish National Board of Health and Welfare. Thus, information was obtained concerning all 461 deaths, during the period 1968–1969 to 2000–2001. Information on causes of death was obtained from death certificates, which were supplemented by studying hospital records.

#### Statistical methods

Cox proportional hazard models assessed the risks during the follow-up periods associated with different consumption categories at baseline, and differences in risk are reported as hazard ratios (HR) with 95% confidence interval (CI). Outcome events analysed were total mortality as well as mortality and morbidity from myocardial infarction, stroke, diabetes, and cancer. Alcohol consumption categories as well as all covariates in the models were recorded in the baseline examination in 1968–1969. The combined two highest alcohol drinking levels, “regularly” and “sometimes”, were compared with the “never” category to obtain the main results. Also, differences between the separate consumption categories were tested. All models included age as a covariate. Furthermore, associations were also tested in larger models that besides age also included four other covariates selected by an initial stepwise procedure, i.e. triglycerides, BMI, leisure-time physical activity, and SES.

The significance level was set at  $< 0.05$  (two-sided tests). SAS™ software (version 9.2; SAS Institute, Cary, NC, USA) was used for the statistical analyses.

## Results

### Alcohol consumption in 1968–1969

Information on the use of alcohol in the different age groups as reported in 1968–1969 is given in Table II. No differences were observed in the use of wine or spirits between the different age cohorts studied.

Table III shows the age-adjusted comparisons of level of lifestyle, anthropometric, and physiological variables between the group with “never” and the group with “sometimes/regularly” levels of intake concerning beer, wine, and spirits, respectively, as reported at the baseline examination in 1968. There were significant differences concerning most variables, for example BMI and triglycerides, mostly in favour of the sometimes/regularly group.

### Mortality from selected diseases during 32 years of follow-up

During the follow-up period, 1968–2001, there were 461 deaths (32% of the women examined at baseline). Of the women who had been free from respective disease at the beginning of the study period, 82 died from myocardial infarction, 41 from stroke, 35 from diabetes, and 162 from cancer. Table IV shows the HRs for total mortality (and mortality from myocardial infarction, stroke, diabetes, and cancer, respectively), and confidence intervals in the age-adjusted model and the multivariate model, in women drinking beer, wine, and spirits at least sometimes/regularly during the recent year compared with women who had never used these beverages or at least not during the past year. In the age-adjusted

Table II. Distribution of alcohol consumption (absolute numbers/percentage), i.e. beer, wine, and spirits, reported by sample participants at baseline (1968–1969), across age-groups.<sup>1</sup>

Alcohol intake <sup>2</sup> n/%	Age in 1968–1969 (years)				
	38	46	50	54	60
Beer:					
Never	101/27.2	142/32.9	141/35.5	62/34.4	26/32.1
Sometimes	166/44.6	178/41.3	148/37.3	69/38.3	40/49.4
Regularly	105/28.2	111/25.8	108/27.2	49/27.2	15/18.5
Wine:					
Never	171/46.1	221/51.3	189/47.7	84/46.7	53/65.4
Sometimes	139/37.5	119/27.6	123/31.1	64/35.6	16/19.8
Regularly	61/16.4	91/21.1	84/21.2	32/17.8	12/14.8
Spirits:					
Never	277/74.9	328/76.1	282/71.2	139/72.8	64/79.0
Sometimes/Regularly	93/26.1	103/23.9	114/28.8	49/27.2	17/21.0

Notes: <sup>1</sup>All participants were asked to report their intake frequency of three different types of alcoholic drinks, i.e. beer, wine, and spirits. The intakes were divided into: Never (including never, earlier, but not during the last 10 years and earlier, but not during the last year), Sometimes (including monthly and weekly), and Regularly (including several times a week and daily). <sup>2</sup>Test of age group difference (Chi-square test): beer  $p = 0.01$ , wine  $p = 0.07$ , spirit  $p = 0.15$ .

