

## Moderate and heavy alcohol consumption among Turks: long-term impact on mortality and cardiometabolic risk

Halkımızda ılımlı ve aşırı alkol tüketimi: mortalite ve  
kardiyometabolik risk üzerine uzun vadeli etkiler

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**Objectives:** The impact of alcohol consumption on various outcomes was prospectively evaluated in the participants of the Turkish Adult Risk Factor Study.

**Study design:** A total of 3,443 men and women (mean age 47.6±12 years) were included at baseline and followed-up for a mean of 7.4 years (range 5 to 9 years). Alcohol drinking status was assessed as abstention and brackets of moderate and heavy intake. Only 19.5% of adults (35% of men and 4.2% of women) reported consumption of alcohol. In each multivariate analysis, individuals with the examined endpoint at baseline were excluded, and alcohol drinking status was adjusted for age, sex, smoking status, and physical activity.

**Results:** Alcohol intake increased overall mortality (by 2-fold) in men drinking heavily, but not in men drinking moderately, nor in women. Heavy drinking in combined sexes predicted the risk for incident coronary heart disease (CHD) (RR 2.3; 95% CI 1.30; 4.05), while moderate drinking tended to be protective (RR 0.72; 95% CI 0.50; 1.035). Heavy intake predicted incident diabetes risk (RR 2.13) and tended to be so for new metabolic syndrome (MetS) in men (RR 1.71), whereas moderate alcohol intake was not significantly associated with subsequent development of diabetes or MetS and the risk for MetS was reduced in women (p=0.10).

**Conclusion:** Risk of alcohol intake depends on the amount used: heavy intake raising the risk for diabetes and CHD in combined sexes, and overall mortality in men, contrasted to moderate intake reducing (borderline) the CHD risk and marginally reducing all-cause mortality. Risk for MetS tends to be reduced in women alone.

**Key words:** Alcohol drinking; cholesterol, HDL; coronary disease; diabetes mellitus, type 2; metabolic syndrome X; mortality; risk factors; Turkey/epidemiology.

**Amaç:** Alkol tüketiminin çeşitli sonuçlar üzerine uzun vadeli etkileri Türk Erişkinlerinde Kalp Hastalığı ve Risk Faktörleri Çalışması'nda ileriye dönük biçimde değerlendirildi.

**Çalışma planı:** Çalışmaya alınan 3443 erkek ve kadın (ort. yaş 47.6±12) ortalama 7.4 yıl (dağılım 5-9 yıl) süreyle izlendi. Alkol içme durumu içmeyenler, ılımlı ve aşırı içenler şeklinde sınıflandırıldı. Katılımcıların sadece %19.5'i (erkeklerin %35'i, kadınların %4.2'si) alkol kullandığını bildirdi. Çokdeğişkenli analizlerde, incelenen sonucu başlangıçta taşıyan bireyler değerlendirmeye alınmadı ve alkol kullanımı durumu yaş, cinsiyet, sigara içiciliği ve fiziksel aktivite için ayarlandı.

**Bulgular:** Alkol tüketiminin genel mortaliteyi aşırı içen erkeklerde iki kat artırdığı görülürken, kadınlar ile ılımlı içici erkeklerde bu etki görülmedi. Aşırı alkol kullanımı koroner kalp hastalığı (KKH) gelişme riskini (RR 2.3; %95 GA 1.30; 4.05) öngördüğü halde, ılımlı kullanım koruyucu olma eğilimindeydi (RR 0.72; %95 GA 0.50; 1.035). İlimli alkol tüketimi diyabet veya metabolik sendrom (MetS) gelişmesiyle ilişkili değilken ve kadında düşük MetS riski (p=0.10) öngörürken, aşırı içicilik yeni diyabet riskini (RR 2.13) öngörmekteydi ve erkekte MetS gelişmesini öngörme eğilimi göstermekteydi (RR 1.71).

**Sonuç:** Alkol içiciliğinin gelecekte yüklediği risk kullanılan miktara bağlıdır: Aşırı içicilik diyabet ile KKH riskini ve erkeklerde ölüm oranını yükseltirken, ılımlı kullanım KKH riskini sınırdan anlamlı, genel mortaliteyi marjinal biçimde düşürmektedir. İlimli içicilik MetS riskini yalnız kadınlarda düşürme eğilimindedir.

