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Alcohol-Related Mortality in the WHO European Region: Sex-Specific Trends and Predictions

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Abstract

Aims: Alcohol is an important risk factor for morbidity and mortality, especially within the European region. Differences in per capita consumption and drinking patterns are possible reasons for regional differences and diverging trends in alcohol-related health outcomes.

Methods: Twenty-nine countries within the World Health Organization (WHO) European region were evaluated for trends and predictions in alcohol-related deaths within the last four decades using data available from the WHO Health for All database.

Results: Between 1979 and 2015, age-standardised death rates due to selected alcohol-related causes decreased significantly for both sexes in all assessed countries of the WHO European region, but regional differences are still pronounced. Assuming a similar trend in the future, the model predicted a further decrease until the year 2030.

Conclusion: Even though alcohol-related mortality may have decreased within the last decades, the detrimental effects of alcohol consumption and alcohol dependence remain a considerable burden of disease within Europe.

INTRODUCTION

Alcohol consumption has been proven to be the seventh leading avoidable risk factor for premature mortality, morbidity and social harm worldwide (Popova *et al.*, 2007; Rehm *et al.*, 2009; Rehm and Scafato, 2011; Collaborators GBDA, 2018).

Europe is traditionally the region with the highest level of per capita alcohol consumption (Popova *et al.*, 2007; Rehm *et al.*, 2009; Jewell and Sheron, 2010; Rehm and Scafato, 2011) with an average 85% of the population aged 15 years and older consuming any alcohol and 9.4% of the population (3.4% female, 15.3% male) being heavy drinkers (\geq 40 g of pure ethanol per day for women, \geq 60 g for men) in the European Union (EU) (Rehm *et al.*, 2013). An

estimated 7.4% of all disability and premature deaths are alcoholattributable within the EU (Popova *et al.*, 2007) with marked regional differences including rates as high as 12.1% in former socialist countries (Room *et al.*, 2005, Rehm *et al.*, 2009).

Disorders related to alcohol consumption include certain types of cancer (e.g. oropharynx, oesophageal, liver or breast cancer) (Schutze *et al.*, 2011), neuropsychiatric disorders (e.g. major depressive disorder), cardiovascular diseases (CVDs) as well as intentional and unintentional injuries (including road traffic accidents, falls, drownings, violence or self-inflicted injuries) (Rehm *et al.*, 2009, 2017). However, the most causally related somatic disorders due to alcohol consumption are liver diseases including cirrhosis and alcoholic hepatitis (Marmet *et al.*, 2014).

A considerable amount of research has been published on alcoholattributable mortality in the European region with detailed analysis of alcohol-attributable fractions (Popova *et al.*, 2007; Rehm *et al.*, 2007, 2011, 2013), yet to our knowledge, no study exists with a longitudinal approach evaluating alcohol-related mortality due to different causes in the European region over a time period of a few decades. To illustrate a bigger picture of alcohol-related mortality in countries of the European region in the last four decades, we conducted an analysis of alcohol-related deaths using data available from the World Health Organization's (WHO) European Health for All database (HFA-DB) (Europe).

MATERIALS AND METHODS

The data source for this study was the WHO HFA-DB, which receives data on basic demographics, health status, health determinants and risk factors from each country's national statistical authorities. The indicator 'selected alcohol-related causes' was used for evaluation, which includes standardised death rates (SDRs) for cancer of oesophagus and larynx (ICD-10 codes: C15, C32), mental and behavioural disorders due to use of alcohol (ICD-10 code: F10), chronic liver disease and cirrhosis (ICD-10 codes: K70, K73, K74, K76) and all external causes including traffic accidents, falls, drowning and assault. Due to disparities in documenting practices in the former USSR countries, some alcohol-related causes such as cancer of liver are not included.

After extracting data for all countries of the WHO European region, data of 49 countries were inspected for noticeable non-random deviations. These may result, for example, due to changes in diagnosis of disease or reporting of disease cases. After excluding data from 20 countries due to deviations, a total of 29 countries entered the analysis (for data specifics, see Supplementary Table S1).

