Alcoholic beverage preference and diabetes incidence across Europe: the Consortium on
 Health and Ageing Network of Cohorts in Europe and the United States (CHANCES)
 project

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61 Genetics, Archiving and Monograph (MORGAM)

Abstract

63	Background/Objectives: It is unknown if wine, beer, and spirit intake lead to a similar
64	association with diabetes. We studied the association between alcoholic beverage preference
65	and type 2 diabetes incidence in persons who reported to consume alcohol.
66	Subjects/Methods: Ten European cohort studies from the Consortium on Health and Ageing:
67	Network of Cohorts in Europe and the United States (CHANCES) were included, comprising
68	participant data of 62 458 adults who reported alcohol consumption at baseline. Diabetes
69	incidence was based on documented and/or self-reported diagnosis during follow-up.
70	Preference was defined as \geq 70% of total alcohol consumed was either beer, wine or spirits.
71	Adjusted hazard ratios (HRs) were computed using Cox proportional hazard regression.
72	Single cohort HRs were pooled by random-effects meta-analysis.
73	Results: Beer, wine, or spirit preference was not related to diabetes risk compared with having
74	no preference. The pooled HRs were HR 1.06 (95%CI 0.93, 1.20) for beer, HR 0.99 (95%CI
75	0.88, 1.11) for wine, and HR 1.19 (95%CI 0.97, 1.46) for spirit preference. Absolute wine
76	intake, adjusted for total alcohol, was associated with a lower diabetes risk: pooled HR per 6
77	grams/day was 0.96 (95% CI 0.93, 0.99). A spirit preference was related to a higher diabetes
78	risk in those with a higher BMI, in men and women separately, but not after excluding
79	persons with prevalent diseases
80	Conclusions: This large individual-level meta-analysis among persons who reported alcohol
81	consumption revealed that the preference for beer, wine, and spirits was similarly associated

- with diabetes incidence compared with having no preference.

83 Introduction

Diabetes mellitus is the fourth to fifth leading cause of death in most high-income countries¹. 84 In 2014, the International Diabetes Federation estimated the prevalence at 7.9% in Europe¹. 85 Two systematic reviews and meta-analyses, including 20 and 26 cohort studies each, revealed 86 a non-linear U-shaped relationship between alcohol consumption and type 2 diabetes 87 incidence in both men and women^{2, 3}. The protective effect of alcohol consumption was 88 largest with light to moderate consumption. Higher levels of ethanol consumption were not 89 associated with diabetes or were associated with a higher risk^{2, 3}. On the other hand, a more 90 recent meta-analysis of 38 studies concluded these risk reductions might have been 91 overestimated by including less healthy former consumers in the reference group⁴. Moreover, 92 the protective association might be confined to women and non-Asian populations only⁴. 93

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Further research has indicated that the associations between alcohol and diabetes might be 95 beverage-specific. A recent systematic review and meta-analysis of 13 prospective studies 96 showed a strong protective association for wine consumption and type 2 diabetes, while for 97 beer or spirits only a slight trend of a protective association was observed⁵. Within the 98 European Prospective Investigation into Cancer and Nutrition (EPIC)-InterAct Study, 99 moderate alcohol consumption was also related to a lower diabetes risk, in particular the 100 consumption of red wine⁶. It was suggested that the association between alcohol and diabetes 101 was likely to be explained by ethanol itself. Indeed, intervention studies have shown that 102 alcohol increases levels of HDL-cholesterol, apoliprotein A1, and adiponectin, and reduces 103 fibrinogen, fasting insulin and HbA_{1c} concentrations^{7, 8}. Hence, the observed differences in 104 association between wine, beer, and spirits and health outcomes might be due to socio-105 demographic and lifestyle factors associated with the preference and consumption of these 106 beverages^{9, 10}. However, differential effects of beer and wine on the glycemic response, as 107

expressed by their glycemic index, have also been observed. Beer induces a higher glucose
response than wine, which may be related to the development of diabetes^{11, 12}. Furthermore,
due to its higher polyphenol content, red wine may exert additional benefits including
reduction of blood pressure and inflammation and improving endothelial function¹³.

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Alcohol consumption is a complex exposure that can be characterized in different ways: the 113 absolute amount, the drinking frequency, and the beverage type. It is statistically difficult to 114 distinguish between the overall alcohol effect and the specific effects of beer, wine, and spirits 115 in observational studies¹⁴. We aimed to disentangle beverage-specific effects, independent of 116 those from the absolute ethanol consumption, by studying the association between alcoholic 117 beverage consumption and preference and type 2 diabetes incidence. This was done by 118 performing a meta-analysis of harmonized individual participant data from several European 119 cohorts including a large proportion of elderly participants. Because this study focused on the 120 type of alcoholic beverage, the analyses were restricted to persons who reported alcohol 121 consumption. Moreover, because the consumption of wine, beer, or spirits is mainly 122 determined by factors including age, sex, socio-economic status, country, and lifestyle, these 123 variables will be taken as much as possible into account in the analyses to strengthen 124 potentially causal inference. 125

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127 Subjects and methods

128 *Study design and population*

The Consortium on Health and Ageing: Network of Cohorts in Europe and the United States
(CHANCES) project is a coordinated multi-country study which aims to harmonize data from
ongoing prospective cohort studies in Europe and the USA in order to produce evidence on

ageing-related health characteristics and on determinants of healthy ageing among the elderly
in these countries¹⁵.

134

The CHANCES project includes cohorts from 14 studies across Europe and the USA. In most 135 CHANCES cohorts, elderly are defined as those who were 60 years or older at recruitment. 136 The CHANCES project as a whole has received ethical approval by the Hellenic Health 137 Foundation Committee on Bioethics (HHFCB). In the individual cohorts, all participants 138 signed informed consent for the original studies. The authors of this study did not have any 139 access to personal information regarding the participants included in this paper. All data that 140 have been analyzed are based on the CHANCES harmonized variables and are completely 141 anonymized. For the present study, the following ten European cohorts were eligible for 142 analysis: the Zutphen Elderly Study (the Netherlands)¹⁶, Rotterdam Study (the Netherlands)¹⁷, 143 the study centers in the Netherlands, Greece, and Sweden from the European Prospective 144 Investigation into Cancer and Nutrition (EPIC) – Elderly study¹⁸, the Tromsø Study 145 (Norway)¹⁹, the Epidemiological Study on Chances for Prevention, Early Detection, and 146 Optimized THERapy of Chronic Diseases at Old Age (ESTHER) study (Germany)²⁰, and 147 from the MOnica Risk, Genetics, Archiving and Monograph (MORGAM) study, the cohorts 148 of FINRISK (Finland), Northern Sweden (Sweden), and MOLI-SANI (Italy)^{21, 22}. An 149 extensive overview of the cohorts included in the CHANCES project and data assessment has 150 been published elsewhere²³. Table 1 displays the main characteristics of the included ten 151 cohorts and participants. 152

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Within the cohorts that were eligible for the present study, analyses were conducted upon all subjects who reported to consume alcohol, without any missing data on alcohol and followed up for diabetes incidence. Subjects with self-reported or independently ascertained prevalent

diabetes at baseline or with missing information on prevalent diabetes at baseline were

excluded from analysis. **Supplemental Figure 1** shows the participant flow-charts of the ten

included cohorts, comprising a total sample size of 63 458.

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161 Data assessment and harmonization

162 Data in the CHANCES project have been collected within the framework of independent

163 cohort studies, with different protocols for data collection and distinct original research foci.

164 Data harmonization was a major task of the project and the data harmonization and

165 conversion rules of the CHANCES project have been described elsewhere²³.

166

167 Alcoholic consumption and beverage preference

Baseline alcohol data were recorded either by self-administered or interview-based 168 questionnaires. The EPIC-Elderly and Rotterdam Study applied a validated food frequency 169 questionnaire (FFQ)^{17, 24, 25} to assess alcohol intake. The Zutphen Elderly Study used a 170 validated dietary history method to assess diet including alcohol¹⁶. The Tromsø Study, the 171 ESTHER study, and MORGAM cohorts derived alcohol consumption from a general 172 questionnaire. In the FINRISK Study, alcohol consumption during the previous week was 173 assessed. If not already defined, average daily alcohol consumption in grams was estimated 174 by adding the amounts of ethanol found in each standard drink or cohort specific size for beer, 175 wine, and spirits. To ensure comparability across cohorts, a conversion rule was applied using 176 standardized portion sizes (330 ml for a bottle of beer, 175 ml for a glass of wine, and 25 ml 177 for a shot of spirit) and alcohol percentages in beer (4.5%), wine (12%), and spirits (37.5%). 178 179

As defined in previous studies, a person was classified as having a preference for beer, wine,
or spirits, when the alcohol consumption from the respective drink comprised 70% or more of

the total alcohol consumption in grams per day. When the average alcohol consumption from beer, wine, or spirits did not add up to 70% of the total alcohol consumption, a person was classified as having no preference^{26, 27}. To assess robustness of this definition, a sensitivity analysis was performed using a cut-off of 50%. Associations between the preference for beer, wine, or spirits and diabetes incidence compared to having no specific preference was assessed. Non-consumers, comprising never and former consumers, were not included in the analyses.

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Next, the association between average daily intake from beer, wine, and spirits and diabetes 190 incidence was studied. The absolute intakes of beer, wine, and spirits were adjusted for total 191 alcohol consumption by the residual method²⁷. In this procedure, intakes of the respective 192 beverage were regressed upon their total alcohol consumption and the residuals from the 193 regression were used in the analysis. These residuals represent the differences between each 194 individual's actual intake and the intake predicted by their total alcohol consumption. Because 195 residuals, by definition, have a mean of zero, a constant representing the mean intake in each 196 population was added to every value to reflect actual consumption values²⁸. The beer, wine, 197 and spirit residuals are uncorrelated with total alcohol consumption and this allows variation 198 due to the intake of beer, wine, and spirits to be evaluated directly. The beer, wine, and spirit 199 residuals were analyzed in tertiles and per 6 g/day. 200

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Information on drinking patterns, i.e. consumption frequency, was not available for all
cohorts. Sensitivity analyses were performed adjusting the associations additionally for
frequency of consumption (less than once a week, 1-2 days/week, 3-5 days/week, or 6-7
days/week) in the Tromsø Study, ESTHER, and MORGAM.

206 Diabetes ascertainment

Diabetes incidence was based on documented or self-reported type 2 diabetes during followup or based on fasting glucose measures, depending on the available options within the cohorts shown in Table 1.

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211 *Covariate assessment*

Socio-demographic, lifestyle, and disease history data were assessed by self-administered 212 questionnaires or in interviews. Weight and height were either measured or self-reported, and 213 blood samples were drawn to determine total and HDL cholesterol. Diet quality was assessed 214 with the Healthy Diet Indicator (HDI) as developed by Jankovic et al.²⁹. The HDI score 215 reflects adherence to the 2003 WHO dietary guidelines. The score ranges from 0 to 70 points 216 and includes 6 nutrients (saturated fatty acids, polyunsaturated fatty acids, mono- and 217 disaccharides, protein, cholesterol, dietary fiber) and 1 food group (fruit and vegetables) of 218 the 14 WHO guideline goals, which were available for the cohorts providing nutrition data²⁹. 219 Dietary intake data to calculate the HDI score were available for the Zutphen Elderly Study, 220 Rotterdam Study, and EPIC-Elderly. Self-reported physical activity was assessed by 221 questionnaires in the Zutphen Elderly Study, Rotterdam Study, EPIC-Elderly the Netherlands 222 and Greece, and ESTHER. 223

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225 Statistical analysis

The statistical analyses were performed using SAS, version 9.3, software (SAS Institute, Inc., Cary, North Carolina). Hazard Ratios (HRs) and 95% confidence intervals (CIs) for diabetes were calculated using Cox proportional hazard regression. The proportional hazard assumption was tested and not violated. Missing values for any of the covariates were imputed using the multiple imputation method, in which all variables included in the

statistical models were included in the procedure. For each cohort, five duplicate datasets 231 were produced and after statistical inference on the duplicate datasets, pooled estimates were 232 calculated with PROC MIANALYZE³⁰. In Model 1, HRs were adjusted for socio-233 demographic factors: age (continuous; years), gender (not applicable for the Zutphen Elderly 234 Study, which is composed only of men), education (categorical: primary or less (low), more 235 than primary but less than college or university (middle), college or university (high)), 236 employment status (categorical: full-time or part-time employment and not of pensionable 237 age, self-employed, housewife and not of pensionable age, pensionable age and still working, 238 pensionable age and not working, stopped work before retirement age due to poor health, 239 unemployed and not of pensionable age; not applicable for SENECA and the Zutphen Elderly 240 Study, where only retired subjects are included), and prevalent coronary heart disease (CHD; 241 yes/no) or cancer (yes/no). Model 2 was additionally adjusted for the lifestyle factors: 242 smoking status (categorical: never, former, current), sports activity (continuous: hours per 243 week; physical activity data were not available for EPIC-Elderly Sweden, the Tromsø Study, 244 and MORGAM; total physical activity was used in the Rotterdam Study), and HDI-score 245 (continuous; dietary intake data to generate the HDI score was not available for ESTHER, the 246 Tromsø Study, and MORGAM). 247