Table III. Body mass index (BMI), blood lipid levels, smoking frequency, and leisure-time physical activity (LTPA) in relation to level of intake of beer, wine, and spirits among women who reported never drinking (level 0–2) compared with women who reported drinking sometimes or regularly (level > 2), at baseline (1968).<sup>1</sup>

	Mean for non-drinkers drinkers	95% CI <sup>2</sup>	p-value
<b>Beer:</b>			
BMI (kg/m <sup>2</sup> )	24.9/23.7	–1.50 to –0.69	< 0.001
Triglycerides (mmol/l)	1.32/1.17	–0.21 to –0.07	< 0.001
Cholesterol (mmol/l)	7.00/6.80	–0.27 to –0.02	< 0.05
Proportion smokers	0.37/0.42	0.97–1.54	n.s.
Proportion physically active <sup>3</sup>	0.79/0.83	1.02–1.78	< 0.05
<b>Wine</b>			
BMI (kg/m <sup>2</sup> )	24.6/23.6	–1.36 to –0.60	< 0.001
Triglycerides (mmol/l)	1.28/1.16	–0.17 to –0.05	< 0.001
Cholesterol (mmol/l)	6.93/6.79	–0.23 to –0.003	n.s.
Proportion smokers	0.38/0.44	1.01–1.55	< 0.05
Proportion physical active	0.77/0.86	1.33–2.30	< 0.001
<b>Spirits</b>			
BMI (kg/m <sup>2</sup> )	24.3/23.3	–1.50 to –0.62	< 0.001
Triglycerides (mmol/l)	1.25/1.15	–0.17 to –0.03	< 0.01
Cholesterol (mmol/l)	6.88/6.81	–0.22 to –0.04	n.s.
Proportion smokers	0.35/0.61	2.45–4.01	< 0.001
Proportion physical active	0.82/0.82	0.71–1.31	n.s.

Notes: <sup>1</sup>Age-adjusted results calculated in regression models (linear or logistic) with age groups as nominal covariate. <sup>2</sup>CI reported for difference in means for BMI, triglycerides, and cholesterol, and odds ratio for smoking and physically active. <sup>3</sup>Leisure-time exercise comparing physical activity of at least four hours/week with less activity.

model, consumption of beer was associated with decreased risk of total mortality and mortality in myocardial infarction, and the reduced risk of mortality in myocardial infarction remained in the multivariate model.

Wine drinkers had less risk of mortality from myocardial infarction than women who did not drink wine (HR = 0.64, 95% CI 0.41–1.00,  $p < 0.05$ ), when analyses were controlled for age.

In the multivariate model, consumption of spirits was associated with decreased risk of mortality from myocardial infarction but increased risk of mortality from cancer.

Risk differences were found between women who never drank beer and women who drank beer; beer drinkers had almost half the risk of mortality from myocardial infarction compared with women who did not drink beer (HR = 0.44, 95% CI 0.28–0.68,  $p < 0.001$ , age-adjusted HR). Women who drank beer sometimes or regularly both had about the same risk reduction compared with women who never drank beer (HR = 0.51, 95% CI 0.33–0.80,  $p < 0.05$ ), in the multivariate model (data not shown).

The total mortality risk was significantly lower for beer drinkers; HR = 0.78, 22% lower risk than women who did not drink beer but did not show any differences for wine or spirit drinkers (Levels < 2).

When dividing the beer drinkers into two groups, the women who drank beer regularly (Levels 5 and 6 vs. 0–2) had about the same risk as women who did not drink beer; however, women who sometimes drank beer (Levels 3 and 4 vs. 0–2) had HR = 0.68, and a 32 % lower risk of mortality than women who never drank beer.

Comparing level 3–4 with all other levels yielded a HR of 0.70, i.e. a 30% lower mortality risk.

To examine whether there was any decrease over time in the effect of the consumption patterns in 1968 on mortality during the follow-up period, the time was divided into three intervals: 0–18 years, 18–28, years and 28–32 years, giving a distribution of number of deaths of 25%, 45%, and 30%, and separate effects were calculated in each. The results showed no significant differences in the change of effect over time (data not shown).

