



ORIGINAL RESEARCH ARTICLE

# Dietary patterns and alcoholic beverage preference in relation to 10-year cardiovascular disease, hypertension, hypercholesterolemia and diabetes mellitus incidence in the ATTICA cohort study

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## ABSTRACT

Literature highlights the need for adjustment for diet quality when the effect of alcohol consumption on health is investigated. We sought to define—a posteriori—dietary patterns according to various drinking preferences as well as to evaluate their combined effect against 10-year cardio-metabolic incidence. During 2001–2002, 3042 CVD-free adults consented to participate in the ATTICA study; of them, 2583 completed the 10-year follow-up (85 % participation rate), but precise information about cardio-metabolic incidence was available in 2020 participants (overall retention rate 66 %). Intake per type of alcoholic beverage was assessed and “a posteriori” dietary patterns were defined. Results showed that among participants not drinking alcoholic beverages, women adhering more to a healthier dietary pattern had 25 % lower CVD risk within the 10-year study follow-up, while men adhering more to an unhealthy dietary pattern had almost two times higher CVD risk (p-values < 0.05). Among beer drinkers, both men and women adhering more to a healthier dietary pattern were found to have at least 26 % lower risk of developing hypertension and at least 15 % lower risk of developing hypercholesterolemia, while men adhering more to a healthier dietary pattern were also found to have 29 % lower CVD risk (all p-values < 0.05). Similarly, among wine drinkers, women adhering more to a healthier dietary pattern were found to have a 16 % and 52 % lower risk of developing hypertension and diabetes mellitus, respectively, whereas men adhering more to a healthier dietary pattern had 22 % lower CVD risk (all p-values < 0.05). Finally, among spirit drinkers, higher adherence to an unhealthy dietary pattern in both genders had an aggravating effect on cardio-metabolic risk. It seems that the quality of dietary pattern stands out as a critical confounding factor in studies assessing the effect of alcohol consumption on cardio-metabolic risk. A Phytochemical-Rich Dietary Pattern is suggested, particularly among drinkers.

**KEYWORDS:** dietary pattern, alcohol, CVD, diabetes mellitus, wine, beer

## INTRODUCTION

The association of alcohol consumption with health outcomes is still hotly debated. Although the effects of excessive alcohol consumption on health are unquestionably detrimental, the question “where do we stand today with regard to the effect of regular alcohol consumption on cardiovascular diseases (CVDs)?” remains unanswered. It has been well acknowledged that the association between alcohol and the development of CVDs in comparison with abstinence or with heavier drinking demonstrates a J- or U-shaped association (Manolis *et al.*, 2019). However, recent meta-analyses (Yoon and Jung, 2020; Zhao *et al.*, 2017), the prospective cohort (Jankhotkaew *et al.*, 2020; Millwood *et al.*, 2019) and genetic epidemiological studies (Holmes *et al.*, 2014) do not confirm these findings.

The drinking pattern has been extensively investigated in the literature; however dietary pattern as a confounder either may be underestimated due to adjustments on selective markers or indexes (Aljuraiban *et al.*, 2020) or even ignored in the majority of studies. “Alcohol” reflects a lifestyle; thus, it should not be studied apart but rather as an integral part of a dietary pattern. In all studies, evaluation of the overall dietary pattern following an “a posteriori” approach reflecting closer real-life situations (Panagiotakos, 2008) has not been applied. Interestingly, in a recent systematic review, authors concluded that the preferred alcoholic beverages are mainly consumed within a dominant dietary pattern (Sluik *et al.*, 2016a). The literature showed that healthy lifestyle behaviours acting simultaneously have been proven to substantially lower the morbidity and mortality of CVD (Barbaresko *et al.*, 2018), whereas the beneficial effect of alcohol on CVD risk can be attenuated by other lifestyle factors (Muscari *et al.*, 2015). Furthermore, contradicting views have been expressed, such as that the alcoholic beverages might not be responsible for the observed health outcomes but their accompanied dietary patterns (Sluik *et al.*, 2016a).

The imperative need for proper adjustment for diet quality in studies of the effects of alcohol consumption on health has been highlighted in the literature (Parekh *et al.*, 2021; Scholz *et al.*, 2016). Taking into account that higher intakes are generally correlated with poorer diets (Parekh *et al.*, 2021), one could assume that the study of dietary patterns following an “a posteriori” approach per type of alcoholic beverage may capture the impact on health outcomes in a more comprehensive way. Therefore, in a sample of apparently healthy individuals from a Mediterranean region, we sought to define – “a posteriori” – dietary patterns according to various drinking habits and to evaluate their combined effect on 10-year incidence of CVD events as well as hypertension, hypercholesterolemia and type II diabetes mellitus.

## MATERIALS AND METHODS

### 1. Study sample

The ATTICA study (Pitsavos, Panagiotakos, Chrysoshoou, and Stefanadis, 2003) is a prospective, observational cohort

investigation initiated in 2001. At baseline (2001–2002), a random, multistage sampling was conducted and 3042 apparently healthy volunteers residing in the greater Athens metropolitan area, Greece, finally agreed to participate (75 % participation rate). Of the enrolled participants, 1514 (49.8 %) were men [Mean (SD) age: 46 (13) years old] and 1528 (50.2 %) were women [Mean (SD) age: 45 (14) years old]. During baseline examination, a detailed clinical evaluation was performed by trained physicians and individuals with pre-existing CVD were excluded according to the study protocol.

### 2. Bioethics

The ATTICA study was approved by the Bioethics Committee of Athens Medical School. The study was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. All participants were informed about the study aims and procedures and provided written informed consent.

### 3. Dietary assessment and alcohol consumption evaluation at baseline examination

Dietary assessment was based on a validated semi-quantitative Food Frequency Questionnaire (FFQ) previously used by the EPIC-Greek project (Katsouyanni *et al.*, 1997). The questionnaire assessed the usual dietary intake of 156 foods and beverages commonly consumed in Greece, with seven non-overlapping frequency-of-consumption response categories ranging from “never or less than once/month” to “ $\geq$  two times/day”. Photographs assisted the responders in defining the portion sizes in several foods included in the questionnaire. Based on this information, twelve common food groups were created according to their nutrient and culinary similarities. Using food composition tables and standard portion sizes, macronutrient consumption was also assessed.

