



# How much is too much alcohol in tuberculosis?

*To the Editor:*

About one-third of the population worldwide have *Mycobacterium tuberculosis* infections, although 90% of infected individuals never develop clinical disease [1, 2].

The association between alcohol consumption and tuberculosis (TB) is well known [3, 4]. Individuals who consume alcohol are considered immune-compromised because they have a greater incidence and severity of infectious diseases than abstainers, and are also more susceptible to lung infections, such as TB and pneumonia [4]. In fact, alcohol users are a group at high risk for TB who should be addressed accordingly with targeted preventative interventions [5, 6].

In the present study, we tried to determine the threshold of alcohol consumption that increased the risk for active TB in men and women.

Cases and controls were recruited from primary healthcare units in the same geographical region. Pregnant or lactating women, and individuals infected with HIV or other immunosuppressive conditions were excluded. Cases were patients with active pulmonary TB (with or without pleural involvement), aged >18 years-old, and diagnosed with TB at outpatient centres in northern Portugal between August 2013 and September 2015. Controls were healthy individuals aged >18 years-old with no suspicion of active TB or history of TB in the participant's household within the previous 5 years.

Registered data included daily alcohol consumption over the previous year (including types of beverages and the quantity consumed), age, sex, area of residence, nationality and current occupation/employment status. The clinical data included co-morbidities (diabetes, chronic kidney disease, rheumatological diseases, solid and haematological cancers, lung disease, silicosis, heart and liver conditions and history of TB) and other risk factors for TB infection (drug abuse, imprisonment, homelessness or residence in a community shelter). This project was approved by Portugal's Northern Region Health Administration Ethics Committee, and all participants provided written informed consent.

We performed separate analyses of men and women in the present study given the fact that the impact of ethanol is different in the two sexes [7]. The crude effect of each evaluated variable on TB infection was investigated by simple logistic regression, except for variables associated with very low numbers of TB infections. Variables that were statistically significant were then included in a multiple binary logistic regression model. The selection of the best model was based on the likelihood-ratio test whenever possible, and otherwise on the Akaike Information Criterion (AIC). The model discriminability was as the area under the receiver operating characteristic curve (AUC). All statistical analyses were performed with R software (version 2.12.1). The level of significance was set at 0.05.

We enrolled 289 subjects in this study, 50.5% of whom were male. The mean $\pm$ SD (range) age was 51.6 $\pm$ 16.9 (19–87) years for men and 50.9 $\pm$ 17.2 (19–85) years for women.

Among men, those with TB were significantly younger (mean $\pm$ SD age 48.1 $\pm$ 17.0 years *versus* 56.8 $\pm$ 15.7 years-old) and more likely to be unemployed (29% *versus* 12%). Smokers were significantly more likely to have TB (55% *versus* 23%). Analysis of alcohol consumption indicated that those who consumed more than 38 g of ethanol per day had a greater risk of TB than those who did not drink at all. The multiple logistic model indicated that drinking more than 38 g of ethanol per day, young age and being unemployed were statistically significant risk factors for TB (AUC 0.715). According to the model estimates, any 1-year increase in age decreased the odds for TB by 3.8% (95% CI 0.938–0.988),



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**Heavy alcohol intake seems to increase risk of TB in males. New measures for alcohol abuse are needed** <http://ow.ly/2Esr304cDg4>

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unemployment increased the risk two-fold (95% CI 0.902–6.247) and daily consumption of more than 38 g of ethanol per day increased the risk for TB four-fold (95% CI 1.508–10.738).

Females with TB were also significantly younger than those without TB (mean±SD age 40.8±15.6 years *versus* 55.4±15.9 years). As with the males, the low prevalence of living in poor conditions precluded analysis of this variable. Smoking was also significantly associated with TB in women (32% *versus* 11%).

The multiple logistic model indicated that young age and smoking were statistically significant risk factors for TB, but there was no significant association between alcohol consumption and TB (table 1, AUC 0.753). Thus, for any 1-year increase in age, the model (table 1) estimated a 5.1% decrease in the odds for TB (95% CI 0.947–6.724). The effect of current smoking was very close to being statistically significant ( $p=0.064$ ), so we left in this variable because it provided a better fit. Current smoking accounted for a 2.5-fold greater risk of TB (95% CI: 0.925–0.974).

Our results showed that men who were younger, drink more than 38 g of ethanol per day and were unemployed had an increased risk for TB, and that women who were younger and smokers had an increased risk for TB.