#### *Morbidity in myocardial infarction, stroke, diabetes, and cancer during 32 years of follow-up*

During the follow-up period, 185 women developed myocardial infarction and 162 developed stroke. Also, 160 women became diabetic and 345 developed cancer of which 63 women died from breast cancer. Table V shows the HRs for myocardial infarction,

Table IV. Total mortality 1968–2000 and mortality from myocardial infarction, stroke, diabetes, and cancer 1968–2000 in women who reported drinking beer, wine, and spirits, respectively, sometimes or regularly (Level > 2), at baseline compared with women who had never used these beverages or at least not during the past year.<sup>1</sup>

End-point studied	Hazard ratio: age-controlled/multivariate controlled (CI age-controlled/CI multivariate controlled)	Statistical significance: age-controlled/multivariate controlled p-value	Test of constant HR (linear interaction test): age-controlled/multivariate controlled p-value	HR first 16 years	HR last 16 years
<b>Beer:</b>					
Death (total, n = 461)	0.80/0.87 (0.66–0.97)/(0.72–1.06)	< 0.05/ns	0.30/ 0.31	0.87 (0.61–1.23) 0.95 (0.67–1.34)	0.78 (0.64–0.96) 0.85 (0.69–1.05)
Trend test:					
Death myocardial infarction (n = 82)	1.00/1.01 (0.93–1.07)/(0.94–1.08)	< 0.001/< 0.05	0.09/ 0.08	0.31 (0.11–0.86) 0.36 (0.13–1.02)	0.47 (0.29–0.74) 0.54 (0.34–0.87)
Death stroke (n = 41)	0.93/0.98 (0.74–1.18)/(0.78–1.24)	ns/ns	0.54/ 0.54	0.19 (0.02–1.58) 0.22 (0.03–1.89)	1.03 (0.53–2.02) 1.21 (0.61–2.38)
Death diabetes (n = 35)	0.89/1.04 (0.46–1.69)/(0.54–2.00)	ns/ns	0.85/ 0.79	0.58 (0.14–2.45) 1.04 (0.24–4.49)	0.54 (0.27–1.10) 0.89 (0.42–1.89)
Death cancer (n = 162)	0.55/0.92 (0.28–1.06)/(0.45–1.89)	ns/ns	0.13/ 0.13	1.15 (0.68–1.94) 1.13 (0.66–1.92)	0.96 (0.66–1.39) 0.94 (0.65–1.38)
1.01/0.99 (0.73–1.41)/(0.71–1.39)					
1.10/1.08 (0.98–1.23)/(0.97–1.21)					
<b>Wine:</b>					
Death (total)	0.90/0.97 (0.75–1.08)/(0.80–1.18)	ns/ns	0.87/0.92	0.85 (0.59–1.24) 0.94 (0.65–1.36)	0.91 (0.75–1.11) 0.99 (0.80–1.22)
Death myocardial infarction	0.95/0.99 (0.85–1.05)/(0.88–1.11)	< 0.05/ns	0.53/ 0.60	0.64 (0.23–1.77) 0.76 (0.27–2.13)	0.64 (0.40–1.04) 0.74 (0.45–1.21)
Death stroke*	0.64/0.74 (0.41–1.00)/(0.47–1.18)	ns/ns	0.25/ 0.28	–	–
Death diabetes*	0.75/0.84 (0.56–0.99)/(0.62–1.14)	ns/ns	0.15/ 0.17	–	–
Death cancer	1.32/1.79 (0.71–2.45)/(0.93–3.42)	ns/ns	0.79/ 0.80	1.05 (0.61–1.78) 1.00 (0.58–1.73)	1.15 (0.81–1.63) 1.10 (0.76–1.60)
0.93/0.98 (0.74–1.18)/(0.78–1.24)					
0.51/0.67 (0.25–1.02)/(0.32–1.38)					
0.59/0.73 (0.36–0.97)/(0.53–1.22)					
1.12/1.07 (0.82–1.52)/(0.77–1.49)					
1.06/1.02 (0.89–1.26)/(0.84–1.23)					
<b>Spirits:</b>					
Death (total)	1.17/1.19 (0.96–1.43)/(0.97–1.46)	ns/ns	0.13/ 0.14	0.97 (0.62–1.51) 1.00 (0.64–1.56)	1.23 (0.98–1.53) 1.25 (0.998–1.56)
Death myocardial infarction	0.49/0.52 (0.27–0.91)/(0.28–0.97)	< 0.05/< 0.05	0.53/ 0.52	0.49 (0.11–2.13) 0.53 (0.12–2.29)	0.49 (0.25–0.96) 0.52 (0.26–1.01)
Death stroke	1.33/1.38 (0.69–2.56)/(0.70–2.69)	ns/ns	0.77/ 0.78	0.79 (0.10–6.46) 0.86 (0.10–7.06)	1.43 (0.72–2.84) 1.49 (0.74–2.99)
Death diabetes*	0.27/0.31 (0.08–0.88)/(0.09–1.03)	< 0.05/ns	0.15/ 0.13	–	–
Death cancer	1.50/1.47 (1.09–2.07)/(1.06–2.05)	< 0.05/< 0.05	0.42/ 0.41	1.40 (0.78–2.53) 1.37 (0.76–2.49)	1.54 (1.06–2.24) 1.52 (1.04–2.21)