**Anahtar sözcükler:** Alkol tüketimi; kolesterol, HDL; koroner hastalık; diabetes mellitus, tip 2; metabolik sendrom X; mortalite; risk faktörü; Türkiye/epidemioloji.

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Chronic excessive alcohol use has been known for long to lead to hypertension, cerebral hemorrhage, coronary heart disease (CHD) and death.<sup>[1-3]</sup> The latter two outcomes have not been conclusively shown in a Turkish population sample prospectively. A previous longitudinal analysis of the Turkish Adult Risk Factor (TARF) study failed to document these adverse relationships<sup>[4]</sup> primarily because a linear type of analysis was utilized. This and the recent recognition that a J-shaped dose-response relationship exists between alcohol use and risk of various vascular events<sup>[5]</sup> call for a renewed assessment of the issue among Turks.

Indeed, moderate chronic alcohol intake, currently defined as 1-2 drinks/day for women and 2-4 drinks for men,<sup>[6]</sup> is associated with a longer life expectancy<sup>[7,8]</sup> and with lower risk of CHD<sup>[3,9]</sup> in the general population and with reduced mortality in patients with established CHD.<sup>[10-12]</sup> The long-term effect of moderate alcohol intake on mortality and new development of CHD needs to be examined among Turkish adults, as does its effect on cardio-metabolic risk such as metabolic syndrome (MetS) and type-2 diabetes.

A cardioprotective effect and survival benefit of light-to-moderate alcohol intake may vary as a function of sex,<sup>[8]</sup> race, and background cardiovascular risk.<sup>[13,14]</sup> It is considered that most of the benefit associated with moderate alcohol intake and diminished risk of CHD is mediated by elevation in HDL-cholesterol;<sup>[15,16]</sup> an elevation was observed in the TARF cohort, as well.<sup>[4,17]</sup> Mediation by improved fibrinolytic activity<sup>[18]</sup> has also been considered in the beneficial effect, while mediation by anti-inflammatory properties of alcohol in moderation has not yet been conclusively documented or refuted.

Several recent reports addressing the association of MetS with alcohol consumption have disclosed a lower prevalence with light-to-moderate alcohol intake<sup>[19-21]</sup> but higher likelihood with heavier intake.<sup>[21]</sup> Fasting serum insulin levels were also found to be favorably influenced by alcohol use in moderation.<sup>[19]</sup>

The purpose of this paper was to assess the long-term impact of moderate and heavy alcohol consumption in men and women on a variety of outcomes among Turkish adults who were recognized to have a high prevalence of MetS.<sup>[22]</sup> End-points included mortality, incident CHD, diabetes, and MetS. Analyses were based on the TARF data with a follow-up of up to nine years.

## PARTICIPANTS AND METHODS

**Population sample.** The TARF study is a prospective survey on the prevalence of cardiac disease and risk factors in adults in Turkey, carried out periodically since 1990 in 59 communities throughout the geographical regions.<sup>[23]</sup> It involves a random sample of the Turkish adult population, representatively stratified for sex, age, geographical regions, and for rural-urban distribution.<sup>[23]</sup> Since combined measurements of waist circumference and HDL-cholesterol were first performed at the follow-up visit in 1997/98, the latter examination formed the baseline. Participants, being 28 years of age or older at baseline, were examined over a period of nine years, up to the survey 2006/07. A total of 3,443 individuals who were examined at baseline comprised the cohort of the current study. The survey conformed to the principles embodied in the Declaration of Helsinki and was approved by the Istanbul University Ethics Committee. Individuals of the cohort were visited at their addresses on the eve of the examination and gave written consent for participation. Data were obtained by history of the past years via a questionnaire, physical examination of the cardiovascular system, sampling of blood, and recording of a resting 12-lead electrocardiogram.