Annual alcohol consumption rates were also extracted using the WHO HFA-DB

Trends were estimated by means of a linear mixed model using the log-transformed standardised rate as the dependent variable in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The independent variable was time including country as a random effect for the intercept and time as a linear continuous random effect. After a preliminary analysis, the regression model was sub-grouped by sex, thereby providing a better model fit than including the variable sex into the model as an independent variable. The aim of this analysis using linear time trend estimates was to provide comparable estimates between countries but not to achieve the best model fit for each country. The latter approach would be feasible by, e.g. joinpoint regression models (e.g. Joinpoint Regression Program, Statistical Research and Applications Branch, National Cancer Institute) but would lead to regression models of different complexity including varying numbers of estimates for sudden changes in time. This in turn would preclude a comparison between countries. Age SDRs are expressed in number of cases per 100,000 person years. Partial Spearman's correlation coefficient was calculated in order to adjust for overall mortality rate in the population as well as with annual per capita alcohol consumption.

RESULTS

Mortality trends

Between 1979 and 2015, age SDRs due to selected alcohol-related causes decreased significantly for both sexes in all included countries

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of the WHO European region (P < 0.0001). This finding also remains significant after adjusting for the countries' overall mortality by partialisation (95% confidence interval).

Mortality trends for female sex

According to our analysis, during the period between 1979 and 2015, mortality due to alcohol-related causes showed a significant overall decrease of 2.7% annual percentage change (APC) (P < 0.0001) in women in the included countries of the WHO European region.

The largest decreases in alcohol-related mortality were observed in Portugal (4.4% APC), Spain, Italy, France and Cyprus (>3.5% APC). The smallest changes were found in Kyrgyzstan (0.9% APC), Great Britain, Slovakia, Switzerland, The Netherlands and Norway (<2.0% APC) (see Fig. 1).

Mortality trends for male sex

Between 1979 and 2015, overall alcohol-related mortality due to selected causes in men declined significantly in the WHO European region with an average APC of 2.5% (P < 0.0001).

Portugal and Italy showed the greatest decline in alcohol mortality (4.0% and 4.1% APC, respectively). The smallest decline was observed in Great Britain and Kyrgyzstan (both 1.0% APC).

Female and male decline of alcohol-related SDRs were observed as parallel and did not show a significant difference in APCs.

Mortality trends and alcohol consumption

Annual alcohol consumption and alcohol-related mortality did not correlate significantly (P = 0.1084).

Tables showing level of alcohol consumption per capita and APCs of countries can be accessed in Supplementary Table S2.

Predictions

Assuming a similar trend in the future, we predicted a further decrease until the year 2030 in both sexes for all included countries (see Fig. 2).

DISCUSSION

In our study, a significant decline in alcohol-related mortality rates was observed for all included countries. Although a clear trend was evident, the countries' SDRs still differed within a considerable range exhibiting a West-East gradient with higher rates in countries such as Hungary and the Baltic states. Whereas in the early 1980s, higher rates were still observed in Mediterranean countries such as France and Portugal, they showed steeper declines over time (APCs around 4% for Portugal, Italy and France) for both sexes. These findings are in alignment with recent data on declining rates of alcohol consumption and liver cirrhosis mortality in these countries (Britton et al., 2003; Zatonski et al., 2010; Mackenbach et al., 2015). Reasons for different rates of alcohol-related mortality are mostly regarded within the spectrum of alcohol exposure and drinking culture (overall volume, patterns of drinking including heavy drinking occasions, type and quality of alcohol) (Popova et al., 2007; Rehm et al., 2009, 2017; Cutright and Fernquist, 2010). In previous studies, substantial variations in the geographical distribution of alcohol-attributable death rates throughout the EU have been reported with rates more than twice as high for men in the Eastern part compared with

