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## Tuberculosis and excess alcohol use in the United States, 1997–2012

T. Volkmann\*, P. K. Moonan†, R. Miramontes†, and J. E. Oeltmann†

\*Epidemic Intelligence Service, assigned to Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta

†Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

### SUMMARY

**BACKGROUND**—Excess alcohol use among tuberculosis (TB) patients complicates TB control strategies.

**OBJECTIVES**—To characterize the role of excess alcohol use in TB control, we describe the epidemiology of excess alcohol use and TB in the United States among those aged ≥ 15 years.

**DESIGN**—Using data reported to the National Tuberculosis Surveillance System, 1997–2012, we examined associations between excess alcohol use and TB treatment outcomes and markers for increased transmission (involvement in a local genotype cluster of cases) using multivariate logistic regression. We used Cox proportional hazards regression analysis to examine the relationship between excess alcohol use and the rate of conversion from positive to negative in sputum culture results.

**RESULTS**—Excess alcohol use was documented for 31 207 (15.1%) of 207 307 patients. Prevalence of excess alcohol use was greater among male patients (20.6%) and US-born patients (24.6%). Excess alcohol use was associated with a positive sputum smear result (aOR 1.23, 95% CI 1.18–1.28) and death during treatment (vs. completion of treatment) (aOR 1.16, 95% CI 1.10–1.22). The rate of culture conversion was higher among patients without excess alcohol use (adjusted hazard ratio 1.20, 95% CI 1.18–1.23).

**CONCLUSIONS**—Excess alcohol use was common among patients with TB, and was associated with TB transmission, lower rates of sputum culture conversion, and greater mortality.

### Keywords

substance use; *Mycobacterium tuberculosis*; directly observed therapy; sputum culture; culture conversion

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Tuberculosis (TB) incidence continues to decrease in the United States, with fewer than 10 000 cases reported nationwide in 2012;<sup>1</sup> however, excess alcohol use remains common.

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Correspondence to: Tyson Volkmann, Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, MS-E-10, 1600 Clifton Road NE, Atlanta, GA 30329, USA. Tel: (+1) 404 639 6469. Fax: (+1) 404 718 8308. xdh4@cdc.gov.

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Excess alcohol use accounted for an estimated 88 000 deaths in the United States each year during 2006–2010,<sup>2</sup> and an estimated US\$224 billion in economic costs in 2006.<sup>3</sup> Excessive alcohol use includes binge drinking, exceeding weekly limits, and any use by pregnant women or persons aged <21 years. In 2011, binge drinking was reported by 18.3% of US adults, who reported doing so an average of four times a month and consuming an average of 8 drinks per occasion.<sup>4</sup> Substance use (including excess alcohol use) among patients with TB remains highly prevalent in the United States<sup>5</sup> and abroad.<sup>6</sup>

Alcohol use might be responsible for a large proportion of TB program burden,<sup>7</sup> which is represented by a strong association between excessive alcohol use and TB.<sup>8</sup> This association may be explained by the progression of latent tuberculous infection to TB disease due to decreased immune system function among excess alcohol users,<sup>9</sup> and exacerbated by other associated factors such as homelessness<sup>10</sup> and smoking.<sup>11</sup> Studies have shown excess alcohol use to be associated with a positive acid-fast bacilli (AFB) sputum smear microscopy result,<sup>12</sup> delay in TB diagnosis,<sup>13</sup> anti-tuberculosis treatment,<sup>13</sup> and poor TB treatment outcomes.<sup>14</sup> Excess alcohol use is also associated with an increased risk of belonging to a localized TB genotype cluster,<sup>15,16</sup> suggesting an association between alcohol use and recent TB transmission.

Despite the high prevalence of excess alcohol use described among TB patients, and the associated comorbidity and mortality, no recent nationwide analysis examining the prevalence of excess alcohol use and potential associations has been published. We investigated the prevalence of excess alcohol use among TB patients reported in the United States from 1997 to 2012. We assessed the association of excess alcohol use with markers for TB transmission and with treatment outcomes, while adjusting for the effects of other demographic and clinical characteristic variables routinely reported in US TB surveillance. We also assessed whether time to sputum culture conversion was associated with excess alcohol use among patients with pulmonary TB.