Regarding the frequency of the alcohol consumption, the consumed alcoholic beverages: wine (red/ white), beer, spirits (including traditional alcoholic drinks and liquor) as well as the daily ethanol intake were recorded in a 7-day food record. Daily alcohol intake (in grams; g) was calculated using food composition tables (USDA, 2015). Based on the FFQ used, participants were categorised into four categories: (i) abstention (no alcohol drinking); (ii) preferably beer consumers (> 70 % of their alcohol intake comes from beer), (iii) preferably wine consumers (> 70 % of their alcohol intake comes from red/white wine) and (iv) spirits’ consumers. Various thresholds have been proposed in the literature to denote preference; the threshold of 70 % was selected here as it has been proposed especially for alcohol drinking in a network of studies in Europe and the US (Sluik *et al.*, 2016b).

### 4. Other baseline measurements

Measurements included demographic characteristics, personal and family medical history, as well as various lifestyle habits. Smoking was defined through pack-years, with smokers

being participants smoking one or more cigarettes per day, including those having quit smoking the past year. Based on their smoking habits, participants were categorised as (i) Current/ Former smokers and (ii) Non-smokers. Participants' physical activity status was evaluated through the validated short Greek version (9 items) of the "International Physical Activity Questionnaire" (IPAQ) (Papathanasiou *et al.*, 2009). For the purposes of the present work, participants were merged into two main categories, inactive (sedentary) and physically active. Details about blood pressure, fasting lipids, blood glucose and circulating pro-inflammatory biomarkers measurements have been presented elsewhere (Pitsavos *et al.*, 2003). Participants who had fasting blood glucose > 125 mg/dl during the examination or who reported the use of antidiabetic medication were defined as having diabetes (Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 2000) (American Diabetes Association, 2014). Hypertension was defined as blood pressure  $\geq$  140/90 mmHg or use of antihypertensive medication and hypercholesterolemia as total cholesterol  $\geq$  200 mg/dL or the use of lipid-lowering agents. Furthermore, weight, height, waist and hip circumferences were also measured and body mass index (BMI) was calculated as weight (in kg) divided by standing height (in square meters, m<sup>2</sup>).

## 5. 10-year follow-up evaluation

During 2011–2012, the 10-year follow-up of the ATTICA Study (mean follow-up duration: 8.41 years) was performed (Panagiotakos *et al.*, 2015). Briefly, 2583 participants of the 3042 initially enrolled were re-evaluated [85 % retention; mean baseline age (years  $\pm$  standard deviation (SD)): 45  $\pm$  14 and 46  $\pm$  14 years for women and men, respectively, with no difference as compared to the overall study sample]. Of the individuals who were lost to the follow-up (i.e., n = 459), n = 224 were not found because of missing or wrong addresses and telephone numbers that they have provided at baseline examination and n = 235 because they denied re-examination. Regarding clinical evaluation, data without any missing information were obtained from 2020 participants (thus, the final retention rate for CVD outcomes was 66 %). No significant differences were observed regarding age and sex distribution, baseline smoking habits, physical activity levels and dietary habits (including alcohol drinking) between those who participated and those who were lost in the follow-up (all p-values > 0.40), which is considered to be of crucial importance for the validity of our conclusions (Tsiampalis and Panagiotakos, 2020). The combined primary endpoint studied in this work was the development of a fatal or non-fatal CVD event. A CVD event was defined according to the World Health Organization (WHO)—International Coding Diseases (ICD)-10 criteria as the development of acute myocardial infarction, unstable angina, or other identified forms of ischemia (WHO-ICD coding 410–414.9, 427.2, 427.6), or heart failure of different types and chronic arrhythmias (WHO-ICD coding 400.0–404.9, 427.0–427.5, 427.9) or stroke (WHO-ICD coding 430–438). For participants who died during follow-up, information was

retrieved from relatives and death certificates. In addition, the 10-year incidence of hypertension (834 participants free of hypertension at baseline), hypercholesterolemia (693 participants free of hypercholesterolemia at baseline) and diabetes mellitus type 2 status (1294 participants free of diabetes mellitus type 2 at baseline) was ascertained using the WHO International Classification of Diseases (ICD-10) coding.

## 6. Statistical analysis

Categorical variables are presented as relative frequencies (%) and continuous variables are presented as mean values (standard deviation: SD). Normality of the continuous characteristics' distribution was tested through the P-P plot and the Shapiro–Wilk test. Associations between the categorical characteristics and the type of alcoholic beverages consumed were evaluated through the Pearson Chi-square test, while the one-way Analysis of Variance (ANOVA) was used for the continuous characteristics. Post hoc analyses using the Bonferroni rule were performed to account for the inflation of the probability of type-I error.

Factor Analysis (FA) using the extraction method of Principal Components was applied to reveal the different dietary patterns consumed. The correlation matrix (instead of the covariance) was preferred to account for the variety in food measurements' scale. To ensure suitability for conducting FA, we used the Kaiser–Mayer–Olkin (KMO) test and Bartlett's test of sphericity. Food groups that were entered in the analysis were coded as servings per month. The identified food groups were orthogonally rotated to simplify the factors' structure and enhance their interpretability. To determine the number of factors to be kept, we used the criteria of eigenvalues > 1.0 and the "elbow" of the scree plot, in addition to the Monte Carlo Parallel analysis, which is an alternative technique that compares the scree plots of factors of the observed data with those of a random data matrix of the same size as the original. For each factor, food items with loadings greater or equal to |0.4| were considered to contribute significantly (Schulze *et al.*, 2003) and were used to calculate the patterns' scores based on the regression method. Univariable and multivariable Cox proportional-hazards regression was used to estimate hazard ratios (HRs) and 95 % confidence intervals (95 % CI) of the main dietary pattern (defined as the pattern explaining the highest variance) with the 10-year incidence of CVD, hypertension, hypercholesterolemia and diabetes, according to the type of alcoholic beverages consumed, as well as the association between the type of alcoholic beverages consumed at baseline with the 10-year incidence of the aforementioned outcomes. The time to each event was recorded on an annual basis. A correlation matrix of the model estimates was used to assess multicollinearity between independent variables. The proportional hazards assumption was tested by including interaction terms between the dietary pattern scores and the calendar year. All statistical analyses were performed using STATA software (version 16.1, TStat S.r.l., Italy) and statistical significance was set at a p-value < 0.05 for two-sided hypotheses.

## RESULTS

### 1. Baseline demographic, socioeconomic and lifestyle characteristics

In Table 1, the baseline demographic, socioeconomic and lifestyle characteristics of the enrolled participants are presented. As was reported by the participants, 43.8 % of women and 56.3 % of men preferred drinking wine, while almost 1 out of 3 women and men preferred drinking beer.