Notes: <sup>1</sup>Age-controlled/multivariate controlled. 95% CI within parentheses. Tested with linear interaction as well as hazard ratio in the first/last 16 years respectively and trend test for death in women reported as drinking beer. \*The small number of women in each group made the division into two different HRs impossible.

Table V. Risk (as hazard ratio with 95% confidence interval CI within parentheses) of myocardial infarction, stroke, cancer, and diabetes during 32 years of follow-up in women in relation to intake of beer, wine and spirits, respectively, reported at baseline (1968–1969) as well as test of linear interaction and hazard ratio in the first/last 16 years respectively.

End-point studied	Hazard ratio (CI): age-controlled/ multivariate controlled (CI age-controlled/CI multivariate controlled)	p-value: age- controlled/multivariate controlled	Test of constant HR: linear interaction test p-value	HR first 16 years	HR last 16 years
<b>Beer:</b>					
Myocardial infarction	0.61/0.70 (0.44–0.85/0.50–0.97)	< 0.05/0.05	0.70 0.76	0.54 (0.31–0.96) 0.63 (0.35–1.13)	0.64 (0.44–0.91) 0.72 (0.50–1.04)
Stroke	0.79/0.84 (0.58–1.08/0.61–1.16)	ns/ns	0.80 0.77	0.42 (0.18–1.01) 0.46 (0.19–1.09)	0.84 (0.61–1.16) 0.90 (0.64–1.25)
Cancer	0.91/0.89 (0.72–1.15/0.70–1.12)	ns/ns	0.40 0.42	0.82 (0.58–1.16) 0.80 (0.57–1.13)	0.96 (0.73–1.26) 0.94 (0.71–1.23)
Diabetes	0.76/1.06 (0.55–1.07/0.75–1.50)	ns/ns	0.40 0.45	0.91 (0.53–1.56) 1.28 (0.74–2.19)	0.72 (0.49–1.04) 0.98 (0.66–1.45)
<b>Wine:</b>					
Myocardial infarction	0.72/0.83 (0.52–1.00/0.59–1.16)	< 0.05/ns	0.13 0.17	0.50 (0.26–0.96) 0.59 (0.30–1.14)	0.81 (0.56–1.16) 0.92 (0.63–1.33)
Stroke	1.01/1.14 (0.75–1.37/0.83–1.57)	ns/ns	0.49 0.49	0.29 (0.09–0.95) 0.33 (0.10–1.09)	1.12 (0.82–1.54) 1.27 (0.91–1.76)
Cancer	1.07/1.01 (0.86–1.34/0.80–1.28)	ns/ns	0.14 0.14	0.84 (0.59–1.20) 0.80 (0.55–1.14)	1.22 (0.94–1.58) 1.15 (0.88–1.52)
Diabetes	0.65/0.80 (0.46–0.90/0.57–1.12)	< 0.05/ns	0.13 0.23	0.64 (0.36–1.14) 0.84 (0.47–1.50)	0.65 (0.45–0.95) 0.79 (0.53–1.16)
<b>Spirits:</b>					
Myocardial infarction	0.94/1.03 (0.65–1.37/0.71–1.51)	ns/ns	0.73 0.79	1.00 (0.50–1.99) 1.08 (0.54–2.17)	0.93 (0.60–1.42) 1.02 (0.66–1.57)
Stroke	0.97/1.00 (0.69–1.38/0.71–1.44)	ns/ns	0.86 0.86	0.62 (0.19–2.06) 0.65 (0.20–2.16)	1.03 (0.72–1.47) 1.06 (0.74–1.53)
Cancer	1.19/1.10 (0.76–1.88/0.86–1.40)	ns/ns	0.42 0.41	0.97 (0.65–1.47) 0.95 (0.63–1.44)	1.21 (0.90–1.62) 1.19 (0.88–1.59)
Diabetes	0.56/0.65 (0.37–0.87/0.42–1.00)	< 0.05/< 0.05	0.25 0.30	0.54 (0.25–1.21) 0.65 (0.29–1.45)	0.57 (0.34–0.94) 0.64 (0.39–1.07)