Previous studies showed there might be a dose-response relationship between the amount of alcohol consumption and risk for TB. However, few studies have focused on the threshold amount of alcohol that increases the risk for TB [8]. In the present study, we classified men as non-drinkers, moderate drinkers (<38 g ethanol per day), or heavy drinkers (>38 g ethanol per day). In terms of standard drinks (1 standard drink=10 g ethanol), 38 g of ethanol is equivalent to about 4 drinks per day. A previous systematic review reported similar results [8]. However, we found no significant association between alcohol consumption and TB in females. This may be due to the small percentage of women who consumed alcohol in our study population (21%). Nonetheless, because of biological differences between men and women, we would expect the threshold (g ethanol per day) for increasing the risk of TB would be lower in women than men.

Our analysis indicated that young age increased the risk for TB. This is in line with previous research that showed that TB mostly affects adults in their most productive years [9]. Moreover, the existing literature also cites numerous social factors, such as unemployment, as significant risk factors for TB [10]. This is supported by our results.

The two major limitations of this study are that we only measured alcohol consumption in the previous year and that we relied on self-reported alcohol consumption, which may not reflect actual drinking pattern.

In conclusion, the epidemiologic data and other evidence presented here indicate that heavy alcohol consumption in men is an independent risk factor for TB. Other variables significantly associated with TB were unemployment in men, current smoking in women, and young age in men and women.

There are specific interventions that could be routinely offered to vulnerable TB patients such as heavy drinkers [11–14].

Other policy measures, such as increasing taxation on alcoholic beverages and more stringent control of the availability of alcoholic beverages, could reduce the problems associated with heavy drinking. Studies of preventive and treatment interventions for heavy drinkers should also be encouraged.

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TABLE 1 Statistical description and multivariate analysis

	Males						Females					
	TB	No TB	p-value	Multivariate analysis			TB	No TB	p-value	Multivariate analysis		
				Estimated OR	95% CI for the estimated OR	p-value				Estimated OR	95% CI for the estimated OR	p-value
<b>Subjects n</b>	86	60					44	90				
<b>Age years</b>	48.1±17.0	56.8±15.7	0.003	0.962	0.938–0.988	0.004	40.8±15.6	55.4±15.9	<0.001	0.949	0.925–0.974	<0.001
<b>Unemployment</b>	25 (29)	7 (12)	0.015	2.374	0.902–6.247	0.080	14 (32)	18 (18)	0.074			
<b>Drug abuse</b>												
No	78 (91)	58 (97)	0.336									
Yes	6 (7)	2 (3)	¶				1 (2)	0 (0)	+			
<b>Imprisonment</b>	1 (1)	0 (0)	+				1 (1)	0 (0)	+			
<b>Homelessness</b>	1 (1)	0 (0)	+				1 (1)	0 (0)	+			
<b>Community shelter</b>	1 (1)	0 (0)	+				1 (1)	0 (0)	+			
<b>Current smoking</b>												
No consumption <sup>#</sup>	23 (27)	29 (48)	¶				30 (68)	89 (63)	¶			
Previous consumption	16 (18)	16 (27)	0.701									
Current consumption	47 (55)	14 (23)	<0.001				14 (32)	10 (11)	0.002	2.523	0.947–6.724	0.064
<b>Co-morbidities</b>												
Diabetes mellitus	3 (3)	31 (52)	<0.001 <sup>§</sup>				6 (14)	46 (46)	<0.001 <sup>§</sup>			
Cancer	1 (1)	1 (2)	+				1 (2)	1 (1)	+			
Silicosis	0 (0)	0 (0)	+				1 (2)	0 (0)	+			
<b>Alcohol consumption</b>												
No	35 (41)	28 (47)	¶				39 (89)	74 (75)	¶			
Yes							5 (11)	25 (25)	0.067			
0–38 g·day <sup>-1</sup>	20 (23)	22 (37)	0.426	1.847	0.679–5.027	0.230						
≥38 g·day <sup>-1</sup>	31 (38)	10 (17)	0.041	4.024	1.508–10.738	0.005						

Data are presented as mean±SD or n (%), unless otherwise stated. TB: tuberculosis. <sup>#</sup>: for females, includes previous consumption; ¶: reference class; +: the effect was not statistically evaluated as frequency numbers were very small; <sup>§</sup>: spurious value, as it results in an OR of 30.

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