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Because the definition of alcoholic beverage preference is not based upon absolute alcohol consumption, persons with a beer preference might, for instance, have a higher absolute alcohol intake than persons with a wine preference. Thus, total alcohol consumption might be a confounding factor. Due to the U-shaped relationship between total alcohol and diabetes^{2,3}, additional adjustment for absolute alcohol consumption (gram/day) was evaluated using fractional polynomials where the best fit regression model was selected with the SAS Macro "Multivariable Fractional Polynomials"³¹. This macro uses an algorithm to determines the

inclusion and transformation of continuous covariates while taking into account their non-256 linearity. In a stepwise approach, the algorithm constructs a fractional polynomial 257 transformation for the continuous covariate. Backward elimination selects the best 258 transformation of the covariate, e.g. linear, first degree or second degree. Depending on the P-259 values associated with the best transformations, covariates may be eliminated from the model. 260 In all cohorts, absolute alcohol consumption was omitted from the best fit model. Because the 261 residuals of beer, wine, and spirit consumption are uncorrelated with total alcohol intake, 262 these HR were not adjusted for total alcohol. 263

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Adjustment model 3 was additionally adjusted for BMI (linearly or second degree; kg/m²); 265 this adjustment for BMI was also evaluated using fractional polynomials. BMI was omitted 266 from the best fit model in the Zutphen Elderly Study, included as a second degree variable in 267 ESTHER and FINRISK, and included linearly in the remaining cohorts. BMI is one of the 268 most important risk factors for diabetes, but is also on a possible causal pathway between 269 alcohol consumption and diabetes. Therefore, crude and adjusted BMI across alcoholic 270 beverage preference categories was estimated with multiple linear regression. To investigate 271 effect modification by BMI, stratified analyses were performed on persons with a BMI <25 272 and $\geq 25 \text{ kg/m}^2$ and the P-value for interaction was checked after including a product term in 273 the regression models. Furthermore, stratified analyses were performed for men and women 274 separately to check for potential effect modification. Finally, subjects with prevalent CHD or 275 cancer at baseline or a follow-up less than 2 years were excluded in a sensitivity analysis. 276

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Cohort-specific HR estimates and 95% CIs for diabetes incidence from having a beer, wine,
or spirit preference compared with no preference and for a beer, wine, or spirit consumption
(per 6 gram/day) were pooled in meta-analyses, using adjustment model 3. Inverse variance

weighting was applied to give the largest weight to the study with the lowest variance. The random-effects model takes into account the between-study variance and the within-study variance. Heterogeneity between studies was assessed by the Q statistic and the I² index. I² was calculated as $I^2 = ((Q - df)/Q)*100$, where "df" stands for degrees of freedom, i.e. total number of studies (k) minus 1. Random-effects meta-analyses with inverse variance weighting were performed using the R package "meta" (R version 3.3.1). Statistical tests were two-sided and P-values <0.05 were considered statistically significant.

288

289 **Results**

In most cohorts, persons with a wine preference constituted the largest group, ranging from 290 44% in ESTHER (Germany) to 79% in MOLI-SANI (Italy) (Supplemental Table 1). In 291 EPIC-Elderly Sweden, the Tromsø Study, FINRISK, and Northern-Sweden persons with no 292 preference formed the largest group and in the Zutphen Elderly Study (the Netherlands), 293 persons with a spirit preference comprised the largest group, i.e. 62%. Across all cohorts, 294 those who preferred wine were relatively more highly educated and were more likely to be a 295 never smoker, and female. Furthermore, those with a beer or spirit preference were more 296 likely to be male and current smoker. Persons with no specific preference generally had the 297 highest absolute alcohol consumption. After adjustment for age, sex, education, employment, 298 prevalent diseases, smoking, alcohol, sports activity, diet, BMI was lowest among those with 299 a beer or wine preference and BMI was highest among persons with a spirit preference 300 (Supplemental Table 1). 301

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The pooled HRs from the random-effects meta-analyses showed no significant association between having a preference for beer, wine, or spirits and diabetes incidence compared with having no specific preference after adjustment for age, sex, education, prevalent diseases, lifestyle factors, and BMI (Figure 1-3). Pooled HR was 1.06 (95%CI 0.93, 1.20) for a beer
preference, HR 0.99 (95%CI 0.88, 1.11) for a wine preference, and HR 1.19 (95%CI 0.97,
1.46) for having a spirit preference. Based on the I² index and the Q-statistic, between-study
heterogeneity was observed for the effect estimates of having a spirit preference.

310

Separate HRs and 95% CIs for the associations between a beer, wine, or spirits and diabetes 311 incidence according to the different levels of adjustment are shown in Supplemental Table 1. 312 Compared with persons with no preference, a preference for beer, wine, or spirits was in most 313 cohorts not significantly associated with diabetes incidence. In the Rotterdam Study, beer or 314 spirit preference had a significant association with a higher diabetes incidence. In EPIC-315 Elderly Greece, having a wine preference tended to be associated with a lower diabetes 316 incidence. Within the cohorts, additional adjustment for BMI (Model 3) had mixed, but small 317 effects on the observed associations. 318

319

The pooled HR for the association between alcohol preference and incident diabetes among 320 sub-groups and with additional adjustments are shown in Table 2. Diabetes risk among 321 persons with a spirit preference was higher in those with a higher BMI, in men and in women, 322 but not after excluding persons with prevalent diseases. Excluding persons with prevalent 323 diseases yielded similar results to the findings including those persons. P-values for 324 interaction by BMI were not significant for all cohorts and did not therefore give indication 325 for effect modification. Furthermore, additional adjustment for consumption frequency and 326 alternative analysis using 50% as a cut-off in the definition of preference showed similar 327 associations. 328

Additionally, the association between the residuals of beer, wine, and spirit intake per 6 gram/day and diabetes incidence was assessed (**Figure 4-6**). Pooled HR was 1.03 (95%CI 0.99, 1.06) per 6 grams of beer intake, HR 0.96 (95%CI 0.93, 0.99) per 6 grams of wine intake, and HR 1.02 (95%CI 0.98, 1.06) per 6 grams of spirit intake. Cohort-specific HR according to tertiles and per 6 grams/day generally showed similar associations (**Supplemental Table 2**).

335

336 **Discussion**

This meta-analysis of individual participant data from ten prospective European cohorts comprising ~60,000 adults who reported at least some alcohol consumption showed that a preference for beer, wine or spirits was not associated with a lower or higher diabetes risk compared with having no specific preference, taking into account several socio-demographic and lifestyle variables.

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To our knowledge, no other studies have investigated the association between alcoholic 343 beverage preference and diabetes risk. However, a number of observational studies have 344 assessed associations of absolute beverage-specific consumption and diabetes, showing 345 inconsistent results. Among 36,527 Australian adults, Hodge et al. observed an inverse 346 association between wine consumption and risk of type 2 diabetes, but not for beer or spirits³². 347 In the EPIC-InterAct Study, a prospective case-cohort study of 16,154 participants and 12,403 348 incident diabetes cases, consumption of wine and fortified wine were most strongly related 349 with a reduced diabetes risk⁶. Moreover, compared with a light consumption, men who did 350 not consume beer had a reduced risk of diabetes in the EPIC-InterAct Study: HR 0.84 (95%CI 351 0.74, 0.95) and in women higher spirit consumption was associated with an higher diabetes 352 risk (P-trend 0.044). Fagherazzi et al. observed an inverse association between wine 353

consumption and diabetes risk when compared to other types of alcoholic beverage among 354 66,485 women from the French E3N-EPIC cohort³³. In contrast, Conigrave et al., did not find 355 a protective effect of red wine on diabetes risk among 46,892 U.S. male health professionals, 356 whereas inverse associations for beer, spirits and white wine were similar and independent³⁴. 357 Moreover, two other studies in large U.S. cohorts also did not observe a specific protective 358 effect of wine consumption on diabetes risk compared with beer or spirit consumption^{35, 36}. In 359 their meta-analysis of 13 prospective studies, Huang, Wang, and Zhang presented a pooled 360 RR of 0.85 (95% CI 0.80-0.89) for wine consumption, and RR 0.96 (95% CI 0.92, 1.00) for 361 beer consumption and RR 0.95 (95%CI 0.89-1.03) for spirit consumption and type 2 diabetes 362 risk compared to no or rare alcohol consumption⁵. In the present study, the pooled HR for 363 residuals of beer, wine, and spirit intake showed similar results: a higher wine intake was 364 related to a lower diabetes risk, even after fully taking into account total alcohol consumption. 365 This further confirms the consistent finding that constituents other than ethanol in red wine 366 may exert additional health benefits¹³. 367

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Several other studies have found differential effects for the type of alcoholic beverage and 369 diabetes risk, with a stronger beneficial association for wine consumption compared to 370 abstinence. These observations could either be explained by a true beneficial effect of wine 371 compared with beer and spirits, or by an artefact arising from residual confounding. Firstly, a 372 true differential effect for beer, wine, and spirits and diabetes incidence might be caused by 373 beneficial compounds other than ethanol in particular those found in wine. For example, a 374 randomized controlled cross-over trial in 67 men at high cardiovascular risk showed that red 375 wine rich in polyphenols with or without alcohol improved glucose metabolism³⁷. This was 376 not confirmed in our study, where we have found no additional beneficial association for 377 having a wine preference compared to having no preference. Secondly, the observation might 378

be an artefact caused by confounding factors associated with the type of alcoholic beverage 379 consumed. Indeed, the choice of alcoholic beverage is associated with a wide range of 380 cultural, socio-demographic and lifestyle factors^{9, 38}, which may confound the association 381 between alcohol and diabetes risk. Moreover, other important determinants of diabetes risk 382 including age, gender, smoking status and overall drinking patterns differ across alcoholic 383 beverage preference and study populations¹⁰. Therefore, we have adjusted the associations for 384 age, gender, socio-economic status, and lifestyle factors including absolute alcohol 385 consumption and BMI. However, we cannot exclude any residual confounding as a result of 386 unmeasured or imprecisely measured confounders. Lastly, in previous studies there is a 387 tendency to find an association for the alcoholic beverage that is most consumed. In the above 388 mentioned studies into beverage type and diabetes risk, most of the alcohol was consumed as 389 wine^{6, 32, 33}. In our study, ten cohorts from seven European countries were included with 390 varying preferences, suggesting this might have less influence on our findings and provided a 391 wider insight into alcohol preference across Europe. 392

393

We observed a tendency toward a higher diabetes risk among persons with a spirit preference 394 compared to those having no specific preference among men and women when analyzed 395 separately and those with a higher BMI. This was also seen within EPIC-InterAct⁶. Cross-396 sectional studies have shown that a spirit preference is associated with an unhealthier lifestyle: 397 persons who preferred spirits have been shown to have a higher BMI, are more likely to be 398 smokers, and display unhealthier diet. Furthermore, spirits may be more often used for heavy 399 binge drinking compared to wine^{9, 10}. In the present study, we could only take consumption 400 frequency into account in a subset of five cohorts. Furthermore, the association was attenuated 401 when excluding persons with prevalent diseases or a short follow-up, indicating that some 402

degree of reverse causation might be present. Finally, we were not able to take diet andphysical activity into account in all cohorts.

