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## Alcohol-attributable mortality in Europe

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# Alcohol-attributable mortality in Europe

Past trends and their effects on overall mortality variations

Sergi Trias Llimós

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# Alcohol-attributable mortality in Europe

Past trends and their effects on overall mortality variations

Phd thesis

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# **Chapter 1**

Introduction

#### 1.1. Introduction and objective

Men and women living in Europe today have longer life expectancies than ever before (Leon, 2011; Mackenbach, 2013). The average life expectancy at birth in Europe is now (2010-15) around 77.2 years, up from 67.1 years in 1955-60 (UN Online, 2017). However, this astonishing increase in life expectancy is not distributed equally across European populations, as there is considerable variation in mortality levels between European countries (especially between Eastern and other European countries) and between men and women. Moreover, the speed of the decline in mortality has not been steady over time across European countries or between the sexes, as life expectancy stagnated or even decreased in Eastern European countries from 1975 onwards, especially among men (Leon, 2011). Understanding of the factors that contribute to this variation in mortality patterns is essential for health policy-makers seeking to reduce health inequalities in Europe.

As lifestyle factors are major avoidable determinants of health and mortality (Dahlgren and Whitehead. 1991), differences in lifestyle could explain the variation in mortality levels observed across countries, between the sexes, and over time. There is strong evidence for Europe that smoking, alcohol consumption, unhealthy eating, and insufficient physical activity (resulting in obesity) are the main lifestyle factors that contribute to increased mortality (WHO, 2009). A large body of literature has analysed the impact of smoking on the variation in mortality in several populations, and over time (e.g., Janssen & van Poppel, 2015; Lopez et al., 1994; Luy & Wegner-Siegmundt, 2015; McCartney et al., 2011; Pampel, 2005). However, there is little existing research on the impact of alcohol and obesity on overall variation in mortality across countries, between the sexes, and over time.

Studying the role of alcohol in mortality variation across Europe is especially meaningful. First, epidemiological studies have confirmed that alcohol consumption has a large impact on several diseases and on overall mortality (Rehm et al., 2010; Rehm & Imtiaz, 2016; Rehm et al., 2017; Wood et al., 2018). Second, alcohol consumption is higher in Europe than in other parts of the world (WHO, 2014). Especially worrisome is the increasing prevalence of alcohol abuse among young people in several European countries (Franco, 2015), as this trend suggests that members of these recent birth cohorts could be at high risk of developing alcohol-related health problems as they grow older (Dawson et al., 2008; Hingson et al., 2006). Third, levels and patterns of

alcohol consumption have been shown to vary across European populations. There is, for example, evidence that on average, men consume more alcohol than women (Leon et al., 2009; Mäkelä et al., 2006); and that compared to Southern European countries, Eastern European countries have a higher prevalence and riskier patterns of alcohol consumption (Popova et al., 2007), as well as less favourable alcohol consumption trends (European health for all database (HFA-DB) WHO/Europe, 2016). Fourth, it has been postulated that these differences in alcohol consumption and drinking patterns across countries, between men and women, and over time contribute to the overall differences in mortality levels across Europe (e.g. McCartney et al., 2011; Meslé et al., 2002). Yet despite this evidence that alcohol consumption plays an important role in mortality, there is little existing research on its impact on variation in overall mortality across countries and between men and women.

Most of the previous studies on alcohol-attributable mortality did not use both a comparative and a temporal approach. These analyses either investigated alcohol-attributable mortality at a single point in time for a group of countries (e.g. Rehm et al., 2007), or they focused on time trends in a single country (e.g. Martikainen et al., 2014). Studies on time trends in alcoholattributable mortality have often ignored the birth cohort dimension, even though it has been proven that taking this dimension into account is essential when examining alcohol use (Keyes et al., 2011). It has, for example, been shown that individuals belonging to the same birth cohort tend to adopt similar drinking behaviours during younger adulthood, which are in turn correlated with their patterns of alcohol use over the life course (Eliasen et al., 2009; Pitkänen et al., 2005) and their subsequent alcohol-related health problems (Hingson et al., 2006; Hingson & Zha, 2009).

There is even less research on the role of alcohol in variation in overall mortality. While one previous study related alcohol-attributable mortality to differences in overall mortality between countries, it did not investigate this relationship over time (Zatoński, 2008). Finland is the only country for which the impact of alcohol on overall mortality trends has been studied (Martikainen et al., 2014). In addition, no previous study has attempted to assess the role of alcohol consumption in sex differences in life expectancy using both a comparative and a temporal approach.

The aim of this PhD thesis is to assess past alcohol-attributable mortality trends in Europe and to examine the role of alcohol in overall mortality differences across countries and between men and women.

More specifically, the sub-objectives of this research are:

- to assess past alcohol-attributable mortality trends, and to look at how these trends differ between countries, the sexes, and birth cohorts (=generations); and
- 2) to assess the role of alcohol in overall mortality differences across countries, between the sexes, and over time.

This study is innovative in a number of ways. First, it focuses on the impact of alcohol consumption on variation in overall mortality across countries, between the sexes, and over time in Europe; whereas previous studies on lifestyle-related mortality trends in Europe focused mainly on the effects of smoking. Second, both a comparative (country, sex) and a temporal approach are used in studying alcohol-attributable mortality. Third, the cross-country comparative approach is applied to both Eastern and Western European countries. Fourth, the study assesses time trends that include not just age and period, but the third temporal dimension of birth cohort, which has often been ignored in previous studies. The results of these analyses are expected to provide us with a more complete understanding of these trends.

#### 1.2. Overall mortality decline

In recent decades, mortality has been gradually declining in most European countries (Leon, 2011). However, this decrease in mortality has not been steady over time, and the speed of the decline has differed considerably across countries. In Eastern Europe, for example, mortality levels have stagnated and even increased during certain periods (e.g. Leon, 2011; Mackenbach, 2013). Nonetheless, in general terms, overall mortality has declined in Europe, in line with the Epidemiological Transition Theory (ETT). The ETT is the most well-regarded theory for explaining the complex changes in patterns of health and diseases and on the interaction between these patterns and their demographic, economic, and sociological determinants and consequences for societies from pre-modern to modern times (Omran, 1971; Omran, 1998). The first stage of the ETT refers to the periods of high and fluctuating mortality that characterised Western Europe until the beginning of the 19th century. The second stage aims to explain the periods of receding pandemics and increasing in life expectancy up until around 50 years. The third and fourth stages of the ETT are directly linked to this PhD research. The third stage of the ETT is characterised by the predominance of degenerative, stress-related, and manmade diseases. The main features of the fourth stage, which started around 1970 in Western countries, are decreases in cardiovascular mortality and intentional lifestyle modifications (e.g., smoking cessation or changes in drinking habits). Finally, Omran has hypothesised that additional stages characterised by paradoxical longevity and persistent inequalities will be observable in the future (Omran, 1998).

The speed of the mortality decline and the timing of the transitions from one stage to another have varied across European countries. The mortality decline was not steady because the extent to which overall mortality decreased varied between countries, resulting in patterns of mortality convergence-divergence across Europe. The clearest example of this variation in trends is the stagnation and decline in life expectancy in Eastern Europe from around 1970 until the 1990s, especially among men; and the stagnation in life expectancy in certain years, especially among men, in some Western European countries, such as the Netherlands or Denmark (Janssen & Kunst, 2005; Lindahl-Jacobsen et al., 2016). In contrast, over the same period, life expectancy in other European countries, especially among women, did not stagnate, but was gradually increasing. Thus, a divergence in mortality trends across Europe could be observed (Leon, 2011; Meslé et al., 2002). Furthermore, at the national level the speed of mortality decline differed between men and women, and clearly affected the life expectancy advantage of women relative to that of men (Luy & Wegner-Siegmundt, 2015; Oksuzyan et al., 2008). In general, these processes of mortality convergence and divergence in Europe are linked to the different ETT stages across populations, and have been well-described in the literature (Vallin & Meslé, 2004). Moreover, these processes reflect differences in the timing of the ETT, which illustrates the growing contributions of lifestyle factors to mortality differentials across Europe. As variation in mortality trends is of considerable concern to policy-makers (Mackenbach, 2013), a more exhaustive analysis of mortality differences is needed.

#### **1.3. Mortality variation in Europe**

While mortality levels are lower now than ever before, there is significant variation in mortality across European countries, between the sexes, and over time. In 2015, life expectancy in the EU-28 ranged from 74.6 years in Lithuania to 83.0 years in Spain (Eurostat, 2017), and was even lower in other non-EU Eastern European countries (Rechel et al., 2013). In recent years, life expectancy was, for example, 73.9 years in Belarus (2015), 71.3 years in Ukraine (2013), and as low as 70.9 years in Russia (2014) (HMD, n.d.). Overall life expectancy was about 11 years lower in Eastern Europe than in the other European regions (Western, Southern, Northern) among men, and was about five to six years lower among women (Kaneda & Dupuis, 2017). Clearly, life expectancy levels differ considerably not just between Eastern Europe and other European regions, but between the individual countries of Eastern Europe.

However, differences in mortality trends have been observed not only between countries, but between population sub-groups within the same country. From a demographic perspective, the higher life expectancy of women relative to that of men is especially relevant. Whereas the gender gap in life expectancy is four years worldwide, it is six years in Europe (Kaneda & Dupuis, 2017). However, the sizes of these gender differences vary across Europe. For example, whereas male life expectancy is five years lower than female life expectancy across the EU-28, the gender differences in life expectancy are even larger in Eastern Europe (10 years), and have been larger still in the past (Rochelle et al., 2015).

#### 1.4. Determinants of mortality variation

Before discussing the determinants of mortality variation, it is crucial that we understand the determinants of mortality levels, or – more broadly – the determinants of individual health.

Determinants of individual health can be broadly divided into individual and contextual determinants (Dahlgren and Whitehead. 1991). Individual determinants include genetic susceptibility, socio-demographic characteristics (e.g., age, gender, educational attainment, or marital status), and individual lifestyle factors (e.g., alcohol or tobacco consumption) (Young. 1998). For example, it is well-known that women live longer than men and that mortality risks increase with age; but also that individual health is negatively affected by unhealthy lifestyle behaviours, such as smoking or drinking alcohol. The health of an individual is, however, also influenced by the context in which s/he lives. These contextual determinants include the individual's socio-economic and socio-cultural circumstances (e.g., societal acceptance of unhealthy behaviours), access to health care, and political context (Shaw, et al. 2002; Young. 1998).