## STUDY POPULATION AND METHODS

### Data collection

We used data from the National Tuberculosis Surveillance System (NTSS), which contains demographic and clinical information for each reported TB case in the United States and the District of Columbia. Incident cases of TB disease in persons aged ≥ 15 years reported to the NTSS for 1997–2012 were selected for this analysis. Molecular genotype data of *Mycobacterium tuberculosis* complex isolates were linked to NTSS case-based records, as described elsewhere.<sup>17</sup> For analyses involving genotyping data, incident culture-positive TB cases in the NTSS for 2009–2012 with matched genotype results were used. Similar to a previous analysis, a genotype cluster was defined as two or more cases of TB with the same genotype matched using 24-locus mycobacterial interspersed repetitive unit (MIRU) and spacer oligonucleotide typing, and reported in the same county and state.<sup>18</sup>

As data for the NTSS are collected as part of routine public health practice and not for the purposes of human subjects' research, the study proposal was reviewed by the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers of Disease Control

and Prevention, Atlanta, GA, and it was determined that institutional review board approval was not required.

Excess alcohol use is defined as having used alcohol in excess within the past 12 months.<sup>19</sup> Information for this variable is either self-reported or medically documented. If excess alcohol use is not self-reported by the patient, the health provider or TB controller is tasked with determining whether excess alcohol use occurs. This determination can be made over the course of numerous appointments. Homelessness, injection drug use, and non-injection drug use are defined as any period of self-reported behavior in the 12 months before the diagnosis of TB disease. Poor treatment outcomes were defined as being lost to follow-up, not complying with or refusing treatment, among those for whom treatment was stopped vs. treatment completion. Patients who died during treatment or whose completion status was unknown or missing were not included in the analysis of poor treatment outcomes. To be included in the variable ‘pulmonary cavity diagnosed by X-ray’, individuals also had to have documentation of an abnormal X-ray. Only those with a positive sputum culture result and initial drug susceptibility testing results were considered for analyses of drug resistance. Patients with documented human immunodeficiency virus (HIV) infection were coded as ‘known positive’, whereas patients with negative or unknown status were coded as ‘other’.

### Statistical analysis

#### **Prevalence of excess alcohol use among TB patients in the United States—**

Trends in the prevalence of excess alcohol use were assessed using a Mantel-Haenszel extension of the  $\chi^2$  test for trend.<sup>20</sup> The prevalence of excess alcohol use was also stratified by state and categorized by quartile.

#### **Bivariate associations between excess alcohol use, select characteristics and TB outcomes—**

Bivariate associations between excess alcohol use and demographic and clinical variables were assessed using crude odds ratios (ORs) and 95% confidence intervals (CIs).

#### **Multivariate associations between excess alcohol use and TB outcomes—**

Multivariate logistic regression analysis was conducted to assess the association of excess alcohol use and select variables. Adjusted odds ratios (aORs) significant at the 95% confidence level are displayed. We did not include the multidrug-resistant and extensively drug-resistant variables in multivariate analysis due to large amounts of missing data in these variables. Analyses of genotype data were restricted to 2009–2012, as 24-locus MIRU data were only available for 2009 onward.

#### **Analyses of time to sputum culture conversion—**

We conducted a Kaplan-Meier analysis to assess whether time to and rate of sputum culture conversion differed between patients with and those without documented excess alcohol use. Time to conversion was defined as the number of days between the start of treatment and the date of the first consistently negative result from sputum culture. Analysis was limited to patients with pulmonary TB who were culture-positive; had confirmed susceptibility to isoniazid, rifampin, and ethambutol; had no known resistance to pyrazinamide; were started on a

standard four-drug regimen;<sup>21</sup> had documentation of a negative sputum culture result; had a temporally valid documentation of date of sputum culture conversion; and, for those who culture converted, before stopping treatment and within 4 months (standard time after which treatment is considered failed);<sup>22</sup> and were reported as either 'yes' or 'no' to the excess alcohol use question.

We plotted time to sputum culture conversion within 4 months of the start of anti-tuberculosis treatment by excess alcohol use using Kaplan-Meier curves. Differences were assessed using log-rank statistics, while hazard ratios (HRs) and 95% CIs for rate of culture conversion were calculated using Cox proportional hazard regression analyses to obtain adjusted hazard ratios (aHRs). The adjusted analysis controlled for age group, sex, race/ethnicity, and homelessness.

