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RELATIONSHIP BETWEEN ALCOHOL INTAKE, HEALTH AND SOCIAL STATUS AND CARDIOVASCULAR RISK FACTORS IN THE URBAN PARIS-ILE-DE-FRANCE COHORT: IS THE CARDIOPROTECTIVE ACTION OF ALCOHOL A MYTH?

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1 **RELATIONSHIP BETWEEN ALCOHOL INTAKE, HEALTH AND SOCIAL**
2 **STATUS AND CARDIOVASCULAR RISK FACTORS IN THE URBAN PARIS-ILE-**
3 **DE-FRANCE COHORT: IS THE CARDIOPROTECTIVE ACTION OF ALCOHOL A**
4 **MYTH?**

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16 Study design: Cross-sectional study

17 Keywords: alcohol, HDL-C, cardiovascular risk factors, epidemiology

18 Running title: alcohol intake and cardiovascular risk profile

19

20

Abstract

21

Background/objective: Observational studies document inverse relationship between cardiovascular disease (CVD) and moderate alcohol intake. Causal role for alcohol in cardioprotection remains however uncertain as such protection may partly arise from confounders and misclassification. The aim of our study was to evaluate potential confounders which may contribute to the putative cardioprotection by alcohol.

26

Subjects/Methods: We evaluated clinical and biological characteristics, including CV risk factors and health status, of 149,773 subjects undergoing examination in our Center for CVD Prevention (The Urban Paris-Ile-de-France Cohort). Subjects were divided into four groups according to alcohol consumption: never, low (≤ 10 g/day), moderate (10 to 30 g/day) and high (>30 g/day); former drinkers were analysed as a separate group.

31

Results: After adjustment for age, moderate male drinkers were more likely to display clinical and biological characteristics associated with lower CV risk, including low BMI, heart rate, pulse pressure, fasting triglycerides, fasting glucose, stress and depression scores together with superior subjective health status, respiratory function, social status and physical activity. Moderate female drinkers equally displayed low waist circumference, blood pressure and fasting triglycerides and LDL-cholesterol. Alcohol intake was strongly associated with plasma HDL-cholesterol in both sexes. Multivariate analysis confirmed that moderate and low drinkers displayed better health status than never drinkers. Importantly, few factors were causally related to alcohol intake.

40

Conclusion: Moderate alcohol drinkers display a more favourable clinical and biological profile, consistent with lower CV risk as compared to non-drinkers and heavy drinkers. Moderate alcohol consumption may therefore represent a marker of higher social level, superior health status and lower CV risk.

44

45 **Introduction**

46 An inverse association between moderate alcohol consumption and cardiovascular disease
47 (CVD) has been established in prospective observational epidemiological studies in several
48 countries. Meta-analysis (Maclure 1993, Cleophas 1999, Corrao, et al. 2000, Di Castelnuovo,
49 et al. 2002, Di Castelnuovo, et al. 2006) have confirmed that self-reported consumption of one
50 (~10 g alcohol) to three (~30 g alcohol) standard alcoholic drinks per day is associated with a
51 20-25% reduction in the risk of CVD. The lower risk of CVD observed in moderate drinkers
52 is often attributed to the beneficial effects of alcohol on plasma lipids and lipoproteins,
53 (Chapman 2006). Other potential explanations include the effect of alcohol on hemostatic
54 factors (Rimm, et al. 1999) and of antioxidants present in red wine (Leikert, et al. 2002).
55 Taken together, these data have been translated into the message that “small to moderate
56 amounts of alcohol are good for your health”. This message is of particular importance in
57 France where the mean alcohol intake per inhabitant is one of the highest in the world.
58 Findings in observational studies should however be viewed with caution because of number
59 of bias not always taken into account. A growing body of evidence suggests that the apparent
60 protection afforded by alcohol intake against CVD might be due in part to misclassification
61 and confounding (Shaper, et al. 1988, Tjonneland, et al. 1999, Mortensen, et al. 2001, Naimi,
62 et al. 2005, Fillmore, et al. 2007, Stockwell, et al. 2007, Fillmore, et al. 2008). In order to
63 evaluate these confounding, we undertook a large population study to analyse the relationship
64 between alcohol intake and other cardiovascular risk factors in a large French population. We
65 assessed a number of key factors not taken into account in earlier well conducted studies;
66 these include social factors, health status (mental well-being, subjective health status),
67 respiratory function, anthropometric values, heart rate and pulse pressure.

68

69

70 **Methods**

71 Subjects were examined at the IPC (*Clinical and Preventive Investigation Center in*
72 *Paris, France*). This Medical Center, which is subsidized by the French National Health Care
73 system (*Social Security-CNAMTS*), offers a complementary medical examination to all
74 working and retired individuals and their families once every five years. It is one of the
75 largest medical centers of this kind in France, carrying out approximately 25,000 health
76 examinations per year for people living in the Paris area.

77 Our study population underwent a health checkup at the IPC Center between January
78 1999 and December 2005 and was composed of 149, 773 subjects (97, 406 men and 52, 367
79 women) with a mean age of 47.6 ± 15 and 47.0 ± 12 years respectively).