Notes: Intake of alcohol sometimes or regularly, during recent years compared with women who had never used these beverages or at least not during the past year. Age-controlled/multivariate controlled 95% CI within parentheses.

stroke, diabetes, and cancer, respectively, in the age-adjusted model and the multivariate model, in women consuming beer, wine, and spirits, at least sometimes/regularly during the past year compared with women who had never used these beverages or at least not during the past year.

In the age-adjusted model, consumption of beer was associated with a decreased risk of myocardial infarction and the reduced risk remained in the multivariate model. Age-adjusted comparisons showed that wine drinkers had less risk of developing myocardial infarction and diabetes than women who did not drink wine.

In the multivariate model, consumption of spirits was associated with decreased risk of diabetes.

The protective effect of beer consumption with regard to myocardial infarction also seemed to persist over a long period of time. Figure 1 plots the cumulative HR of morbidity in myocardial infarction related to women’s intake of beer during eight to 32 years of follow-up. As shown in Figure 1, women

who sometimes drank beer had a constant 30% lower risk of developing myocardial infarction during the entire follow-up period compared with women who did not drink at all.

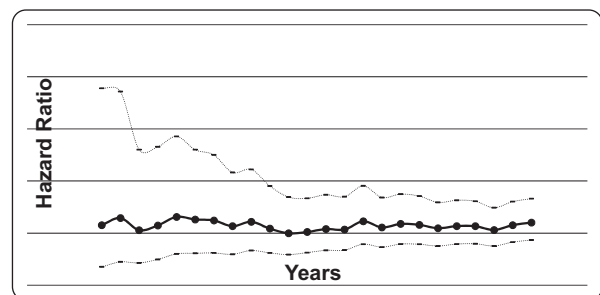


Figure 1. Cumulative hazard ratio of morbidity in myocardial infarction related to women’s intake of beer during eight to 32 years of follow-up. Women who sometimes drank beer (weekly to monthly) had a 30% lower risk of developing myocardial infarction that was constant throughout the entire follow-up period, compared with women who did not drink at all. Hazard ratio for drinking beer, age adjusted, with 95% CI.

## Discussion

The Population Study of Women in Gothenburg has been ongoing since 1968. In our previous study of alcohol consumption in women, we have shown that the proportion of women drinking alcohol every day increased with regard to wine and spirits during the period 1968 to 1993 [21]. The most robust outcome of the present study was that women who sometimes drank beer had a lower risk of mortality in myocardial infarction, compared with both women never drinking beer and women drinking regularly. The decreased risk remained over 30 years of follow-up. This association between moderate drinking and reduced mortality has been observed in earlier studies [5,9].