There were no significant differences among the different types of alcoholic beverages consumed and the majority of participants' characteristics, with the exception of their age, physical activity and smoking status. Specifically, participants preferring drinking wine were significantly older when compared to the other types of alcoholic beverages ( $p \leq 0.001$  both in men and women); a significantly higher percentage of non-drinkers women followed a sedentary lifestyle ( $p = 0.048$ ) and were non-smokers ( $p = 0.003$ ) (Table 1).

**TABLE 1.** Baseline demographic, socioeconomic, lifestyle and anthropometric characteristics of the ATTICA study participants according to the type of alcohol intake reported at baseline (N = 2020), (Part 1/2).

Women (N = 1014)					
	No alcohol (N = 187)	Preferably beer spirits (N = 326)	Preferably wine (N = 444)	Other alcoholic drink (N = 57)	<i>p-value</i>
DEMOGRAPHIC - SOCIOECONOMIC CHARACTERISTICS					
Age [years; Mean (SD)]	37.8 (12.5)	37.5 (11.2)	40.1 (11.2)	28.8 (9.9)	0.001
Educational level (%)					
Low (0–6 years)	16.9	12.6	6.4	0.0	0.106
Middle (7–12 years)	52.5	43.7	50.0	61.1	
High (> 14 years)	30.5	43.7	43.6	38.9	
Socioeconomic status (%)					
Low	13.7	11.7	5.8	0.0	0.150
Middle	66.7	55.3	57.5	70.6	
High	19.6	33.0	36.7	29.4	
LIFESTYLE - ANTHROPOMETRIC CHARACTERISTICS					
Physical activity (%)					
Sedentary	61.0	62.1	45.7	50.0	0.048
Physically active	39.0	37.9	54.3	50.0	
Smoking status (%)					
Non-smoker	76.3	46.6	54.3	55.6	0.003
Current/former smoker	23.7	53.4	45.7	44.4	
Body Mass Index (BMI; kg/m <sup>2</sup> ) (%)					
≤ 24.99	34.5	28.1	27.5	46.2	0.365
25.0–29.99	41.4	49.6	55.9	38.5	
≥ 30	24.1	22.3	16.6	15.4	
Mean (SD)	24.7 (5.4)	24.8 (5.6)	24.1 (4.0)	23.4 (4.6)	0.559

**TABLE 1.** Baseline demographic, socioeconomic, lifestyle and anthropometric characteristics of the ATTICA study participants according to the type of alcohol intake reported at baseline (N = 2020), (Part 2/2).

Men (N = 1006)					
	No alcohol (N = 76)	Preferably beer spirits (N = 326)	Preferably wine (N = 567)	Other alcoholic drink (N = 37)	<i>p-value</i>
DEMOGRAPHIC - SOCIOECONOMIC CHARACTERISTICS					
Age [years; Mean (SD)]	40.2 (12.4)	39.3 (9.5)	43.4 (10.4)	31.3 (10.7)	<b>&lt; 0.001</b>
Educational level (%)					
Low (0–6 years)	6.9	8.9	8.4	7.1	
Middle (7–12 years)	58.6	42.3	41.1	64.3	<b>0.439</b>
High (> 14 years)	34.5	48.8	50.5	28.6	
Socioeconomic status (%)					
Low	0.0	6.5	7.0	9.1	
Middle	69.6	48.6	43.9	72.7	<b>0.154</b>
High	30.4	44.9	49.1	18.2	
LIFESTYLE - ANTHROPOMETRIC CHARACTERISTICS					
Physical activity (%)					
Sedentary	44.8	59.3	54.7	50.0	
Physically active	55.2	40.7	45.3	50.0	<b>0.513</b>
Smoking status (%)					
Non-smoker	75.9	49.6	57.0	42.9	
Current/former smoker	24.1	50.4	43.0	57.1	<b>0.052*</b>
Body Mass Index (BMI; kg/m <sup>2</sup> ) (%)					
≤ 24.99	34.5	28.1	27.5	46.2	
25.0–29.99	41.4	49.6	55.9	38.5	<b>0.481</b>
≥ 30	24.1	22.3	16.6	15.4	
Mean (SD)	27.4 (3.9)	27.6 (4.6)	27.1 (3.7)	26.0 (4.0)	<b>0.499</b>

Continuous variables are presented as mean (standard deviation (SD)) and categorical variables as relative frequencies. P values for the comparisons between the types of alcohol intake are derived from using the one-way ANOVA (continuous variables) and the Pearson chi-squared test (categorical variables). One standard glass being equivalent to 12 g of alcohol. Reporting physical activity on the International Physical Activity Questionnaire (IPAQ). Significant p-values ( $p < 0.05$ ) are presented in bold. \*p-value < 0.10.

## 2. Baseline dietary patterns and macronutrient intakes

There were no significant differences regarding the total energy intake, macronutrient contributions to total energy intake and weekly consumption of food groups among the different types of alcoholic beverages consumed in women (Table 2). However, men preferring to drink spirits were found to have a significantly higher total energy intake ( $p = 0.049$ ) and consume a significantly higher portion of nuts every week ( $p = 0.014$ ). As for the protein contribution to the total energy intake, it was found to be higher in the non-drinkers group of men, as well as in those preferring to drink spirits ( $p < 0.001$ ), while the PUFA contribution to the total energy intake was found to be significantly higher

among men preferring to drink beer instead of wine and spirits ( $p = 0.040$ ). Among men and women that reported systematic drinking, daily ethanol intake was quite similar among subgroups (all  $p > 0.052$ ); hence the alcoholic beverage preference did not seem to alter the amount of alcohol consumed (Table 2).

## 3. Dietary patterns analysis

Based on the factor analysis (Table 3), two dietary patterns were identified in each type of alcoholic beverage, with each one of them explaining at least 20 % of the total variation in intake. Specifically, among women not drinking alcohol, the major dietary pattern was characterised by higher consumption of fruits, vegetables, legumes, dairy products,

**TABLE 2.** Total energy intake, macronutrient contributions to total energy intake, daily ethanol intake and weekly consumption of food groups according to the type of alcohol intake reported at baseline (N = 2020), Part 1/2.