80 Supine blood pressure (BP) was measured in the right arm using a manual mercury
81 sphygmomanometer, after a 10-minute resting period. The first and the fifth Korotkoff phases
82 were used to define systolic blood pressure (SBP) and diastolic blood pressure (DBP). The
83 mean of three measurements was considered as the BP value. Pulse pressure (PP) was defined
84 as the difference between SBP and DBP. Waist circumference (WC) was measured using an
85 inelastic tape placed midway between the lower ribs and iliac crests on the mid-axillary line.
86 Standard biological parameters (enzymatic method, automat HITACHI 917; colorimetric
87 method for albumin dosage and hematology: ABX, Pentra 120) were measured under fasting
88 conditions; HDL-C was measured by direct enzymatic assay with cyclodextrin (Roche
89 Diagnostics, Basel, Switzerland). A resting electrocardiogram was recorded. Respiratory
90 function was assessed by spirometry by measuring forced expiratory volume (FEV1).
91 Tobacco consumption (never smoker, ex-smoker and current smoker), physical activity
92 (regular physical activity: yes or no), personal medical history, current medications and
93 alcohol consumption, social status and occupational activity were assessed using a self-
94 administered questionnaire. Stress and depression scores were assessed by validated

95 questionnaires (Cohen, et al. 1983) (Beck, et al. 1974); Subjected Health Status (SHS) score
96 were collected with a self-estimation on a scale between 0 to 10. Alcohol intake was
97 quantified as the number of standardized glasses of alcohol (10 g/glass) consumed per day.
98 Each type of alcoholic beverage (i.e. cider and beer, wine, appetizer) was recorded. Total
99 alcohol intake was calculated as the sum of all types of alcohol consumed and the
100 corresponding quantity (as grams of alcohol) was estimated. All clinical and biological
101 parameters were evaluated on the same day of the examination.

102 The IPC Center received authorization from the *National Committee of Information and*
103 *Civil Liberty* to conduct these analyses. All subjects gave their informed consent at the time of
104 the examination.

105 **Statistical analysis**

106 Alcohol consumption was divided into 5 classes : (1): Never alcohol consumption, (2): Low
107 alcohol consumers (less than one glass per day), (3): moderate alcohol consumers (between 1
108 and 3 glasses per days), (4): High alcohol consumers (more than 3 glasses), (5): subjects who
109 previously consumed alcohol but who no longer consume alcohol (former drinkers). As a
110 consequence of the heterogeneity in the group of former drinkers (time elapsed since
111 cessation of alcohol consumption, reason for this cessation...), data in this group were
112 analysed separately.

113 For quantitative variables, the four first groups were compared by multivariate model
114 analysis, which included age in order to take into account the difference in age observed
115 between the different groups; respiratory function (FEV1) was compared across the groups
116 before and after further adjustment for tobacco status. For qualitative variables, comparisons
117 were made using the Chi2 test. As one may hypothesize that the relationships between alcohol
118 and health and social status are not identical in males and females, we analysed these
119 relationships on the basis of stratification by gender. All parameters associated with alcohol

120 consumption in univariate analysis were included in a multivariate model. Forward regression
121 analysis was carried out and all variables remaining in the model were significant with
122 $p < 0.05$. All statistical analyses were performed with SAS statistical software (version 8.2).

123 **Results**

124 Data from a total of 149, 773 subjects (97, 406 men and 52, 367 women) were analyzed. The
125 average ages of men and women were 47.6 ± 15 and 47.0 ± 12 years respectively. In this
126 population, 13.7% of the men and 23.9% of the women were abstinent (4.5% former drinkers
127 and 9.2% never drinkers in men; 20.1% never drinkers and 3.1% former drinkers in women).
128 Total alcohol intake increased with age both in men and women. **Figure 1** presents the type of
129 alcoholic beverage preferred according to sex and age. With the exception of the subgroup of
130 young subjects (<30 years of age), alcoholic beverages mainly consisted of wine. In addition,
131 wine consumption increased with age whereas those of beer and appetizers decreased
132 ($p < 0.0001$).

133 Age-adjusted clinical characteristics of the study population according to alcohol
134 consumption (never, low, moderate and heavy drinkers) are presented in **Table 1** for men and
135 in **Table 2** for women. In women, BMI, WC, hip circumference, waist-to-hip ratio as well as
136 the prevalence of obesity ($BMI > 30 \text{ kg/m}^2$) were all lowest in moderate drinkers and highest
137 in never drinkers. No clear relationship was observed between alcohol consumption and
138 anthropometric variables in men; however, moderate drinkers were less likely to be obese as
139 compared to other groups. In women, SBP and DBP differed as a function of alcohol
140 consumption, being lowest in moderate drinkers and highest in never drinkers. Moreover, in
141 women, PP was negatively associated with alcohol intake, being highest in female never
142 drinkers. In men, the lowest value for SBP was observed in low drinkers, whereas there was a
143 progressive increase in DBP with increment in alcohol intake; PP was the lowest in low and

144 moderate drinkers as compared to never drinkers. Heart rate was the lowest in moderate
145 drinkers in both men and women.

146 There was a significant positive relationship between smoking and alcohol consumption. In
147 women, moderate drinkers were more likely to declare that they practiced regular physical
148 activity as compared to the other groups. By contrast in men, never drinkers reported the
149 highest level of physical activity. In both genders, respiratory function assess by FEV1 was
150 highest in moderate drinkers and lowest in never drinkers. Similar results were observed after
151 adjustment for tobacco consumption (data not shown). In men, the percentage of subjects
152 living alone was the highest among never drinkers and lowest among moderate drinkers. By
153 contrast, in women, moderate drinkers were more likely to live alone than never drinkers.