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To avoid any bias by the inclusion of former drinkers, the current analysis was restricted to 406 persons who reported some alcohol consumption. Furthermore, persons with no specific 407 preference, i.e. mixed drinkers, were used as a reference. Most other observational studies 408 have used non-consumers as a reference; however, this has been contested. Non-consumers 409 are in general a heterogeneous group comprising lifetime abstainers and former drinkers. In 410 many high-income countries, lifetime abstinence of alcohol is not normative and this group 411 differs from alcohol consumers in other health determinants³⁹. Moreover, former drinkers may 412 have quit because of ill health arising from their former (heavy) alcohol use. As a result, these 413 individuals are more vulnerable for morbidity and mortality and their ill health may confound 414 the association between alcohol consumption and health outcomes. Using non-consumers as a 415 reference group may overestimate the beneficial effects of alcohol⁴⁰. On the other hand, in the 416 meta-analysis of Di Castelnuovo et al., there was still a protective effect of alcohol 417 consumption in the general population after exclusion of former drinkers⁴¹. We were unable 418 to take into account former alcohol consumption in all cohorts, but by restricting the analyses 419 to alcohol consumers, possible confounding by abstinence or former alcohol consumption 420 could not influence our results. 421

422

The association between alcoholic beverage preference and diabetes may be partly driven by obesity: since adiposity is on one causal pathway between absolute alcohol consumption and diabetes, adjusting for BMI may lead to overadjustment bias⁴². However, after multiple adjustments, those with a spirit preference had the highest BMI and persons with a beer or wine preference had the lowest BMI. Because BMI is a strong risk factor for developing

diabetes, the effect of moderate alcohol consumption might be strongest, in absolute terms, in 428 those at higher risk. In our analysis, the association between spirit preference and diabetes 429 incidence was higher among those with overweight or obese (BMI>25 kg/m²). In contrast, 430 Beulens et al. found that moderate alcohol consumption was more strongly related to a 431 reduced diabetes risk in overweight men and women than in their normal weight 432 counterparts⁶. Moreover, in the French E3N-EPIC cohort, overweight women consuming two 433 or more glasses of wine per day had a lower diabetes risk, whereas in normal weight women 434 consuming the same amount, no association was observed³³. 435

436

We aimed to disentangle beverage-specific effects, independent of those from the absolute 437 ethanol consumption, by studying the association between alcoholic beverage preference and 438 type 2 diabetes incidence. Beverage preference was used to classify the study population 439 according to their alcohol intake. This approach of studying preference rather than absolute 440 intake can thus be considered as a qualitative approach. Independent from the biological 441 mechanisms associated with the chemical composition of the beverages, beverage preference 442 per se may not be directly associated with diabetes incidence. Therefore, we have additionally 443 studied the residuals of beer, wine and spirit intake, fully adjusted for total alcohol 444 consumption by the residual method²⁸; these analyses yielded similar findings. The number of 445 cases distributed by beverage preference differed across the cohorts and were in some cohorts 446 quite low, which may have affected the statistical power of the analyses. Non-consumers were 447 excluded from the analysis to prevent non-consumers and former (heavy) consumers to affect 448 the results. As a result, these findings only apply to alcohol consumers. 449

450

451 The CHANCES project is a large-scale multi-national collaboration of cohort studies

452 including a large number of elderly persons. Pooled analyses of the individual participant data

from the different cohorts is a cost-efficient analytical approach and increases statistical 453 power considerably. However, we had to rely on secondary data collected according to 454 different study objectives and protocols, which may be a weakness¹⁵. With respect to type 2 455 diabetes incidence, the identification and verification of diabetes cases varied across the 456 cohorts. The oral glucose tolerance test is considered the gold standard of diabetes 457 ascertainment, but recently fasting glucose has been shown to be the most accurate method of 458 diabetes diagnosis⁴³. Most cohort studies relied on self-reports, linkage with registries, HbA_{1c}, 459 or fasting blood glucose measures. As a result, misclassification could have been present and 460 we might have underestimated the number of diabetes cases. However, only if this 461 misclassification is differential and related to alcohol preference, would it have influenced the 462 direction of the effect estimates, and yet our observed associations across cohorts were 463 broadly consistent. Furthermore, it is difficult to distinguish between type 1 and type 2 464 diabetes; therefore, some cohorts may not have been able to appropriately distinguish between 465 the types. Moreover, this issue is not restricted to this study only. Diagnosing diabetes can be 466 equivocal: the clinical diagnosis is based on a pre-specified cut-off point on a continuous 467 scale of declining glycemic control, but clinical practice will dictate how assiduously the 468 necessary tests are applied. Furthermore, the diagnosis is often based on the occurrence of 469 complications of the disease and the disease can remain asymptomatic for years. Hence, it has 470 been estimated that up to 50% of all type 2 diabetes patients are undiagnosed⁴⁴. As a result, 471 the true association may have been underestimated. 472

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This meta-analysis of individual participant data from ten cohorts among Europeans who
reported at least some alcohol consumption showed that beer, wine, and spirits were similarly
associated with diabetes incidence. The recommendations of the American Diabetes
Association for the prevention of diabetes suggest that if adults choose to drink alcohol, daily

intake should be limited to a moderate amount, i.e. no more than one drink per day for women
and two drinks per day for men⁴⁵. Our analysis offers little support for making beverage
specific recommendation for diabetes prevention.

481

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493 DS, FK, EJMF designed the study and formulated the research question; OHF, DK, AT, TW,

HB, KK, TL, SS, LI, and PB acquired the data and contributed reagents/materials/analysis
tools; DS carried out the study, analyzed the data, and drafted the manuscript; All authors

496 critically revised the manuscript for important intellectual content and approved of the final497 version to be published.

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499 **References**

International Diabetes Federation. IDF Diabetes Atlas, Sixth Edition [Retrieved 12
 March 2015]. Available from: <u>http://www.idf.org/diabetesatlas</u> 2014.

- Li XH, Yu FF, Zhou YH, He J. Association between alcohol consumption and the risk
 of incident type 2 diabetes: a systematic review and dose-response meta-analysis. *The American journal of clinical nutrition* 2016; **103**(3): 818-829. e-pub ahead of print
 2016/02/05; doi: 10.3945/ajcn.115.114389
- Baliunas DO, Taylor BJ, Irving H, Roerecke M, Patra J, Mohapatra S *et al.* Alcohol as
 a risk factor for type 2 diabetes: A systematic review and meta-analysis. *Diabetes care*2009; **32**(11): 2123-2132. e-pub ahead of print 2009/10/31; doi: 10.2337/dc09-0227
- 4. Knott C, Bell S, Britton A. Alcohol Consumption and the Risk of Type 2 Diabetes: A
- 510 Systematic Review and Dose-Response Meta-analysis of More Than 1.9 Million
- 511 Individuals From 38 Observational Studies. *Diabetes care* 2015; **38**(9): 1804-1812. e-
- 512 pub ahead of print 2015/08/22; doi: 10.2337/dc15-0710
- 5135.Huang J, Wang X, Zhang Y. Specific Types of Alcoholic Beverage Consumption and514Risk of Type 2 Diabetes: A Systematic Review and Meta-analysis. Journal of diabetes
- 515 *investigation* 2016. e-pub ahead of print 2016/05/18; doi: 10.1111/jdi.12537
- 6. Beulens JW, van der Schouw YT, Bergmann MM, Rohrmann S, Schulze MB, Buijsse
- 517 B *et al.* Alcohol consumption and risk of type 2 diabetes in European men and
- women: influence of beverage type and body size The EPIC-InterAct study. *Journal of*
- 519 *internal medicine* 2012; **272**(4): 358-370. e-pub ahead of print 2012/02/23; doi:
- 520 10.1111/j.1365-2796.2012.02532.x
- 521 7. Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol
- 522 consumption on biological markers associated with risk of coronary heart disease:
- 523 systematic review and meta-analysis of interventional studies. *Bmj* 2011; **342:** d636. e-
- 524 pub ahead of print 2011/02/24; doi: 10.1136/bmj.d636
- 525 8. Schrieks IC, Heil AL, Hendriks HF, Mukamal KJ, Beulens JW. The effect of alcohol
- 526 consumption on insulin sensitivity and glycemic status: a systematic review and meta-

- analysis of intervention studies. *Diabetes care* 2015; **38**(4): 723-732. e-pub ahead of
 print 2015/03/26; doi: 10.2337/dc14-1556
- Gronbaek M. Confounders of the relation between type of alcohol and cardiovascular
 disease. *Annals of Epidemiology* 2007; 17(5): S13-S15. doi:
- 531 10.1016/j.annepidem.2007.01.004
- 532 10. Sluik D, Bezemer R, Sierksma A, Feskens E. Alcoholic Beverage Preference and
- 533 Dietary Habits: A Systematic Literature Review. *Critical reviews in food science and* 534 *nutrition* 2015: 0. e-pub ahead of print 2015/02/13; doi:
- 535 10.1080/10408398.2013.841118
- 11. Brand-Miller JC, Fatema K, Middlemiss C, Bare M, Liu V, Atkinson F et al. Effect of
- alcoholic beverages on postprandial glycemia and insulinemia in lean, young, healthy
 adults. *The American journal of clinical nutrition* 2007; **85**(6): 1545-1551.
- 12. Hatonen KA, Virtamo J, Eriksson JG, Perala MM, Sinkko HK, Leiviska J et al.
- 540 Modifying effects of alcohol on the postprandial glucose and insulin responses in
- healthy subjects. *The American journal of clinical nutrition* 2012; **96**(1): 44-49. e-pub
- ahead of print 2012/06/01; doi: 10.3945/ajcn.111.031682
- 13. Arranz S, Chiva-Blanch G, Valderas-Martinez P, Medina-Remon A, Lamuela-
- 544 Raventos RM, Estruch R. Wine, beer, alcohol and polyphenols on cardiovascular
- 545 disease and cancer. *Nutrients* 2012; **4**(7): 759-781. e-pub ahead of print 2012/08/02;
- 546 doi: 10.3390/nu4070759
- 14. Wacholder S, Schatzkin A, Freedman LS, Kipnis V, Hartman A, Brown CC. Can
- energy adjustment separate the effects of energy from those of specific
- 549 macronutrients? *American journal of epidemiology* 1994; **140**(9): 848-855.
- 15. Boffetta P, Bobak M, Borsch-Supan A, Brenner H, Eriksson S, Grodstein F et al. The
- 551 Consortium on Health and Ageing: Network of Cohorts in Europe and the United

552		States (CHANCES) projectdesign, population and data harmonization of a large-
553		scale, international study. European journal of epidemiology 2014; 29(12): 929-936.
554		e-pub ahead of print 2014/12/17; doi: 10.1007/s10654-014-9977-1
555	16.	Buijsse B, Feskens EJ, Kok FJ, Kromhout D. Cocoa intake, blood pressure, and
556		cardiovascular mortality: the Zutphen Elderly Study. Archives of internal medicine
557		2006; 166 (4): 411-417. e-pub ahead of print 2006/03/01; doi:
558		10.1001/archinte.166.4.411
559	17.	Hofman A, Brusselle GG, Darwish Murad S, van Duijn CM, Franco OH,
560		Goedegebure A et al. The Rotterdam Study: 2016 objectives and design update.
561		European journal of epidemiology 2015; 30 (8): 661-708. doi: 10.1007/s10654-015-
562		0082-x
563	18.	Trichopoulou A, Orfanos P, Norat T, Bueno-de-Mesquita B, Ocke MC, Peeters PH et
564		al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study.
565		<i>Bmj</i> 2005; 330 (7498): 991. e-pub ahead of print 2005/04/12; doi:
566		10.1136/bmj.38415.644155.8F
567	19.	Jacobsen BK, Eggen AE, Mathiesen EB, Wilsgaard T, Njolstad I. Cohort profile: the
568		Tromso Study. Int J Epidemiol 2012; 41(4): 961-967. e-pub ahead of print
569		2011/03/23; doi: 10.1093/ije/dyr049
570	20.	Schottker B, Haug U, Schomburg L, Kohrle J, Perna L, Muller H et al. Strong
571		associations of 25-hydroxyvitamin D concentrations with all-cause, cardiovascular,
572		cancer, and respiratory disease mortality in a large cohort study. The American journal
573		of clinical nutrition 2013; 97(4): 782-793. e-pub ahead of print 2013/03/01; doi:
574		10.3945/ajcn.112.047712