Our study showed no significances for the level of cholesterol in relation to level of intake of wine or spirits among women who reported never drinking compared with women who reported drinking sometimes or regularly. Earlier studies have shown that level of triglycerides is more important than cholesterol, as risk factor for CVDs in women. Another outcome of the study was that women who sometimes drank wine had a lower risk of developing diabetes compared with the other two groups. An earlier meta-analysis of observational studies found a J-shaped relationship for both women and men, with a risk reduction for the development of diabetes among persons with moderate alcohol intake [22].

High alcohol intake is associated with social problems, mental illness, somatic disease, and reduced length of life both in men and women [23,24]. Women who died from alcohol-related diseases in the Population Study of Women in Gothenburg had reported a high intake of alcohol, further supporting the notion that the information obtained from the women was valid, as well as supporting the deleterious effects of high alcohol consumption also in women.

Studies of men have shown that non-consumers of alcohol have a less favourable prognosis than subjects drinking moderate amounts [25]. These previous observations are supported also in women by the results from our study, where a tendency for increased mortality was found in women who had never drunk alcohol ( $p < 0.10$ ). However, this observation needs to be confirmed by other studies.

Among the advantages of this study are its cross-sectional and longitudinal design, the long follow-up, i.e. from 1968–1969 to 2000–2001, with exactly the same examination protocol, as well as the maintenance of a high level of consistency of contact between investigators and study participants during the long study period, such that participants to a large extent met the same investigators throughout the assessment

period. Due to the high participation rates at baseline as well as in the follow-up studies, the participants are known to be representative of women in Gothenburg for the birth and age groups studied.

The study has also some limitations. Participants were asked about frequency of intake of beer, wine, and spirits, respectively, and not about alcohol consumption in grams/day or drinks/week. We did not ask whether the women were teetotalers or recovering alcoholics. Women who reported the frequency of alcohol intake according to the “earlier, but not during the last ten years” and respectively “earlier, but not during the last year” were very few: one woman for beer and two women each for wine and spirit. They were analysed in the same group as women who “never consumed alcohol”. The exposure was measured at only one point in time, at baseline. Taking into account the change in alcohol consumption during every follow-up during the 32 years would imply a substantial reduction of the total number of women included in the analyses. This would influence the possibility to test associations in regard to separating between beverage types as well as differentiating morbidity and mortality endpoints. Another limitation is the problem of mass significance as some of the associations shown in the present study could be caused by chance. On the other hand the significant associations are in a uniform direction, which makes the assumptions of true associations probable.

Women’s drinking habits might have changed by now compared with during the 1960s. At that time, as well as today, the literature included statements on the protective effects of alcohol use. One question is the extent to which the protective effect is directly or indirectly related to better health outcome. Survival and disease patterns may be related to other factors, for example diet, rather than being due to direct effects of alcohol. Low-income households had the least healthy diets combined with a preference for beer or spirits [26]. A great shift in women’s working situation towards work outside the home showed an influence on their mood [27] as well as their perception of health and position in society. This may in turn lead to increased alcohol consumption.

An English study wished to determine the optimal level of alcohol consumption for prevention of chronic disease. The conclusion was that the existing recommendation from the government on alcohol consumption was above this level [28]. It may be that the recommended level is too high and possibly harmful, and further studies are needed regarding the optimal level of alcohol consumption.

It has been reported that low to moderate consumption of alcohol was associated with a reduced risk of myocardial infarction in both men and women



[29]. The risk of myocardial infarction was partly negatively associated with the level of drinking, but higher consumption also conferred a lower risk. However, when level of alcohol consumption increased even further, the risk increased to a level twice as high among women as among men [2]. A previous report concerning alcohol and dementia from the Prospective Study of Women in Gothenburg showed a protective effect of wine and a reverse albeit non-significant trend for beer and spirits [30]. Adding up the results from this present study, the discrepant associations with different endpoints illustrate the existing difficulties in considering any plain health-promotion recommendations on alcohol intake in women.