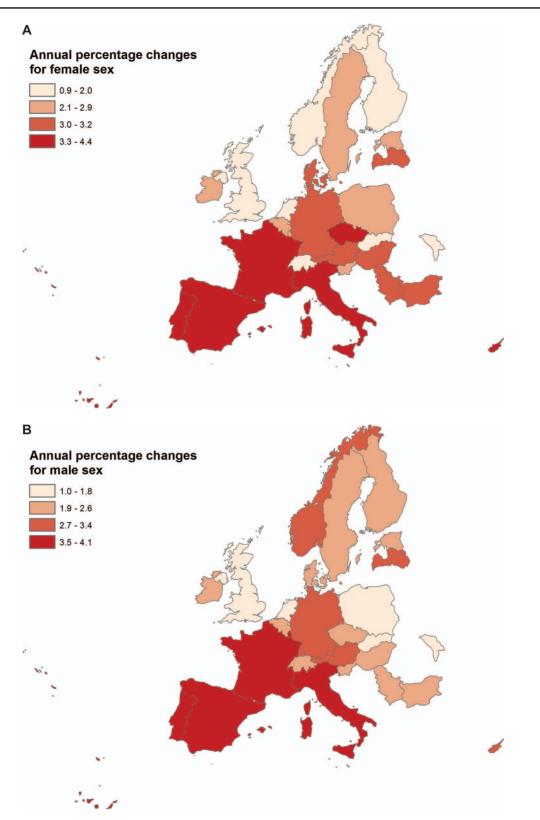


Fig. 1. (A) APCs (numbers in per cent) for female sex. (B) APCs (numbers in per cent) for male sex.

the older EU countries. Alcohol-related SDRs in the Baltics were even four times higher for men and almost three times higher for women (Rehm *et al.*, 2011). Although our data did not show such pronounced differences for female sex, a similar trend was revealed for male sex with Estonia and Latvia showing 2- to 3-fold higher SDRs compared with countries such as France and Italy.

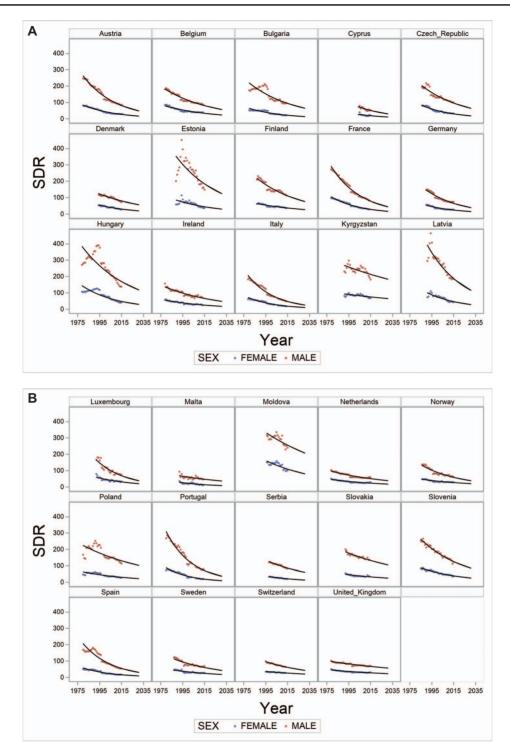


Fig. 2. Trends and predictions in alcohol-related mortality in the European region, 1979–2030; men (age-standardized mortality rates per 100,000); women (age-standardized mortality rates per 100,000).

These marked dissimilarities may not only be due to greater volume of consumed alcohol but also differences in drinking cultures with higher prevalence of heavy drinking occasions in Nordic countries as well as Eastern regions (Rehm *et al.*, 2013) and a traditional spirits culture in the Baltics (Rehm *et al.*, 2007).

In addition to different drinking cultures, research has shown that there is a socioeconomic gradient of alcohol-attributable harm (Marmot, 1997). People of lower socioeconomic status suffer to a greater extent from alcohol-related problems compared with people with higher socioeconomic status drinking the same amount of alcohol (Grittner *et al.*, 2012; Probst *et al.*, 2015).