575	21.	Evans A, Salomaa V, Kulathinal S, Asplund K, Cambien F, Ferrario M et al.
576		MORGAM (an international pooling of cardiovascular cohorts). Int J Epidemiol 2005;
577		34 (1): 21-27. e-pub ahead of print 2004/11/25; doi: 10.1093/ije/dyh327
578	22.	Di Castelnuovo A, de Curtis A, Costanzo S, Persichillo M, Olivieri M, Zito F et al.
579		Association of D-dimer levels with all-cause mortality in a healthy adult population:
580		findings from the MOLI-SANI study. Haematologica 2013; 98(9): 1476-1480. e-pub
581		ahead of print 2013/05/07; doi: 10.3324/haematol.2012.083410
582	23.	Kuulasmaa K, Palosaari T, editors. Contributors from Partners of the Consortium on
583		Health and Ageing: Network of Cohorts in Europe and the United States
584		(CHANCES). CHANCES cohort descriptions, assessment of the availability and
585		quality of data, and definitions of variables. MORGAM Project e-publications
586		[Internet]. 2015; (6). URN:NBN:fi-fe201501151161. Available from
587		URL: <u>http://www.thl.fi/publications/morgam/chances_d9/index.html</u> . Available from:
588		URL (Accessed n Date Accessed Year) .
589	24.	Klipstein-Grobusch K, den Breeijen JH, Goldbohm RA, Geleijnse JM, Hofman A,
590		Grobbee DE et al. Dietary assessment in the elderly: validation of a semiquantitative
0,0		
591		food frequency questionnaire. European journal of clinical nutrition 1998; 52(8): 588-
591 592		food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52 (8): 588- 596. e-pub ahead of print 1998/09/02;
591 592 593	25.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588-596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European
591 592 593 594	25.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588- 596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl
591 592 593 594 595	25.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588-596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl 1: S6-14. e-pub ahead of print 1997/01/01;
591 592 593 594 595 596	25. 26.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588-596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl 1: S6-14. e-pub ahead of print 1997/01/01; Sluik D, van Lee L, Geelen A, Feskens EJ. Alcoholic beverage preference and diet in
591 592 593 594 595 596 597	25. 26.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588- 596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl 1: S6-14. e-pub ahead of print 1997/01/01; Sluik D, van Lee L, Geelen A, Feskens EJ. Alcoholic beverage preference and diet in a representative Dutch population: the Dutch national food consumption survey 2007-
591 592 593 594 595 596 597 598	25. 26.	 food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52(8): 588-596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl 1: S6-14. e-pub ahead of print 1997/01/01; Sluik D, van Lee L, Geelen A, Feskens EJ. Alcoholic beverage preference and diet in a representative Dutch population: the Dutch national food consumption survey 2007-2010. <i>European journal of clinical nutrition</i> 2014; 68(3): 287-294. e-pub ahead of
591 592 593 594 595 596 597 598 599	25. 26.	food frequency questionnaire. <i>European journal of clinical nutrition</i> 1998; 52 (8): 588- 596. e-pub ahead of print 1998/09/02; Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. <i>Int J Epidemiol</i> 1997; 26 Suppl 1: S6-14. e-pub ahead of print 1997/01/01; Sluik D, van Lee L, Geelen A, Feskens EJ. Alcoholic beverage preference and diet in a representative Dutch population: the Dutch national food consumption survey 2007- 2010. <i>European journal of clinical nutrition</i> 2014; 68 (3): 287-294. e-pub ahead of print 2014/01/09; doi: 10.1038/ejcn.2013.279

600 27. Sluik D, Jankovic N, O'Doherty MG, Geelen A, Schottker B, Rolandsson O *et al.*

- Alcoholic Beverage Preference and Dietary Habits in Elderly across Europe: Analyses
- within the Consortium on Health and Ageing: Network of Cohorts in Europe and the
- United States (CHANCES) Project. *PloS one* 2016; **11**(8): e0161603. e-pub ahead of
- 604 print 2016/08/23; doi: 10.1371/journal.pone.0161603
- 605 28. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in
- epidemiologic studies. *The American journal of clinical nutrition* 1997; **65**(4 Suppl):
- 607 1220S-1228S; discussion 1229S-1231S. e-pub ahead of print 1997/04/01;
- 608 29. Jankovic N, Geelen A, Streppel MT, de Groot LC, Orfanos P, van den Hooven EH et
- *al.* Adherence to a healthy diet according to the World Health Organization guidelines
- and all-cause mortality in elderly adults from Europe and the United States. *American*
- *journal of epidemiology* 2014; **180**(10): 978-988. e-pub ahead of print 2014/10/17;
- 612 doi: 10.1093/aje/kwu229
- 30. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG *et al.* Multiple
 imputation for missing data in epidemiological and clinical research: potential and
- 615 pitfalls. *Bmj* 2009; **338:** b2393. e-pub ahead of print 2009/07/01; doi:
- 616 10.1136/bmj.b2393
- Sauerbrei W, Meier-Hirmer C, Benner A, Royston P. Multivariable regression model
 building by using fractional polynomials: Description of SAS, STATA, and R
- 619 programs. *Computational Statistics & Data Analysis* 2006; **50:** 3464-3485.
- 620 32. Hodge AM, English DR, O'Dea K, Giles GG. Alcohol intake, consumption pattern
- and beverage type, and the risk of Type 2 diabetes. *Diabetic medicine : a journal of*
- *the British Diabetic Association* 2006; **23**(6): 690-697. doi: 10.1111/j.1464-
- 623 5491.2006.01864.x

624	33.	Fagherazzi G, Vilier A, Lajous M, Boutron-Ruault MC, Balkau B, Clavel-Chapelon F
625		et al. Wine consumption throughout life is inversely associated with type 2 diabetes
626		risk, but only in overweight individuals: results from a large female French cohort
627		study. European journal of epidemiology 2014; 29(11): 831-839. doi:
628		10.1007/s10654-014-9955-7
629	34.	Conigrave KM, Hu BF, Camargo CA, Jr., Stampfer MJ, Willett WC, Rimm EB. A
630		prospective study of drinking patterns in relation to risk of type 2 diabetes among men.
631		Diabetes 2001; 50 (10): 2390-2395.
632	35.	Kao WH, Puddey IB, Boland LL, Watson RL, Brancati FL. Alcohol consumption and
633		the risk of type 2 diabetes mellitus: atherosclerosis risk in communities study.
634		American journal of epidemiology 2001; 154(8): 748-757. e-pub ahead of print
635		2001/10/09;
636	36.	Wannamethee SG, Camargo CA, Jr., Manson JE, Willett WC, Rimm EB. Alcohol
637		drinking patterns and risk of type 2 diabetes mellitus among younger women. Archives
638		of internal medicine 2003; 163(11): 1329-1336. e-pub ahead of print 2003/06/11; doi:
639		10.1001/archinte.163.11.1329
640	37.	Chiva-Blanch G, Urpi-Sarda M, Ros E, Valderas-Martinez P, Casas R, Arranz S et al.
641		Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid
642		profile: a randomized clinical trial. <i>Clinical nutrition</i> 2013; 32 (2): 200-206. e-pub
643		ahead of print 2012/09/25; doi: 10.1016/j.clnu.2012.08.022
644	38.	Gronbaek M. Factors influencing the relation between alcohol and mortalitywith
645		focus on wine. Journal of internal medicine 2001; 250(4): 291-308. e-pub ahead of
646		print 2001/09/29;
647	39.	Rehm J, Irving H, Ye Y, Kerr WC, Bond J, Greenfield TK. Are lifetime abstainers the
648		best control group in alcohol epidemiology? On the stability and validity of reported

649		lifetime abstention. American journal of epidemiology 2008; 168(8): 866-871. e-pub
650		ahead of print 2008/08/15; doi: 10.1093/aje/kwn093
651	40.	Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men:
652		explaining the U-shaped curve. Lancet 1988; 2(8623): 1267-1273. e-pub ahead of
653		print 1988/12/03;
654	41.	Di Castelnuovo A, Costanzo S, Bagnardi V, Donati MB, Iacoviello L, de Gaetano G.
655		Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34
656		prospective studies. Archives of internal medicine 2006; 166(22): 2437-2445. e-pub
657		ahead of print 2006/12/13; doi: 10.1001/archinte.166.22.2437
658	42.	Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment
659		in epidemiologic studies. <i>Epidemiology</i> 2009; 20 (4): 488-495. e-pub ahead of print
660		2009/06/16; doi: 10.1097/EDE.0b013e3181a819a1
661	43.	Collaboration NCDRF. Effects of diabetes definition on global surveillance of
662		diabetes prevalence and diagnosis: a pooled analysis of 96 population-based studies
663		with 331 288 participants. The lancet. Diabetes & endocrinology 2015; 3(8): 624-637.
664		e-pub ahead of print 2015/06/26; doi: 10.1016/S2213-8587(15)00129-1
665	44.	Ryden L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, de Boer MJ et al.
666		Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary.
667		The Task Force on Diabetes and Cardiovascular Diseases of the European Society of
668		Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD).
669		European heart journal 2007; 28(1): 88-136. e-pub ahead of print 2007/01/16; doi:
670		10.1093/eurheartj/ehl260
671	45.	American Diabetes Association. Nutrition recommendations and interventions for
672		diabetes: a position statement of the American Diabetes Association. Diabetes care
673		2008; 31 Suppl 1: S61-78. e-pub ahead of print 2008/01/10; doi: 10.2337/dc08-S061

674	46.	Feskens EJ, Loeber JG, Kromhout D. Diet and physical activity as determinants of
675		hyperinsulinemia: the Zutphen Elderly Study. American journal of epidemiology. Aug
676		15 1994; 140 (4):350-360.
677	47.	Beulens JW, Stolk RP, van der Schouw YT, Grobbee DE, Hendriks HF, Bots ML.
678		Alcohol consumption and risk of type 2 diabetes among older women. Diabetes Care.
679		Dec 2005; 28 (12):2933-2938.
680	48.	Kulathinal S, Niemelä M, Niiranen T, Saarela O, Palosaari T, Tapanainen H, et al.
681		Description of MORGAM Cohorts. MORGAM Project e-publications [Internet].
682		2005-; (2). URN:NBN:fi-fe20051214. Available from URL:

683 <u>http://www.thl.fi/publications/morgam/cohorts/index.html</u>.

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Figure 1. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between beer preference and diabetes incidence compared to having no
preference adjusted for age, sex, education, employment status, prevalent coronary heart
disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator
score (if available), and BMI.

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Figure 2. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between wine preference and diabetes incidence compared to having no
preference adjusted for age, sex, education, employment status, prevalent coronary heart
disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator
score (if available), and BMI.

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Figure 3. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between spirit preference and diabetes incidence compared to having no
preference adjusted for age, sex, education, employment status, prevalent coronary heart
disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator
score (if available), and BMI.

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Figure 4. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between residuals of beer consumption per 6 g/d and diabetes incidence
adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent
coronary heart disease and cancer, smoking status, physical activity (if available), Healthy
Diet Indicator score (if available), and BMI.

Figure 5. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between residuals of wine consumption per 6 g/d and diabetes incidence
adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent
coronary heart disease and cancer, smoking status, physical activity (if available), Healthy
Diet Indicator score (if available), and BMI.
Figure 6. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs)
for the association between residuals of spirit consumption per 6 g/d and diabetes incidence

adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent

- coronary heart disease and cancer, smoking status, physical activity (if available), Healthy
- 718 Diet Indicator score (if available), and BMI.