**Categories of alcohol intake.** We categorized a daily alcohol intake of less than 1 drink (32 ml raki, or 300 ml beer, or 120 ml wine) as light drinking, and anyone consuming 1 to 3 units of alcohol daily was classified as a moderate drinker. A daily alcohol intake of >3 units was designated as heavy drinking. This greatly overlaps with the standard definition of moderate drinking, which is 1-2 drinks daily for women and 2-4 drinks daily for men.<sup>[6]</sup> In logistic regression analyses, however, light alcohol intake was included in the moderate drinking category with the purpose of attaining greater statistical power. Light drinkers made up 10.2% (n=350) of the cohort, moderate drinkers 6.6% (n=227), and heavy drinkers 2.7% (93 men and women). Since alcohol use was relatively uncommon among females, they were grouped together with males in some analyses.

**Definitions and outcomes.** Hypertension was defined as a systolic blood pressure (BP)  $\geq 140$  mmHg and/or diastolic BP  $\geq 90$  mmHg, and/or use of antihypertensive medication. Individuals with diabetes were diagnosed with the criteria of the American Diabetes Association,<sup>[24]</sup> namely when plasma fasting glucose was  $\geq 126$  mg/dl (or 2-hr postprandial glucose  $> 200$  mg/dl) and/or the current use of diabetes medication. Individuals with MetS were identified when three

out of the five criteria of the National Cholesterol Education Program (ATP III)<sup>[25]</sup> were met, modified for prediabetes (fasting glucose 100-125 mg/dl<sup>[26]</sup> and further for abdominal obesity using the cutpoint  $\geq 95$  cm in men, as recently assessed in the TARF stud.<sup>[27]</sup> Missing data on triglycerides in 1/6 of the sample did not preclude the identification of MetS, since availability of no more than three criteria was required, and the MetS status of the subsequent survey was adopted in few individuals presenting two positive criteria. HOMA was calculated with the following formula:<sup>[28]</sup>  $\text{insulin (mIU/l)} \times \text{glucose (in mmol/l)} / 22.5$ . Values of the baseline examination were used to evaluate prospective developments. Diagnosis of non-fatal CHD was based on the presence of angina pectoris, of a history of myocardial infarction with or without accompanying Minnesota codes of the ECG,<sup>[29]</sup> or on a history of myocardial revascularization. Typical angina and, in women, age  $>45$  years were prerequisites for a diagnosis when angina was isolated. ECG changes of "ischemic type" of greater than minor degree (Codes 1.1-2, 4.1-2, 5.1-2, 7.1) were considered to represent myocardial infarct sequelae or myocardial ischemia, respectively. Diagnosis of CHD did not include chronic heart failure or isolated atrial fibrillation.

**Measurements of risk variables.** Blood pressure was measured in the sitting position and on the right arm, and the mean of two recordings at least 3 min apart was recorded. Waist circumference was measured with a tape (Roche LI95 63B 00), with the subject standing and wearing only underwear, at the level midway between the lower rib margin and the iliac crest. Body mass index (BMI) was computed as weight divided by height squared ( $\text{kg/m}^2$ ). Self-reported cigarette smoking was categorized into never smokers, former smokers (discontinuance of 3 months or more), and current smokers (regularly 1 or more cigarettes daily), as elicited from interviews during examination. Physical activity was graded by the participant himself into four categories of increasing order with the aid of a standard scheme.<sup>[23]</sup> Grades I and II were collectively designated as sedentary, grades III and IV as physically active.

Serum concentrations of cholesterol, fasting triglycerides, HDL-cholesterol, and glucose were determined at baseline examination by the enzymatic dry chemistry method using the Reflotron system (Boehringer Mannheim, Germany). In the final three surveys, the stated parameters, as well as C-reactive protein (CRP) values were assayed at the same cen-

tral laboratory. Blood samples, collected into dry vacutainers were spun and sera shipped on cooled gel packs to İstanbul to be stored in deep-freeze at  $-75$  °C, until analyzed at the laboratory. Concentrations of serum CRP were measured by the Behring nephelometry (Behring Diagnostics, Marburg, Germany).