When the aim is to explain variation in mortality across countries, between the sexes, and over time, the same determinants apply, but in a different manner. Thus, in relation to the determinants of mortality/health at the population level, contextual versus compositional factors are distinguished (Shaw, et al. 2002). The contextual factors are the contextual determinants of individual health outlined in the previous paragraph. The compositional factors are the composition of the individual determinants in a country, such as the share of elderly, the share of people with higher education, or the share of people with unhealthy lifestyles (Sloggett & Joshi, 1994). The composition by age is of particular importance. For this reason, previous research on variation in mortality often controlled for the role of age composition by means of age-standardisation (e.g. Jasilionis et al., 2011; Mäkelä, 1998).

In addition to examining the role of differences in age composition, previous research on the determinants of variation in mortality over time and between countries has highlighted the importance of contextual factors and differences in shares of people with unhealthy lifestyles. For example, East-West life expectancy differences have been directly linked to socioeconomic and health care system differences (Leon, 2011; Moskalewicz & Österberg, 2016; Shkolnikov et al., 1998). However, most of the existing research on the impact of lifestyle factors on overall mortality variation has focused exclusively focused on smoking behaviours (e.g. Janssen et al., 2015; Lindahl-Jacobsen et al., 2016; Renteria et al., 2016), while only a few studies have also investigated the impact of alcohol consumption on overall mortality variation (Martikainen et al., 2014; Zatoński, 2008).

Previous research on the determinants of sex differences in mortality has highlighted the importance of biological factors, socio-economic factors, and behavioural factors (especially smoking) (Luy & Wegner-Siegmundt, 2015). The biological explanations that have been proposed are mainly related to hormones, autoimmunity, and genetics (Austad, 2006; Oksuzyan et al., 2008). In Western Europe, an individual's socio-economic circumstances – i.e., his/her socio-economic position and employment status – seems to have limited influence on his/her life expectancy (Vallin, 1995). However, significant gender differences been observed in social role determinants, health care access, and use of treatment; and these differences have been found to contribute to the overall female mortality advantage (Oksuzyan et al., 2008; Waldron, 1985). Moreover, the lifestyle factors that influence mortality differ by gender: in general, men are more likely than women to take risks; a pattern that has been attributed to gender-specific ways of coping with stress and behavioural norms (Byrnes et al., 1999; Weidner & Cain, 2003). For example, compared to women, men are more likely to use unhealthy substances like alcohol, tobacco, and psychoactive drugs; and to engage in risky driving behaviours (Oksuzyan et al., 2008).

It has been estimated that biological factors account for up to two years of the gender differences in life expectancy in low-mortality countries (Luy, 2003); whereas individual factors – and lifestyle behaviours in particular – account for a bigger share of these differences, especially in low-mortality countries with a large gender gap in mortality. As smoking has been widely considered the lifestyle factor with the greatest impact on mortality, gender differences in smoking are often cited to explain gender differences in mortality (e.g. Janssen & van Poppel, 2015; McCartney et al., 2011; Preston & Wang, 2006).

Much of the previous research on the determinants of mortality variation over time and across countries has postulated that macro-economic factors are the main determinants of mortality variation. For example, it has been argued that in the former Soviet republics, the socio-economic and health crises of the early 1990s contributed to life expectancy stagnation or decline (Leon, 2011). It has also been posited that the contextual situations of these countries triggered the collapse of the health system and led to social deprivation, which in turn contributed to increased psychological distress levels and the adoption of unhealthy lifestyle behaviours like alcohol abuse (Shkolnikov et al., 1998). In other European countries, where the contextual situation did not abruptly change, smoking has been described as an important determinant of temporal stagnation in the increase in life expectancy, particularly among men (Janssen & Kunst, 2005; Janssen et al., 2013; Lindahl-Jacobsen et al., 2016). In general, women appear to have adopted unhealthy lifestyle behaviours decades later than men; a pattern that has been explained by changes in the position of women in society (changes in gender roles), and by the increased participation of women in the labour market (Waldron, 1985).

In sum, it is important to consider lifestyle factors when seeking to explain variation in mortality between countries and between the sexes; and changes in these trends over time. Whereas previous research on lifestyle-attributable mortality has focused on the impact of smoking, this PhD thesis will focus on the impact of alcohol consumption on mortality patterns.

#### 1.5. The important role of alcohol consumption

Studying the role of alcohol consumption in mortality variation in Europe is meaningful for four important reasons, which will be explained in detail in this section: 1) alcohol consumption has a large impact on mortality; 2) alcohol consumption levels are high in Europe; 3) alcohol consumption levels vary between European countries; and 4) the impact of alcohol on mortality varies across Europe.

#### 1.5.1. The effect of alcohol consumption on mortality

Alcohol consumption has a significant impact on the risk of contracting several diseases and on overall mortality. Alcohol use and abuse can have both acute and chronic effects. The main diseases linked to alcohol abuse are liver cirrhosis, alcohol use disorders, cancers, cardiovascular diseases, infectious diseases, and injuries (Rehm et al., 2017). The relationship between alcohol consumption and specific health outcomes is, however, complex and multidimensional; and can vary depending on both the volume of alcohol consumed and the

patterns of drinking (e.g., binge drinking, or drinking several alcoholic drinks on a single occasion) (Rehm et al., 2010; Rehm et al., 2017).

Most of the cohort studies and meta-analyses that have looked at the impact of alcohol on allcause mortality have found a J-shaped relationship between the volume of drinking and mortality (Di Castelnuovo et al., 2006; Gmel et al., 2003; Jayasekara et al., 2015); whereby moderate drinking is associated with a lower mortality risk than abstaining, but drinking more than moderately is associated with a higher mortality risk. However, the claim that moderate alcohol consumption has a protective effect on health has recently been criticised (Chikritzhs et al., 2015; GBD 2016 Alcohol Collaborators, 2018; Knott et al., 2015; Wood et al., 2018). Importantly, the effects of overall consumption on mortality appear to be moderated by drinking patterns, as studies from Eastern Europe have clearly shown that binge drinking is especially risky (e.g. Leon et al., 2007).

The most important alcohol-attributable causes of death are alcoholic liver cirrhosis and mental and behavioural disorders due to the use of alcohol. These causes of death are wholly attributable to alcohol, as they would not have occurred without alcohol consumption. At the same time, alcohol consumption can contribute to mortality from injuries and other diseases, including ischaemic stroke, several cancers, and pancreatitis. These causes of death are partly attributable to alcohol.

#### **1.5.2.** Alcohol consumption in Europe

Alcohol consumption patterns in Europe are worrisome. Worldwide, Europe is the region with the highest levels of alcohol consumption: the volume of pure alcohol consumed per capita per year has been estimated at 10.9 litres in Europe, compared to 8.4 litres in the WHO region of the Americas, 6.8 litres in the WHO Western Pacific region, and 6.2 litres worldwide (World Health Organization, 2014).

There are, however, significant differences in alcohol consumption levels between European countries. Especially striking is the gap in consumption between Eastern and Western Europe, with most Eastern European countries having higher alcohol consumption levels than Mediterranean and Nordic countries. According to WHO estimates, the volume of pure alcohol consumed per capita per year is more than 12.5 litres in most Eastern European countries, but is lower in other European countries, and especially in the Netherlands (9.9), Sweden (9.2), Norway (7.7), and Italy (6.7) (World Health Organization, 2014). Furthermore, compared to

Western European countries, Eastern European countries have traditionally had higher levels of unrecorded alcohol consumption and riskier drinking patterns (Moskalewicz & Österberg, 2016; Popova et al., 2007), which are known to be especially harmful to health (Szcs et al., 2005). Moreover, the gender differences in alcohol consumption patterns are greater in Eastern Europe than elsewhere. In Europe as a whole, men consume 1.5-2 times more alcohol than women (Mäkelä et al., 2006); but in Eastern Europe, men consume up to 5-6 times more alcohol than women, largely through binge drinking (Popova et al., 2007).

#### 1.5.3. Time trends in alcohol consumption in Europe

The important differences in alcohol consumption levels across Europe that were mentioned above have not been steady over time. In recent years, overall alcohol consumption levels and patterns of drinking have tended to converge across countries, mainly due to a convergence in the types of beverages consumed (increasing beer consumption in Southern and Eastern Europe) across Europe (Franco, 2015; Gual & Colom, 1997; Moskalewicz & Österberg, 2016). In Southern European countries, where alcohol consumption was extremely high in the 1970s and wine has traditionally been the most consumed beverage, alcohol consumption has clearly been declining from the mid-1970s onwards (Gual & Colom, 1997). But in other countries (e.g., Russia and the Baltic states), alcohol consumption trends have been more irregular over the last two decades (World Health Organization, 2014). Specifically, over the 1992-2012 period, alcohol consumption declined by about 20% in most of the Southern European countries, but increased by 50% in countries such as Russia and Estonia (Franco, 2015).

Worrisome as well is the increase in alcohol consumption among adolescents and young adults in Europe. For example, an analysis of survey data for 20 OECD countries found that the proportion of individuals who reported having consumed their first drink by age 15 increased from 56% in 2001-02 to 70% in 2009-10, and from 50% to 69% among men and women, respectively (Franco, 2015). Similarly, there is evidence that heavy episodic drinking has increased in most European countries among both adolescents and young adults (Franco, 2015; Harkonen & Mäkelä, 2011; Meng et al., 2014; Pabst et al., 2010). Patterns of alcohol consumption among the younger generations are especially important, as the link between overall consumption and alcohol-related problems over the life course is well-established (Courtney et al., 2018; Pitkänen et al., 2005). Individuals belonging to the same birth cohort are more likely to adopt relatively similar drinking behaviours than individuals belonging to other cohorts who have been influenced by other contextual situations. Collecting information on the recent trends in alcohol consumption and patterns of drinking among the younger generations may provide insights into their consumption patterns over the life course, and their future health problems.

Furthermore, there is evidence that the gender gap in alcohol consumption is currently shrinking because of the changing position of women in society and the overall convergence of alcohol drinking patterns among young adults (Slade et al., 2016).

#### 1.5.4. The impact of alcohol on mortality variation

The abovementioned differences in alcohol consumption and drinking patterns across countries, between men and women, and over time appear to contribute significantly to overall mortality differences across Europe (McCartney et al., 2011; Meslé et al., 2002).