Figure 1. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between beer preference and diabetes incidence compared to having no preference adjusted for age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W(random)
Zutphen Elderly Study, the Netherlands		1.00 (0.31-3.27)	1.1
Rotterdam Elderly Study, the Netherlands		2.21 (1.33-3.68)	5.4
EPIC-Elderly, the Netherlands		0.91 (0.30-2.74)	1.3
EPIC-Elderly, Greece		0.92 (0.71-1.19)	15.3
EPIC-Elderly, Sweden		0.81 (0.52-1.26)	6.8
The Tromsø Study, Norway		1.23 (0.86-1.77)	9.6
ESTHER, Germany		0.98 (0.78-1.24)	17.9
MORGAM: FINRISK, Finland	•	1.05 (0.93-1.18)	31.2
MORGAM: Northern-Sweden, Sweden		1.06 (0.72-1.56)	8.5
MORGAM: MOLI-SANI, Italy		1.29 (0.63-2.65)	2.9
Combined – Random Effects Model	•	1.06 (0.93-1.20)	
Q=12.08 (P-value: 0.21); I ² : 26% (0%-64%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 2. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between wine preference and diabetes incidence compared to having no preference adjusted for age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W (random)
Zutphen Elderly Study, the Netherlands		1.60 (0.55-4.63)	1.1
Rotterdam Elderly Study, the Netherlands		1.49 (0.99-2.24)	6.5
EPIC-Elderly, the Netherlands		1.14 (0.72-1.80)	5.5
EPIC-Elderly, Greece	-	0.82 (0.70-0.95)	24.1
EPIC-Elderly, Sweden		1.00 (0.53-1.87)	3.1
The Tromsø Study, Norway	- -------------	1.03 (0.73-1.44)	9.0
ESTHER, Germany		0.96 (0.76-1.20)	16.0
MORGAM: FINRISK, Finland		0.94 (0.80-1.10)	23.1
MORGAM: Northern-Sweden, Sweden		1.15 (0.69-1.93)	4.4
MORGAM: MOLI-SANI, Italy		1.22 (0.83-1.80)	7.2
Combined – Random Effects Model	•	0.99 (0.88-1.11)	
Q=12.14 (P-value: 0.21); l ² :26% (0%-64%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 1. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between beer preference and diabetes incidence compared to having no preference adjusted for age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W(random)
Zutphen Elderly Study, the Netherlands		1.00 (0.31-3.27)	1.1
Rotterdam Elderly Study, the Netherlands		2.21 (1.33-3.68)	5.4
EPIC-Elderly, the Netherlands		0.91 (0.30-2.74)	1.3
EPIC-Elderly, Greece		0.92 (0.71-1.19)	15.3
EPIC-Elderly, Sweden		0.81 (0.52-1.26)	6.8
The Tromsø Study, Norway		1.23 (0.86-1.77)	9.6
ESTHER, Germany		0.98 (0.78-1.24)	17.9
MORGAM: FINRISK, Finland	•	1.05 (0.93-1.18)	31.2
MORGAM: Northern-Sweden, Sweden		1.06 (0.72-1.56)	8.5
MORGAM: MOLI-SANI, Italy		1.29 (0.63-2.65)	2.9
Combined – Random Effects Model	•	1.06 (0.93-1.20)	
Q=12.08 (P-value: 0.21); I ² : 26% (0%-64%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 2. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between wine preference and diabetes incidence compared to having no preference adjusted for age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W (random)
Zutphen Elderly Study, the Netherlands		1.60 (0.55-4.63)	1.1
Rotterdam Elderly Study, the Netherlands		1.49 (0.99-2.24)	6.5
EPIC-Elderly, the Netherlands		1.14 (0.72-1.80)	5.5
EPIC-Elderly, Greece	-	0.82 (0.70-0.95)	24.1
EPIC-Elderly, Sweden		1.00 (0.53-1.87)	3.1
The Tromsø Study, Norway	- -------------	1.03 (0.73-1.44)	9.0
ESTHER, Germany		0.96 (0.76-1.20)	16.0
MORGAM: FINRISK, Finland		0.94 (0.80-1.10)	23.1
MORGAM: Northern-Sweden, Sweden		1.15 (0.69-1.93)	4.4
MORGAM: MOLI-SANI, Italy		1.22 (0.83-1.80)	7.2
Combined – Random Effects Model	•	0.99 (0.88-1.11)	
Q=12.14 (P-value: 0.21); l ² :26% (0%-64%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 3. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between spirit preference and diabetes incidence compared to having no preference adjusted for age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W (random)
Zutphen Elderly Study, the Netherlands		1.60 (0.55-4.63)	3.9
Rotterdam Elderly Study, the Netherlands		1.49 (0.99-2.24)	12.5
EPIC-Elderly, the Netherlands		1.14 (0.72-1.80)	8.3
EPIC-Elderly, Greece		0.82 (0.70-0.95)	17.0
EPIC-Elderly, Sweden		1.00 (0.53-1.87)	5.8
The Tromsø Study, Norway		1.03 (0.73-1.44)	15.4
ESTHER, Germany		0.96 (0.76-1.20)	8.7
MORGAM: FINRISK, Finland	•	0.94 (0.80-1.10)	23.2
MORGAM: Northern-Sweden, Sweden		1.15 (0.69-1.93)	5.3
Combined – Random Effects Model	•	1.19 (0.97-1.46)	
Q=17.47 (P-value: 0.03); I ² :54% (3%-78%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 4. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between the residuals of beer consumption per 6 g/d and diabetes incidence adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI) %W(random)
Zutphen Elderly Study, the Netherlands		0.97 (0.77-1.21) 2.1
Rotterdam Elderly Study, the Netherlands	•	0.97 (0.87-1.09) 8.1
EPIC-Elderly, the Netherlands		1.13 (0.89-1.44) 1.8
EPIC-Elderly, Greece	•	1.03 (0.95-1.12) 14.9
EPIC-Elderly, Sweden		1.20 (0.56-2.56) 0.2
The Tromsø Study, Norway		1.16 (0.95-1.41) 2.7
ESTHER, Germany	•	1.05 (0.95-1.16) 9.5
MORGAM: FINRISK, Finland	•	1.02 (0.98-1.07) 52.7
MORGAM: Northern-Sweden, Sweden		1.49 (0.86-2.60) 0.4
MORGAM: MOLI-SANI, Italy	P	1.01 (0.90-1.14) 7.5
Combined – Random Effects Model	•	1.03 (0.99-1.06)
Q=5.17 (P-value: 0.82); l ² : 0% (0%-35%)	0.1 0.2 0.4 0.8 1.6 3.2	

Figure 5. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between the residuals of wine consumption per 6 g/d and diabetes incidence adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W(random)
Zutphen Elderly Study, the Netherlands		0.84 (0.59-1.21)	0.9
Rotterdam Elderly Study, the Netherlands		0.92 (0.82-1.04)	7.6
EPIC-Elderly, the Netherlands	—	0.90 (0.78-1.04)	5.3
EPIC-Elderly, Greece		0.95 (0.90-1.01)	37.5
EPIC-Elderly, Sweden		0.44 (0.17-1.10)	0.1
The Tromsø Study, Norway		0.91 (0.73-1.15)	2.0
ESTHER, Germany		0.96 (0.87-1.07)	9.7
MORGAM: FINRISK, Finland	•	0.98 (0.92-1.04)	28.1
MORGAM: Northern-Sweden, Sweden		0.98 (0.49-1.96)	0.2
MORGAM: MOLI-SANI, Italy	•	1.00 (0.89-1.12)	8.5
Combined – Random Effects Model	•	0.96 (0.93-0.99)	
Q=5.80 (P-value: 0.76); l ² : 0% (0%-42%)	0.1 0.2 0.4 0.8 1.6 3.2		

Figure 6. Forest plot with pooled Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) for the association between the residuals of spirit consumption per 6 g/d and diabetes incidence adjusted for absolute alcohol intake, age, sex, education, employment status, prevalent coronary heart disease and cancer, smoking status, physical activity (if available), Healthy Diet Indicator score (if available), and BMI.

Study	Hazard Ratio	HR (95% CI)	%W(random)
Zutphen Elderly Study, the Netherlands		1.08 (0.90-1.31)	3.7
Rotterdam Elderly Study, the Netherlands		1.07 (0.98-1.17)	15.2
EPIC-Elderly, the Netherlands	- -	1.08 (0.93-1.26)	5.6
EPIC-Elderly, Greece		1.05 (0.99-1.11)	30.2
EPIC-Elderly, Sweden		1.65 (0.74-3.68)	0.2
The Tromsø Study, Norway	-8-	0.84 (0.57-1.25)	0.9
ESTHER, Germany		0.93 (0.64-1.35)	1.0
MORGAM: FINRISK, Finland		0.99 (0.94-1.03)	41.4
MORGAM: Northern-Sweden, Sweden		0.51 (0.21-1.26)	0.2
MORGAM: MOLI-SANI, Italy	-0-	0.93 (0.69-1.26)	1.5
Combined – Random Effects Model	•	1.02 (0.98-1.06)	
Q=9.89 (P-value: 0.36); I ² : 9% (0%-66%)	0.1 0.2 0.4 0.8 1.6 3.2		

Supplemental Figure 1: Participant flow-charts of the ten included European cohort studies from the Consortium on Health and Ageing: Network of Cohorts in Europe and the United States (CHANCES) project.

Zutphen Elderly Study	Rotterdam Study	EPIC-Elderly the Netherlands	EPIC-Elderly Greece	EPIC-Elderly Sweden
-		-		
N=876	N=7983	N=6896	N=9863	N=3364
	8			
Persons excluded with: - Prevalent diabetes (n=82) N=237 non-consumers excluded N=557	Persons excluded with: - Missing data on alcohol consumption (n=2551) - Prevalent diabetes at baseline (n-506) - Prevalent diabetes between baseline and start of follow- up and missing follow-up data (n=2459) N=490 non-consumers excluded N=2428	Persons excluded with: • Missing data on alcohol consumption (n=42) • Prevalent diabetes or missing data on diabetes revalence (n=357) • Missing follow-up data on diabetes (n=1967) N=896 non-consumers excluded	Persons excluded with: - Missing data on alcohol consumption (n=25) - Prevalent diabetes or missing data on diabetes prevalence (n=1460) - Missing follow-up data on diabetes (n=674) N=2567 non-consumers excluded N=5316	Persons excluded with: - Prevalent diabetes or missing data on diabetes prevalence (n=131) - Missing follow-up data on diabetes (n=4) N=410 non-consumers excluded N=2819
The Tromsø Study	ESTHER	MORGAM: FINRISK	MORGAM: MOLI-SANI	MORGAM: Northern-Sweden
N=10262	N=7983	N=38333	N=24325	N=5094
Persons excluded with: - Missing data on alcohol consumption (n=2464) - Prevalent diabetes or missing data on diabetes prevalence (n=453) Missing follow up data are	Persons excluded with: - Missing data on alcohol consumption (n=966) - Prevalent diabetes or missing data on diabetes prevalence (n=1580) Micine follow up data are	Persons excluded with: - Missing data on alcohol consumption (n=929) - Prevalent diabetes or missing data on diabetes prevalence (n=1808)	Persons excluded with: - Missing data on alcohol consumption (n=1843) - Prevalent diabetes or missing data on diabetes prevalence (n=1737)	Persons excluded with: - Missing data on alcohol consumption (n=217) - Prevalent diabetes or missing data on diabetes prevalence (n=160)
diabetes (n=153)	diabetes (n=1454)		8	
		N=15213 non-consumers	N=6402 non-consumers excluded	N=1672 non-consumers excluded
N=2474 non-consumers	N=2295 non-consumers	excluded	1	
excluded	excluded	*	N=14510	N=3032
	*	N=19759	., 14510	
N=4958	N=5286			

	Beer preference	Wine preference	Spirit preference	No preference
Zutphen Elderly Study				
N (%)	65 (12)	73 (13)	344 (62)	75 (13)
Age, years	70.5 (5.8)	72.1 (5.0)	72.2 (5.2)	71.8 (5.5)
Men, %	100	100	100	100
Ethanol consumption, g/day	13.5 [4.0-25.0]	3.8 [1.7-12.0]	18.8 [6.2-37.5	20.3 [8.4-44.9
University or college education, %	0	14	3	10
Current smokers, %	32	23	41	29
BMI, kg/m ²				
- Crude	26.0 (0.4)	24.7 (0.4)*	25.5 (0.2)	25.3 (0.4)
- Adjusted ^a	25.9 (0.4)	25.0 (0.4)	25.5 (0.2)	25.3 (0.4)
Diabetes cases / Person Years	6 / 756	9 / 747	27 / 3529	6 / 848
HR (95% CI): Model 1	1.00 (0.32-3.18)	1.34 (0.46-3.89)	0.95 (0.39-2.32)	1.00 (ref)
HR (95% CI): Model 2	1.04 (0.32-4.15)	1.46 (0.52-4.15)	0.96 (0.38-2.42)	1.00 (ref)
HR (95% CI): Model 3	1.00 (0.31-3.27)	1.60 (0.55-4.63)	1.07 (0.42-2.77)	1.00 (ref)
Rotterdam Study				
N (%)	182 (7)	1292 (53)	582 (24)	372 (15)
Age, years	62.4 (5.8)	64.8 (6.8)	66.2 (6.5)	64.0 (6.1)

	Beer preference	Wine preference	Spirit preference	No preference
Men, %	88	17	72	71
Ethanol consumption, g/day	11.7 [3.0-25.7]	2.9 [0.6-9.1]	18.9 [7.5-31.8]	11.3 [3.6-24.9]
University or college education, %	13	8	11	18
Current smokers, %	31	17	28	22
BMI, kg/m ²				
- Crude	25.4 (0.3)	26.1 (0.1)*	26.2 (0.1)*	25.7 (0.2)**,***
- Adjusted ^a	25.6 (0.3)	26.0 (0.1)	26.4 (0.2)***	26.0 (0.2)***
Diabetes cases / Person Years	30 / 1756	155 / 13447	100 / 5321	32 / 3920
HR (95% CI): Model 1	2.10 (1.27-3.47)	1.43 (0.96-2.15)	2.30 (1.54-3.43)	1.00 (ref)
HR (95% CI): Model 2	2.15 (1.29-3.57)	1.48 (0.98-2.24)	2.38 (1.58-3.57)	1.00 (ref)
HR (95% CI): Model 3	2.21 (1.33-3.68)	1.49 (0.99-2.24)	2.28 (1.52-3.43)	1.00 (ref)
EPIC-Elderly the Netherlands				
N (%)	82 (2)	2802 (74)	384 (10)	525 (14)
Age, years	63.7 (2.6)	64.2 (2.7)	64.1 (2.5)	64.2 (2.7)
Men, %	39	2	13	12
Ethanol consumption, g/day	7.3 [1.3-20.1]	4.4 [1.3-13.1]	10.1 [1.8-25.7]	4.9 [1.5-12.8]
University or college education, %	7	16	8	12
Current smokers, %	40	15	29	17