## RESULTS

### Prevalence of excess alcohol use among confirmed TB patients in the United States

During the study period, 207 307 TB cases were reported among persons aged 15 years (Figure 1). Of these, excess alcohol use was documented for 31 207 (15.1%; yearly range 12.4–17.3) (data not shown); 22 733 (72.8%) were born in the United States (US-born) and 8474 (28.2%) outside the United States (foreign-born). For 1997–2012, the prevalence of excess alcohol use differed significantly between US-born and foreign-born patients (24.3%, range 22.8–25.6 vs. 7.5%, range 6.5–8.4;  $P < 0.001$ ; Figure 1). The prevalence of excess alcohol use for 1997–2012 decreased significantly, from 25.3% to 23.1%, among US-born persons ( $P < 0.001$ ), but did not change significantly among foreign-born persons ( $P = 0.842$ ). Beginning in 2005 for US-born ( $P = 0.429$ ) and in 2008 for all patients with TB ( $P = 0.051$ ), there was no significant change in excess alcohol use prevalence. Excess alcohol use prevalence among TB patients varied by state by a factor of nearly nine, ranging from 5.1% in Rhode Island to 44.5% in Montana (Figure 2).

**Bivariate associations between excess alcohol use and select characteristics and TB outcomes**—Excess alcohol use was more common among males than females, among patients aged 45–64 years than among other age groups, among American Indians or Alaska Natives than other races, and among US-born than foreign-born patients (Table 1). TB patients with excess alcohol use were more likely to be homeless and to have used injection or non-injection drugs during the past year. Those with excess alcohol use were also more likely to be HIV-positive.

**Multivariate associations between excess alcohol use and TB outcomes**—Excess alcohol use was independently associated with positive AFB sputum smear microscopy results (aOR 1.23, 95% CI 1.18–1.28), pulmonary vs. extra-pulmonary site of disease (aOR 1.31, 95% CI 1.23–1.39), having a pulmonary cavity diagnosed on X-ray (aOR 1.21, 95% CI 1.16–1.25), and genotype cluster involvement (aOR 1.36, 95% CI 1.23–1.50). With regard to measures of anti-tuberculosis treatment, excess alcohol use was associated with receiving directly observed therapy (DOT) vs. self-administered therapy (SAT) (aOR 1.92, 95% CI 1.81–2.03). Compared with completion of treatment, rates of death (aOR 1.16, 95% CI 1.10–1.22) or loss to follow-up (aOR 1.25, 95% CI 1.15–1.37) were significantly

higher in those with excess alcohol use (Table 1). A total of 67 patients (0.03%) had treatment outcome information missing and were excluded from further analyses. The proportion of patients with missing treatment outcome information and reported excess alcohol use was not significantly different from that observed among those with no reported excess alcohol use ( $P > 0.99$ ).

**Analyses of time to culture conversion**—The proportion of patients with culture conversion was significantly lower for those who reported excess alcohol use (88.6%) than those who did not (92.3%,  $P < 0.001$ ; Table 2). Analysis of time to culture conversion indicated a significant difference between median days to culture conversion for those for whom excess alcohol use was reported vs. those for whom it was not (54 days, interquartile range [IQR] 31–76 vs. 43 days, IQR 25–66;  $P = 0.001$ ). After adjustment for race/ethnicity, age, sex, and homelessness, the rate of sputum culture conversion remained significantly higher for those without excess alcohol use (aHR 1.20, 95% CI 1.18–1.23). When the adjusted analysis was stratified by therapy, the rate of conversion among those without excess alcohol use was significantly higher for those treated with DOT (aHR 1.22, 95% CI 1.19–1.25), but not for those who underwent SAT (aHR 1.11, 95% CI 0.99–1.25) (Figure 3).

## DISCUSSION

Nearly one in six TB patients consumes alcohol in excess, and this behavior complicates TB control at every level. These findings echo research from abroad and from other US states and cities.<sup>5,6,23,24</sup> The burden of alcohol and TB is distributed disproportionately in the United States, with 12 states reporting an overall prevalence of excess alcohol use among TB patients ranging between 19% and 44%. Among US-born patients with TB, the prevalence of excess alcohol use has been >20% each year since 1997, suggesting that excess alcohol use needs to be considered when addressing TB control in the United States. The prevalence of excess alcohol use among US-born patients with TB has remained steady since 2005 and among foreign-born patients with TB since 1997. While the prevalence of excess alcohol use among TB patients appears to be lower than that of binge drinking in the general population of the United States, it should be noted that these measures of alcohol use are not equivalent, and that the proportion of foreign-born TB patients in the United States is approaching 50%, among whom only 7.5% had excess alcohol use reported. This drives down the overall prevalence of excess alcohol use compared to that of the general population in the United States. As a common factor among patients with TB, excess alcohol use may represent a large portion of the morbidity and mortality associated with TB in the United States, and may be a marker for other factors that were not included in this analysis, including smoking and poverty.