Studies that have examined the contributions of specific broader causes of death to overall mortality trends have suggested that alcohol consumption plays an important role, especially in Eastern European countries (Meslé et al., 2002; Shkolnikov et al., 1998; Shkolnikov et al., 2001). Indeed, the large impact of alcohol use on overall and cause-specific mortality is well-documented, especially for Eastern European countries (Bobak et al., 2016; Leon et al., 2007; Zaridze et al., 2009). It is therefore likely that differences in alcohol consumption trends help to explain East-West differences in mortality. Furthermore, it has been suggested that alcohol consumption plays a major role in overall gender differences in mortality, especially in Eastern Europe (Luy & Wegner-Siegmundt, 2015; McCartney et al., 2011).

Despite the evidence that drinking patterns influence mortality, the impact of alcohol consumption on the variation in overall mortality across countries and between men and women has scarcely been researched. As only a few previous studies have formally quantified the role of alcohol in mortality variation, a careful study of past trends in alcohol-attributable mortality is clearly needed.

The few studies that have assessed alcohol-attributable mortality across multiple European countries found important differences across countries, with the levels generally being higher in Eastern European countries than elsewhere in Europe (Rehm et al., 2007). The studies that took gender into consideration found that the alcohol-attributable mortality rates and fractions for men were at least twice as high as those for women (Kraus et al., 2015; Rehm et al., 2007). These studies also confirmed that there are large time trend differences between countries. It has, for example, been shown that mortality has been decreasing in France and increasing in

Finland over the last three decades, but that the gender differences in these trends have remained roughly similar within the same country (Kraus et al., 2015).

However, most of the previous studies that examined alcohol-attributable mortality did not simultaneously employ a cross-national and a temporal perspective. Furthermore, the studies that assessed past trends in alcohol-attributable mortality have often ignored the cohort dimension, and have mostly focused on a selection of countries. But as was outlined in section 1.5.3, studying birth cohorts is useful for understanding alcohol consumption, and possibly for understanding mortality trends as well.

The few existing studies that assessed the birth cohort dimension in alcohol-related mortality did not focus on trends over a long historical period, and they did not make pan-European comparisons. The overall results of these studies did, however, confirm the importance of the birth cohort dimension when examining alcohol-attributable mortality trends (Corrao et al., 1997; Kraus et al., 2015; Rosén & Haglund, 2006).

Research on the impact of alcohol consumption on overall mortality variation has been even more sporadic. To the best of our knowledge, only one previous study compared the effect of alcohol use on life expectancy across European countries and at a single point in time (Zatoński, 2008). In this study, the impact of alcohol consumption – as measured by wholly alcohol-attributable mortality plus shares of partly alcohol-attributable mortality – was estimated to account up to 30% of the differences between individual Eastern European countries and the EU-15 in 2002 (Zatoński, 2008). Research on the impact of alcohol on overall mortality over time is scare, and has so far been conducted for Finland only. It has, for example, been estimated that the impact of alcohol on life expectancy in Finland was around two years in 1990 (Mäkelä, 1998), and remained at that level at least up until 2005 (Martikainen et al., 2014).

In addition, none of the previous assessments of the effect of alcohol consumption on sex differences in life expectancy used both a comparative and a temporal approach. The one previous comparative study on this topic examined 30 European countries, but did so only for the year 2005. The main conclusion of this study was that alcohol appears to play an important role in the gender gap in life expectancy, especially in Eastern European countries (between 20% and 30%) (McCartney et al., 2011).

#### 1.6. This study

#### 1.6.1. Approach

This PhD thesis adopts an interdisciplinary approach by conducting research at the intersection of demography, epidemiology, and public health.

The main aim of this research is to investigate the impact of alcohol consumption on health. While this topic is often addressed in epidemiology, the current study investigates it from a demographic population-level perspective, and with a focus on mortality. By examining the impact of alcohol on mortality variation across countries, between the sexes, and over time, this PhD thesis has a high degree of public health relevance.

More specifically, this PhD research uses both a comparative and a temporal approach when studying alcohol-attributable mortality and assessing the impact of alcohol consumption on mortality variation. This aspect of the thesis is novel, as previous research on this topic used either a temporal or a comparative approach, but not both. The differences between and within Eastern and Western Europe and the differences between the sexes are studied from a comparative point of view. The long-term trends and the role of birth cohort effects are studied from a temporal perspective.

To obtain population-level estimates of the impact of alcohol consumption on mortality, this PhD research evaluates and employs a range of techniques for linking the available demographic and epidemiological information. Thus, this PhD research carefully compares different methods for estimating alcohol-attributable mortality.

Furthermore, several advanced demographic techniques and statistical modelling techniques are used, including life table analysis, decomposition techniques, and age-period-cohort modelling (see 1.6.3).

#### 1.6.2. Setting

This PhD thesis draws upon newly available demographic and epidemiological data that cover a selection of the adult national populations aged 20 or older of both Central and Eastern European (CEE) and Western European countries from the 1950s onwards. Depending on the research question and the specific data needed, the countries, time periods, and age ranges studied differ across the chapters.

#### 1.6.3. Data and methods

The demographic data used in the analyses are population-level all-cause and cause-specific mortality data by country, year, sex, and age that are drawn from the Human Mortality Database (HMD, n.d.) the WHO Mortality database (WHO Mortality Database, n.d.), and the newly released Human Cause-of-Death Database (HCD, n.d.). All of these datasets provide comparable age- and sex-specific mortality for several countries.

The epidemiological data used in the research are estimates of overall alcohol-attributable mortality from the Global Burden of Disease Study 2013 (Global Burden of Disease Study, 2013; Lim et al., 2013); alcohol prevalence data from national health surveys (e.g., Health and Social Protection Survey for France and the Health and Well-being for Residents Survey for Finland); and estimates of the relative risks (RR) of dying from alcohol use drawn from various meta-analyses following previous work (Rehm et al., 2007).

Different families of approaches and methods for estimating alcohol-attributable mortality are evaluated and used within the PhD thesis. These include five methods that employ cause-of-death approaches and three methods that use attributable fraction (AF) approaches. The cause-of death approaches merely include a set of causes of death that are wholly attributable to alcohol use (i.e., that would not have occurred in the absence of alcohol consumption). The AF approaches indirectly estimate the share of alcohol-attributable mortality that is from causes of death that are only partly related to alcohol consumption, and combine these estimates with the deaths from causes that are wholly attributable to alcohol use. The methods applied in each chapter depend on the research question, data availability, and the results of an evaluation.

The main advanced demographic techniques used in this thesis are age-standardisation to life table techniques and decomposition techniques for analysing the contribution of alcohol consumption to life expectancy, and for assessing differences in the size of this contribution across countries and between men and women. Furthermore, advanced statistical age-periodcohort models are used to analyse differences in alcohol-attributable mortality by birth cohort; and to assess the role of cohort effects in past alcohol-attributable mortality trends.

#### 1.7. Outline of the thesis

This PhD thesis consists of seven chapters. The current Chapter 1 introduces the reader to the key elements of this research, and to their importance based on the literature. The focus of

Chapter 2 is on methodology. Chapters 3 to 5 present the most relevant results. Finally, Chapter 6 provides an overall discussion of the results.

In the methodological chapter (**Chapter 2**), different approaches for estimating alcoholattributable mortality by age are compared, and the strengths and limitations of each approach are discussed.

The four results chapters are ordered according the sub-objectives of the PhD thesis as formulated above (section 1.1). In **Chapter 3**, an examination of the impact of birth cohorts on long-term trends in liver cirrhosis mortality across eight European countries is presented (sub-objective 1). Chapters 4 and 5 provide the results of an assessment of the impact of alcohol consumption on overall mortality differences over time, across countries, and between the sexes (sub-objective 2). In **Chapter 4**, estimates of the impact of alcohol use on life expectancy are presented for 24 European countries and from 1990 onwards. Furthermore, the extent to which alcohol consumption patterns explain the differences in life expectancy between EU-15 and individual Central and Eastern European (CEE) countries is investigated. In **Chapter 5**, the impact of alcohol use on long-term trends in the gender gap in life expectancy is examined for eight CEE countries.

The final chapter, **Chapter 6**, provides a summary of the main results, a discussion of the methodological strengths and limitations of the approach used, a discussion of the main results, and a summary of the implications of the results for both further research and policy-making.

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# **Chapter 2**

Comparison of different approaches for estimating age-specific alcohol-attributable mortality: The cases of France and Finland

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#### Abstract

*Background*: Accurate estimates of the impact of alcohol on overall and age-specific mortality are crucial for formulating health policies. However, different approaches to estimating alcohol-attributable mortality provide different results, and a detailed comparison of age-specific estimates is missing.

*Methods*: Using data on cause of death, alcohol consumption, and relative risks of mortality at different consumption levels, we compare eight estimates of sex- and age-specific alcohol-attributable mortality in France (2010) and Finland (2013): five estimates using cause-of-death approaches (with one accounting for contributory causes), and three estimates using attributable fraction (AF) approaches.

*Results*: AF-related approaches and the approach based on alcohol-related underlying and contributory causes of death provided estimates of alcohol-attributable mortality that were twice as high as the estimates found using underlying cause-of-death approaches in both countries and sexes. The differences across the methods were greatest among older age groups. An inverse U-shape in age-specific alcohol-attributable mortality (peaking at around age 65) was observed for cause-of-death approaches, with this shape being more pronounced in Finland. AF-related approaches resulted in different estimates at older ages: i.e., mortality was found to increase with age in France; whereas in Finland mortality estimates depended on the underlying assumptions regarding the effects of alcohol consumption on cardiovascular mortality.

*Conclusions*: While the most detailed approaches (i.e., the AF-related approach and the approach that includes underlying and contributory causes) are theoretically able to provide more accurate estimates of alcohol-attributable mortality, they–especially the AF approachesdepend heavily on data availability and quality. To enhance the reliability of alcoholattributable mortality estimates, data quality for older age groups needs to be improved.