	Women (N = 1014)				p-value
	No alcohol (N = 187)	Preferably beer (N = 326)	Preferably wine (N = 444)	Other alcoholic drink (N = 57)	
Energy intake (kcal/day)	2036.24 (796.95)	2106.74 (843.24)	2092.59 (721.45)	2151.36 (1219.69)	0.939
Carbohydrates (% of energy)	38.5 (5.7)	36.6 (5.8)	37 (6.4)	38.6 (5.1)	0.176
Proteins (% of energy)	14.6 (1.9)	14.5 (1.9)	14.5 (2.1)	14.5 (2.2)	0.990
Total fat (% of energy)	35.8 (4.0)	35.6 (3.8)	35.1 (4.1)	35 (3.3)	0.641
MUFA (% of energy)	24.2 (4.1)	23.7 (3.8)	23.7 (4.1)	22.8 (2.7)	0.596
PUFA (% of energy)	6.5 (1.8)	6.5 (1.9)	6.6 (2.0)	6.4 (1.6)	0.972
SFA (% of energy)	14.5 (3.3)	14.8 (2.9)	14.2 (3.2)	15.2 (3.6)	0.310
Daily ethanol intake (grams)	0.02 (0.04)	6.5 (11.5)	7.1 (11.7)	2.7 (3.6)	< 0.001
Weekly consumption (servings) of:					
Fruits	30.1 (12.4)	26.4 (13.3)	28.2 (13.2)	25.5 (16.4)	0.311
Vegetables	34.0 (11.2)	33.4 (13.0)	36.6 (14.0)	33.9 (18.6)	0.277
Legumes	4.6 (2.5)	4.4 (2.2)	4.9 (2.4)	4.1 (2.0)	0.395
Potatoes	11.3 (7.8)	11.4 (5.7)	10.3 (6.0)	12.4 (6.6)	0.356
Red meat	4.1 (1.8)	4.6 (1.9)	4.1 (2.6)	4.9 (3.2)	0.244
Poultry	1.4 (1.0)	1.3 (0.9)	1.3 (0.9)	1.7 (1.3)	0.388
Dairy products	12.5 (5.0)	12.3 (4.7)	12.6 (5.8)	10.9 (5.2)	0.635
Fish	2.0 (1.1)	2.0 (0.9)	2.2 (1.3)	1.9 (0.7)	0.451
Nuts	1.5 (1.5)	1.4 (1.7)	1.3 (1.2)	1.3 (1.9)	0.890
Sweets	4.7 (2.3)	4.7 (2.2)	5.0 (2.1)	4.9 (2.9)	0.794
Eggs	1.2 (1.3)	1.0 (0.8)	1.1 (0.9)	1.0 (0.4)	0.713
Cereals	50.7 (22.7)	51.9 (19)	53.8 (16.8)	50.7 (19.5)	0.691

**TABLE 2.** Total energy intake, macronutrient contributions to total energy intake, daily ethanol intake and weekly consumption of food groups according to the type of alcohol intake reported at baseline (N = 2020), Part 2/2.

	Men (N = 1006)				p-value
	No alcohol (N = 76)	Preferably beer spirits (N = 326)	Preferably wine (N = 567)	Other alcoholic drink (N = 37)	
Energy intake (kcal/day)	2020.45 (663.27)	2507.37 (903.58)	2359.44 (818.12)	2560.48 (1008.19)	0.049
Carbohydrates (% of energy)	38.9 (9.0)	36.3 (6.0)	36.2 (6.4)	35.2 (6.4)	0.166
Proteins (% of energy)	15.8 (2.7)	14.4 (1.9)	14.2 (2.0)	15.1 (2.7)	<0.001
Total fat (% of energy)	34.6 (5.4)	35.2 (3.9)	34.7 (4.2)	35.2 (5.1)	0.796
MUFA (% of energy)	23.1 (3.9)	23.2 (3.7)	23.7 (4.2)	23.7 (3.7)	0.653
PUFA (% of energy)	6.1 (1.6)	7.1 (2.3)	6.7 (1.9)	6.3 (1.4)	0.040
SFA (% of energy)	14.4 (6.4)	14.2 (2.9)	13.4 (2.7)	14.7 (3.2)	0.074*
Daily ethanol intake (grams)	0.03 (0.03)	12.0 (14.3)	14.2 (14.4)	13.0 (19.0)	< 0.001
Weekly consumption (servings) of:					
Fruits	26.5 (16.0)	26 (14.7)	26.1 (13.4)	24.2 (10.4)	0.964
Vegetables	30.5 (17.3)	33.2 (12.0)	35.7 (15.1)	30 (17.8)	0.124
Legumes	5.9 (7.0)	5.3 (2.6)	5.7 (2.6)	5.5 (2.6)	0.633
Potatoes	13.1 (10.4)	12.9 (6.3)	11.6 (6.3)	15.3 (10.0)	0.103
Red meat	5.1 (3.2)	4.9 (2.0)	4.6 (2.3)	6.1 (3.9)	0.096*
Poultry	1.4 (1.1)	1.4 (0.8)	1.2 (0.7)	1.4 (0.7)	0.194
Dairy products	10.7 (7.3)	11.6 (4.2)	11 (5.1)	13.1 (4.5)	0.341
Fish	2.5 (1.3)	2.0 (0.8)	2.2 (1.0)	2.1 (2.1)	0.146
Nuts	1.5 (1.8)	1.9 (1.7)	1.6 (1.4)	2.9 (2.5)	0.014
Sweets	5.1 (2.7)	5.1 (2.3)	4.9 (2.5)	5.0 (2.9)	0.761
Eggs	1.6 (1.7)	1.1 (1.0)	1.0 (1.0)	1.4 (1.3)	0.041
Cereals	49.4 (21.2)	51.3 (18.1)	52.3 (17.0)	52.0 (12.5)	0.833

Variables are presented as mean (standard deviation (SD)). P values for the comparisons between the types of alcohol intake are derived from using the one-way ANOVA (continuous variables). One standard glass being equivalent to 12 g of alcohol. MUFA: Monounsaturated Fatty Acid. PUFA: Polyunsaturated Fatty Acid. SFA: Saturated Fatty Acid. Significant p-values ( $p < 0.05$ ) are presented in bold. \*p-value < 0.10.

fish, eggs and cereals (“Towards healthy”), while among men not drinking alcohol, the major dietary pattern was characterised by higher consumption of fruits, potatoes, red meat, nuts and sweets («Poor in vegetables, high in calories towards unhealthy»). Among women preferring to drink beer, the major dietary pattern was characterised by higher consumption of fruits, vegetables, legumes, poultry, fish and cereals (“Towards healthy”), while among men preferring to drink beer, the major dietary pattern was characterised by higher consumption of fruits, vegetables, legumes, eggs and cereals (“Mainly plant-based-healthy”).

Furthermore, among women preferring to drink wine, the major dietary pattern was characterised by higher consumption of fruits, vegetables, legumes, dairy products, fish, sweets and cereals (“Towards healthy”), similarly among men preferring to drink wine, the major dietary pattern was characterised by higher consumption of fruits, vegetables, legumes, dairy products, fish and cereals (“Towards healthy”). Finally, among women preferring to drink spirits, the major dietary pattern was characterised by higher consumption of potatoes, red meat, dairy products, nuts and sweets (“Poor in plant-based foods high in energy-dense

**TABLE 3.** Factor loadings of food groups with high loadings ( $|\geq 0.4|$ ) after Factor Analysis with VARIMAX rotation according to the preferred alcoholic beverage intake reported at baseline (N = 2020).