### Conclusions

The effect of alcohol intake upon health remains a key issue. Regular consumption of, e.g., one glass of wine seems to be associated with low prevalence of various diseases while excessive consumption may give rise to serious disease. In this study, women with moderate consumption of beer had a reduced risk of myocardial infarction over 32 years. However, it is premature to recommend that women should drink beer regularly, as this protection must be compared with the possible disadvantages of alcohol consumption.

### Ethical approval and participants consent

The Ethics Committee of the University of Gothenburg approved the study. All subjects gave informed consent to participate, in accordance with the provisions of the Declaration of Helsinki.

### Acknowledgements

This study was supported by grants from the Swedish Medical Research Council, the Swedish Research Council (2002-3724), and the Swedish Council for Life and Social Research (no 2005-0794, 2007-1958FAS, and FAS WISH). The Bank of Sweden Tercentenary Foundation also supported this work.

### Declaration of interest

There are no conflicts of interest in connection with the paper. The authors alone are responsible for the content and writing of the paper.

### References

[1] Goddard E. Drinking and health: An official survey of new information from British households. *J Epidemiol Community Health* 1994;48:106.

[2] Russell M, Chu BC, Banerjee A, Fan AZ, Trevisan M, Dorn JM, et al. Drinking patterns and myocardial infarction: A linear dose-response model. *Alcohol Clin Exp Res* 2009; 33:324-31.

[3] St Leger AS, Cochrane AL, Moore F. Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. *Lancet* 1979;1: 1017-20.

[4] Gronbaek M, Becker U, Johansen D, Gottschau A, Schnohr P, Hein HO, et al. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. *Ann Intern Med* 2000;133:411-19.

[5] Klatsky AL. Epidemiology of coronary heart disease: Influence of alcohol. *Alcohol Clin Exp Res* 1994;18:88-96.

[6] Makela P, Fonager K, Hibell B, Nordlund S, Sabroe S, Simpura J. Episodic heavy drinking in four Nordic countries: A comparative survey. *Addiction* 2001;96:1575-88.

[7] Beaglehole R, Jackson R. Alcohol, cardiovascular diseases and all causes of death: A review of the epidemiological evidence. *Drug Alcohol Rev* 1992;11:275-89.

[8] Rimm EB, Klatsky A, Grobbee D, Stampfer MJ. Review of moderate alcohol consumption and reduced risk of coronary heart disease: Is the effect due to beer, wine, or spirits. *BMJ* 1996;312:731-6.

[9] Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kawachi I, et al. Alcohol consumption and mortality among women. *N Engl J Med* 1995;332:1245-50.

[10] Rehm J, Fichter MM, Elton M. Effects on mortality of alcohol consumption, smoking, physical activity, and close personal relationships. *Addiction* 1993;88:101-12.

[11] Iso H, Baba S, Mannami T, Sasaki S, Okada K, Konishi M, et al. Alcohol consumption and risk of stroke among middle-aged men: The JPHC Study Cohort I. *Stroke* 2004;35: 1124-9.

[12] Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, Mohapatra S, et al. Alcohol consumption and the risk of morbidity and mortality for different stroke types: A systematic review and meta-analysis. *BMC Public Health* 2010;10:258.

[13] Hart CL, Smith GD, Hole DJ, Hawthorne VM. Alcohol consumption and mortality from all causes, coronary heart disease, and stroke: Results from a prospective cohort study of Scottish men with 21 years of follow up. *BMJ* 1999; 318:1725-9.

[14] Howard AA, Arnsten JH, Gourevitch MN. Effect of alcohol consumption on diabetes mellitus: A systematic review. *Ann Intern Med* 2004;140:211-19.