This study has limitations. First, the variable ‘excess alcohol use’ collected in the NTSS and used in this study lacks a specific definition. The specificity of this variable could be increased by systematically implementing a reliable, valid use measure, such as the single-question screen measure used by the National Institute on Alcohol Abuse and Alcoholism (National Institutes of Health, Bethesda, MD).<sup>25</sup> However, the current, broad definition remains in place due to requests from TB programs that are striving to ensure that all patients with excess alcohol use are captured. Second, the reliability of self-reported or

medically documented data on excess alcohol use is unknown. As a potentially stigmatized behavior, it is probable that the prevalence of excess alcohol use is underreported. Importantly, our analysis was unable to analyze the potential confounding effects of smoking on the excess alcohol use/TB outcome association. Unfortunately, as the NTSS does not collect information on tobacco smoking, we were not able to perform an analysis that controlled for smoking.

Alcohol use is associated with the development of TB disease,<sup>8</sup> probably due to impaired immune function.<sup>26</sup> In addition, excess alcohol use among TB patients has been linked to TB transmission<sup>27</sup> and adverse treatment outcomes.<sup>28</sup> Our results are consistent with these findings, as excess alcohol use was associated with pulmonary vs. extra-pulmonary disease, a positive sputum smear result, having a diagnosed pulmonary cavity and being included in a local genotype cluster. Each of these factors can influence transmission, including clustering, which has been linked to recent transmission.<sup>29</sup> Furthermore, excess alcohol use was associated with non-injection drug use and homelessness, both of which negatively impact our ability to control TB through the difficulty in locating contacts and ensuring treatment adherence.<sup>30,31</sup>

The odds of documented excess alcohol use were greater among those with poor treatment outcomes and for those who died vs. those who completed treatment. These findings support those from past studies that reported that patients who used alcohol in excess were more likely to experience adverse treatment outcomes.<sup>32,33</sup> A recent study in India found that persons who consumed alcohol during treatment missed on average 18 (95% CI 13–22) more intensive phase doses than those who did not.<sup>34</sup> A variety of factors probably account for poor treatment outcomes: TB patients who drink excessively may be less likely to have adequate social support, housing, and transportation to appointments for care, and may be unable to attend appointments for treatment due to factors related to substance use.<sup>35</sup> Furthermore, medication failure is possible due to immunosuppression<sup>36</sup> and changes in pharmacokinetics<sup>8,37</sup> caused by alcohol consumption. In the current study, among patients who culture converted within 4 months, those for whom excess alcohol use was not documented completed treatment more than a week sooner on average, demonstrating that patients who use alcohol in excess may be more likely to fail treatment and require additional resources from TB control programs.

Further complicating anti-tuberculosis treatment among TB patients who consume alcohol in excess is the additional hepatic damage caused by the metabolism of alcohol. The majority of anti-tuberculosis medications are processed in the liver,<sup>38</sup> where additive hepatotoxic effects can occur.<sup>39</sup> This outcome is more commonly found in those who consume alcohol in excess than in those who do not.<sup>40</sup> For people who are known to be currently using alcohol in excess or have a history of alcohol abuse, the American Thoracic Society recommends treatment with fewer TB medications to reduce the hepatotoxic effects from the additive effects of excess alcohol use and anti-tuberculosis treatment.<sup>41</sup> Cigarette smoking is more common among those who use excess alcohol than among those who do not, and is also associated with tuberculous infection and progression to TB disease.<sup>11</sup> Smoking might complicate anti-tuberculosis treatment through poor TB outcomes (e.g., relapse after treatment).<sup>42</sup> The association between smoking and TB may also be responsible

for some of the effects observed between excess alcohol use and the outcomes in the current study.