		<b>Women (N = 1014)</b>							
		No alcohol (N = 187)		Preferably beer (N = 326)		Preferably wine (N = 444)		Preferably spirits (N = 57)	
Food groups		"Towards healthy"	"Towards unhealthy"	"Towards healthy"	"Towards unhealthy"	"Towards healthy"	"Towards unhealthy"	"Poor in plant-based foods high in energy-dense foods"	"Towards healthy"
		Fruits	0.588	.	0.619	.	0.708	.	.
	Vegetables	0.720	.	0.670	.	0.662	.	.	0.871
	Legumes	0.674	.	0.710	.	0.615	.	.	.
	Potatoes	.	0.729	.	0.643	.	0.710	0.701	.
	Red meat	.	0.677	.	0.414	.	0.756	0.630	.
	Poultry	.	0.448	0.636	.	.	0.586	.	0.765
	Dairy products	0.554	.	.	0.430	0.402	0.546	0.762	.
	Fish	0.482	.	0.581	.	0.626	.	.	.
	Nuts	.	.	.	0.727	.	.	0.886	.
	Sweets	.	0.627	.	0.798	0.458	.	0.862	.
	Eggs	0.495	.	.	.	.	.	.	0.670
	Cereals	0.701	.	0.547	.	0.535	.	.	0.586
Total Variance explained		39.4 %	21.8 %	41.4 %	20.4 %	38.2 %	28.7 %	52.1 %	26.0 %

  

		<b>Men (N = 1006)</b>							
		No alcohol (N = 76)		Preferably beer (N = 326)		Preferably wine (N = 567)		Preferably spirits (N = 37)	
Food groups		"Poor in vegetables, high in calories towards unhealthy"	"Towards healthy"	"Mainly plant-based-healthy"	"Mainly animal-based and towards unhealthy"	"Towards healthy"	"Mainly animal-based and towards unhealthy"	"Mainly animal-based - unhealthy"	"Mainly unbalanced"
		Fruits	0.678	.	0.748	.	0.749	.	.
	Vegetables	.	0.708	0.625	.	0.663	.	0.550	.
	Legumes	.	0.694	0.642	.	0.605	.	.	0.747
	Potatoes	0.860	.	.	0.590	.	0.700	0.830	.
	Red meat	0.769	.	.	0.783	.	0.825	0.835	.
	Poultry	.	0.701	.	0.645	.	0.405	0.639	.
	Dairy products	.	0.454	.	0.546	0.504	.	0.723	.
	Fish	.	.	.	.	0.523	.	.	0.877
	Nuts	0.783	.	.	.	.	.	.	.
	Sweets	0.830	.	.	.	.	0.550	0.858	.
	Eggs	.	0.616	0.518	.	.	0.470	0.799	.
	Cereals	.	0.589	0.597	.	0.491	.	.	.
Total Variance explained		35.6 %	30.2 %	39.2 %	27.8 %	38.7 %	26.7 %	55.4 %	24.0 %



foods”), while the major dietary pattern of men preferring to drink spirits, was characterised by higher consumption of vegetables, potatoes, red meat, poultry dairy products, sweets and eggs (“*Mainly animal-based- unhealthy*”).

#### **4. Baseline clinical characteristics and alcohol drinking pattern**

As is shown in Table 4, only the prevalence of hypercholesterolemia at baseline was found to be significantly higher among women preferring to drink wine when compared to the rest types of alcoholic beverages ( $p = 0.007$ ). No significant differences were found among the different types of alcoholic beverages, both in men and women, in any of the other baseline characteristics of the participants (all  $p$ -values  $> 0.05$ ; Table 4).

#### **5. 10-year incidence of CVD events, hypertension, hypercholesterolemia and diabetes mellitus in relation to alcohol drinking pattern**

In Table 5, the effect sizes of the association between the intake of the preferred alcoholic beverage reported at baseline and the 10-year risk of CVD events, as well as the development of hypertension, hypercholesterolemia and diabetes mellitus (among participants free of the aforementioned disease conditions at baseline examination) are presented. Women drinking no alcoholic beverages had almost 1.5 times higher risk of developing CVD [HR = 1.47; 95 % CI = 1.05–4.25] and almost two times higher risk of developing diabetes mellitus [HR = 1.71; 95 % CI = 1.26–6.34] within the 10-year study follow-up, as compared to women preferring to drink mainly wine, while women preferring to drink spirits were found to have 63 % higher risk of developing CVD, in comparison with the women preferring mainly wine [HR = 1.63; 95 % CI = 1.13–4.09]. As for men, it was found that those not drinking alcoholic drinks had a 28 % higher risk of developing CVD within the 10-year study follow-up when compared to men preferring to drink mainly wine [HR = 1.28; 95 % CI = 1.03–3.61].

#### **6. 10-year risk of CVD, hypertension, hypercholesterolemia and diabetes mellitus and overall dietary patterns**

In Table 6, the effect size measures of the association between the main dietary pattern (derived through factor analysis) and the 10-year risk of cardiovascular disease events, as well as hypertension, hypercholesterolemia and diabetes mellitus, according to the preferred alcoholic beverage intake reported at baseline. Among participants not drinking alcoholic beverages, women adhering more to their major dietary pattern had a 25 % lower risk of developing CVD [HR = 0.75; 95 % CI = 0.20–0.96] and hypertension [HR = 0.75; 95 % CI = 0.25–0.97] within the 10-year study follow-up, while men adhering more to their major dietary pattern, had almost two times higher risk of developing CVD [HR = 1.82; 95 % CI = 1.10–4.70]. At the same time, among participants preferring to drink beer, both men and women adhering more to their major dietary pattern, were found to have at least 26% lower risk of developing hypertension

[Women: HR = 0.74; 95 % CI = 0.26–0.92 and Men: HR = 0.72; 95 % CI = 0.28–0.97] and at least 15 % lower risk of developing hypercholesterolemia [Women: HR = 0.83; 95 % CI = 0.41–0.97 and Men: HR = 0.85; 95 % CI = 0.39–0.97], while men adhering more to their major dietary pattern were also found to have 29 % lower risk of developing CVD within the 10-year study follow-up [HR = 0.71; 95 % CI = 0.32–0.94]. Similarly, among participants preferring to drink wine, women adhering more to their major dietary pattern were found to have 16 % and 52 % lower risk of developing hypertension [HR = 0.84; 95 % CI = 0.65–0.96] and diabetes mellitus [HR = 0.48; 95 % CI = 0.25–0.93], respectively, while men adhering more to their major dietary pattern, had 22% lower risk of developing CVD within the 10-year study follow-up [HR = 0.78; 95 % CI = 0.52–0.98]. Finally, among participants preferring to drink spirits, higher adherence to the major dietary pattern among women was significantly associated with at least 1.3 times higher risk of developing CVD [HR = 1.35; 95 % CI = 1.11–1.58], hypertension [HR = 1.48; 95 % CI = 1.12–1.85] and diabetes mellitus [HR = 1.28; 95 % CI = 1.08–1.50], while among men, higher adherence to their major dietary pattern was associated with 20 % higher risk of developing CVD [HR = 1.22; 95 % CI = 1.05–1.41] and diabetes mellitus [HR = 1.19; 95 % CI = 1.02–1.36].