The observed decline in alcohol-related mortality may have various reasons. For one, overall per capita consumption of alcohol in Europe has decreased in recent years (Rehm *et al.*, 2018). Another

explanation could be advances in healthcare including improved treatment options for cancer and liver diseases as well as better treatment for alcohol use disorders (Kraus et al., 2015). Considering liver cirrhosis rates, diverging trends were observed in recent decades with a significant decrease of rates in the Mediterranean and central European countries (e.g. France, Greece, Austria, Germany) and an increase in Eastern countries such as Hungary and the Republic of Moldova, but also the United Kingdom and Ireland (Zatonski et al., 2010). The decrease in mortality due to cirrhosis in the Mediterranean region has been described as being in accordance with a considerable decline of alcohol consumption in those countries. Also, liver transplantation, the only curative treatment for alcohol-related liver cirrhosis and severe alcoholic hepatitis, has become more widely used (Parker and Holt, 2018). Frequency of transplantation is highly variable by locality (Beresford and Lucey, 2018), but a 6-month abstinence rule pre-transplant is widely applied (Parker and Holt, 2018; Im et al., 2019). Yet, this practice has been challenged by data showing a comparable outcome in transplant procedures not adhering to this rule, as alcohol relapse rates and injury to the new liver graft were not increased in patient collectives with a shorter abstinence period pre-transplant (Mathurin et al., 2011; Beresford and Lucey, 2018; Im et al., 2019).

Other important factors for decline in alcohol consumption are legal regulations like increasing prices of alcoholic beverages as well as stricter laws and controls for drinking and driving such as breath testing and penalising drivers with illegally high concentrations of alcohol (Rehm *et al.*, 2011; Mackenbach *et al.*, 2015).

Declining trends in alcohol-related death rates did not differ significantly between men and women in the countries included in our analysis. Yet, there were marked differences in absolute values of SDRs between sexes with men showing higher rates than women. The most pronounced differences were observed for Latvia (SDR in men 4 times as high as in women), Portugal (3.6 times higher in men) and Slovakia (3.5 times higher in men). These rates are similar to findings of earlier studies (Rehm *et al.*, 2009, 2011).

Limitations

Whereas the Global Burden of Disease studies are based on alcohol attributable fractions and require information on amount of alcohol consumed, prevalence of diseases and relative risk for outcomes (Rehm *et al.*, 2009; Whiteford *et al.*, 2013) to create a more accurate estimate of actual deaths caused by alcohol, we solely relied on data containing total SDRs due to selected causes, which are known to be related to alcohol consumption. Consequently, we cannot report on actual alcohol-attributable deaths. Yet, in our opinion, our data depict an important trend. For one, they include crucial outcomes like mortality due to liver diseases such as cirrhosis, which has been regarded as one of the most immediate indicators for reductions in consumption, since it has a much shorter latency than the development of cancer (Jewell and Sheron, 2010; Rehm *et al.*, 2011).

The HFA-DB data are not restricted to reporting deaths from liver disease, which were coded as 'alcoholic liver disease/cirrhosis' leading to a possible overestimation. On the other hand, it has been suggested that deaths from alcoholic liver disease might often be reported under different causes due to stigmatisation. Even in liver damage due to different aetiologies, further continuation of alcohol use, also at relatively low quantities, can lead to death (Rehm *et al.*, 2017). Therefore, it seems plausible to include other diagnoses as well.

Another limitation of our data is that it does not include CVDs, which have been established as a common alcohol-related cause of death (Bobak *et al.*, 2016; Rehm *et al.*, 2017, 2018).

Lastly, an inherent problem with using national registries is potential variance in reporting practices between countries, which may be due to different factors such as autopsy rates (Britton *et al.*, 2003), differences in coding for cause of death (Mackenbach *et al.*, 2015) or stigma.

CONCLUSION

According to our data, alcohol-related causes of death have significantly declined in the WHO European region. Yet, a West–East gradient can still be observed with Eastern countries exhibiting markedly higher rates of alcohol-related mortality. This is in alignment with the findings of earlier studies showing pronounced socioeconomic inequality concerning morbidity and mortality due to alcohol consumption. Even though rates in mortality may have decreased within the last decades, the detrimental effects of alcohol consumption and alcohol dependence remain a considerable burden of disease within Europe.