	Beer preference	Wine preference	Spirit preference	No preference
BMI, kg/m ²				
- Crude	25.2 (0.4)	25.5 (0.1)	26.4 (0.2)*,**	25.6 (0.2)***
- Adjusted ^a	25.0 (0.4)	25.7 (0.1)	26.3 (0.2)*,**	25.6 (0.2)***
Diabetes cases / Person Years	4 / 416	167 / 13601	26 / 1927	22 / 2559
HR (95% CI): Model 1	0.75 (0.25-2.22)	1.28 (0.81-2.02)	1.22 (0.69-2.17)	1.00 (ref)
HR (95% CI): Model 2	0.88 (0.29-2.57)	1.23 (0.78-1.94)	1.20 (0.67-2.13)	1.00 (ref)
HR (95% CI): Model 3	0.91 (0.30-2.74)	1.14 (0.72-1.80)	1.11 (0.63-1.98)	1.00 (ref)
EPIC-Elderly Greece				
N (%)	510 (10)	2561 (48)	361 (7)	1884 (35)
Age, years	66.2 (4.5)	67.4 (4.5)	67.0 (4.3)	66.3 (4.3)
Men, %	47	46	74	52
Ethanol consumption, g/day	1.3 [0.6-8.5]	8.0 [1.2-16.0]	13.2 [4.4-21.3]	2.8 [1.3-12.5]
University or college education, %	4	2	3	7
Current smokers, %	12	13	29	16
BMI, kg/m ²				
- Crude	29.2 (0.2)	28.9 (0.1)	28.9 (0.2)	28.8 (0.1)
- Adjusted ^a	29.0 (0.2)	28.7 (0.1)	29.4 (0.2)**	29.0 (0.1)
Diabetes cases / Person Years	72 / 5407	377 / 28107	58 / 3717	308 / 20618
HR (95% CI): Model 1	0.99 (0.77-1.28)	0.78 (0.67-0.91)	1.37 (1.03-1.82)	1.00 (ref)

	Beer preference	Wine preference	Spirit preference	No preference
HR (95% CI): Model 2	0.98 (0.76-1.27)	0.80 (0.69-0.94)	1.32 (1.00-1.76)	1.00 (ref)
HR (95% CI): Model 3	0.92 (0.71-1.19)	0.82 (0.70-0.95)	1.27 (0.95-1.68)	1.00 (ref)
EPIC-Elderly Sweden				
N (%)	958 (34)	413 (15)	137 (5)	1311 (47)
Age, years	60.4 (1.3)	60.3 (0.9)	60.4 (1.2)	60.3 (0.8)
Men, %	58	15	77	54
Ethanol consumption, g/day	0.9 [0.3-2.7]	1.6 [0.1-3.3]	2.0 [0.2-2.4]	2.9 [0.4-5.4]
University or college education, %	11	18	5	13
Current smokers, %	13	13	40	22
BMI, kg/m ²				
- Crude	25.6 (0.1)	25.5 (0.2)	26.7 (0.3)*,**	25.9 (0.1)***
- Adjusted ^a	25.5 (0.1)	25.5 (0.2)	26.8 (0.3)*,**	26.0 (0.1)*,***
Diabetes cases / Person Years	33 / 12680	14 / 5406	9 / 1821	53 / 17276
HR (95% CI): Model 1	0.81 (0.52-1.25)	1.00 (0.54-1.86)	1.34 (0.65-2.74)	1.00 (ref)
HR (95% CI): Model 2	0.80 (0.52-1.25)	1.00 (0.53-1.86)	1.31 (0.63-2.81)	1.00 (ref)
HR (95% CI): Model 3	0.81 (0.52-1.26)	1.00 (0.53-1.87)	0.92 (0.44-1.93)	1.00 (ref)
The Tromsø Study				
N (%)	722 (15)	1502 (30)	1042 (21)	1692 (34)

	Beer preference	Wine preference	Spirit preference	No preference
Age, years	59.6 (8.4)	59.8 (8.8)	62.1 (8.6)	58.7 (7.7)
Men, %	76	28	74	71
Ethanol consumption, g/day	3.3 [1.7-6.1]	4.7 [2.4-7.1]	1.1 [1.1-2.6]	4.7 [2.8-8.1]
University or college education, %	18	33	10	28
Current smokers, %	38	29	50	34
BMI, kg/m ²				
- Crude	25.4 (0.1)	25.4 (0.1)	25.9 (0.1)*,**	25.9 (0.1)*,**
- Adjusted ^a	25.3 (0.1)	25.6 (0.1)	25.9 (0.1)*,**	25.8 (0.1)**
Diabetes cases / Person Years	45 / 9158	65 / 19853	72 / 12715	96 / 22094
HR (95% CI): Model 1	1.12 (0.78-1.60)	0.95 (0.68-1.34)	1.32 (0.96-1.81)	1.00 (ref)
HR (95% CI): Model 2	1.12 (0.78-1.60)	0.96 (0.68-1.34)	1.32 (0.96-1.81)	1.00 (ref)
HR (95% CI): Model 3	1.23 (0.86-1.77)	1.03 (0.73-1.44)	1.17 (0.85-1.61)	1.00 (ref)
ESTHER				
N (%)	1466 (28)	2305 (44)	107 (2)	1408 (27)
Age, years	61.5 (6.4)	61.5 (6.6)	63.2 (6.8)	62.0 (6.6)
Men, %	77	32	22	64
Ethanol consumption, g/day	6.6 [2.6-13.2]	5.6 [3.7-11.0]	0.8 [0.8-2.5]	9.1 [5.3-15.8]
Middle education, %	21	35	25	34
Current smokers, %	26	13	13	14

	Beer preference	Wine preference	Spirit preference	No preference
BMI, kg/m ²				
- Crude	27.6 (0.1)	26.8 (0.1)*	28.0 (0.4)**	27.1 (0.1)*,**,***
- Adjusted ^a	27.4 (0.1)	27.0 (0.1)*	28.2 (0.4)*,**	27.1 (0.1)*,***
Diabetes cases / Person Years	165 / 9671	207 / 16394	14 / 736	140 / 9792
HR (95% CI): Model 1	1.07 (0.85-1.35)	0.98 (0.79-1.23)	1.42 (0.81-2.47)	1.00 (ref)
HR (95% CI): Model 2	1.05 (0.83-1.32)	0.97 (0.78-1.22)	1.39 (0.80-2.43)	1.00 (ref)
HR (95% CI): Model 3	0.98 (0.78-1.24)	0.96 (0.76-1.20)	1.25 (0.71-2.18)	1.00 (ref)
MORGAM: FINRISK				
N (%)	6410 (32)	3200 (16)	3410 (17)	6739 (34)
Age, years	41.5 (11.5)	47.3 (12.3)	46.8 (11.8)	44.6 (11.7)
Men, %	63	26	66	62
Ethanol consumption, g/day	7.0 [4.0-15.0]	3.0 [2.0-9.0]	8.0 [3.0-14.0]	13.0 [7.0-21.0]
University or college education, %	9	19	6	15
Current smokers, %	38	17	34	29
BMI, kg/m ²				
- Crude	25.7 (0.1)	25.9 (0.1)*	25.9 (0.1)*,**	26.2 (0.1)*,**,***
- Adjusted ^{aw}	25.9 (0.1)	26.1 (0.1)	25.5 (0.1)*,**	26.2 (0.1)*,***
Diabetes cases / Person Years	487 / 101570	229 / 50342	437 / 59893	557 / 105820
HR (95% CI): Model 1	0.98 (0.87-1.11)	0.89 (0.76-1.05)	1.08 (0.95-1.22)	1.00 (ref)

	Beer preference	Wine preference	Spirit preference	No preference
HR (95% CI): Model 2	0.97 (0.86-1.10)	0.91 (0.78-1.07)	1.07 (0.94-1.21)	1.00 (ref)
HR (95% CI): Model 3	1.05 (0.93-1.18)	0.94 (0.80-1.10)	1.00 (0.88-1.13)	1.00 (ref)
MORGAM: Northern-Sweden				
N (%)	794 (26)	511 (17)	146 (5)	1581 (52)
Age, years	45.5 (13.4)	46.6 (11.6)	49.7 (11.6)	44.3 (11.7)
Men, %	72	10	81	65
Ethanol consumption, g/day	2.0 [1.0-6.0]	2.0 [1.0-2.0]	2.0 [1.0-2.0]	4.0 [3.0-6.0]
University or college education, %	15	26	2	19
Current smokers, %	23	27	40	30
BMI, kg/m ²				
- Crude	25.4 (0.1)	24.8 (0.2)*	26.7 (0.3)*,**,***	25.2 (0.1)**,***
- Adjusted ^a	25.2 (0.2)	25.2 (0.2)	26.1 (0.3)*,**	25.2 (0.1)***
Diabetes cases / Person Years	40 / 15215	25 / 10413	7 / 2728	77 / 31392
HR (95% CI): Model 1	0.99 (0.67-1.46)	1.05 (0.63-1.73)	0.88 (0.40-1.93)	1.00 (ref)
HR (95% CI): Model 2	1.04 (0.71-1.54)	1.10 (0.66-1.83)	0.87 (0.40-1.90)	1.00 (ref)
HR (95% CI): Model 3	1.06 (0.72-1.56)	1.15 (0.69-1.93)	0.68 (0.31-1.50)	1.00 (ref)
MORGAM: MOLI-SANI				
N (%)	618 (4)	11522 (79)	102 (1)	2268 (16)

	Beer preference	Wine preference	Spirit preference	No preference
Age, years	49.6 (9.9)	56.7 (11.7)	50.7 (9.3)	49.6 (9.7)
Men, %	62	60	34	64
Ethanol consumption, g/day	4.0 [1.0-17.0]	18.0 [10.0-34.0]	2.0 [2.0-7.0]	8.0 [3.0-20.0]
University or college education, %	13	12	14	17
Current smokers, %	35	22	25	27
BMI, kg/m ²				
- Crude	27.3 (0.2)	27.8 (0.0)*	26.9 (0.4)**	27.6 (0.1)**
- Adjusted ^a	27.7 (0.2)	27.7 (0.0)	27.5 (0.4)	28.0 (0.1)**
Diabetes cases / Person Years	10 / 2758	255 / 20198	0 / 478	30 / 10319
HR (95% CI): Model 1	1.21 (0.59-2.49)	1.17 (0.80-1.73)	no cases	1.00 (ref)
HR (95% CI): Model 2	1.19 (0.58-2.44)	1.17 (0.80-1.73)	no cases	1.00 (ref)
HR (95% CI): Model 3	1.29 (0.63-2.65)	1.22 (0.89-1.80)	no cases	1.00 (ref)

* P-value <0.05 versus beer preference; ** P-value <0.05 versus wine preference; *** P-value <0.05 versus spirit preference.

^a BMI adjusted for age, sex, education, employment, prevalent coronary heart disease or cancer, smoking status, sports activity (if available), and Healthy Diet Indicator (if available).

Model 1: Adjusted for age, sex, education, employment, and prevalent coronary heart disease or cancer;

Model 2: Model 1 additionally adjusted for smoking status, sports activity (if available), and Healthy Diet Indicator score (if available). Model 3: Model 2 additionally adjusted for BMI.