154 SHS across the groups is presented on **Figure 3**. The proportion of subjects with a low
155 evaluation of their SHS was lowest in the group of moderate alcohol consumers and the
156 highest in never drinkers; this finding was observed in both genders. Score values of
157 depression and stress differed significantly among groups distinguished by the level of
158 alcohol consumption. For both scores, minimal values were observed among moderate
159 alcohol consumers in both women and men. Higher values of these scores were observed
160 among individuals who were abstainers. Intermediate values were observed among heavy
161 drinkers.

162 **Tables 3 and 4** show age-adjusted means of biological parameters in men and women
163 respectively. MGV as well as GGT were positively associated with self-reported alcohol
164 consumption, thereby confirming the validity of data collection concerning alcohol intake. In
165 both genders, total cholesterol levels were positively associated with alcohol consumption.
166 The lowest levels of total cholesterol were observed among never drinkers while the highest
167 were observed among heavy drinkers. In men, LDL-Cholesterol (LDL-C) levels were also
168 positively associated with alcohol consumption. In women, the lowest values of LDL-C were

169 observed among moderate drinkers. In both genders, the lowest values of plasma triglycerides
170 and fasting blood glucose were observed among low or moderate drinkers.

171 Mean values (SEM) of HDL-C concentration are presented in **Tables 3** (for men) and **4** (for
172 women) and in **figure 2**. In both genders, the level of HDL-C was the lowest among never
173 drinkers and increased linearly with alcohol consumption. This relationship was similar across
174 age groups, and equally persisted in hypertriglyceridemic subjects. Moreover, this
175 relationship was independent of the type of alcoholic beverage consumed (data not shown). A
176 multivariate analysis was performed in order to determine the factors associated with low or
177 moderate alcohol consumption (Table 5). This analysis revealed that FEV1, age, current
178 smoking, HDL-C, general health status, a lower anxiety score, cholesterol, Gamma-GT, a
179 lower heart rate, the absence of diabetes and an absence of regular physical activity were the
180 major factors which were positively associated with low or moderate alcohol consumption.

181

182 **Discussion**

183 In this-cross sectional study, alcohol consumption was strongly associated with several
184 clinical, social and biological characteristics that favour a superior overall health status and a
185 lower risk of CVD in moderate alcohol drinkers as compared to never drinkers. Our
186 multivariate analysis, which included all factors associated with alcohol consumption in the
187 univariate analysis, confirmed that moderate and low drinkers display a superior health status
188 as compared with never drinkers. Importantly, few of these factors seem causally related to
189 alcohol consumption.

190 In this study, the relationship between alcohol intake and HDL-C levels was strong and
191 constant in both sexes. Moreover, it was independent of the type of alcoholic beverage
192 consumed. In this context, it is relevant that Rimm and colleagues quantified the effect of
193 alcohol consumption in a metaanalysis of 25 studies (Rimm, et al. 1999), and clearly

194 established a causal relationship between alcohol and HDL-C levels. However, to our
195 knowledge, the causal relationship between alcohol-related increment in HDL-C levels and
196 reduction in cardiovascular risk remains to be established. Previous studies have focused on
197 the importance of HDL functionality, i.e the capacity of HDL particles to protect against
198 atherosclerosis, which might be more informative than quantitative data on HDL-C (Kontush,
199 et al. 2006). Alcohol may impact HDL metabolism and functionality, but there are few data
200 which demonstrate that this effect is beneficial. Some studies suggest that ethanol may impair
201 HDL function despite an increase in HDL-C. (Marmillot, et al. 2007). (Hannuksela, et al.
202 1992). Thus, the influence of alcohol on HDL cannot simply be interpreted as a
203 cardioprotective effect.

204 In our study, the BMI and the percentage of obese subjects in both men and women, as well
205 as the WC in women, were lowest in moderate drinkers. The earliest observational studies
206 reported discordant results concerning the association between alcohol intake and
207 anthropometric variables (Suter 2005). Several studies reported a J-shaped relationship
208 between alcohol consumption and BMI and waist-to-hip ratio, such that light to moderate
209 drinking was believed to exert beneficial effects in reducing weight, whereas non-drinking
210 and heavy or risky drinking exerted the opposite effect (Colditz, et al. 1991, Arif, et al. 2005)
211 (Lukasiewicz, et al. 2005). Other studies have revealed a positive relationship between
212 alcohol intake and BMI and/or WC. Thus, there is no clear evidence of a favourable or
213 unfavourable effect of alcohol intake on weight and body fat distribution. Lower WC non-
214 causally related with moderate alcohol intake might thus, in part, account for the apparent
215 protective effect of alcohol intake.

216 SBP in both sexes, as well as DBP, was lower in moderate drinkers as compared to abstainers.
217 Moreover PP, which might represent a potent CV risk factor (Panagiotakos, et al. 2005), was
218 significantly lower in drinkers. These results are strongly suggestive of a confounding effect.

219 Indeed, moderate alcohol consumption is known to have no effect or even to increase blood
220 pressure (Suter 2005).

221 Importantly, social status was strikingly different across the groups. Our findings demonstrate
222 that moderate alcohol consumption is a powerful general indicator of optimal social status.
223 These findings are concordant with those of other published reports. Thus, Mortensen et al.
224 concluded that the association between drinking habits and social and psychological
225 characteristics in Denmark may in large part explain the apparent health benefits of wine
226 (Mortensen, et al. 2001). Another study conducted by Naimi et al. led to a similar conclusion
227 in a population-based telephone survey of US adults (Naimi, et al. 2005). The majority of well
228 conducted studies which have assessed CVD as a function of alcohol intake do not take into
229 account adjustment for social status. Residual confounding is likely when a single index of
230 social status is used as a covariate in other studies of the beneficial CV effect of alcohol.