SUPPLEMENTARY MATERIAL

Supplementary material is available at Alcohol and Alcoholism online.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Beresford TP, Lucey MR. (2018) Towards standardizing the alcoholism evaluation of potential liver transplant recipients. Alcohol Alcohol 53:135–44.
- Bobak M, Malyutina S, Horvat P, et al. (2016) Alcohol, drinking pattern and all-cause, cardiovascular and alcohol-related mortality in Eastern Europe. Eur J Epidemiol 31:21–30.
- Britton A, Nolte E, White IR, *et al.* (2003) A comparison of the alcoholattributable mortality in four European countries. *Eur J Epidemiol* 18:643–51.
- Collaborators GBDA. (2018) Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 392:1015–35.
- Cutright P, Fernquist RM. (2010) Predictors of per capita alcohol consumption and gender-specific liver cirrhosis mortality rates: thirteen European countries, circa 1970-1984 and 1995-2007. Omega 62:269–83.
- Grittner U, Kuntsche S, Graham K, et al. (2012) Social inequalities and gender differences in the experience of alcohol-related problems. Alcohol Alcohol 47:597–605.
- Im GY, Cameron AM, Lucey MR. (2019) Liver transplantation for alcoholic hepatitis. J Hepatol 70:328–34.
- Jewell J, Sheron N. (2010) Trends in European liver death rates: implications for alcohol policy. *Clin Med (Lond)* 10:259–63.
- Kraus L, Osthus S, Amundsen EJ, et al. (2015) Changes in mortality due to major alcohol-related diseases in four Nordic countries, France and Germany between 1980 and 2009: a comparative age-period-cohort analysis. Addiction 110:1443–52.
- Mackenbach JP, Kulhanova I, Bopp M, et al. (2015) Inequalities in alcoholrelated mortality in 17 European countries: a retrospective analysis of mortality registers. PLoS Med 12:e1001909.
- Marmet S, Rehm J, Gmel G, et al. (2014) Alcohol-attributable mortality in Switzerland in 2011—age-specific causes of death and impact of heavy versus non-heavy drinking. *Swiss Med Wkly* 144:w13947.
- Marmot M. (1997) Inequality, deprivation and alcohol use. *Addiction* **92**(Suppl 1): \$13–20.
- Mathurin P, Moreno C, Samuel D, et al. (2011) Early liver transplantation for severe alcoholic hepatitis. N Engl J Med 365:1790–800.

- Parker R, Holt A. (2018) Transplanting patients with alcohol-related liver disease in the National Health System: new rules and decisions. *Alcohol Alcohol* 53:145–50.
- Popova S, Rehm J, Patra J, et al. (2007) Comparing alcohol consumption in central and eastern Europe to other European countries. Alcohol Alcohol 42:465–73.
- Probst C, Roerecke M, Behrendt S, et al. (2015) Gender differences in socioeconomic inequality of alcohol-attributable mortality: a systematic review and meta-analysis. Drug Alcohol Rev 34:267–77.
- Rehm J, Gmel GE Sr, Gmel G, et al. (2017) The relationship between different dimensions of alcohol use and the burden of disease-an update. Addiction 112:968–1001.
- Rehm J, Guiraud J, Poulnais R, et al. (2018) Alcohol dependence and very high risk level of alcohol consumption: a life-threatening and debilitating disease. Addict Biol 23:961–8.
- Rehm J, Mathers C, Popova S, *et al.* (2009) Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet* 373:2223–33.
- Rehm J, Scafato E. (2011) Indicators of alcohol consumption and attributable harm for monitoring and surveillance in European Union countries. *Addiction* 106(Suppl 1):4–10.

- Rehm J, Shield KD, Gmel G, et al. (2013) Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. Eur Neuropsychopharmacol 23:89–97.
- Rehm J, Sulkowska U, Manczuk M, et al. (2007) Alcohol accounts for a high proportion of premature mortality in central and eastern Europe. Int J Epidemiol 36:458–67.
- Rehm J, Zatonksi W, Taylor B, *et al.* (2011) Epidemiology and alcohol policy in Europe. *Addiction* **106**(Suppl 1):11–9.
- Room R, Babor T, Rehm J. (2005) Alcohol and public health. Lancet 365:519–30.
- Schutze M, Boeing H, Pischon T, et al. (2011) Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. BMJ 342:d1584.
- Whiteford HA, Degenhardt L, Rehm J, et al. (2013) Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. Lancet 382: 1575–86.
- Zatonski WA, Sulkowska U, Manczuk M, *et al.* (2010) Liver cirrhosis mortality in Europe, with special attention to Central and Eastern Europe. *Eur Addict Res* 16:193–201.