**Keywords**: alcohol, mortality, alcohol harm, population attributable fraction, cause-specific mortality

#### **2.1. Introduction**

Excessive alcohol consumption is one of the major risk factors for morbidity and mortality, and the causal effects of the different dimensions of alcohol on various diseases and causes of death are relatively well established (Rehm & Imtiaz, 2016; Rehm et al., 2017). The effects of alcohol consumption on morbidity and mortality are more severe in Europe than elsewhere in the world (Forouzanfar et al., 2015; World Health Organization, 2014) because of the high prevalence of drinking in Europe (World Health Organization, 2013). Estimates of alcohol-attributable mortality provide essential information about the harmful effects of alcohol at the population level. However, different estimation techniques yield different estimates. Moreover, the existing approaches seldom provide age-specific estimates, which can convey crucial information about the risk groups that should be targeted.

The estimation of alcohol-attributable mortality is a challenge for demographers, epidemiologists, and public health experts. Mortality statistics report data on 'underlying causes of death' (e.g., heart diseases, malignant neoplasm, cerebrovascular disease), and do not classify death according to the proximate behavioural cause of the occurrence of disease and injuries, such as alcohol consumption. While drinking alcohol is the only factor in some leading causes of death considered wholly attributable to alcohol (e.g., alcoholic liver cirrhosis or mental and behavioural disorders due to alcohol), alcohol can also be a contributing factor in the development of other diseases (e.g., ischaemic heart diseases or different types of cancer) and injuries (Rehm et al., 2017).

In previous studies, a range of methods have been used to estimate alcohol-attributable mortality. These methods can be broadly divided into two groups that differ in their specifications. In the first group, only cause-specific mortality data are used. Studies using a selection of causes of death wholly attributable to alcohol have generally included the main underlying alcohol-attributable causes: i.e., mental and behavioural disorders due to the use of alcohol, alcoholic liver cirrhosis, accidental poisoning by alcohol, and other diseases that differ across studies (Jasilionis et al., 2011; Kraus et al., 2015; Mackenbach et al., 2015; Rosén & Haglund, 2006). These studies vary in the extent to which they take into account other causes of death when estimating alcohol-attributable mortality. For example, some studies include non-alcoholic liver cirrhosis (Jasilionis et al., 2011; Leon & McCambridge, 2006; Trias-Llimós et al., 2017) while others include causes of death that are partly attributable to alcohol (Grigoriev & Andreev, 2015). Less frequently, both the contributing and the underlying causes

of death are taken into account when estimating alcohol-attributable deaths (*underlying* + *contributory*) (Durkin et al., 2010; Mäkelä, 1998; Martikainen et al., 2014; Polednak, 2016).

The second group of methods used to estimate alcohol-attributable mortality are methods based on attributable fractions (AF). By combining data on cause-of-death mortality, alcohol consumption, and dose-specific relative risks at different levels of drinking (Rehm et al., 2007), these approaches take into account all deaths that are both wholly and partly attributable to alcohol. AF approaches have been widely used to estimate recent alcohol-attributable mortality not only in individual countries, such as in France (Guerin et al., 2013; Rey et al., 2010); but also worldwide using a harmonised methodology in the Comparative Risk Assessments at the Global Burden of Disease studies (Forouzanfar et al., 2015).

The choice of the estimation technique obviously affects the estimates obtained. Because AF approaches include mortality from causes of death that are both wholly and partly attributable to alcohol, studies that have used these approaches have provided information for selected countries and years on the relative importance of causes of death that are wholly and partly attributable to alcohol. These studies have shown that the estimates derived from AF approaches are at least twice as high as those derived from cause-of-death approaches, as the latter only include conditions that are wholly attributable to alcohol (Guerin et al., 2013; Rey et al., 2010). Marked differences in alcohol-attributable mortality estimates can also be observed when comparing approaches that include both the underlying and the contributing causes of death with approaches that include only the underlying causes that are wholly attributable to alcohol (Durkin et al., 2010; Mäkelä, 1998; Polednak, 2016).

Many of the previous studies that provided alcohol-attributable mortality estimates distinguished between very broad age groups (Guerin et al., 2013; Marmet et al., 2016; Rehm et al., 2007), and rarely between specific (five-year) age groups (Martikainen et al., 2014; Martin et al., 2010). Age is, however, an essential determinant of alcohol-attributable mortality because of the age-specific differences in both current alcohol consumption (including drinking patterns) and the history of consumption over the individual life course (Mäkelä et al., 2012); and in the relationship between alcohol consumption and overall mortality (Klatsky & Udaltsova, 2007). Indeed, a study that distinguished between age groups noted the relative importance of including and dealing with older age groups in particular when estimating overall levels of alcohol-attributable mortality (Marmet et al., 2016). However, to the best of our

knowledge, no previous study has directly compared the different methods used to estimate age-specific alcohol-attributable mortality.

We examine and compare for the first time the overall and the age-specific alcohol-attributable mortality estimates obtained by applying eight different estimation techniques to French and Finnish data. We chose to compare France and Finland because these two countries represent different drinking cultures with similar levels of current per capita consumption, but with very different levels of past per capita alcohol consumption. In France, per capita consumption of pure alcohol among adults (ages 15+) dropped from 21.1 litres in 1975 to 11.7 litres in 2010 (HFA-DB, 2016). Over the same period, per capita consumption of pure alcohol among adults in Finland increased from 8.0 to 9.7 litres (HFA-DB, 2016); or from nine to 12 litres, if consumption that was not officially recorded is included (Jääskeläinen et al., 2016). Additionally, there are important differences in the drinking cultures of France and Finland, as the patterns of drinking and the levels of acceptance of drinking differ between the two countries (Allamani et al., 2014; Mäkelä et al., 2012). For example, in France, alcohol (mostly wine) has traditionally been consumed in a daily basis within meals. In Finland, by contrast, risky single-occasion drinking is still much more common than in France (Moskalewicz et al., 2017).

Recent studies for France have used AF approaches to estimate alcohol-related mortality, and have focused on causes of death more than on age-specific patterns. These studies provided estimates ranging from 20,255 (ages 15-75) to 36,500 (ages 15+) annual deaths (45-71 per 100,000) (Guerin et al., 2013; Rey et al., 2010). In Finland, a recent study that used the *underlying* + *contributory* approach as the benchmark method provided an estimate of around 2,500 (ages 25+) annual deaths (67 per 100,000) (Martikainen et al., 2014). Because of the different methods used in these studies, levels of alcohol-attributable mortality in France and Finland cannot be readily compared.

#### 2.2. Materials and methods

#### 2.2.1. Data

We estimated sex-specific and five-year age-specific (ages 25-79) alcohol-attributable mortality in France (2010) and Finland (2013) using eight different definitions and methodologies that were previously used in the literature: namely, five specifications of the cause-of-death approach and three specifications of the AF approach (see further details under "methods"). For each method, alcohol-attributable mortality rates were estimated by five-year

age groups by dividing death counts (estimates) by the corresponding population exposure. Due to the small sample size at younger ages, and in order to avoid potentially random variation in rates, we included deaths at ages 25 and older. We used the 75-79 age group as the oldest age group to ensure an accurate comparison across methods, which would not be possible with an open-ended age group.

For these estimates, mortality data by (underlying) causes of death and population exposures by age groups and sex were retrieved from the WHO Mortality Database (WHO Mortality Database, 2016). In addition, detailed data and specifically tabulated data on underlying and contributory causes of death were obtained from Inserm CépiDc for France, and from the Statistics Finland for Finland.

For the attributable fractions (AF) approaches, we performed two estimations based on the methods and relative risks (RR) in Rehm and colleagues (Rehm et al., 2007). The alcohol consumption data used in these estimations were obtained from the Health and Social Protection Survey (*Enquête Santé et Protection Sociale*) (ESPS, 2010) for France in 2010 and from the Health and Well-being for Residents Survey (ATH, 2013) for Finland in 2013. We also included the corresponding estimates from the Global Burden of Disease (GBD) Study 2013 (Forouzanfar et al., 2015; GBD, 2016).

All data was secondary and totally anonymized. No patients were involved in the design and implementation of the study.

# 2.2.2. Methods

We used the following five cause-of-death approaches:

Underlying causes of death wholly attributable to alcohol (*underlying-wholly*): We considered 12 underlying causes of death (ICD-10) with an alcoholic aetiology: mental and behavioural disorders due to alcohol (F10), alcohol-related degeneration of the nervous system (G312), alcoholic polyneuropathy (G621), alcoholic myopathy (G721), alcoholic cardiomyopathy (I426), alcoholic gastritis (K292), alcoholic liver disease (K70), chronic pancreatitis with alcoholic aetiology (K860), fetal alcohol syndrome (Q860), accidental poisoning by alcohol (X45), intentional self-poisoning and exposure to alcohol (X65), and exposure and poisoning by alcohol with undetermined intent (Y15) (Semyonova et al., 2014).

Liver cirrhosis (*liver cirrhosis*): We considered cirrhosis-related underlying causes of death: alcoholic liver disease (K70), chronic hepatitis, not elsewhere classified (K73), and fibrosis and cirrhosis of liver and (K74) (Leon & McCambridge, 2006; Trias-Llimós et al., 2017).

Short list of underlying causes of death wholly attributable to alcohol and liver cirrhosis (*main underlying*): We considered the three main diseases that are wholly attributable to alcohol, which accounted for >80% of the (underlying) causes of deaths that are wholly attributable to alcohol in both countries and for both sexes: behavioural disorders due to alcohol (F10), alcoholic liver disease (K70), and accidental poisoning by alcohol (X45). In addition, in line with previous studies (Jasilionis et al., 2011), and in order to account for potential differences in coding practices in alcoholic liver cirrhosis (Rehm et al., 2017), we included chronic hepatitis not elsewhere classified (K73) and fibrosis and cirrhosis of the liver (K74). Moreover, in contrast to the underlying approach, this specification has the advantage of only requiring three-digit ICD-10 codes.

The European Health for All Database definition (*HFA-DB*): The definition of alcoholattributable mortality from the European Health for All Database (HFA-DB, 2016) includes a selection of underlying causes of death that are wholly or partly attributable to alcohol consumption: cancer of the oesophagus (C15), cancer of the larynx (C32), alcohol dependence syndrome (F10), chronic liver disease and cirrhosis (K70, K73, K74, K76), and all external causes (V00-V99, W00-W99, X00-X99 and Y00-Y99) (McCartney et al., 2011).

Underlying and contributory (*underlying* + *contributory*) causes of death: We included deaths for which alcohol consumption (ICD-10 codes: F10, G312, G4051, G621, G721, I426, K292, K70, K852, K860, O354, P043, Q860 and X45) was the underlying or a contributory cause (Mäkelä, 1998; Martikainen et al., 2014).