In addition to being less likely to complete anti-tuberculosis treatment, a significantly higher proportion of those who used alcohol in excess were prescribed DOT than those who did not use alcohol in excess; those who consumed alcohol in excess were nearly twice as likely to receive DOT as SAT. As DOT requires active supervision by a health care worker, the cost in terms of human resources is higher for each TB patient treated with DOT.<sup>43</sup> Despite this extra attention from the system, TB patients who used alcohol in excess were still less likely to complete treatment than those who did not. After adjusting for race/ethnicity, sex, age, and homelessness, the rate of culture conversion among those who did not use alcohol in excess was significantly greater. The conversion rate maintained statistical significance after stratification among those who did not use alcohol in excess who were receiving DOT, which indicates that, even with supervised treatment, those who used alcohol in excess take longer to cure. The increased treatment time under DOT ostensibly means that those who use alcohol in excess may require an even larger proportion of resources during anti-tuberculosis treatment than those who do not.

One strategy that may provide an opportunity for clinical intervention is alcohol screening and brief intervention. Since 2004, the US Preventive Services Task Force (Rockville, MD) has recommended alcohol screening and behavioral counseling (also known as alcohol screening and brief intervention [ASBI]) for all adults in primary care to address excessive alcohol use. This review of evidence indicated that brief (6–15 min) intervention sessions were effective in significantly reducing weekly alcohol consumption (by 3.6 fewer drinks/week for adults) and binge level episodes (reported by 12% fewer participants) and increasing adherence to recommended drinking limits (achieved by 11% more participants).<sup>44</sup> Furthermore, the effects can last for years and show improvement in health care utilization outcomes, including fewer hospital days and lower costs.<sup>44</sup>

Another strategy consists of an integrated approach to concurrently treating both excessive alcohol use and TB. This is an approach that represents a dual-purpose opportunity. While very few programs appear to have utilized such an approach to co-treating excess alcohol use and TB,<sup>45</sup> and few current programs with TB and alcohol treatment exist, this model is fairly well established in the literature on injection drug use in populations at high risk for transmission of HIV-TB.<sup>46</sup> A similar model might utilize a holistic approach that addresses a variety of factors, such as the concomitant social (e.g., homelessness), psychological (e.g., unmet mental health needs), physiological (e.g., alcohol dependence), and physical health issues (e.g., TB) that are simultaneously affecting a disproportionately large number of TB persons. This strategy presents an opportunity for the health system to manage multiple related issues, which could result in an overall cost savings to the system and respond to calls in the literature for integrative approaches to co-treating infectious disease and substance use disorders.<sup>46–49</sup>

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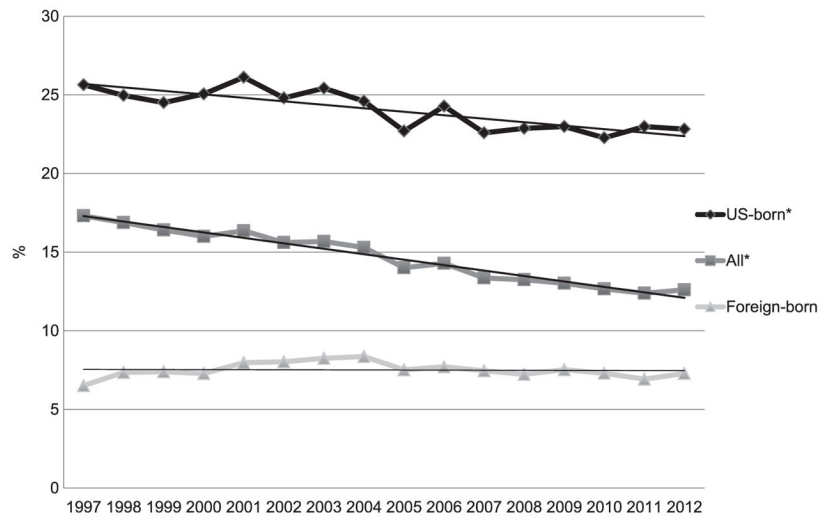
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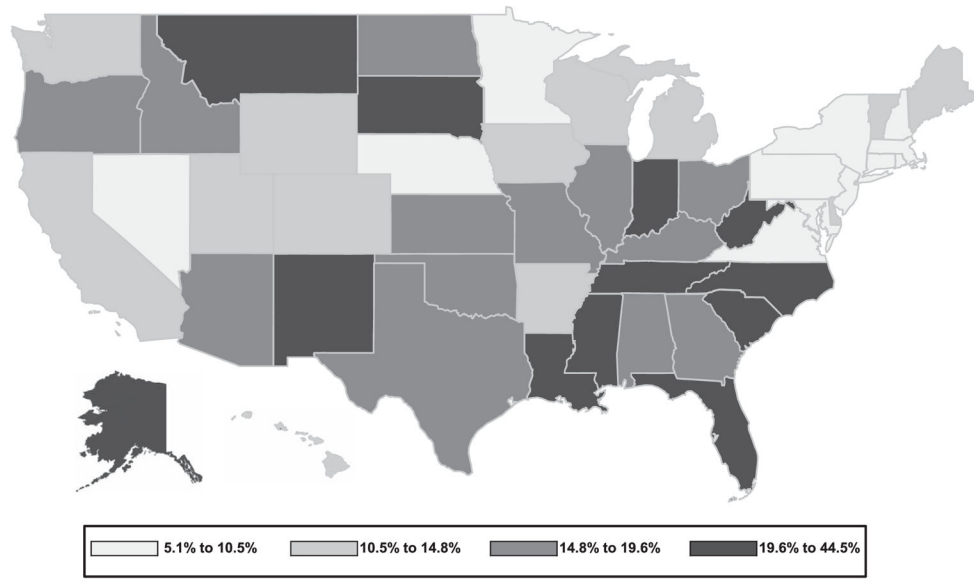