231 Global health status assessed by a scale of SHS was highest in moderate drinkers. Subjective
232 health provides a global assessment of health status and is a strong predictor of total mortality
233 (Idler, et al. 1997). Our present findings are consistent with those of the study by Stranges and
234 al., in which non-current drinkers reported poorer physical and mental health than life-time
235 abstainers and current drinkers (Stranges, et al. 2006). A similar pattern was observed for the
236 relationship between depression score, anxiety score and alcohol intake. No evidence was
237 obtained to support the conclusion that this relationship might be causal in nature.

238 Our data collection included measurement of respiratory function. Drinkers displayed higher
239 forced expiratory volume in one second and forced vital capacity. Impaired pulmonary
240 function is a strong predictor of cardiovascular and all-cause mortality in the general
241 population independent of smoking (Friedman, et al. 1976) (Schunemann, et al. 2000). Thus,
242 our findings may partially explain the apparent protective effect of alcohol. Whether the
243 relationship between alcohol intake and pulmonary function is causal remains indeterminate

244 since published literature shows conflicting results. (Lebowitz 1981) (Lange, et al. 1988)
245 (Zureik, et al. 1996). (Sparrow, et al. 1983) (Twisk, et al. 1998) (Murray, et al. 1998) (Cohen,
246 et al. 1980). Our findings therefore support the need to integrate pulmonary function in
247 multivariate analysis when studying the effect of alcohol on CVD or health status.

248 Our data thus show that several social, clinical and biological variables differ markedly
249 according to alcohol consumption. Other studies are consistent with our data and show that
250 moderate drinkers, particularly wine drinkers, consume a healthy diet and have a healthy
251 behavioural pattern as compared to other drinkers or abstainers (Ruidavets, et al. 2004)
252 (Tjonneland, et al. 1999).

253 Our multivariate analysis showed that several risk factors which are rarely or never taken into
254 account in previous observational studies are associated with alcohol intake independently of
255 traditional risk factors. Interestingly, FEV1, socio-professional status, SHS, anxiety score,
256 waist circumference and HR all remained associated with alcohol consumption with a more
257 favourable profile in low or moderate drinkers vs never drinkers. These results emphasise the
258 caution with which one must interpret results of observational studies. Another concern in
259 observational studies is misclassification. Shaper and al. proposed that ex-drinkers who
260 ceased drinking because of illness or cardiovascular risk factors were often misclassified with
261 never drinkers, thus artifactually raising the cardiovascular risk of abstainers (Shaper, et al.
262 1988). This hypothesis was discarded in some studies which reported association after
263 exclusion of ex-drinkers (Fagrell, et al. 1999). However, in two meta-analyses (Fillmore, et al.
264 2007) (Stockwell, et al. 2007), the apparent protective effect of alcohol disappeared when
265 occasional and ex-drinkers were excluded from the group of abstainers subjects.

266 Taken together, our results raise the possibility that the protective effect of alcohol may be an
267 artifactual association due to uncontrolled confounding. Although several observational
268 studies on alcohol consumption were of very high quality, bias cannot be excluded. As

269 emphasized by previous examples with hormonal replacement therapy or antioxidant
270 supplementation (Neuzil, et al. 2001), the observational design cannot lead to conclude to
271 causal relationships. However, our results cannot eliminate the cardioprotective effect of
272 alcohol.

273 The strength of the present report emanates from the use of a relatively healthy large cohort of
274 subjects who were characterized with standardized and validated clinical and biological
275 methods. The main weakness of our study is its cross-sectional design. Another potential
276 limitation concerns the fact that alcohol intake was based on self-reported data with the
277 possibility of misclassification of exposure. However all previous studies have assessed
278 alcohol intake in a similar manner. The positive relationship observed between plasma levels
279 of GGT, MCV and the ordered groups of alcohol consumption led us to conclude that
280 classification on the basis of the quantity of alcohol consumed was satisfactory. Furthermore,
281 misclassification would have reduced the relationship between alcohol intake and risk factors.
282 The third limitation in our study involved the self-selection of subjects who attended the
283 screening centers. However, analysis of the co-morbidity and causes of mortality of subjects
284 in our cohort lead us to consider this population as representative of the population of the
285 urban region of Paris-Ile-de -France.

286 In conclusion, our data reveal that mild and moderate drinkers display a more favourable
287 health status and a lower cardiovascular risk profile (especially when we consider non-
288 traditional CV risk factors) than never drinkers and heavy drinkers. No human clinical data
289 other than those from observational studies are currently available to support a causal
290 relationship between alcohol intake and CVD. Rather than a beneficial effect of alcohol
291 consumption on classic or emerging cardiovascular risk factors, we must hypothesize that
292 moderate drinking is a marker of a higher social level, superior general health status and
293 lower cardiovascular risk. Future epidemiological studies assessing the relationship between

294 alcohol and CVD should cautiously select the covariates for the multivariate analysis. Our
295 data suggest that it is clearly premature to promote alcohol consumption as the basis of
296 cardiovascular protection until such time as the causal role of alcohol in cardioprotection is
297 fully proven.