We included three attributable fraction approaches in which estimates of deaths from conditions that are wholly attributable to alcohol are combined with estimates of deaths from conditions that are partly attributable to alcohol:

The conventional attributable-fraction approach (*AF-conventional*): Following Rehm and colleagues, we estimated the alcohol-attributable fractions (AAF) for the causes of death partly attributable to alcohol for each country, sex, and age using Levin's formula (Rehm et al., 2007):

$$AAF_{i} = \frac{\sum_{i=1}^{n} p_{i}(RR_{i}-1)}{1 + \sum_{i=1}^{n} p_{i}(RR_{i}-1)}$$
(1)

Where *n* is the number of drinking categories, *p* is the proportion of drinkers, and *RR* are the relative risks of dying for each *i* alcohol consumption category. We defined four drinking categories: 0-19, 20-39, 40-59, and 60 or more grams of pure alcohol consumed per day. As is the case in most health surveys, the survey-based estimate of alcohol consumption underestimated total alcohol consumption based on sales in both countries. To adjust for unreported consumption, we followed previous work and modelled alcohol consumption using a Gamma distribution, shifting its parameters until the total matched the level of alcohol sales (Rehm et al., 2010) that was obtained from the European Health for All Database (HFA-DB, 2016).

The attributable-fraction approach, excluding (cardio)protective effects of alcohol (AF ( $RR \ge 1$ )): This approach is identical to the conventional AF approach except that it excludes the (cardio)protective effects of alcohol on mortality, as these effects are disputed (Holmes et al., 2014), and because none of the cause-of-death approaches includes the potential protective effects of alcohol on mortality.

Global Burden of Disease estimates (*AF-GBD*): the GBD 2013 study (Forouzanfar et al., 2015), which has often been cited in recent studies (Agardh et al., 2016; Trias-Llimós et al., 2018), estimated alcohol-attributable mortality by applying an alcohol-attributable fractions approach. GBD estimates differ from the other two AF methods in that they are based on different alcohol consumption estimates, the measure the risk of alcohol consumption on a continuous scale, and they use a narrower specification of causes of death (Forouzanfar et al., 2015; GBD 2013 Mortality and Causes of Death Collaborators, 2015) than is used in the conventional AF approach, which relies on detailed four-digit ICD-10 causes of death.

# 2.3. Analyses & Comparison

For all eight approaches, we estimated and compared the overall age-standardised (ages 25-79) and age-specific (five-year age groups) alcohol-attributable mortality rates (per 100,000) for each method, sex, and country.

In order to provide further insight into the differences between the more detailed methods (AF approaches and the *underlying* + *contributory* approach), we disentangled different forms of age-specific alcohol-attributable mortality into groups of underlying causes of death: cancers (ICD-10 codes: C00-D48), cardiovascular diseases (I00-I99), digestive disorders (K00-K99),

external causes (S00-Y98), mental diseases (F00-F99), and other causes. For reasons of data availability, we could not perform such an analysis for the *underlying* + *contributory* method in Finland.

### 2.4. Results

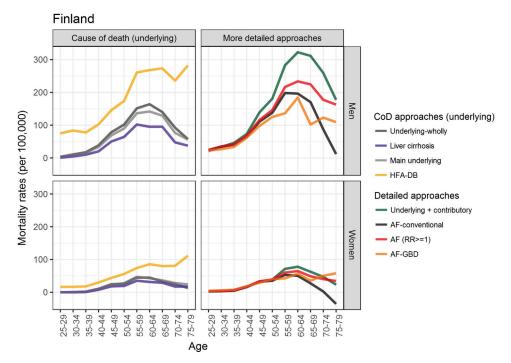
At ages 25-79, the age-standardised alcohol-attributable mortality rates among men ranged from 24.7 to 129.9 deaths per 100,000 in France, and from 49.2 to 165.5 deaths in Finland (Table 2.1). Among women, the alcohol-attributable mortality rates ranged from 8.4 to 42.9 deaths in France, and from 16.7 to 54.2 deaths in Finland. The lowest estimates were obtained by selecting *liver cirrhosis* only, while the highest estimates were obtained by applying the *HFA-DB* approach. The most detailed approaches (the AF-related approaches and the *underlying* + *contributory* approach) resulted in estimates of alcohol-attributable mortality that were around twice as high as the estimates provided by the *underlying-wholly*, *liver cirrhosis*, and *main underlying* approaches in both countries and for both sexes. The *underlying* + *contributory* approach resulted in higher estimates than the AF-related approaches in Finland, but not in France. The alcohol-attributable mortality rates were generally higher in Finland than in France, except when the *AF-GBD* approach (men only) and the *AF-conventional* approach (women only) were applied. Regardless of the method used, alcohol-attributable mortality was found to be higher among men than among women.

| Table 2.1. Total alcohol-attributable deaths and age-standardised alcohol-attributable mortality rates |
|--|
| (per 100,000) in France (2010) and Finland (2013) for men and women, ages 25-79.                       |

|           |                           | France (2010)  | Finland (2013) |               |               |
|-----------|---------------------------|----------------|----------------|---------------|---------------|
|           |                           | Men            | Women          | Men           | Women         |
| Approach  | Method                    | deaths (rate)  | deaths (rate)  | deaths (rate) | deaths (rate) |
|           | Underlying-wholly         | 5,875 (30.2)   | 1,746 (8.4)    | 1,423 (79.4)  | 393 (21.5)    |
| Cause-of- | Liver cirrhosis           | 4,806 (24.7)   | 1,748 (8.4)    | 8,81 (49.2)   | 304 (16.7)    |
| death     | Main underlying           | 7,202 (37.0)   | 2,329 (11.2)   | 1,265 (70.6)  | 416 (22.8)    |
| (CoD)     | HFA-DB                    | 25,302 (129.9) | 8,901 (42.9)   | 3,104 (173.2) | 990 (54.2)    |
|           | Underlying + Contributory | 12,581 (64.6)  | 3,221 (15.5)   | 2,966 (165.5) | 665 (36.4)    |
|           | AF-conventional           | 17,147 (88.1)  | 5,644 (27.2)   | 1,869 (104.3) | 381 (20.9)    |
| AF        | AF (RR>=1)                | 18,720 (96.1)  | 6,546 (31.6)   | 2,314 (129.2) | 600 (32.9)    |
|           | AF-GBD                    | 19,034 (97.7)  | 5,770 (27.8)   | 1,655 (92.4)  | 569 (31.2)    |

With the exception of the estimates from the *HFA-DB* method, the age-specific estimates from the methods that use cause-of-death data exhibited similar patterns, regardless of gender and country: an increase until around age 65 and a decline at older ages, which is depicted as a reverse U-shape (Figures 2.1 and 2.2). The decline at older ages seems to be less pronounced in France than in Finland, however (Figure S2.1). Among the older age groups, the AF approaches resulted in a wide range of estimates for Finland. In addition, differences between the countries were observed: e.g., there was a clear increase in alcohol-attributable mortality rates with age in France, but not in Finland (except among Finnish women when the *AF-GBD* approach was applied). When the estimates derived from the AF-related approaches were compared with those from the *underlying* + *contributory* method, differences in the results from the *AF* method and the other AF-related approaches were observed, but only among Finns aged 50+. In France, the *underlying* + *contributory* method estimated lower mortality than the AF-related methods for both men and women, and especially for the older age groups.

Figure 2.1. Age-specific alcohol-attributable mortality rates in Finland (2013) for men and women, ages 25-79



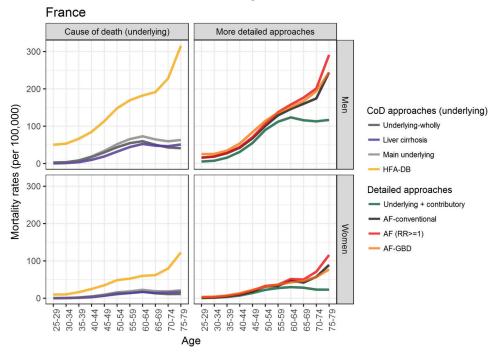
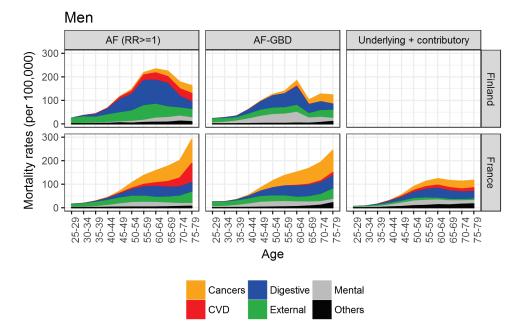


Figure 2.2. Age-specific alcohol-attributable mortality rates in France (2010) for men and women, ages 25-79

The cause-specific results of the AF-related approaches showed that the composition of the causes of death was relatively similar for both countries and for both men and women until around age 50 (Figures 2.3 and 2.4). Among the older age groups, the differences increased, especially in terms of cardiovascular and cancer mortality. These increases in rates of cancer and cardiovascular alcohol-related mortality with age seem to have been less pronounced in Finland. There were important differences between the estimates of cardiovascular mortality using AF-related approaches, with the estimates from the AF  $(RR \ge 1)$  method being higher than the estimates from the AF-GBD method. When comparing AF-related methods to the underlying + contributory method in France, we observed that the higher estimates from AFrelated methods among younger age groups were mostly due to external causes. Among older age groups, the higher alcohol-attributable mortality estimates provided by AF-related approaches were mainly due to higher estimates of cancer and cardiovascular alcoholattributable mortality, which also increased more with age than in the estimates generated by the underlying + contributory approach. Finally, and across all age groups, estimates of mortality from external causes were lower when the *underlying* + *contributory* method was used than when AF-related methods were applied.



**Figure 2.3.** Cause-specific alcohol-attributable mortality rates in France (2010) and Finland (2013) for men, ages 25-79, by detailed method<sup>ab</sup>

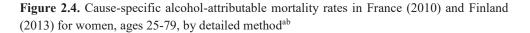
<sup>a.</sup> Preventive mortality (negative numbers) was excluded in the AF-GBD method (only for CVD diseases and among men): for France, the minimum rates at ages 30-59 were equal to -1.23/100,000; for Finland, the rates at ages 55-59, 70-74, and 75-79 were -2.80, -4.20, and -13.94 per 100,000, respectively.