Zutphen Elderly Study	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N	185	186	186	557
Cases / Person Years	14 / 1968	18 / 1903	16 / 2009	48 / 5880
HR (95% CI): Model 1	1.00 (ref)	1.47 (0.71-3.02)	1.25 (0.60-2.64)	0.98 (0.80-1.20)
HR (95% CI): Model 2	1.00 (ref)	1.47 (0.71-3.05)	1.30 (0.61-2.77)	0.98 (0.79-1.21)
HR (95% CI): Model 3	1.00 (ref)	1.47 (0.70-3.07)	1.23 (0.58-2.62)	0.97 (0.77-1.21)
Wine consumption (residuals)				
Ν	190	181	186	557
Cases / Person Years	15 / 1915	14 / 1859	19 / 2106	48 / 5880
HR (95% CI): Model 1	1.00 (ref)	0.92 (0.44-1.91)	1.25 (0.62-2.52)	0.89 (0.64-1.23)
HR (95% CI): Model 2	1.00 (ref)	0.93 (0.45-1.95)	1.19 (0.58-2.43)	0.85 (0.60-1.20)
HR (95% CI): Model 3	1.00 (ref)	0.90 (0.43-1.90)	1.12 (0.55-2.30)	0.84 (0.59-1.21)
Spirit consumption (residuals)				
Ν	189	184	184	557
Cases / Person Years	20 / 2095	13 / 1952	15 / 1833	48 / 5880
HR (95% CI): Model 1	1.00 (ref)	0.69 (0.34-1.41)	0.77 (0.39-1.54)	1.06 (0.88-1.26)
HR (95% CI): Model 2	1.00 (ref)	0.73 (0.35-1.50)	0.81 (0.41-1.63)	1.07 (0.89-1.28)
HR (95% CI): Model 3	1.00 (ref)	0.81 (0.39-1.68)	0.94 (0.47-1.90)	1.08 (0.09-1.31)

Rotterdam Study	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N (%)	809	815	804	2428
Cases / Person Years	109 / 8118	112 / 8283	96 / 8042	317 / 24444
HR (95% CI): Model 1	1.00 (ref)	1.07 (0.82-1.41)	0.88 (0.67-1.17)	0.98 (0.87-1.10)
HR (95% CI): Model 2	1.00 (ref)	1.08 (0.82-1.42)	0.88 (0.66-1.17)	0.97 (0.86-1.10)
HR (95% CI): Model 3	1.00 (ref)	1.06 (0.80-1.39)	0.87 (0.62-1.15)	0.97 (0.87-1.09)
Wine consumption (residuals)				
N (%)	810	819	799	2428
Cases / Person Years	125 / 7627	99 / 8250	93 / 8567	317 / 24444
HR (95% CI): Model 1	1.00 (ref)	0.74 (0.55-1.00)	0.67 (0.50-0.90)	0.89 (0.79-1.01)
HR (95% CI): Model 2	1.00 (ref)	0.74 (0.55-1.00)	0.68 (0.50-0.91)	0.90 (0.79-1.01)
HR (95% CI): Model 3	1.00 (ref)	0.79 (0.54-0.98)	0.72 (0.54-0.98)	0.92 (0.82-1.04)
Spirit consumption (residuals)				
N (%)	810	819	799	2428
Cases / Person Years	89 / 8471	110 / 8359	118 / 7613	317 / 24444
HR (95% CI): Model 1	1.00 (ref)	1.28 (0.96-1.70)	1.43 (1.08-1.91)	1.09 (0.99-1.19)
HR (95% CI): Model 2	1.00 (ref)	1.30 (0.97-1.72)	1.41 (1.06-1.87)	1.09 (0.99-1.19)
HR (95% CI): Model 3	1.00 (ref)	1.26 (0.95-1.68)	1.33 (1.00-1.77)	1.07 (0.98-1.17)

EPIC-ELDERLY: The Netherlands	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N	1264	1265	1264	3793
Cases / Person Years	67 / 6097	71 / 6120	81 / 6286	219 / 18503
HR (95% CI): Model 1	1.00 (ref)	1.01 (0.72-1.41)	0.97 (0.69-1.35)	1.07 (0.85-1.36)
HR (95% CI): Model 2	1.00 (ref)	0.95 (0.67-1.35)	0.96 (0.68-1.35)	1.10 (0.87-1.40)
HR (95% CI): Model 3	1.00 (ref)	0.79 (0.55-1.14)	0.83 (0.59-1.17)	1.13 (0.89-1.44)
Wine consumption (residuals)				
N	1265	1264	1264	3793
Cases / Person Years	78 / 6291	87 / 6172	54 / 6040	219 / 18503
HR (95% CI): Model 1	1.00 (ref)	1.20 (0.88-1.64)	0.87 (0.61-1.24)	0.90 (0.79-1.03)
HR (95% CI): Model 2	1.00 (ref)	1.16 (0.84-1.59)	0.85 (0.59-1.22)	0.88 (0.76-1.01)
HR (95% CI): Model 3	1.00 (ref)	1.03 (0.66-1.37)	0.95 (0.66-1.37)	0.90 (0.78-1.04)
Spirit consumption (residuals)				
N	1265	1266	1262	3793
Cases / Person Years	54 / 6068	87 / 6159	78 / 6276	219 / 18503
HR (95% CI): Model 1	1.00 (ref)	1.43 (1.01-2.02)	1.18 (0.83-1.69)	1.09 (0.95-1.26)
HR (95% CI): Model 2	1.00 (ref)	1.41 (0.99-2.00)	1.19 (0.83-1.70)	1.12 (0.97-1.29)
HR (95% CI): Model 3	1.00 (ref)	1.14 (0.79-1.63)	1.04 (0.72-1.49)	1.08 (0.93-1.26)

EPIC-ELDERLY: Greece	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N	1784	1775	1757	5316
Cases / Person Years	251 / 19614	296 / 19127	268 / 19109	815 / 57849
HR (95% CI): Model 1	1.00 (ref)	1.48 (1.24-1.76)	1.29 (1.09-1.54)	1.04 (0.96-1.12)
HR (95% CI): Model 2	1.00 (ref)	1.46 (1.23-1.74)	1.26 (1.06-1.50)	1.02 (0.94-1.10)
HR (95% CI): Model 3	1.00 (ref)	1.39 (1.17-1.66)	1.20 (1.00-1.43)	1.03 (0.95-1.12)
Wine consumption (residuals)				
Ν	1769	1765	1782	5316
Cases / Person Years	273 / 18828	280 / 19263	262 / 19759	815 / 57849
HR (95% CI): Model 1	1.00 (ref)	0.84 (0.71-1.00)	0.66 (0.55-0.78)	0.93 (0.88-0.98)
HR (95% CI): Model 2	1.00 (ref)	0.88 (0.73-1.04)	0.69 (0.58-0.82)	0.94 (0.90-0.99)
HR (95% CI): Model 3	1.00 (ref)	0.89 (0.63-0.89)	0.75 (0.63-0.89)	0.95 (0.90-1.01)
Spirit consumption (residuals)				
N	1770	1820	1726	5316
Cases / Person Years	260 / 19497	284 / 20037	271 / 18315	815 / 57849
HR (95% CI): Model 1	1.00 (ref)	1.23 (1.0346)	1.49 (1.26-1.78)	1.08 (1.02-1.14)
HR (95% CI): Model 2	1.00 (ref)	1.21 (1.02-1.45)	1.45 (1.22-1.72)	1.06 (1.01-1.12)
HR (95% CI): Model 3	1.00 (ref)	1.12 (0.94-1.34)	1.35 (1.13-1.61)	1.05 (0.99-1.11)

EPIC-ELDERLY: Sweden	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N	932	949	936	2819
Cases / Person Years	27 / 12276	48 / 12507	34 / 12400	109 / 37183
HR (95% CI): Model 1	1.00 (ref)	1.99 (1.22-3.25)	1.14 (0.68-1.91)	0.99 (0.48-2.03)
HR (95% CI): Model 2	1.00 (ref)	2.02 (1.24-3.31)	1.16 (0.69-1.95)	1.00 (0.48-2.06)
HR (95% CI): Model 3	1.00 (ref)	1.99 (1.22-3.77)	1.31 (0.78-2.22)	1.20 (0.56-2.56)
Wine consumption (residuals)				
Ν	941	921	957	2819
Cases / Person Years	39 / 12435	43 / 12173	27 / 12576	109 / 37183
HR (95% CI): Model 1	1.00 (ref)	1.31 (0.83-2.08)	0.85 (0.50-1.45)	0.54 (0.23-1.29)
HR (95% CI): Model 2	1.00 (ref)	1.32 (0.83-2.10)	0.85 (0.50-1.45)	0.54 (0.23-1.29)
HR (95% CI): Model 3	1.00 (ref)	1.21 (0.46-1.35)	0.79 (0.46-1.35)	0.44 (0.17-1.10)
Spirit consumption (residuals)				
N	939	956	924	2819
Cases / Person Years	21 / 12366	43 / 12604	45 / 12213	109 / 37183
HR (95% CI): Model 1	1.00 (ref)	2.14 (1.26-3.62)	2.04 (1.21-3.44)	1.76 (0.86-3.61)
HR (95% CI): Model 2	1.00 (ref)	2.13 (1.26-3.63)	2.02 (1.19-3.43)	1.76 (0.85-3.64)
HR (95% CI): Model 3	1.00 (ref)	2.05 (1.20-3.49)	1.86 (1.10-3.15)	1.65 (0.74-3.68)

Tromsø	Q1	Q2	Q3	Per 6 g/d	
Beer consumption (residuals)					
Ν	1562	1752	1644	4958	
Cases / Person Years	79 / 20158	97 / 22559	102 / 21103	278 / 63819	
HR (95% CI): Model 1	1.00 (ref)	1.11 (0.82-1.50)	1.07 (0.79-1.45)	1.11 (0.91-1.36)	
HR (95% CI): Model 2	1.00 (ref)	1.11 (0.82-1.50)	1.07 (0.79-1.45)	1.11 (0.91-1.36)	
HR (95% CI): Model 3	1.00 (ref)	1.03 (0.76-1.39)	1.16 (0.85-1.57)	1.16 (0.95-1.41)	
Wine consumption (residuals)					
Ν	1662	1733	1563	4958	
Cases / Person Years	114 / 20596	100 / 22534	64 / 20689	278 / 63819	
HR (95% CI): Model 1	1.00 (ref)	0.92 (0.70-1.21)	0.70 (0.50-0.97)	0.88 (0.71-1.09)	
HR (95% CI): Model 2	1.00 (ref)	0.92 (0.70-1.22)	0.70 (0.50-0.98)	0.88 (0.71-1.09)	
HR (95% CI): Model 3	1.00 (ref)	0.95 (0.56-1.10)	0.79 (0.56-1.10)	0.91 (0.73-1.15)	
Spirit consumption (residuals)					
Ν	1708	1617	1633	4958	
Cases / Person Years	80 / 22496	80 / 21103	118 / 20220	278 / 63819	
HR (95% CI): Model 1	1.00 (ref)	1.02 (0.75-1.40)	1.41 (1.05-1.91)	1.07 (0.74-1.54)	
HR (95% CI): Model 2	1.00 (ref)	1.02 (0.75-1.40)	1.41 (1.04-1.92)	1.06 (0.73-1.53)	
HR (95% CI): Model 3	1.00 (ref)	0.85 (0.62-1.16)	1.08 (0.79-1.46)	0.84 (0.57-1.25)	

<u>ESTHDR</u>	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
Ν	1589	1932	1765	5286
Cases / Person Years	143 / 11176	186 / 13686	197 / 11731	526 / 36593
HR (95% CI): Model 1	1.00 (ref)	1.08 (0.86-1.34)	1.12 (0.89-1.40)	1.06 (0.95-1.18)
HR (95% CI): Model 2	1.00 (ref)	1.10 (0.88-1.37)	1.11 (0.89-1.39)	1.05 (0.95-1.17)
HR (95% CI): Model 3	1.00 (ref)	1.07 (0.86-1.34)	1.05 (0.84-1.32)	1.05 (0.94-1.16)
Wine consumption (residuals)				
Ν	1667	1792	1827	5286
Cases / Person Years	191 / 11018	175 / 12681	160 / 12894	526 / 36593
HR (95% CI): Model 1	1.00 (ref)	0.88 (0.71-1.10)	0.83 (0.67-1.04)	0.94 (0.85-1.05)
HR (95% CI): Model 2	1.00 (ref)	0.90 (0.72-1.13)	0.84 (0.67-1.06)	0.95 (0.85-1.05)
HR (95% CI): Model 3	1.00 (ref)	0.92 (0.72-1.13)	0.90 (0.72-1.13)	0.96 (0.87-1.07)
Spirit consumption (residuals)				
Ν	1865	1834	1687	5286
Cases / Person Years	166 / 12075	184 / 12834	176 / 11683	526 / 36593
HR (95% CI): Model 1	1.00 (ref)	1.18 (0.94-1.47)	1.11 (0.89-1.37)	1.06 (0.74-1.53)
HR (95% CI): Model 2	1.00 (ref)	1.20 (0.96-1.49)	1.12 (0.91-1.39)	1.05 (0.73-1.51)
HR (95% CI): Model 3	1.00 (ref)	1.12 (0.90-1.39)	1.03 (0.83-1.27)	0.93 (0.64-1.35)