298

299

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305

306 **Conflicts of interest**

307 The authors have no conflict of interest to declare for this paper.

308

309

310 **Table 1: Age-adjusted clinical characteristics of men in the urban Paris-Ile-de- France**311 **Cohort**

Alcohol intake	never	Low	Moderate	Heavy	P for trend
N (%)	8921 (9.2)	46 550 (47.8)	24 221 (24.9)	13 311 (13.7)	
Age (years)	42.8 (14.0)	45.4 (12.1)	49.4 (12.0)	51.1 (11.3)	<0.0001
Weight (kg)	75.6 (0.13)	77.7 (0.06)	77.3 (0.08)	78.3 (0.10)	<0.0001
BMI (kg/m ²)	25.4 (0.04)	25.5 (0.02)	25.3 (0.02)	25.6 (0.03)	<0.0001
% Obesity (n) *	11.6 (1026)	10.1 (4705)	9.2 (2214)	12.3 (1628)	<0.0001
WC (cm)	88.4 (0.10)	89.4 (0.05)	89.4 (0.06)	90.1 (0.09)	<0.0001
Hip circumference (cm)	99.3 (0.08)	100.1 (0.04)	99.9 (0.05)	99.7 (0.07)	<0.0001
WHR	0.89(0.0007)	0.89 (0.0002)	0.89 (0.0004)	0.90 (0.001)	<0.0001
SBP (mmHg)	133.8(0.18)	133.1 (0.08)	133.4 (0.11)	136.1 (0.15)	<0.0001
DBP (mmHg)	78.8 (0.12)	79.3 (0.05)	79.7 (0.07)	81.6 (0.10)	<0.0001
PP (mmHg)	54.9 (0.12)	53.7 (0.05)	53.7 (0.07)	54.4 (0.10)	<0.0001
HR (bt/mn)	63.6 (0.11)	62.0 (0.05)	62.0 (0.07)	63.5 (0.09)	<0.0001
FEV1	0.86 (0.002)	0.93 (0.0008)	0.94 (0.001)	0.91 (0.001)	<0.0001
% Current smokers (n)	8.6 (1656)	29.4 (13664)	31.9 (7722)	44.9 (5981)	<0.0001
Anxiety score**	4.48 (0.03)	3.45 (0.01)	3.45 (0.02)	3.92 (0.03)	<0.0001
Depression score***	1.35 (0.02)	1.23 (0.01)	1.25 (0.02)	1.69 (0.02)	<0.0001
SHS score #	20.2 (1798)	12.0 (5570)	12.0 (2906)	17.2 (2285)	<0.0001
% Physical activity (yes) (n)	49.0 (4367)	47.2 (21 970)	48.1 (11 641)	47.0 (6249)	<0.05
% Hypertensives (n)	29.9 (2560)	32.4 (14 418)	38.2 (8964)	46.8 (5699)	<0.0001
% Diabetics (n)	4.7 (416)	2.8 (1236)	3.1 (742)	4.6 (568)	<0.0001
% Subjects Living alone (n)	29.4 (2608)	21.9 (10195)	18.8 (4548)	23.9 (3172)	<0.0001
Education (% ,n)					
-No educational or professional diploma	17.4 (1151)	6.3 (2119)	6.3 (782)	10.3 (902)	<0.0001
-High school diploma, or superior	21.0 (1390)	39.0 (13040)	42.9 (5327)	34.6 (3019)	<0.0001
SPC (% ,n)					
-Unemployed	28.1 (2452)	12.5 (5617)	9.9 (2357)	16.0 (1985)	
-Profession, White collar	18.6 (1626)	49.2 (22170)	56.5 (13409)	48.2 (5978)	<0.0001

-Employés, Blue collar 53.3 (4660) 38.3 (17261) 33.6 (7978) 35.8 (4430)

312

Values are (means (SEM)); BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP,
313 systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; HR, heart rate, FEV1, forced
314 expiratory volume in one second; VC, vital capacity; SHS subjective health status; * BMI > 30 kg/m², **,
315 (Cohen, et al. 1983); *** (Beck, et al. 1974); # % (n) of subjects with a less favourable SHS (score ≤ 5/10);
316 SPC, socio-professional category.
317

318 **Table 2: Age adjusted clinical characteristics of women in the urban Paris-Ile-de- France**319 **Cohort**