**Data analysis.** Descriptive parameters were shown as mean  $\pm$  standard deviation or as sex- and age-adjusted mean estimates, and in percentages. Log-transformed values were used for CRP and insulin due to their skewed distribution. Two-sided t-tests and Pearson's chi-square test served to analyze the differences in means and proportions between groups. ANOVA comparisons and pairwise comparisons with Bonferroni adjustment were made to detect significance between groups of estimated means. After exclusion of the participants with each dependent variable at baseline examination, estimates (and 95% confidence intervals) for relative risk (RR) of a dependent variable (outcome) were obtained by use of logistic regression analyses in models that were controlled for potential confounders. A value of  $p < 0.05$  on the two-sided test was considered statistically significant. Statistical analyses were performed using SPSS-10 for Windows (SPSS Inc., Chicago, Ill., Nr. 9026510).

## RESULTS

### Baseline characteristics

Before exclusion of prevalent CHD cases, 3,443 individuals (1,708 men, 1,735 women; mean age  $47.6 \pm 12$  years) were available at baseline examination. Light drinkers consisted of 294 men and 56 women, moderate drinkers of 215 men and 12 women, heavy drinkers of 88 men and 5 women, and abstainers of 1,111 men and 1,662 women. Estimated marginal means of certain sex- and age-adjusted risk variables related to non-users of alcohol were compared with those of light, moderate, and heavy drinkers (Table 1). Alcohol users were on average 5.4 years younger than abstainers ( $p < 0.001$ ); they differed from abstainers in serum sex- and age-adjusted total, LDL- and HDL-cholesterol, triglyceride levels ( $p < 0.001$ ). A fairly linear increase in HDL-cholesterol was observed across drinking groups so that levels were 5.4 mg/dl (13%) higher in heavy drinkers than in abstainers. Compared to abstainers, systolic and diastolic BP were higher only in heavy drinkers ( $p < 0.05$ ). In contrast, physical activity grade, BMI, waist circumference, blood glucose and CRP concentrations were similar across the groups of alcohol status. Noteworthy was that hypertension and MetS were less prevalent in

**Table 1. Sex- and age-adjusted<sup>†</sup> characteristics of the sample by alcohol intake at baseline examination**

	n	Non-users	Mild	Moderate	Heavy	p
		Mean±SE (n=2,773)	Mean±SE (n=350)	Mean±SE (n=227)	Mean±SE (n=93)	
Crude age (years)		49.7±13**	43.4±10.3	45±10.6	46±10.5	
Body mass index (kg/m <sup>2</sup> )		27.9±0.1	28.1±0.4	27.7±0.4	27.9±0.7	0.84
Waist circumference (cm)		92.5±0.2	92.2±0.2	92.1±0.7	94.8±1.2	0.24
Fasting triglycerides (mg/dl)	2,850	142±2.0	155±5.8	154.3±7.2	188±11**	0.000
HDL-cholesterol (mg/dl)	3,306	40.6±0.2	42±0.7	44.7±0.9*	46±1.3*	0.000
LDL-cholesterol (mg/dl)	2,850	115.6±0.7*	123±2.0	123±2.5	126±3.9	0.000
Total cholesterol (mg/dl)	3,332	182.3±0.8**	191.6±2.1	199.3±2.6*	204.3±3.4*	0.000
Fasting glucose (mg/dl)	2,911	100±0.6	99.4±1.8	101.7±2.2	94±3.4	0.27
C-reactive protein (mg/l) <sup>¶</sup>	2,703	2.12±1.03	2.07±1.07	2.13±1.09	2.74±1.14	0.28
Blood pressure (mmHg)	3,424					
Systolic		130±0.4	129.3±1.2	131.7±1.5	137.1±2.3*	0.016
Diastolic		81.6±0.3	81.4±0.7	82.9±0.9	85.8±1.4*	0.015
Physical activity grade (I to IV)		2.31±0.02	2.27±0.05	2.39±0.6	2.25±0.9	0.38
Hypertension (n; %)		1,366; %50.5	124; %36.3	84; %37.5	49; %54.4	0.000
Diabetes (n; %)	3,142	402; %14.5	39; %11.1	28; %12.3	16; %17.2	0.24
Metabolic syndrome (n; %)		1,322; %48.9	143; %42.2	97; %43.3	47; %52.2	0.045

P \* $<0.05$  and \*\* $<0.001$  from both of the extreme values; <sup>†</sup>adjusted to age 48.6 years; <sup>¶</sup>log-transformed values.

light and moderate drinkers than heavy drinkers or abstainers.