MORGAM: FINRISK	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
N	6455	6069	7235	19759
Cases / Person Years	645 / 103702	493 / 99754	572 / 114169	1710 / 317624
HR (95% CI): Model 1	1.00 (ref)	0.82 (0.73-0.92)	0.96 (0.86-1.08)	0.97 (0.93-1.02)
HR (95% CI): Model 2	1.00 (ref)	0.85 (0.75-0.96)	0.96 (0.86-1.07)	0.97 (0.93-1.02)
HR (95% CI): Model 3	1.00 (ref)	0.95 (0.84-1.07)	1.09 (0.97-1.22)	1.02 (0.98-1.07)
Wine consumption (residuals)				
Ν	6643	6477	6639	19759
Cases / Person Years	705 / 108162	548 / 108167	457 / 101296	1710 / 317624
HR (95% CI): Model 1	1.00 (ref)	0.81 (0.72-0.91)	0.79 (0.69-0.89)	0.95 (0.88-1.02)
HR (95% CI): Model 2	1.00 (ref)	0.84 (0.75-0.95)	0.82 (0.72-0.93)	0.96 (0.89-1.02)
HR (95% CI): Model 3	1.00 (ref)	0.95 (0.78-1.01)	0.89 (0.78-1.01)	0.98 (0.92-1.04)
Spirit consumption (residuals)				
Ν	7069	6188	6502	19759
Cases / Person Years	511 / 105964	445 / 1005545	754 / 111116	1710 / 317624
HR (95% CI): Model 1	1.00 (ref)	0.81 (0.71-0.92)	1.03 (0.92-1.16)	1.06 (1.01-1.11)
HR (95% CI): Model 2	1.00 (ref)	0.85 (0.75-0.97)	1.05 (0.94-1.18)	1.05 (1.01-1.10)
HR (95% CI): Model 3	1.00 (ref)	0.83 (0.73-0.95)	0.92 (0.82-1.03)	0.99 (0.94-1.03)

MORGAM: MOLI-SANI	Q1	Q2	Q3	Per 6 g/d
Beer consumption (residuals)				
Ν	4811	5065	4634	14510
Cases / Person Years	110 / 20994	117 / 22226	68 / 20533	295 / 63753
HR (95% CI): Model 1	1.00 (ref)	1.32 (1.00-1.74)	1.04 (0.76-1.42)	1.04 (0.92-1.18)
HR (95% CI): Model 2	1.00 (ref)	1.33 (1.00-1.75)	1.04 (0.76-1.42)	1.04 (0.92-1.17)
HR (95% CI): Model 3	1.00 (ref)	1.26 (0.95-1.66)	1.03 (0.75-1.41)	1.01 (0.90-1.14)
Wine consumption (residuals)				
Ν	4797	5271	4442	14510
Cases / Person Years	75 / 21702	115 / 23140	105 / 18911	295 / 63753
HR (95% CI): Model 1	1.00 (ref)	1.15 (0.85-1.56)	0.97 (0.71-1.33)	0.98 (0.87-1.10)
HR (95% CI): Model 2	1.00 (ref)	1.16 (0.85-1.57)	0.97 (0.71-1.33)	0.98 (0.87-1.10)
HR (95% CI): Model 3	1.00 (ref)	1.14 (0.73-1.36)	1.00 (0.73-1.36)	1.00 (0.89-1.12)
Spirit consumption (residuals)				
Ν	4750	5075	4685	14510
Cases / Person Years	104 / 19857	106 / 22123	85 / 21772	295 / 63753
HR (95% CI): Model 1	1.00 (ref)	1.23 (0.92-1.64)	1.08 (0.80-1.45)	0.93 (0.68-1.27)
HR (95% CI): Model 2	1.00 (ref)	1.23 (0.92-1.65)	1.09 (0.81-1.46)	0.93 (0.68-1.27)
HR (95% CI): Model 3	1.00 (ref)	1.21 (0.91-1.62)	1.02 (0.76-1.37)	0.93 (0.69-1.26)

consumption of beer, wine, and spirits and diabetes incidence in 10 European cohorts.

MORGAM: North-Sweden	Q1	Q2	Q3	Per 6 g/d	
Beer consumption (residuals)					
Ν	1101 911		1020	3032	
Cases / Person Years	55 / 21790	44 / 18329	50 / 19628	149 / 59748	
HR (95% CI): Model 1	1.00 (ref)	1.11 (0.74-1.65)	1.04 (0.70-1.55)	1.44 (0.84-2.46)	
HR (95% CI): Model 2	1.00 (ref)	1.15 (0.77-1.73)	1.11 (0.74-1.65)	1.46 (0.87-2.47)	
HR (95% CI): Model 3	1.00 (ref)	1.15 (0.77-1.72)	1.11 (0.75-1.66)	1.49 (0.86-2.60)	
Wine consumption (residuals)					
Ν	784	1224	1024	3032	
Cases / Person Years	40 / 14853	63 / 24261	46 / 20633	149 / 59748	
HR (95% CI): Model 1	1.00 (ref)	0.96 (0.64-1.44)	0.93 (0.58-1.48)	0.87 (0.44-1.69)	
HR (95% CI): Model 2	1.00 (ref)	0.98 (0.65-1.48)	0.92 (0.57-1.48)) 0.87 (0.45-1.67)	
HR (95% CI): Model 3	1.00 (ref)	0.99 (0.66-1.68)	1.05 (0.66-1.68)	0.98 (0.49-1.96)	
Spirit consumption (residuals)					
Ν	1042	1012	978	3032	
Cases / Person Years	46 / 20310	47 / 20377	56 / 19060	149 / 59748	
HR (95% CI): Model 1	1.00 (ref)	0.98 (0.65-1.48)	1.09 (0.72-1.65)	0.93 (0.68-1.27)	
HR (95% CI): Model 2	1.00 (ref)	0.99 (0.66-1.50)	1.05 (0.70-1.60)	0.67 (0.29-1.54)	
HR (95% CI): Model 3	1.00 (ref)	0.89 (0.59-1.34)	0.88 (0.58-1.33)	0.51 (0.21-1.26)	

Model 1: Adjusted for age, sex, education, employment, and prevalent coronary heart disease or cancer;

Model 2: Model 1 additionally adjusted for smoking status, sports activity (if available), and Healthy Diet Indicator score (if available). Model 3: Model 2 additionally adjusted for BMI.

 Table 1. Cohort characteristics of the ten included European cohorts from the Consortium on Health and Ageing: Network of Cohorts in Europe

 and the United States (CHANCES) project and number of included persons who reported to consume alcohol.

Cohort	Sub-cohort or country	Baseline period	Follow- up period	Follow-up length, median [P25- P75]	Ascertainment of incident diabetes type 2	Ν	Age category	Males, %
Zutphen	The	1985	1985-	9.7 [5.0-15.0]	Self-report and current treatment and non-	557	≥60 y	100
Elderly Study	Netherlands		2010		fasting glucose measures using the WHO definition ⁴⁶ .			
Rotterdam Study	The Netherlands	1990	1997- 2013	12.2 [7.0- 13.1]	Followed-up using information from general practitioners, pharmacies' databases, and follow-up examinations. Defined as being registered by a general practitioner as having type 2 diabetes and meeting at least one of the following four criteria: fasting plasma glucose concentration \geq 7.0 mmol/L, random plasma glucose concentration \geq 11.1 mmol/L,	2428	≥55 y	44
					use of anti-diabetic mediation, and/or following dietary guidelines for type 2 diabetes.			
EPIC-Elderly	The Netherlands	1993- 1997	1993- 2005	4.9 [4.1-5.0]	Self-reported diagnosis in the follow-up questionnaires and/or a urinary glucose strip test for detection of glucosuria, and/or linkage with the Dutch register of hospital discharge diagnoses ⁴⁷ .	3793	≥60 y	6

Table 1 (continued). Cohort characteristics of the ten included European cohorts from the Consortium on Health and Ageing: Network of

Cohorts in Europe and the United States (CHANCES) project and number of included persons who reported to consume alcohol.

Cohort	Sub-cohort or country	Baseline period	Follow- up period	Follow-up length, median [P25- P75]	Ascertainment of incident diabetes type 2	Ν	Age category	Males, %
	Greece	1994-	1994-	11.4 [9.9-	Collected during follow-up through self-	5316	≥60 y	50
		1999	2011	12.5]	report and current treatment; cases were not validated.			
	Sweden	1992-	1992-	13.2 [12.1-	Followed up through linkage with the	2819	≥60 y	51
		1996	2011	14.2]	Swedish diabetes register and verified by			
					biomarker measurements of impaired			
					glucose tolerance and impaired fasting			
					glucose in a few cases.			
The Tromsø	Norway	1994-	1994-	15.6 [10.0-	Linkage with diabetes-related or	4958	≥45 y	59
Study		1995	2010	16.0]	cardiovascular diseases discharge diagnosis			
					at the only hospital serving the Tromsø			
					population or verified by self-report or			
					observed HbA1c-values >6.5% during			
					follow-up. Some of the cases were validated			
					using medical records or a non-fasting			
					glucose measurement.			

Table 1 (continued). Cohort characteristics of the ten included European cohorts from the Consortium on Health and Ageing: Network of

Cohorts in Europe and the United States (CHANCES) project and number of included persons who reported to consume alcohol.

Cohort	Sub-cohort or country	Baseline period	Follow- up period	Follow-up length, median [P25- P75]	Ascertainment of incident diabetes type 2	Ν	Age category	Males, %
ESTHER	Germany	2000- 2003	2000- 2007	7.9 [5.3-8.1]	The cohort was systematically searched for diabetes events and incident cases were validated with medical records during follow-up. In addition, subjects with HbA _{1c} $\geq 6.5\%$ at 8-year follow-up were classified as subjects with incident type 2 diabetes in order to identify undiagnosed cases.	5286	48-75 y	53
MORGAM	FINRISK	1982-	1982-	14.0 [8.9-	Through linkage to the national Hospital	19759	24-74 y	57
	(Finland)	2002	2010	23.8]	Discharge Register, Causes of Death Register, and drug reimbursement registers ⁴⁸ .			
	MOLI-SANI	2005-	2005-	4.3 [3.3-5.4]	Cases were identified and validated through	14510	35-99 у	60
	(Italy)	2010	2011		linkage to the National Medication Register and to the Local Diagnosis Registers ⁴⁸ .			
	Northern-	1986-	1986-	20.8 [17.8-	Based on self-reported diagnosis in a phone	3032	24-74 y	58
	Sweden	1994	2011	24.5]	interview and/or linkage with Hospital			
	(Sweden)				Discharge Records ⁴⁸ .			

Table 2. Pooled Hazard Ratios (95% CI) from random-effects meta-analyses for the association between having a beer, wine, or spirit preference compared to having no preference according to sub-groups and additional analyses.

Beer preference	Wine preference	Spirit preference	No preference
1.24 (0.95-1.61)	1.07 (0.85-1.36)	0.89 (0.44-1.82)	1.00 (ref)
1.05 (0.95-1.15)	0.95 (0.85-1.06)	1.26 (1.06-1.51)	1.00 (ref)
1.26 (0.93-1.71)	1.17 (0.92-1.50)	1.27 (1.01-1.59)	1.00 (ref)
1.23 (0.89-1.70)	1.08 (0.85-1.37)	1.33 (1.11-1.60)	1.00 (ref)
1.04 (0.95-1.15)	0.99 (0.87-1.13)	1.16 (0.95-1.42)	1.00 (ref)
1.05 (0.95-1.16)	0.98 (0.87-1.10)	1.01 (0.90-1.14)	1.00 (ref)
1.06 (0.93-1.21)	0.93 (0.77-1.12)	1.10 (0.93-1.31)	1.00 (ref)
	Beer preference 1.24 (0.95-1.61) 1.05 (0.95-1.15) 1.26 (0.93-1.71) 1.23 (0.89-1.70) 1.04 (0.95-1.15) 1.05 (0.95-1.16) 1.06 (0.93-1.21)	Beer preference Wine preference 1.24 (0.95-1.61) 1.07 (0.85-1.36) 1.05 (0.95-1.15) 0.95 (0.85-1.06) 1.26 (0.93-1.71) 1.17 (0.92-1.50) 1.23 (0.89-1.70) 1.08 (0.85-1.37) 1.04 (0.95-1.15) 0.99 (0.87-1.13) 1.05 (0.95-1.16) 0.98 (0.87-1.10) 1.06 (0.93-1.21) 0.93 (0.77-1.12)	Beer preference Wine preference Spirit preference 1.24 (0.95-1.61) 1.07 (0.85-1.36) 0.89 (0.44-1.82) 1.05 (0.95-1.15) 0.95 (0.85-1.06) 1.26 (1.06-1.51) 1.26 (0.93-1.71) 1.17 (0.92-1.50) 1.27 (1.01-1.59) 1.23 (0.89-1.70) 1.08 (0.85-1.37) 1.33 (1.11-1.60) 1.04 (0.95-1.15) 0.99 (0.87-1.13) 1.16 (0.95-1.42) 1.05 (0.95-1.16) 0.98 (0.87-1.10) 1.01 (0.90-1.14)

* Defined as persons with prevalent heart disease or cancer or a follow-up ≤ 2 years.

Models adjusted for age, sex, education, employment, prevalent coronary heart disease or cancer, smoking status, sports activity (if available), Healthy Diet Indicator score (if available), and BMI.