Alcohol intake	never	low	Moderate	heavy	P
N (%)	10523 (20.1)	30547 (58.4)	7705 (14.7)	1581 (3.0)	
Age (years)	43.1 (15.9)	47.6 (14.4)	53.4 (14.0)	51.5 (13.3)	
Weight (kg)	64.3 (0.12)	62.0 (0.07)	60.9 (0.14)	62.3 (0.30)	<0.0001
BMI (kg/m ²)	25.4 (0.04)	23.9 (0.03)	23.2 (0.05)	23.5 (0.11)	<0.0001
% Obesity (n) *	17.5 (1825)	9.0 (2746)	6.7 (512)	8.1 (128)	<0.0001
WC (cm)	79.4 (0.10)	76.0 (0.06)	75.2 (0.12)	76.5 (0.27)	<0.0001
Hip circumference (cm)	99.3 (0.09)	97.1 (0.05)	96.1 (0.11)	96.5 (0.23)	<0.0001
WHR	0.80 (0.0006)	0.78 (0.0004)	0.78 (0.001)	0.79 (0.002)	<0.0001
SBP (mmHg)	130.5 (0.18)	127.7 (0.10)	127.3 (0.21)	128.6 (0.46)	<0.0001
DBP (mmHg)	76.3 (0.11)	75.2 (0.06)	75.1 (0.13)	76.6 (0.28)	<0.0001
PP (mmHg)	54.3 (0.12)	52.5 (0.07)	52.3 (0.14)	52.0 (0.32)	<0.0001
HR (bt/mn)	66.7 (0.10)	64.3 (0.06)	64.0 (0.12)	64.5 (0.26)	<0.0001
FEV1	0.90 (0.002)	0.93 (0.001)	0.94 (0.002)	0.91 (0.004)	<0.0001
% Current smokers (n)	13.5 (1419)	24.8 (7575)	28.0 (2163)	46.2 (731)	<0.0001
Anxiety score**	5.33 (0.03)	4.59 (0.02)	4.61 (0.04)	5.10 (0.08)	<0.0001
Depression score***	2.70 (0.03°)	2.26 (0.02)	2.33 (0.04)	2.99 (0.08)	<0.0001
SHS score #	32.0 (3359)	19.5 (5937)	18.2 (324)	22.9 (361)	<0.0001
% Hypertensives (n)	27.2 (2743)	27.7 (8193)	34.2 (2513)	35.4 (506)	<0.0001
% Diabetics (n)	3.7 (378)	1.52 (457)	1.76 (131)	2.19 (32)	<0.0001
% Subjects Living alone (n)	29.5 (3100)	35.7 (10 891)	33.5 (2579)	38.0 (600)	<0.0001
Education (% ,n)					
-No educational or professional diploma	17.6 (1379)	7.6 (1531)	6.4 (263)	6.4 (74)	<0.0001
-High school diploma, or superior	15.3 (1200)	27.4 (5525)	29.8 (1219)	33.7 (390)	<0.0001
SPC (% ,n)					
-Unemployed	43.4 (4474)	23.7 (7147)	24.5 (1832)	31.2 (456)	
-Profession, White collar	9.4 (974)	23.7 (7128)	28.6 (2138)	30.5 (445)	<0.0001
-Employés, Blue collar	47.2 (4873)	52.6 (15842)	46.9 (3501)	38.3 (558)	

320 Values are (means (SEM)); BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; SBP,
321 systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; HR, heart rate, FEV1, forced
322 expiratory volume in one second; SHS, subjective health status; *BMI > 30 kg/m², **, (Cohen, et al. 1983); ***
323 (Beck, et al. 1974); # % (n) of subjects with a less favourable SHS (score ≤ 5/10); SPC, socio-professional
324 category.

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329 **Tale 3: Age-adjusted biological characteristics of men in the urban Paris-Ile-de- France Cohort**

Alcohol intake	never	Low	Moderate	Heavy	P
	8921 (9.2%)	46 55(47.8%)	24 221 (24.9%)	13 311 (13.7%)	
CT (mg/dl)	200 (0.004)	214 (0.002)	217 (0.003)	222 (0.003)	<0.0001
FBG (mg/dl)	99 (0.002)	98 (0.001)	98 (0.001)	100 (0.002)	<0.0001
Triglycerides (mg/dl)	109 (0.008)	111 (0.004)	110 (0.005)	122 (0.007)	<0.0001
HDL-C (mg/dl)	52.2 (0.15)	55.9 (0.07)	58.2 (0.09)	60.1(0.12)	<0.0001
LDL-C (mg/dl)	126.8 (0.38)	135.8 (0.17)	137.4 (0.23)	138.1 (0.31)	<0.0001
MGV (μ 3)	89.2 (0.09)	90.9 (0.04)	92.3 (0.05)	93.8 (0.08)	<0.0001
Gamma-Gt (UI/l)	30.0 (0.59)	34.5 (0.26)	38.7 (0.36)	58.9 (0.48)	<0.0001

330 Values are (means (SEM)); TC, total cholesterol, FBG, fasting blood glucose; LDL-C, LDL-cholesterol; HDL-C,

331 HDL-cholesterol; MGV, mean globular volume; P, difference between groups, by ANCOVA

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333 **Table 4: Age-adjusted biological characteristics of women in the urban Paris-Ile-de- France**

334 **Cohort**

Alcohol intake	never	Low	Moderate	heavy	P
N (%)	10523 (20.1%)	30547 (58.4%)	7705 (14.7%)	1581 (3.0%)	
Cholesterol (mg/dl)	206 (0.004)	212 (0.004)	212 (0.004)	216 (0.01)	<0.0001
FBG (mg/dl)	94 (0.01)	92 (0.001)	93 (0.002)	94 (0.004)	<0.0001
Triglycerides (mg/dl)	90 (0.004)	82 (0.003)	81 (0.005)	90 (0.01)	<0.0001
HDL-C (mg/dl)	64.0 (0.16)	70.1 (0.10)	73.1 (0.2)	75.1 (0.4)	<0.0001
LDL-C (mg/dl)	124.6 (0.33)	125.2 (0.19)	122.8 (0.38)	123.1 (0.84)	<0.0001
MGV (μ 3)	88.8 (0.10)	90.9 (0.06)	92.5 (0.11)	94.1 (0.27)	<0.0001
Gamma-Gt (UI/l)	21.7 (0.3)	21.1 (0.2)	24.6 (0.4)	38.4 (0.9)	<0.0001

335 Values are (means (SEM)); TC, total cholesterol, FBG, fasting blood glucose; HDL-C, HDL-cholesterol; LDL-

336 C, LDL-cholesterol; MGV, mean globular volume, P, difference between groups, by ANCOVA

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339 **Table 5: Multivariate analysis of determinants of moderate or low alcohol consumption vs**
 340 **never consumption**