### Prospective evaluation

The mean follow-up was 7.4 years (total 25,300 person-years), during which 298 deaths (8.8%; or 1.15% per year) occurred and new fatal or nonfatal CHD developed in 433 cases (13.0%; or 1.67% per year).

**Multivariable prediction of all-cause mortality by alcohol usage.** Table 2 depicts predictors of all-cause mortality in a logistic regression model. After adjustment for sex, age, smoking status, and physical activity grade, heavy alcohol drinking predicted the outcome of death in combined sexes (RR 2.33; 95% CI 1.15; 4.72) and in men at borderline significance. Moderate drinking in men was not associated with any excess mortality, nor was so for any drinking category in women.

**Prediction of incident CHD and diabetes.** Sex was adjusted but not analyzed separately. Distribution of incident CHD cases (crude and adjusted) across the categories of alcohol usage is given in Fig. 1. As seen in Table 3, after adjustment for sex, age, smoking status, and physical activity grade, heavy intake of alcohol was predictive of future CHD risk (RR 2.3; 95% CI 1.30; 4.05) whereas moderate drinking tended to be protective (RR 0.72; 95% CI 0.50; 1.035). Likewise, diabetes risk was significantly increased among heavy drinkers (RR 2.13; 95% CI 1.15; 3.96) but not in moderate drinkers compared with abstainers. Noteworthy was that current cigarette smoking in these models significantly protected against both diabetes and MetS (Table 3 and 4).

**Prediction of incident MetS.** Risk for MetS was not influenced by moderate alcohol consumption among 951 men presenting no MetS at baseline, while heavy

**Table 2. Alcohol consumption and all-cause mortality by gender**

	Total (n=3,391)		Men (n=1,681)		Women (n=1,710)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex (Female)	<b>0.65</b>	0.46; 0.91				
Age (years)	<b>1.126</b>	1.11; 1.14	<b>1.106</b>	1.09; 1.12	<b>1.16</b>	1.13; 1.19
Moderate alcohol	0.90	0.58; 1.40	0.81	0.52; 1.27	0.79	NS
Heavy drinking	<b>2.33</b>	1.15; 4.72	1.95	0.98; 3.89	0.30	NS
Former smokers	1.08	0.70; 1.67	1.24	NS	1.48	NS
Current smokers	<b>2.22</b>	1.53; 3.23	<b>2.59</b>	1.65; 4.07	1.39	NS
Physically active/sedentary	<b>0.81</b>	0.69; 0.95	<b>0.805</b>	0.68; 0.96	0.90	NS
Deaths	298		186		112	

NS: Not significant; 567/93 moderate/heavy drinkers; 414/1197 former/current smokers.

**Table 3. Adjusted outcomes for incident CHD and diabetes in alcohol users**

	CHD (n=3,273)*		Diabetes (n= 3142)*	
	RR	95% CI	RR	95% CI
Sex (Female)	0.80	NS	0.91	NS
Age (years)	<b>1.063</b>	1.05; 1.07	<b>1.02</b>	1.01; 1.03
Moderate alcohol	0.72	0.50; 1.035	1.12	NS
Heavy drinking	<b>2.30</b>	1.30; 4.05	<b>2.13</b>	1.15; 3.96
Former smokers	1.02	NS	0.92	NS
Current smokers	1.03	NS	<b>0.66</b>	0.48; 0.91
Physically active/sedentary	0.885	0.78; 1.004		
Developed events	423		321	

\*Cases identified at baseline examination were excluded; CHD: Coronary heart disease; NS: Not significant; 555/86 moderate/heavy drinkers; 393/1171 former/current smokers.

drinking conferred an increased RR (1.71; 95% CI 0.92; 3.18) at borderline significance (Table 4). Women, however, differed from men in having a tendency to be protected against MetS by alcohol consumption; moderate intake tended to reduce the related RR ( $p=0.10$ ).