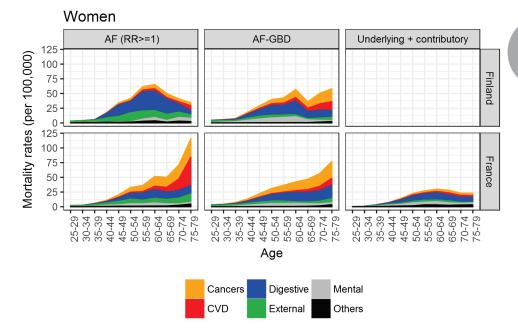
<sup>b.</sup> Cause-specific death rates for the underlying + contributory approach for Finland were not available.

#### 2.5. Discussion

This study compared the overall and the age-specific alcohol-attributable mortality rates provided by eight different estimation techniques in France (2010) and Finland (2013). The overall mortality rates varied widely depending on the method applied: the methods that used additional data on either contributory causes or alcohol consumption and information on the association with mortality provided estimates that were around twice as high as the estimates generated by methods based solely on underlying causes of death that are wholly attributable to alcohol. The differences in the estimates provided by the various methods were especially large at older ages. Cause-of-death approaches generally estimated an inverse U-shaped age pattern, with a decline in alcohol-attributable mortality rates beyond age 65. Approaches that included alcohol consumption data and information on the association between alcohol

consumption and mortality resulted in a similar inverse U-shaped pattern in Finland, but in increasing mortality with age in France due to high levels of alcohol-related cancer and cardiovascular mortality. Overall, however, higher levels of alcohol-attributable mortality were observed in Finland than in France.





<sup>a.</sup> Preventive mortality (negative numbers) was excluded in the *AF-GBD* method (only for CVD diseases and among men): for France, the minimum rates at ages 30-59 were equal to -1.23/100,000; for Finland, the rates at ages 55-59, 70-74, and 75-79 were -2.80, -4.20, and -13.94 per 100,000, respectively.

<sup>b.</sup> Cause-specific death rates for the *underlying* + *contributory* approach for Finland were not available.

#### 2.5.1. Interpretation of the results

The substantial differences in the estimates of alcohol-attributable mortality provided by the eight methods studied are in line with the differences that were previously found between the underlying approach and the AF approach in France (Guerin et al., 2013), and between the underlying approach and the *underlying* + *contributory* approach in Finland (Mäkelä, 1998). The differences in the estimates can be traced back to both to the general approach used (cause-of-death approaches versus AF approaches) and to the details and the data associated with the

particular methods. In general, more detailed approaches (AF approaches and underlying + *contributory*) theoretically provide more accurate estimates, as they account for the impact of alcohol on diseases and causes of death that are not fully attributable to alcohol, as well as on those that are wholly attributable to alcohol. These higher estimates should therefore be considered more reliable estimates of the total impact of alcohol on mortality than the estimates that account for a selection of underlying causes of death only. On the other hand, the estimates that account for underlying causes of death only can be considered estimates of the minimum burden of alcohol on mortality. In addition, causes of death wholly attributable to alcohol may not be fully recorded in death certificates due to stigma associated with alcohol-related health problems, which has been shown to be the case at least for alcoholic liver cirrhosis and alcoholic cardiomyopathy (Manthey et al., 2017; Room, 2005). One of the approaches using underlying causes of death included all underlying liver cirrhosis (main underlying), and showed a similar age-specific pattern as the other underlying cause-of-death approaches (except the HFA-DB). Therefore, it seems that the underreporting of causes wholly attributable to alcohol by the physicians writing death certificates only has a rather minor impact on the age-specific alcoholattributable mortality pattern. The estimates provided by the HFA-DB approach, which were the largest in both countries and for both men and women, were the most likely to be overestimates of the total burden of alcohol on mortality because the approach defined all external deaths as alcohol-related. By contrast, the AF-conventional approach defined only 25% of external deaths in Finland and 12% of external deaths in France as alcohol-related.

The differences in the alcohol-attributable mortality rates found using the various methods were largest at older ages, with the differences being greater between the different AF approaches than between the different underlying cause-of-death approaches (with the exception of the HFA-DB approach) (Figure S2.2). The differences between the results of the AF approaches can be at least partly explained by data demands and methodological details. The AF approaches require not only data on cause-specific mortality; but also data on alcohol consumption and on the association between alcohol consumptions. The limitations and the potential biases of AF-related methods have been described elsewhere by several authors, including Rehm, Marmet, and Rey; see, e.g. (Marmet et al., 2016; Rehm et al., 2007; Rey & Jougla, 2014). The estimates for older age groups in particular are more sensitive to the data and assumptions used (Marmet et al., 2016). In our application, at least four specific factors that may cause bias should be taken into account. First, alcohol consumption estimates at older ages

might be less reliable because of the smaller sample sizes for these age groups in surveys. Indeed, for France we had a sample size of less than 310 for each age group and sex at ages 65 and older (Table S2.1). Second, because of the lack of questions in health surveys about lifetime alcohol consumption patterns, estimates of current drinking behaviour, especially at older ages, may not provide a full picture of the respondents' lifetime exposure to alcohol. Third, efforts to estimate cause-specific mortality could be hampered by competing causes at older ages (Alpérovitch et al., 2009). Furthermore, the estimates of the association between alcohol consumption and mortality are often derived from adult (and not older) populations (Corrao et al., 1999), even though it is not clear that the risks are identical over age groups. Finally, the differences we observed between the AF-conventional approach and the AF-GBD approach seem to be mostly related to differences in alcohol consumption data, and less on the choice of a categorical measurement scale in the *conventional-AF* methods vs. a continuous scale in the AF-GBD method. Indeed, the observed differences between these two methods were rather tiny, except for older Finns. In the calculation of the AF-conventional estimates we used alcohol consumption data from the Health and Well-being for Residents Survey, which had a rather large sample size, also at old ages (Table S2.1), and is considered a good source of consumption data, whereas the AF-GBD used forecasted data using different sources as input.

Our observation that alcohol-related mortality estimates at older ages vary greatly for Finland depending on the AF-based approach used, but are relatively similar for France, seems to point to another important factor driving old-age estimates. This difference between the countries may be related to the relative importance of causes of death for which alcohol has large cardioprotective effects in combination with the prevalence of moderate drinkers, to whom these cardioprotective effects tend to apply. The details of our analyses showed that the impact of alcoholic ischaemic heart disease on total alcohol-attributable mortality was much larger in Finland than in France. In general, we found that ischaemic heart disease mortality was three to four times higher in Finland than in France, which has also been documented elsewhere (Finegold et al., 2013). Ischaemic heart disease is not only the most prevalent cardiovascular cause of death; it is also the cause with the greatest cardioprotective effect (Rehm et al., 2007). This could explain the large differences observed between the results from the AF-conventional and AF  $(RR \ge 1)$  approaches for Finland. In addition, the larger shares of moderate older drinkers in Finland than in France (Table S2.2) contributed to the differences in the results from the AF-related methods in Finland. Clearly, the estimates of the (cardioprotective) effects of alcohol consumption on mortality have a notable impact on the estimates of alcohol-related

mortality at older ages (when mortality itself is higher), especially in populations with higher mortality from causes of death for which cardioprotective effects may be significant, and with large shares of moderate drinkers.

In Finland, the estimates at older ages differed substantially depending on the AF approach used. However, we observed a reverse U-shaped age pattern irrespective of the method applied (except for the HFA-DB method). A reverse U-shaped pattern was also observed in France when the causes-of-death approach was used, albeit with a less pronounced decline in alcoholrelated mortality at old ages; but not when the AF approaches were applied, as the estimates of these approaches showed an exponential increase in mortality rates at older ages. Because this exponential increase was observed only for the estimates from the AF approaches in France, and because of the above-mentioned data issues with the use of AF approaches at older ages, particularly given the small survey sample available, we are sceptical about this age pattern. Although the other approaches, including the detailed *underlying* + *contributory* approach, estimated an inverse U-shaped pattern for both countries and sexes, we cannot be fully certain that this is indeed the correct age pattern in France. Although the underlying + contributory approach seems to have been less affected by data quality issues than the AF approaches, underestimation could have occurred. Only in cases in which autopsies were carried out we can be relatively confident about the cause of death. Because autopsies are carried out less often when the cause of death is from a chronic disease than when it is accidental, underestimation is more likely to occur at old ages (Mäkelä, 1998). In addition, cancer-related alcohol-attributable mortality is likely to be underestimated because alcohol consumption and other risk factors that may have increased the likelihood of cancer are often not recorded in the death certificate. As a result, the decline in alcohol-attributable mortality rates with age that we observed at older ages may have been overestimated, and may have concealed a slightly different pattern than the observed inverse U-shaped age pattern.

In addition to these methodological and data differences between France and Finland, the overall patterns and the age patterns of alcohol-related mortality vary by the national context. Overall, higher levels of alcohol-attributable mortality were observed in Finland than in France, except when the *AF-GBD* method was applied to men and the *AF-conventional* method was applied to women. Examining the age patterns more in detail, we observed that when cause-of-death approaches were used, the differences between France and Finland were especially large among the middle-aged groups; and that when AF approaches were applied, alcohol-related mortality at older ages was higher in France than in Finland (Figure S2.1). Alcohol-attributable

mortality declined abruptly with age in Finland, but more moderately or not at all in France. Although the comparison between countries was hampered by data quality issues (see above), and by differences in how the physicians in each country have been trained to record causes of death (Ramstedt, 2002), the observed differences can be at least partly linked to national differences in the patterns of drinking. Alcohol consumption is slightly higher in France than in Finland (HFA-DB, 2016), but drinking patterns are riskier in Finland than in France (Moskalewicz et al., 2017; World Health Organization. 2014). These risky drinking patterns likely explain the higher rates observed in Finland, especially among young and middle-aged individuals. Additionally, the older generations in France and Finland were exposed to very different country-specific cultural practices related to alcohol use in their younger adulthood (Allamani et al., 2014), which likely shaped their drinking behaviour over the life course. For example, older Finns have grown up in a dry society, and most have remained light drinkers or abstainers through their lives (Mäkelä et al., 2012); whereas older French people have grown up in a rather permissive alcohol culture, and overall levels of alcohol consumption have been much higher among this generation than among their younger counterparts (Cogordan et al., 2014). The different patterns of lifetime exposure to alcohol use among the older generations in the two countries explain the more pronounced decline observed (using all methods) in alcohol-attributable mortality rates with age in Finland than in France, and illustrate that the actual age pattern depends on the context as well.