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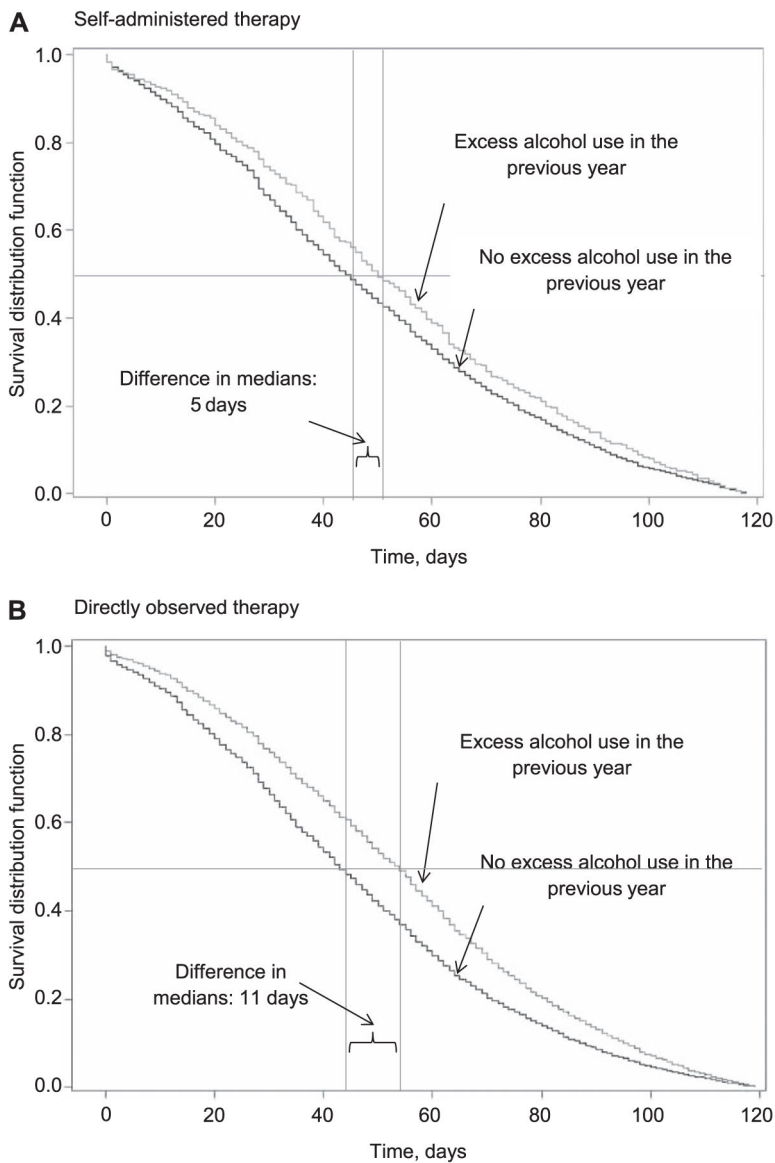
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**Figure 1.** Proportion of excess alcohol use among confirmed TB cases aged 15 years reported to the National TB Surveillance System, United States, 1997–2012 ( $n = 207\ 307$ ). \* Trend  $P < 0.0001$ .



**Figure 2.** Excess alcohol use in previous year among persons aged 15 years with reported tuberculosis diagnosis, United States, 1997–2012.