## **DISCUSSION**

To the best of our knowledge, this study is the first of its kind, at least in Greece, to evaluate the effect of the main dietary pattern on the 10-year cardio-metabolic incidence considering the preferred alcoholic beverage intake. The findings revealed that the quality of overall diet is a strong confounder in the association between alcohol consumption and cardio-metabolic risk. The beneficial role of wine and beer consumption on cardio-metabolic risk is more profound when it is combined with a high-quality diet.

More men than women drink alcohol, a consumption pattern that has been extensively reported in the literature (Sluik *et al.*, 2016a). The higher preference for wine in both genders compared to other alcoholic beverages is justified by the fact that wine is an inherent part of the Mediterranean culture and, in particular, its consumption is more pronounced in older ages, as it was also found in the present study.

Regarding the main dietary patterns and their macronutrient contributions to total energy intake, it seems that significant differences exist among alcoholic beverage preference, with spirit drinkers in both genders having lower diet quality. These findings are in line with the findings of a systematic review (Sluik *et al.*, 2016a), whereas other studies (Sluik *et al.*, 2016b) suggested that these differences were not significant in elderly populations. In accordance with the literature (Vari *et al.*, 2016), in abstainers, gender differences were observed in terms of their dietary habits, with women having healthier dietary habits compared to men.

Although beer drinking is believed to be associated with inferior diet quality compared to wine drinking (Sluik *et al.*, 2016a), in the present study, this observation

**TABLE 4.** Baseline clinical characteristics, measurements of oxidative-inflammatory biomarkers and 10-year incidence of fatal/non-fatal CVD events, hypertension, hypercholesterolemia and diabetes mellitus of the ATTICA study participants according to the type of alcohol intake reported at baseline (N = 2020).

<b>Women (N = 1014)</b>					
	No alcohol (N = 187)	Preferably beer spirits (N = 326)	Preferably wine (N = 444)	Other alcoholic drink (N = 57)	<i>p</i> -value
BASELINE CLINICAL CHARACTERISTICS					
Hypertension, %	24.6	14.3	15.2	0.0	0.083
Diabetes Mellitus, %	1.7	1.0	1.4	5.6	0.547
Hypercholesterolemia, %	18.6	12.6	30.7	16.7	0.007
BASELINE OXIDATIVE AND INFLAMMATORY BIOMARKERS					
Triglycerides [mg/dl; Mean (SD)]	84 (46)	87 (65)	81 (48)	80 (42)	0.833
HDL-cholesterol [mg/dl; Mean (SD)]	55 (12)	52 (12)	55 (13)	53 (12)	0.373
Lp(a) [mg/dl; Mean (SD)]	17 (17)	18 (22)	19 (22)	20 (18)	0.931
C-reactive protein [mg/L; Mean (SD)]	1.6 (2.3)	2.2 (3.0)	1.8 (2.6)	1.3 (1.3)	0.330
TNF-α [ng/mL; Mean (SD)]	4.9 (3.0)	4.9 (3.1)	5.3 (3.4)	5.1 (4.3)	0.737
Fibrinogen [mg/dl; Mean (SD)]	300 (49)	307 (64)	317 (70)	318 (99)	0.406
Homocysteine [μmol/L; Mean (SD)]	10 (4)	10 (6)	11 (9)	11 (6)	0.625
Oxidised LDL-C [mg/dl; Mean (SD)]	55 (21)	66 (30)	59 (33)	49 (16)	0.237
10-year incidence of:					
Cardiovascular diseases (CVD), %	10.2	4.9	7.1	11.1	0.564
Hypertension, %	25.8	18.6	18.1	9.1	0.640
Hypercholesterolemia, %	17.6	30.6	29.4	11.1	0.348
Diabetes mellitus, %	9.8	6.5	6.3	0.0	0.717
<b>Men (N = 1006)</b>					
	No alcohol (N = 76)	Preferably beer spirits (N = 326)	Preferably wine (N = 567)	Other alcoholic drink (N = 37)	<i>p</i> -value
BASELINE CLINICAL CHARACTERISTICS					
Hypertension, %	37.0	35.9	42.1	21.4	0.364
Diabetes Mellitus, %	0.0	4.9	7.5	7.1	0.398
Hypercholesterolemia, %	34.5	35.8	41.6	14.3	0.178
BASELINE OXIDATIVE AND INFLAMMATORY BIOMARKERS					
Triglycerides [mg/dl; Mean (SD)]	156 (298)	126 (66)	127 (72)	91 (47)	0.292
HDL-cholesterol [mg/dl; Mean (SD)]	43 (8)	44 (11)	45 (11)	50 (8)	0.233
Lp(a) [mg/dl; Mean (SD)]	23 (36)	22 (67)	20 (24)	8 (7)	0.682
C-reactive protein [mg/L; Mean (SD)]	1.5 (2.1)	2.2 (2.7)	2.1 (2.4)	3.0 (4.2)	0.343
TNF-α [ng/mL; Mean (SD)]	7.5 (2.6)	7.6 (2.6)	7.7 (2.1)	7.9 (3.7)	0.958
Fibrinogen [mg/dl; Mean (SD)]	295 (59)	299 (69)	300 (63)	290 (54)	0.935
Homocysteine [μmol/L; Mean (SD)]	13 (5)	13 (6)	12 (5)	13 (5)	0.907
Oxidised LDL - C [mg/dl; Mean (SD)]	52 (16)	61 (29)	56 (23)	73 (37)	0.320
10-year incidence of:					
Cardiovascular diseases (CVD), %	17.2	14.6	14.0	14.3	0.975
Hypertension, %	23.1	26.4	18.8	20.0	0.773
Hypercholesterolemia, %	33.3	52.7	41.5	16.7	0.232
Diabetes mellitus, %	11.1	8.1	11.1	14.3	0.895