#### 2.5.2. Reflections on the choice of method for assessing alcohol-related mortality

The more detailed approaches used to estimate alcohol-attributable mortality (*AF-conventional*, *AF-GBD*, and *underlying* + *contributory*) theoretically provide more accurate estimates of the overall level of alcohol-related mortality. However, these more detailed approaches all require detailed data of high quality. The AF-related approaches require data drawn from three main sources, and rely on (often problematic) data on alcohol prevalence and on disease incidence at various levels of alcohol consumption. We argue that if highly accurate cause-specific (underlying and contributory) mortality data are available, the use of the *underlying* + *contributory* approach is recommended, as the estimates from this approach are less affected by additional assumptions. The underlying + contributory approach has commonly been applied in Finland (Mäkelä, 1998; Martikainen et al., 2014) and Sweden (Hemstrom, 2002), which have high-quality, cause-specific mortality data (Lahti & Penttilä, 2001; Mathers et al., 2005); and has only recently been applied to other countries (Durkin et al., 2010; Polednak, 2016). The application of the *contributory* approach in our study resulted in estimates that were lower than

the estimates from AF-related approaches for France, especially among the younger and the older age groups; but not for Finland. However, adding the contributory cause of death to estimate alcohol-attributable mortality increased the rates in France by 75% for men and by 40% for women relative to the estimates from the method based on underlying causes only.

In addition to assessing the pros and cons of various methods for estimating alcohol-attributable mortality in one point of time it is also interesting to discuss the main strengths and limitations of the different methods to examine trends over time and in cross-national comparisons. Despite its high degree of accuracy of the *underlying* + *contributory* approach, it is impossible to use this approach to assess time trends in most European countries or to conduct cross-national comparisons on a large scale because contributory cause-of-death data are scarcely available for many countries and periods of time. Of the methods that use underlying causes of death, the underlying and the main underlying methods are, by definition, the most accurate, as the age patterns found when using these methods are similar to those observed when using the *underlying* + *contributory* method. Obviously, the overall levels found when using methods that take into account only the underlying causes of death are underestimates. However, these methods estimated an age pattern that was similar to the pattern found when using the underlying + contributory approach, but are easier to use because they do not require additional data or a set of assumptions. Because of potential country differences in the classification of liver disease mortality (alcoholic or other) (Rehm et al., 2017), we recommend using the main *underlying* method, at least for comparative studies across countries and over time, although country-specific coding practices and changes therein over time should be carefully considered in the comparison. Generally, approaches that take into account underlying causes of death that are wholly attributable to alcohol follow the trends in per capita alcohol consumption over time (with a certain lag time) (Ramstedt, 2001; Rosén & Haglund, 2006). Thus, the estimates from these approaches may be seen as indicating the presence of other chronic conditions partly attributable to alcohol (Kraus et al., 2015), especially when we examine time trends, and not merely levels.

#### 2.6. Conclusions

To the best of our knowledge, this is the first study that has compared underlying cause-ofdeath methods and methods based on more detailed data to estimate overall and age-specific alcohol-attributable mortality in different European countries. Our comparison of the overall and the age-specific alcohol-attributable mortality estimates from the application of eight different estimation techniques to French and Finnish data showed that the methods that relied on more detailed data (on either contributory causes of death or alcohol prevalence, and on their association with mortality) were more likely than other methods to provide accurate estimates of overall alcohol-attributable mortality levels; but are also dependent on the level of detail and the quality of these data. In the approaches that require information on the association between alcohol consumption and mortality, and in particular in the AF approaches, these data quality issues could explain the different age patterns we observed. A clear inverse U-shaped age pattern in alcohol-attributable mortality rates was found for Finland; but not for France, where the age-specific alcohol-attributable mortality pattern was different, in part because the older population in France had a long history of drinking. To enhance our knowledge about the impact of alcohol on mortality, and in order to further improve overall estimates of alcohol-attributable mortality, particular attention should be paid to the older age groups.

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# Supporting information

**Table S2.1.** Valid cases by age, sex, and survey in France (2010) and Finland (2013)

|       | France | e (ESPS) | Finland (ATH) |       |  |  |
|-------|--------|----------|---------------|-------|--|--|
| Age   | Men    | Women    | Men           | Women |  |  |
| 25-29 | 366    | 408      | 1,029         | 1,525 |  |  |
| 30-34 | 353    | 487      | 1,134         | 1,528 |  |  |
| 35-39 | 487    | 546      | 1,178         | 1,529 |  |  |
| 40-44 | 491    | 547      | 1,167         | 1,512 |  |  |
| 45-49 | 533    | 607      | 1,386         | 1,873 |  |  |
| 50-54 | 486    | 597      | 1,652         | 2,182 |  |  |
| 55-59 | 485    | 503      | 1,992         | 2,364 |  |  |
| 60-64 | 432    | 467      | 2,325         | 2,763 |  |  |
| 65-69 | 308    | 294      | 2,300         | 2,544 |  |  |
| 70-74 | 256    | 285      | 1,431         | 1,794 |  |  |
| 75-79 | 248    | 267      | 2,132         | 2,767 |  |  |
|       |        |          |               |       |  |  |

# Table S2.2. Adjusted alcohol prevalence in France (2010) and Finland (2013), by age and sex Finland

#### Men

|              | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 0 gr/day     | 10%   | 8%    | 8%    | 10%   | 11%   | 11%   | 13%   | 15%   | 19%   | 25%   | 31%   |
| 0-20 gr/day  | 46%   | 47%   | 43%   | 39%   | 37%   | 35%   | 38%   | 38%   | 38%   | 42%   | 41%   |
| 20-40 gr/day | 23%   | 23%   | 23%   | 22%   | 22%   | 21%   | 21%   | 21%   | 20%   | 19%   | 17%   |
| 40-60 gr/day | 11%   | 11%   | 12%   | 13%   | 13%   | 13%   | 12%   | 12%   | 11%   | 8%    | 7%    |
| 60+ gr/day   | 10%   | 11%   | 14%   | 16%   | 17%   | 20%   | 16%   | 15%   | 12%   | 6%    | 4%    |

#### Women

25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74 75-79 0 gr/day 13% 13% 15% 14% 13% 15% 17% 23% 30% 39% 56% 65% 0-20 gr/day 71% 66% 63% 58% 57% 55% 54% 53% 52% 39% 20-40 gr/day 17%14%15% 18%20%19% 19% 17%13% 8% 5% 40-60 gr/day 4% 2% 3% 4% 6% 6% 6% 5% 3% 1% 0% 60+ gr/day1% 0% 1% 1% 3% 3% 3% 2% 1% 0% 0%

2

# Table S2.2. (continued)

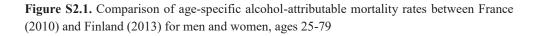
# France

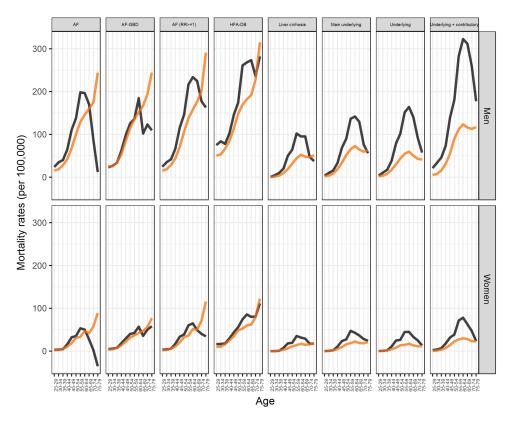
# Men

|              | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 0 gr/day     | 16%   | 18%   | 14%   | 13%   | 17%   | 10%   | 10%   | 12%   | 11%   | 16%   | 16%   |
| 0-20 gr/day  | 49%   | 43%   | 41%   | 40%   | 34%   | 36%   | 33%   | 32%   | 30%   | 30%   | 28%   |
| 20-40 gr/day | 18%   | 18%   | 19%   | 19%   | 17%   | 19%   | 18%   | 18%   | 17%   | 17%   | 17%   |
| 40-60 gr/day | 9%    | 9%    | 11%   | 11%   | 11%   | 12%   | 12%   | 12%   | 12%   | 11%   | 12%   |
| 60+ gr/day   | 9%    | 12%   | 16%   | 17%   | 21%   | 23%   | 26%   | 27%   | 30%   | 26%   | 28%   |

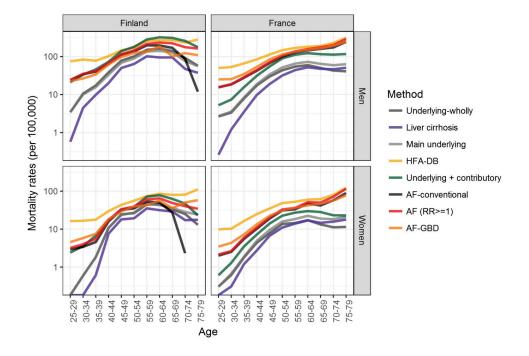
#### Women

|              | 25-29 | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 |
|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 0 gr/day     | 34%   | 38%   | 27%   | 30%   | 24%   | 24%   | 30%   | 21%   | 28%   | 35%   | 39%   |
| 0-20 gr/day  | 49%   | 45%   | 51%   | 48%   | 45%   | 43%   | 42%   | 41%   | 40%   | 31%   | 28%   |
| 20-40 gr/day | 10%   | 10%   | 12%   | 12%   | 15%   | 15%   | 14%   | 16%   | 14%   | 13%   | 12%   |
| 40-60 gr/day | 4%    | 4%    | 5%    | 5%    | 7%    | 8%    | 7%    | 9%    | 7%    | 8%    | 7%    |
| 60+ gr/day   | 3%    | 3%    | 4%    | 5%    | 8%    | 10%   | 8%    | 13%   | 10%   | 12%   | 13%   |





- Finland - France



**Figure S2.2.** Age-specific alcohol-attributable mortality rates in France (2010) and Finland (2013) for men and women, ages 25-79 (logarithmic scale)

\*AF method for Finnish women aged 75-79 is not shown as the rate is negative (-35.4).