**Figure 3.** Time (in days) from start of treatment to conversion to negative sputum culture by excess alcohol use vs. no excess alcohol use in past year in individuals treated with **A)** self-administered therapy and **B)** directly observed therapy, among persons reported with TB, United States, 1997–2012. (Horizontal line indicates the median time point and vertical lines indicate the median time point to culture conversion.)

**Table 1**

Factors associated with excess alcohol use among persons aged 15 years reported with a TB diagnosis, United States, 1997–2012 ( $n = 207\,307$ )

Variable	$n$ (%) <sup>*</sup>	Subjects with documented excess alcohol use $n$ (%) <sup>*</sup>	Crude OR (95%CI)	Adjusted OR (95%CI) <sup>†</sup>
Demographic characteristics and behaviors				
Male sex	128 713 (62.10)	27 051 (20.62)	4.31 (4.17–4.45)	3.34 (3.21–3.47)
Age group, years				
15–24	22 559 (10.88)	1 317 (5.84)	1.0 (reference)	1.0 (reference)
25–44	74 706 (36.04)	12 117 (16.22)	3.12 (2.95–3.31)	2.82 (2.63–3.02)
45–64	63 789 (30.77)	14 920 (23.39)	4.92 (4.65–5.214)	4.094 (3.82–4.389)
65	46 253 (22.31)	2 604 (5.63)	0.96 (0.90–1.03)	1.21 (1.12–1.32)
Racial/ethnic group				
White	41 959 (20.30)	7 947 (18.94)	1.0 (reference)	1.0 (reference)
American Indian	2 544 (1.23)	1 040 (40.88)	2.96 (2.72–3.21)	2.73 (2.45–3.03)
Asian	49 922 (24.15)	1 662 (3.33)	0.15 (0.14–0.16)	0.49 (0.45–0.52)
Black	58 149 (28.13)	12 507 (21.51)	1.17 (1.14–1.21)	0.97 (0.94–1.01)
Hispanic	52 622 (25.46)	7 919 (15.05)	0.76 (0.73–0.78)	1.35 (1.29–1.43)
Multiple	676 (0.33)	49 (7.32)	0.34 (0.25–0.45)	0.80 (0.56–1.14)
Hawaiian/Pacific Islander	829 (0.40)	72 (8.68)	0.41 (0.36–0.46)	0.97 (0.72–1.32)
US born vs. foreign born	92 489 (44.69)	22 733 (24.58)	3.95 (3.85–4.06)	2.51 (2.40–2.63)
Homeless during last year	12 762 (6.21)	7 186 (56.31)	9.27 (8.93–9.62)	2.83 (2.70–2.97)
Injection drug use, past year	4 621 (2.25)	2 699 (58.41)	9.03 (8.52–9.57)	1.80 (1.67–1.95)
Non-injection drug use, past year	15 956 (7.78)	9 438 (59.15)	12.00 (11.59–12.41)	5.29 (5.05–5.53)
Clinical and epidemiological characteristics				
Known HIV-positive	17 600 (8.49)	4 247 (24.13)	1.77 (1.70–1.84)	1.40 (1.34–1.48)
Sputum smear result				
Negative	85 789 (44.13)	10 664 (12.43)	1.0 (reference)	1.0 (reference)
Positive	76 156 (39.17)	16 297 (21.40)	1.92 (1.87–1.97)	1.23 (1.18–1.28)
Not tested	32 477 (16.70)	2 137 (6.58)	0.50 (0.47–0.52)	1.06 (0.91–1.23)
Sputum culture result				
Negative	44 080 (22.80)	4 544 (10.31)	1.0 (reference)	1.0 (reference)
Positive	115 929 (59.95)	22 358 (19.31)	2.08 (2.01–2.15)	1.36 (1.29–1.43)
Not tested	33 360 (17.25)	2 135 (6.40)	0.60 (0.57–0.63)	0.85 (0.73–0.99)
Disease site				
Extra-pulmonary	41 367 (19.96)	2 622 (6.34)	1.0 (reference)	1.0 (reference)
Pulmonary	147 540 (71.20)	25 568 (17.33)	3.10 (2.97–3.23)	1.31 (1.23–1.39)
Both	18 316 (8.84)	2 744 (14.98)	2.60 (2.46–2.75)	1.20 (1.11–1.29)
Pulmonary cavity diagnosed by X-ray	47 160 (27.69)	10 238 (21.71)	1.55 (1.51–1.59)	1.21 (1.16–1.25)
Cluster involvement <sup>‡</sup>	7 209 (23.60)	1 010 (14.01) <sup>†</sup>	2.52 (2.35–2.70)	1.36 (1.23–1.50)
First-line drug resistance	16 893 (8.15)	2 083 (12.33)	0.79 (0.75–0.82)	0.90 (0.85–0.95)
Multidrug-resistant TB <sup>§</sup>	1 558 (1.35%)	164 (10.55)	0.563 (0.48–0.66)	—