◀ Continuous variables are presented as mean (standard deviation (SD)) and categorical variables as relative frequencies. P values for the comparisons between the types of alcohol intake are derived from using the one-way ANOVA (continuous variables) and the Pearson chi-squared test (categorical variables). One standard glass being equivalent to 12 g of alcohol. Significant p-values ( $p < 0.05$ ) are presented in bold. HDL high-density lipoprotein cholesterol. LDL-C low-density lipoprotein cholesterol. TNF- $\alpha$  tumour necrosis factor- $\alpha$ . Diabetes mellitus was defined as a fasting blood sugar  $> 125$  mg/dl or the use of antidiabetic medication; patients whose average blood pressure levels were greater or equal to 140/90 mm Hg or were under antihypertensive medication were classified as hypertensives; the definition of hypercholesterolemia was based on the total serum cholesterol levels ( $\geq 200$  mg/dl).

**TABLE 5.** Results from the additive Cox proportional hazards models that were developed to evaluate the association between the type of alcohol intake reported at baseline and the 10-year risk of cardiovascular disease events, hypertension, hypercholesterolemia and diabetes mellitus, separately in men and women.

10-year risk of:	Type of alcohol intake at baseline	Hazard Ratio (HR)	95 % Confidence Interval (CI)	p-value
<b>Women</b>				
Cardiovascular Diseases (CVD)	No alcohol		Reference category	
	Preferably wine	0.68	0.24–0.95	<b>0.036</b>
	Preferably beer spirits	0.51	0.18–0.89	<b>0.027</b>
	Other alcoholic drink	1.17	0.22–6.20	0.855
Hypertension	No alcohol		Reference category	
	Preferably wine	0.91	0.36–2.27	0.844
	Preferably beer spirits	0.83	0.36–1.89	0.651
	Other alcoholic drink	3.13	0.35–15.00	0.310
Hypercholesterolemia	No alcohol		Reference category	
	Preferably wine	1.49	0.61–3.70	0.377
	Preferably beer spirits	1.40	0.67–2.93	0.373
	Other alcoholic drink	2.38	0.27–20.00	0.430
Diabetes mellitus	No alcohol		Reference category	
	Preferably wine	0.58	0.16–0.79	<b>0.022</b>
	Preferably beer spirits	0.77	0.22–2.69	0.687
	Other alcoholic drink	1.15	0.18–11.63	0.837
<b>Men</b>				
Cardiovascular Diseases (CVD)	No alcohol		Reference category	
	Preferably wine	0.78	0.28–0.97	<b>0.043</b>
	Preferably beer spirits	0.75	0.23–0.94	<b>0.040</b>
	Other alcoholic drink	0.99	0.18–5.40	0.986
Hypertension	No alcohol		Reference category	
	Preferably wine	0.83	0.21–3.23	0.789
	Preferably beer spirits	0.90	0.59–2.13	0.807
	Other alcoholic drink	1.79	0.16–15.20	0.635
Hypercholesterolemia	No alcohol		Reference category	
	Preferably wine	1.43	0.42–5.00	0.566
	Preferably beer spirits	1.80	0.88–3.67	0.109
	Other alcoholic drink	3.57	0.35–33.33	0.280
Diabetes mellitus	No alcohol		Reference category	
	Preferably wine	0.95	0.20–4.55	0.953
	Preferably beer spirits	0.69	0.24–1.99	0.492
	Other alcoholic drink	1.12	0.10–12.40	0.925

Results are adjusted for age, smoking (current/former smoker/non-smoker), physical activity (active/inactive), BMI, education in years of school and total ethanol intake (in grams); Hazard Ratios (HR) and the respective 95 % Confidence Intervals (CIs) were derived from semiparametric Cox proportional hazards models; One standard glass being equivalent to 12 g of ethanol; Significant p-values ( $p < 0.05$ ) are presented in bold; \*p-value  $< 0.10$ .

**TABLE 6.** Results from the additive Cox proportional hazards models that were developed to evaluate the association between the main dietary pattern and the 10-year risk of cardiovascular disease events, hypertension, hypercholesterolemia and diabetes mellitus, according to the preferred alcoholic beverage intake reported at baseline.

10-year risk of:		Hazard Ratio (HR)	95 % Confidence Interval (CI)	p-value
<b>Non-consumers</b>				
Cardiovascular Diseases (CVD)	Women	<b>0.75</b>	<b>0.20–0.96</b>	0.035
	Men	<b>1.82</b>	<b>1.10–4.70</b>	0.049
Hypertension	Women	<b>0.75</b>	<b>0.25–0.97</b>	0.007
	Men	0.94	0.43–2.07	0.878
Hypercholesterolemia	Women	0.37	0.12–1.16	0.089*
	Men	1.84	0.55–6.18	0.327
Diabetes mellitus	Women	0.87	0.28–2.70	0.805
	Men	1.37	0.48–3.92	0.559
<b>Preferably beer</b>				
Cardiovascular Diseases (CVD)	Women	0.97	0.40–1.10	0.053*
	Men	<b>0.71</b>	<b>0.32–0.94</b>	0.001
Hypertension	Women	<b>0.74</b>	<b>0.26–0.92</b>	0.023
	Men	<b>0.72</b>	<b>0.28–0.97</b>	0.007
Hypercholesterolemia	Women	<b>0.83</b>	<b>0.41–0.97</b>	0.002
	Men	<b>0.85</b>	<b>0.39–0.97</b>	<0.001
Diabetes mellitus	Women	0.95	0.31–2.86	0.930
	Men	0.52	0.18–1.46	0.212
<b>Preferably wine</b>				
Cardiovascular Diseases (CVD)	Women	0.74	0.42–1.28	0.276
	Men	<b>0.78</b>	<b>0.52–0.98</b>	<0.001
Hypertension	Women	<b>0.84</b>	<b>0.65–0.96</b>	<0.001
	Men	0.87	0.45–1.11	0.065*
Hypercholesterolemia	Women	0.67	0.35–1.27	0.218
	Men	0.72	0.45–1.14	0.158
Diabetes mellitus	Women	<b>0.48</b>	<b>0.25–0.93</b>	0.032
	Men	0.87	0.48–1.59	0.653
<b>Spirit</b>				
Cardiovascular Diseases (CVD)	Women	<b>1.35</b>	<b>1.11–1.58</b>	<0.001
	Men	<b>1.22</b>	<b>1.05–1.41</b>	0.015
Hypertension	Women	<b>1.48</b>	<b>1.12–1.85</b>	<0.001
	Men	1.14	0.98–1.30	0.354
Hypercholesterolemia	Women	1.09	0.88–1.32	0.516
	Men	0.97	0.84–1.25	0.805
Diabetes mellitus	Women	<b>1.28</b>	<b>1.08–1.50</b>	0.028
	Men	<b>1.19</b>	<b>1.02–1.36</b>	0.046