## DISCUSSION

In a prospective analysis of a representative sample of middle-aged and elderly Turkish adults, outcome among consumers of alcohol depended on the amount of alcohol intake. Heavy drinking, representing a daily average of over 40 ml ethanol, leads to approximately 2-fold risk for incident type-2 diabetes, CHD, and in men, at a borderline significance, risk for all-cause death and MetS. In contrast, moderate intake of alcohol was not associated with any adverse outcome; future CHD risk was reduced at a borderline significance, as was risk for MetS in women, and RR for all-cause mortality stood at a non-significant 0.8 in each gender.

The present study differs greatly in the overlap with the previous longitudinal study:<sup>[4]</sup> the latter's period involved the 1990s while the current analysis

involves primarily the current decade, the current cohort is one-quarter larger in size and is six years older; finally, the figures of outcomes for death and incident CHD are substantially higher. The approach of consistently analyzing heavy and moderate drinkers separately also differed between these studies.

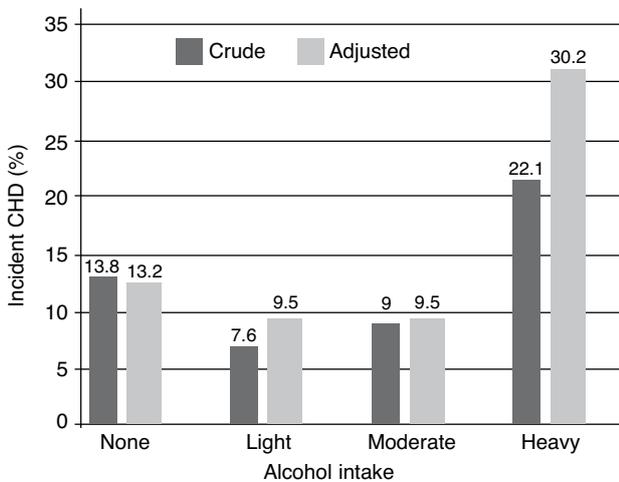
As far as the types of alcoholic drinks are concerned, as can be derived from official sources,<sup>[30]</sup> 62% of ethanol consumed in Turkey is in the form of beer, 26% as raki, 5% as vodka, and 5% as wine. The distribution in our study was in general agreement with these data and was at large variance from the drinking pattern in populations of South Europe where wine predominates. This knowledge might be of use in interpreting the effects.

**Impact of heavy alcohol intake.** Heavy alcohol consumption is known to raise the risk of all-cause death<sup>[8,10]</sup> as well as of CHD,<sup>[9]</sup> and we confirmed this now among Turks. Compared with abstainers, a significant and approximately 2-fold risk for mortality, incident CHD, and diabetes was observed in heavy drinkers, after adjustment for sex, age, smoking status, and sedentariness.

**Table 4. Adjusted outcomes for incident MetS in male and female alcohol users**

	Total (n=1,888)*		Men (n=951)		Women (n=937)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex (Female)	0.91	NS				
Age (years)	1.01	NS	0.99	NS	<b>1.025</b>	1.01; 1.04
Moderate alcohol	1.06	NS	1.11	NS	0.48	0.20; 1.16
Heavy drinking	1.72	0.95; 3.12	1.71	0.92; 3.18	1.35	NS
Former smokers	1.025	NS	1.27	NS	0.93	NS
Current smokers	<b>0.76</b>	0.59; 0.986	0.86	NS	0.79	0.54; 1.17
Physical activity (grade I-IV)	0.95	NS	0.91	0.79; 1.06	1.01	NS
Developed MetS	513		262		251	

\*Cases identified at baseline examination were excluded; MetS: Metabolic syndrome; NS: Not significant; 294/48 moderate/heavy male drinkers; 49/4 moderate/heavy female drinkers.



**Figure 1.** Risk for incident CHD in 3,273 men and women at 7.4 years' follow-up among non-drinkers and individuals with moderate (2 units per month to 3 units daily) and heavy alcohol intake (>3 units daily). Crude and multi-adjusted incidence rates are given.