Variable	Score chi-square	OR	CI
High vs low socio professional status	3069.7	0.571	0.551-0.592
FEV1	953.8	1.007	1.006-1.008
Age	1506.3	1.038	1.036-1.041
Current smoker (Y/N)	1044.2	2.86	2.69-3.04
HDL-C (mg/dl)	827.5	1.021	1.019-1.022
Good Health Evaluation (SHS<5)	323.3	1.533	1.446-1.626
Cholesterol (mg/dl)	164.6	1.003	1.002-1.004
Gamma-Gt	114.8	1.009	1.007-1.010
Anxiety score	112.6	0.957	0.950-0.965
HR	81.8	0.989	0.986-0.991
Diabetes (Y/N)	22.2	0.716	0.622-0.825
Waist circumference (cm)	27.11	0.990	0.987-0.994
Gender (M/F)	12.0	1.13	1.06-1.21
Hypertension (Y/N)	5.1	1.07	1.009-1.131

341 All parameters associated with alcohol consumption in univariate analysis were included in the multivariate
 342 model. Forward regression analysis was carried out and all variables remaining in the model were significant with
 343 $p < 0.05$. FEV1, forced expiratory volume in one second, SHS, score health status; HR, heart rate; CI, confidence
 344 interval, OR, odd ratio

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Figure legends

Figure 1: Nature of the preferred alcoholic beverage according to sex and age.

Figure 2: Mean plasma HDL-C concentration expressed as a function of the level of alcohol intake in both women and men.

Figure 3: % of subjects with a less favourable SHS (score ≤ 5) as a function of alcohol intake in both women and men. SHS, Subjective Health Status.

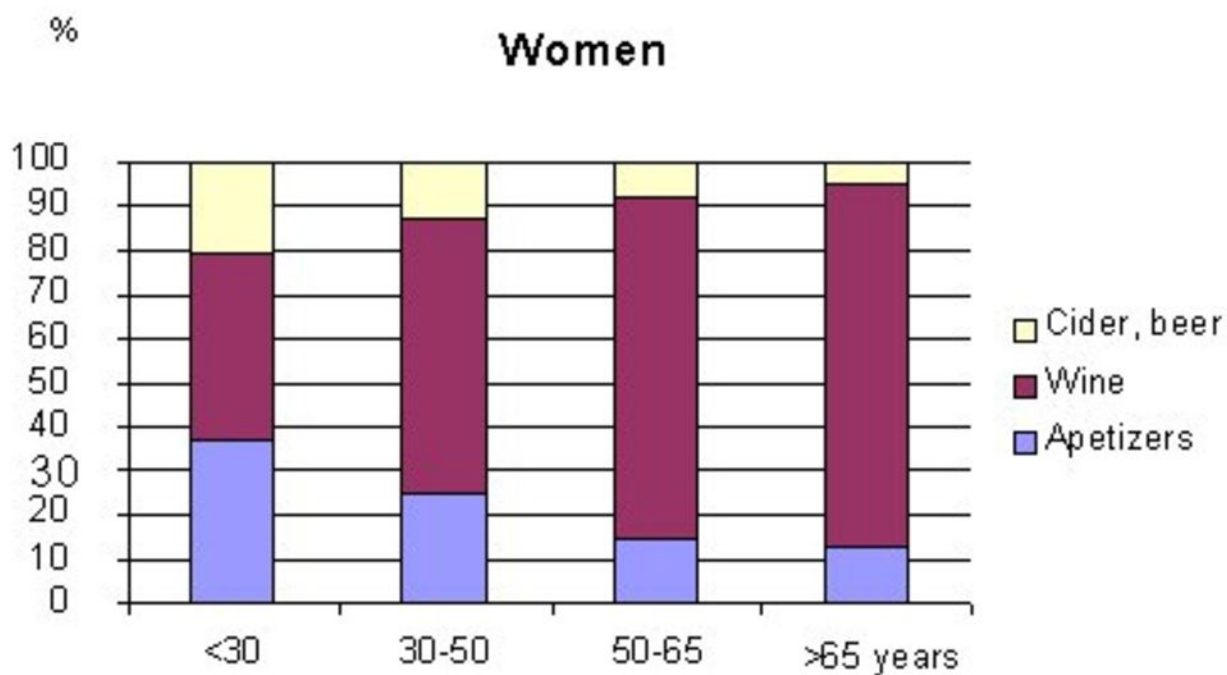
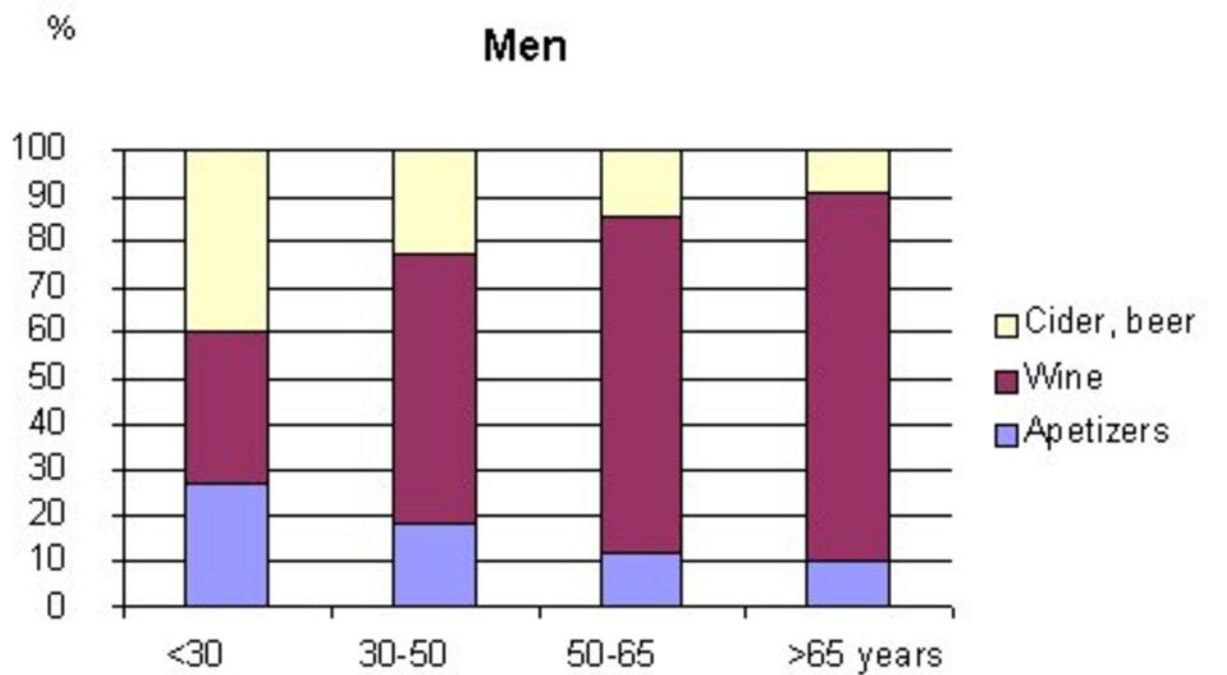