[15] Tjonneland A, Christensen J, Olsen A, Stripp C, Thomsen BL, Overvad K, et al. Alcohol intake and breast cancer risk: The European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes Control* 2007;18:361-73.

[16] Li CI, Chlebowski RT, Freiberg M, Johnson KC, Kuller L, Lane D, et al. Alcohol consumption and risk of postmenopausal breast cancer by subtype: The Women's Health Initiative Observational Study. *J Natl Cancer Inst* 2010;102:1422-31.

[17] Bengtsson C, Gredmark T, Hallberg L, Hallstrom T, Isaksson B, Lapidus L, et al. The population study of women in Gothenburg 1980-81: The third phase of a longitudinal study. Comparison between participants and non-participants. *Scand J Soc Med* 1989;17:141-5.

[18] Bengtsson C, Blohme G, Hallberg L, Hallstrom T, Isaksson B, Korsan-Bengtson K, et al. The study of women in Gothenburg 1968-1969: A population study. General design, purpose and sampling results. *Acta Med Scand* 1973;193:311-18.

[19] Lissner L, Skoog I, Andersson K, Beckman N, Sundh V, Waern M, et al. Participation bias in longitudinal studies: Experience from the Population Study of Women in Gothenburg, Sweden. *Scand J Prim Health Care* 1989;21:242-7.

- [20] Carlsson G. Socialgruppering: Social mobility and class structure. Lund, Sweden: University of Lund, GWK Gleerup; 1958.
- [21] Bengtsson C, Allebeck P, Lissner L, Bjorkelund C, Hallstrom T, Sigurdsson JA. Alcohol habits in Swedish women: Observations from the population study of women in Gothenburg, Sweden 1968–1993. *Alcohol Alcohol* 1998;33:533–40.
- [22] Bonnet F, Disse E, Laville M, Mari A, Hojlund K, Anderwald CH, et al. Moderate alcohol consumption is associated with improved insulin sensitivity, reduced basal insulin secretion rate and lower fasting glucagon concentration in healthy women. *Diabetologia* 2012;55:3228–37.
- [23] McKinney CM, Chartier KG, Caetano R, Harris TR. Alcohol availability and neighborhood poverty and their relationship to binge drinking and related problems among drinkers in committed relationships. *J Interpersonal Violence* 2012; 27:2703–27.
- [24] Holahan CJ, Schutte KK, Brennan PL, North RJ, Holahan CK, Moos BS, et al. Wine consumption and 20-year mortality among late-life moderate drinkers. *J Stud Alcohol Drugs* 2012;73:80–8.
- [25] Kloner RA, Rezkalla SH. To drink or not to drink? That is the question. *Circulation* 2007;116:1306–17.
- [26] Gell L, Meier P. The nature and strength of the relationship between expenditure on alcohol and food: An analysis of adult-only households in the UK. *Drug Alcohol Rev* 2012; 31:422–30.
- [27] Lundh C, Bengtsson C, Bjorkelund C. Generation shift in family vs. working conditions as most important influence on women's mood? The Prospective Population Study of Women in Gothenburg, Sweden. *Scandinavian J Prim Health Care* 2004;22:101–5.
- [28] Nichols M, Scarborough P, Allender S, Rayner M. What is the optimal level of population alcohol consumption for chronic disease prevention in England? Modelling the impact of changes in average consumption levels. *BMJ Open*. 2012; 2(3): e000957. Published online 2012 May 30. doi: 10.1136/bmjopen-2012-000957 PMID: PMC3367150.
- [29] Kabagambe EK, Baylin A, Ruiz-Narvaez E, Rimm EB, Campos H. Alcohol intake, drinking patterns, and risk of nonfatal acute myocardial infarction in Costa Rica. *Am J Clin Nutr* 2005;82:1336–45.
- [30] Mehlig K, Skoog I, Guo X, Schutze M, Gustafson D, Waern M, et al. Alcoholic beverages and incidence of dementia: 34-year follow-up of the prospective population study of women in Goteborg. *Am J Epidemiol* 2008;167:684–91.