#### ***Favorable outcomes with moderate alcohol intake.***

Our finding of moderate alcohol consumption being associated with a borderline significantly lower risk for fatal and incident nonfatal CHD than abstinence is in agreement with other prospective studies<sup>[31,32]</sup> and confirms validity in Turkish adults. This is a novel documentation for this population. It is worth noting that, in a prospective evaluation of the same TARF sample as the present one, only Turkish women responded to moderate alcohol consumption with lower triglycerides and CRP, while men showed a log-linear positive association of drinking categories with BP, LDL-cholesterol, apolipoprotein B, and CRP.<sup>[33]</sup> The magnitude of the reduced risk, 28%, is consistent with the reported reduction of 32% associated with drinking wine in overall vascular risk.<sup>[5]</sup> In 1,675 men and 465 women undergoing coronary angiography, alcohol intake was independently associated with lower atherosclerosis score, and in a nearly 8-year follow-up, alcohol consumption was the only negative predictor of cardiac mortality (RR 0.84).<sup>[34]</sup>

As regards total mortality, consumption of alcohol, up to 4 drinks per day in men and 2 drinks per day in women, was inversely associated in a huge meta-analysis of over one million subjects, maximum protection conferred being 18% in women and 17% in men.<sup>[8]</sup> Higher doses of alcohol were associated with increased mortality. Our finding of an insignificant reduction of 19% in mortality in men who consumed moderate alcohol is in agreement with the findings of this meta-analysis.

Other interpretations offered for the observed net benefit of alcohol in moderation include unmeasured confounding<sup>[35]</sup> and reverse causality, namely, the inclusion of nondrinker individuals who do not drink because of their poor health status.<sup>[36]</sup> But studies with separate analysis of former drinkers yielded similar benefit with light-to-moderate alcohol intake.<sup>[13]</sup>

In regard to diabetes, the relative risk with current alcohol consumption depended on BMI, being high among low-BMI ( $\leq 22$  kg/m<sup>2</sup>) individuals, but low among middle- (22-25 kg/m<sup>2</sup>) and high-BMI individuals, in a cohort of 5,636 Japanese.<sup>[37]</sup>

Different outcomes for MetS in sexes among moderate drinkers, e.g., the finding that only women tended to benefit, merit explanatory commenting. Despite an increase in concentrations of HDL-cholesterol in both sexes, our unpublished observations indicate that female Turks alone respond to alcohol with a significant decline in triglycerides and a tendency to reduced systolic and diastolic BPs and CRP concentrations.

This study provided evidence that the dose-response relationship of alcohol intake with mortality and cardiovascular risk is clearly J-shaped depending on the excessiveness of the amount consumed. It is likely that the effect of certain factors such as blood pressure, fibrinolytic activity, subclinical inflammation rises steeply with heavy drinking, thus offsetting the beneficial effects on insulin sensitivity and the stimulated HDL-mediated processes like reverse cholesterol transport and antioxidative effects; hence, a J-shaped risk curve results. It has been suggested that the beneficial effects of moderate alcohol intake may be more important in subjects with a deteriorated risk profile, such as those with MetS.<sup>[14]</sup>

**Limitations and strengths.** The low proportion (1 in every 23) of alcohol drinkers among women somewhat limits the sex-related differential evaluation of the effects of alcohol intake, though this does reflect the prevalence in this population at large. Assessment based on a single self-report on alcohol intake at one point in time constitutes another limitation inherent virtually to all such studies, but consistency of series of reports on the drinking pattern was described in a previous study by us.<sup>[4]</sup> Any misclassification of alcohol intake category or any potential cause in terms of inaccurate classification in the diagnosis of CHD may have tended to dilute the noted association between alcohol intake and outcomes. Our data have the strength of documenting the predictive value of alcohol intake categories in a large representative

population of both sexes in whom death and cardio-metabolic events were identified.

### Conclusion

Prospective evaluation of a representative sample of Turkish adults confirmed adverse outcomes among heavy consumers of alcohol (>3 units daily) compared with abstainers: 2-fold risk for incident diabetes, CHD and, in men, at a borderline significance, for all-cause mortality and MetS. Moderate intake of alcohol, in contrast, was not associated with any adverse outcome. Lifestyle-adjusted risks for incident CHD and, in women, for MetS were borderline significantly lower, and risk for all-cause mortality was non-significantly reduced. The apparent diverging beneficial effect of light-to-moderate alcohol intake in women (compared with men) in regard to MetS warrants further study in this population.

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