Figure 1

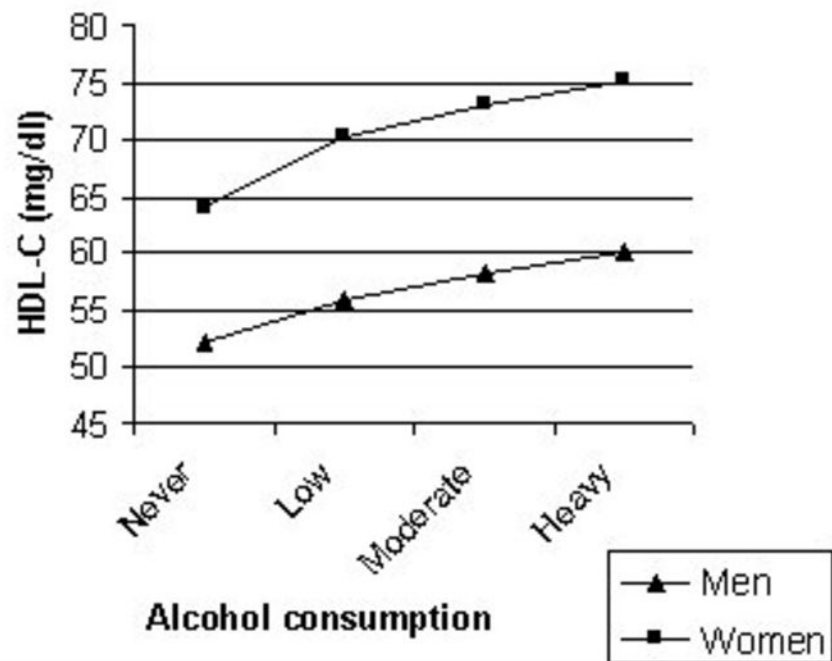


Figure 2

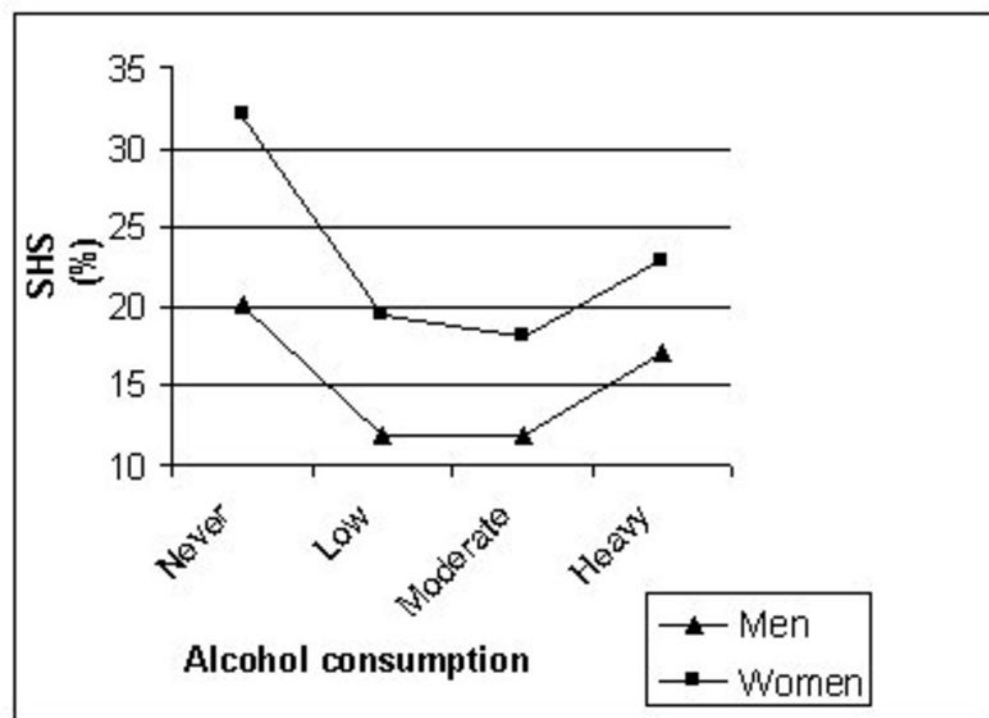


Figure 3