Results are adjusted for age, smoking (current/former smoker/non-smoker), physical activity (active/inactive), BMI, education in years of school and total ethanol intake (in grams); Hazard Ratios (HR) and the respective 95 % Confidence Intervals (CIs) were derived from semiparametric Cox proportional hazards models and they are presented per 1 unit increment in the dietary pattern score; One standard glass being equivalent to 12 g of ethanol; Main dietary pattern among participants drinking no alcohol was characterised by: higher consumption of: Fruits, Vegetables, Legumes, Dairy products, Fish, Eggs and Cereals (in women) and Fruits, Potatoes, Red meat, Nuts and Sweets (in men); Main dietary pattern among participants drinking mainly beer was characterised by higher consumption of: Fruits, Vegetables, Legumes, Poultry, Fish and Cereals (in women) and Fruits, Vegetables, Legumes, Eggs and Cereals (in men); Main dietary pattern among participants drinking mainly wine was characterised by higher consumption of: Fruits, Vegetables, legumes, Dairy products, Fish, Sweets and Cereals (in women) and Fruits, Vegetables, Legumes, Dairy products, Fish and Cereals (in men); Main dietary pattern among participants drinking other alcoholic drinks was characterised by higher consumption of: Potatoes, Red meat, Dairy products, Nuts and Sweets (in women) and Vegetables, Potatoes, Red meat, Poultry, Dairy products, Sweets and Eggs (in men); significant p-values ( $p < 0.05$ ) are presented in bold; \*p-value  $< 0.10$

was not confirmed, probably because beer preference is more pronounced among younger ages, who are more likely to use the Internet and social media for health information (Tennant and Stollefson, 2015). This finding is in line with another study conducted among young adults (Scholz *et al.*, 2016).

When the correlation between the intake of the preferred alcoholic beverage and the 10-year cardio-metabolic risk was evaluated in the “conventional” way (adjusted for the well-known risk factors), results showed the beneficial cardio-protective effects of wine and beer consumption while no significant associations were found among spirits’ drinkers. These findings are in accordance with the literature (Chiva-Blanch *et al.*, 2013; Costanzo *et al.*, 2011; Grønbaek *et al.*, 2000) whereas other authors (Mukamal *et al.*, 2003) suggested that only drinking pattern and not the type of beverage matters. An inverse correlation between wine consumption and diabetes mellitus incidence was found in agreement with the literature (Restani *et al.*, 2020). Although the differential health effects among the different alcoholic beverages could be derived from their differences in their chemical composition with spirits being the worst in terms of bioactive components (Sacanella Anglés *et al.*, 2019) whether or not the protective role is attributed to the alcohol content or their phenolic content (Sato *et al.*, 2002) through various mechanisms (Di Castelnuovo *et al.*, 2009) still remains unanswered and has been discussed controversially (Chiva-Blanch and Badimon, 2019; Olas and Bryś, 2020; Rehm and Hasan, 2020).

Furthermore, our study showed that when the association between the main dietary pattern and the 10-year cardio-metabolic risk was evaluated according to the preferred alcoholic beverage intake, the findings demonstrated other significant associations hidden in the previous “conventional” analysis. Results demonstrated that the effect of the quality of the dietary pattern could strengthen, attenuate or even alter the direction of the association with the aforementioned health risks. For instance, among wine and especially among beer drinkers, the effect of the higher adherence to a healthier dietary pattern strengthened the above-mentioned associations with cardio-metabolic risk.

Additionally, in accordance with the literature (Jayedi *et al.*, 2020), the pronounced protective role of the higher adherence to a healthier dietary pattern among women abstainers against cardio-metabolic risk was shown compared to men with higher adherence to an unhealthy dietary pattern. Similarly, an aggravating effect on cardio-metabolic risk was observed among spirits drinkers adhering more to an unhealthy dietary pattern.

The effect of a high-quality dietary pattern on health could be attributed to the higher consumption of fruits, vegetables and legumes probably consumed with olive oil and cereals (Grosso *et al.*, 2017), with all of them sharing a high capacity of phytochemicals with proven cardio-protective properties among others (Leitzmann, 2016). This observation implies that various components of a healthy dietary pattern could

probably act either in concert with the constituents of wine and beer or could even counteract any potential harmful effect as a consequence of their consumption.

Therefore, the question of reducing the cardio-metabolic risk is not “what I drink” or “what I eat” but rather “what I eat when drinking”, certainly in conjunction with other proven healthy behaviours (Barbaresko *et al.*, 2018). The promotion of a Phytochemical-Rich Dietary Pattern resembling the Mediterranean Dietary Pattern (Billingsley and Carbone, 2018) seems particularly important among drinkers to reduce the cardio-metabolic risk.

## 1. Limitations

Although the data of the present study were derived using robust and reliable epidemiological methods, there are also some study limitations that need to be mentioned. Firstly, the baseline examination was performed once and so may be susceptible to random measurement error, whereas possible underreporting and misclassification should be further acknowledged as an inherent limitation in this type of research. Furthermore, there is a possibility of a suboptimal retention rate, but the main characteristics of the participants who were not found in the follow-up examination were similar to those of the participants who participated in the follow-up, limiting the possibility of potential selection bias (Naimi *et al.*, 2017) due to selective dropouts. Regarding potential suboptimal statistical power, according to the final working sample, the statistical power was adequate to evaluate the observed HRs. Moreover, the *n* of subjects in the “Other alcoholic drink” group was much lower than the other groups; however, the achieved statistical power was adequate for all post-hoc comparisons. As the aim of the present study was not to assess the risk of alcohol consumption on cardio-metabolic risk, therefore the lack of both the distinction between lifetime and current (during the past year) alcohol abstention and detailed information relevant to drinking patterns does not underestimate the importance of findings.

## CONCLUSIONS

The emergence of the quality of the dietary pattern as a crucial confounder when investigating the association of alcohol with cardio-metabolic risk is highlighted and, thus, the results of existing literature should be interpreted with caution. Both wine and beer consumption are associated with lower cardio-metabolic incidence, particularly in the frame of a healthy dietary pattern. The promotion of a Phytochemical-Rich Dietary Pattern is suggested especially among drinkers.

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