Variable	<i>n</i> (%) <sup>*</sup>	Subjects with documented excess alcohol use <i>n</i> (%) <sup>*</sup>	Crude OR (95%CI)	Adjusted OR (95%CI) <sup>†</sup>
Extensively drug-resistant TB <sup>§</sup>	31 (0.36)	4 (12.90)	1.40 (0.57–3.42)	—
Directly observed therapy				
No (self-administered)	32 694 (16.79)	2 056 (6.29)	1.0 (reference)	1.0 (reference)
Yes	106 140 (54.49)	18 829 (17.74)	3.21 (3.06–3.37)	1.92 (1.81–2.03)
Both	55 941 (28.72)	8 251 (14.75)	2.58 (2.45–2.71)	1.82 (1.71–1.93)
Poor treatment outcomes	5 929 (3.41)	1 309 (22.09)	1.64 (1.54–1.75)	1.55 (1.04–2.31)
Reason for stopping treatment				
Completed	167 985 (86.92)	24 576 (14.63)	1.0 (reference)	1.0 (reference)
Died	15 057 (7.79)	2 569 (17.06)	1.20 (1.15–1.25)	1.16 (1.10–1.22)
Lost	4 678 (2.42)	1 100 (23.51)	1.79 (1.68–1.92)	1.25 (1.15–1.37)
Moved	4 189 (2.17)	547 (13.05)	0.88 (0.80–0.96)	1.11 (0.99–1.24)
Refused treatment	1 251 (0.65)	209 (16.73)	1.17 (1.01–1.36)	1.35 (1.11–1.62)

\* Numbers may not reflect 100% of data due to missing data.

<sup>†</sup> Variables with adjusted ORs were adjusted for all other variables in the table except for multidrug resistance, extensive drug resistance, and cluster involvement.

<sup>‡</sup> Variables that had >10% missing data were not included in the adjusted analysis.

<sup>§</sup> Data from 2009–2012 only.

TB = tuberculosis; OR = odds ratio; CI = confidence interval; HIV = human immunodeficiency virus.

**Table 2**

HRs for sputum culture conversion from start of treatment for incident TB cases\* and excess alcohol use by DOT vs. SAT

	Total <sup>†</sup> (n = 60 034) <sup>‡</sup>	Total converted by 4 months n (%)	Time to culture conversion, days, median [IQR]	HR (95%CI)	Adjusted HR <sup>§</sup>
All					
No excess alcohol use	46 925	43 311 (92.3)	43 [25–66]	1.23 (1.22–1.26)	1.20 (1.18–1.23)
Excess alcohol use	12 512	11 082 (88.6)	54 [31–76]	Reference	Reference
SAT					
No excess alcohol use	3 392	2 907 (85.7)	45 [26–69]	1.14 (1.01–1.27)	1.11 (0.99–1.25)
Excess alcohol use	308	255 (82.8)	50 [31–76]	Reference	Reference
DOT					
No excess alcohol use	30 041	27 751 (92.4)	43 [24–65]	1.27 (1.23–1.30)	1.22 (1.19–1.25)
Excess alcohol use	8 887	7 878 (88.6)	54 [31–75]	Reference	Reference

\* Limited to US cases aged 15 years, 1997–2012, with culture positivity, confirmed susceptibility to isoniazid, rifampin, and ethambutol, no known resistance to pyrazinamide, alive at the time of diagnosis, started on four-drug regimen, had documentation of negative sputum, had valid documentation date of conversion, culture converted before stopping treatment, culture converted within 4 months, responded either ‘yes’ or ‘no’ to excess alcohol use.

<sup>†</sup> Columns may not sum to 100% due to missing data.

<sup>‡</sup> Total with documented conversion.

<sup>§</sup> Adjusted for race/ethnicity, sex, age and homelessness. Missing cases excluded from analysis.

HR = hazard ratio; TB = tuberculosis; IQR = interquartile range; CI = confidence interval; DOT = directly observed therapy; SAT = self-administered therapy.