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2

# **Chapter 3**

The role of birth cohorts in long-term trends in liver cirrhosis mortality across eight European countries

This chapter was published as: Trias-Llimós, S., Bijlsma, M. J., Janssen, F. (2017). The role of birth cohorts in long-term trends in liver cirrhosis mortality across eight European countries. *Addiction*, 112(2), 250-258.

#### Abstract

*Background and aims:* Understanding why inequalities in alcohol-related mortality trends by sex and country exist, is essential for developing health policies. Birth cohort effects, indicative of differences by generation in drinking, have rarely been studied. We estimate the relative contribution of birth cohorts in liver cirrhosis mortality trends and compare sex- and country-specific cohort patterns across eight European countries.

*Design, setting and participants:* Time-series analysis of population-level mortality data of Austria Finland, Hungary, Italy, the Netherlands, Poland, Spain and Sweden; 1950-2011; ages 15-94.

*Measurements:* We modelled country- and sex-specific liver cirrhosis mortality (from national vital registers) adjusting for age, period and birth cohort.

*Findings:* Birth cohorts (adjusted for age and period) made statistically significant contributions to liver cirrhosis mortality in all countries and for both sexes (p-values < 0.001), and more so among women (average contribution to deviance reduction of 38.8%) than among men (17.4%). The observed cohort patterns were statistically different between all, but two, country pairs (p-values < 0.001). Sex differences existed overall (p-value < 0.001), but not in the majority of countries (p-values > 0.999). Visual inspection of birth cohort patterns reveals that birth cohorts at higher risk of liver cirrhosis mortality were born around 1935-1949 in Sweden and Finland, around 1950 in Austria and the Netherlands, and around 1960 or later in the other analysed countries.

*Conclusions:* Birth cohorts are a significant component of liver cirrhosis mortality trends. Clear differences in the analysed European countries exist in birth cohorts that experience smaller risks than their predecessors.

Keywords: alcohol, cohort, age-period-cohort analysis, Europe, liver cirrhosis

#### **3.1. Introduction**

Alcohol-attributable mortality, or the share of overall mortality attributable to alcohol, is higher in Europe than elsewhere in the world because of the high prevalence of alcohol consumption (World Health Organization, 2014). However, the levels of and the trends in alcohol prevalence and subsequent alcohol-related mortality differ substantially across European countries and between the sexes (Popova et al., 2007; Rehm et al., 2007; Rehm et al., 2011; Simpura & Karlsson, 2001). Understanding the long-term trends in alcohol-related mortality, the differences in these trends across countries and between the sexes, and the factors that explain these trends, is essential for developing health policies.

Previous studies that assessed the long-term trends in alcohol-related mortality mainly focused on calendar time as the time component, and on liver cirrhosis mortality as the indicator of alcohol-attributable mortality (Leon & McCambridge, 2006; Munoz-Perez & Nizard, 1999; Ramstedt, 2001; Ramstedt, 2007; Zatonski et al., 2010). However, the inclusion of another time dimension, such as birth cohort, has been crucial to understanding mortality (Janssen et al., 2005) and cancer incidence trends (Dhillon et al., 2011; McNally et al., 2012). Individuals who were born in the same period, and thus belong to the same birth cohort, have similar experiences at the same age, and are likely to adopt similar behaviours. In the particular case of alcohol, restrictions, prices, and advertisements related to alcohol directly influence drinking behaviour at younger ages (Paschall et al., 2009), which tends to predict patterns of alcohol use over the life course (Eliasen et al., 2009; Pitkänen et al., 2005). In addition, individuals who started drinking at younger ages are more prone to suffer from alcohol dependence (Hingson et al., 2006) and to develop other alcohol-related problems, such as alcohol use disorders or injuries (Dawson et al., 2008; Hingson & Zha, 2009). Therefore, in studying trends in alcohol prevalence and subsequent mortality, it is necessary to not only look at changes over age (= age effects)-increasing mortality with age-and calendar time (= period effects)-mortality change over subsequent years, but also to examine the role of birth cohorts (= birth cohort effects), i.e. differences in mortality between those born in 1950 and those born in 1960. Indeed, recent studies on alcohol consumption trends have found that birth cohorts are significant explanatory factors (Kraus et al., 2015; Meng et al., 2014). These findings indicate that drinking habits are formed not just collectively (= period effects), as Skog posited (Skog, 1985), but also by generation (= birth cohort effects).

The relevance of birth cohorts has been also proved in the few studies that have assessed alcohol-attributable mortality. Analysing data for the period 1970-1989, Corrao et al. (1997) found increasing liver cirrhosis mortality risks for cohorts born in the first half of the 20<sup>th</sup> century in Northern and Eastern Europe. Recent studies at the country-specific level found a decline in alcohol-related mortality risks for birth cohorts born after World War II in Sweden (Rosén & Haglund, 2006); and in Nordic countries, Germany, and France, based on data from 1980 to 2009 (Kraus, Osthus et al., 2015).

However, these previous studies did not examine trends over a long historical period, nor did they make pan-European country comparisons. Longer time series make it possible to compare more birth cohorts at the same age, and are therefore likely to provide more precise cohort estimates. In addition, because alcohol consumption and liver cirrhosis mortality trends are not always similar across European countries (Popova et al., 2007; Zatonski et al., 2010), it is important to examine the country-specific role of birth cohorts across European countries.

#### Objectives

First, we estimate the extent to which birth cohorts explain liver cirrhosis mortality trends in countries across different European regions by simultaneously examining the age, period and birth cohort effects. Second, we compare the birth cohort patterns across countries and between sexes.

# 3.2. Methods

# 3.2.1. Design

We estimated liver cirrhosis mortality trends from 1950 to 2011 for the national populations aged 15 to 94 of eight European countries belonging to different regions and with different alcohol consumption levels, patterns and trends: Austria, Finland, Hungary, Italy, the Netherlands, Poland, Spain and Sweden.

#### 3.2.2. Data

Liver cirrhosis mortality data by calendar year, five-year age groups, and sex from national vital registration systems were retrieved from the WHO Mortality database (WHO Mortality Database, 2016). These data were complete and of medium or high quality for all countries except Poland, because of a more substantial proportion of ill-defined causes (Mathers et al., 2005). Because only a small share of ill-defined causes of death can be attributed to liver

cirrhosis (Mokdad et al., 2014), the potential underestimation of liver cirrhosis mortality in Poland is small. We used International Classification of Diseases (ICD) codes 581 in ICD-7, 571 in ICD-8 and ICD-9, and K70, K73, and K74 in ICD-10 (Leon & McCambridge, 2006). We redistributed the deaths in the open-ended age group 85+ in ICD-7, ICD-8 and ICD-9 to the age groups 85-89 and 90-94 by means of their average relative share in ICD-10 by country and sex. The mortality rates were obtained by dividing the deaths by the age-, sex-, and year-specific exposure population which we obtained from the Human Mortality Database (HMD, 2014). These five-year age group mortality rates were subsequently turned into one-year age group mortality rates by applying two-dimensional P-splines smoothing (Camarda, 2012). The combination of ages 15-94 and years 1950-2011 resulted in the inclusion of the two-year overlapping birth cohorts (1855/56, ..., 1995/1996). Because of missing data, in some countries different years and birth cohorts were included (see Table S3.1).

#### 3.2.3. Statistical analysis

#### Descriptive analysis

All analyses were done separately for men and women. To compare liver cirrhosis mortality across countries, the liver cirrhosis mortality rates were directly age-standardised using the European population of 2011 from Eurostat (Eurostat, n.d.) as the standard. Age-standardised and age-specific liver cirrhosis mortality trends were plotted and visually inspected.

#### Age-period-cohort (APC) modelling

Liver cirrhosis mortality rates were modelled as a function of age, period, and birth cohort. We fitted four different Poisson regression models for each country-sex combination (see Box 1), with the natural logarithm of population at risk as the offset term. To deal with the identification problem in APC modelling that results from the linear dependency between age, period, and birth cohort (age = calendar year (period) minus year of birth (cohort)), we applied the standard Clayton and Schifflers approach (Clayton & Schifflers, 1987a,b). This approach distinguishes the shared linearity between period and birth cohort by means of identifying the drift, next to age, period and cohort. Drift represents the linear change in the outcome that is shared between period and birth cohort. By constraining two categories in the variable of interest (birth cohort), we can estimate and visualize non-linear birth cohort effects unaffected by linear time-trend changes. We used as reference categories age 50, calendar year 1980, and birth cohorts 1900 and 1960. We examined country differences (in the full data set and between pairs of countries)

and sex differences (in the full data set and in each country) by performing likelihood ratio tests comparing an APC model with sex-APC interactions or country-APC interactions with the same model excluding the sex-cohort or country-cohort interactions, respectively.

| Box 1. APC modelling                          |   |
|---|---|
| Model parameters                              | Statistical notation  |
| Age (A)                                       | $\ln[\lambda_a] = \mu + \alpha_a$   |
| Age + drift (AD)                              | $\ln[\lambda_{ad}] = \mu + \alpha_a + \delta$                                   |
| Age + period (AP)                             | $\ln[\lambda_{ap}] = \mu + \alpha_a + \beta_p$                                  |
| Age + period + cohort (APC)                   | $\ln[\lambda_{ap}] = \mu + \alpha_a + \beta_p + \gamma_c$                       |
| Where $\lambda$ is the liver cirrhosis mortal | ity rate. $\mu$ is the intercept, $\alpha$ , $\beta$ and $\gamma$ represent the |
| age, period and birth cohort effects,         | and $\delta$ represents the drift.  |
|   |   |

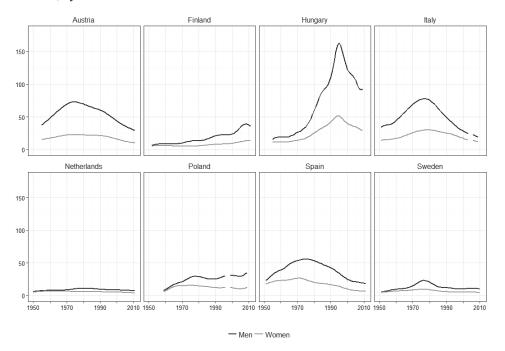
To assess the relative contributions of birth cohorts to the model fit, we calculated the percentage of scaled deviance between the models A and APC that is attributed to the drift, to the non-linear period, and to the non-linear birth cohort components. We also assessed the fit of the different models to the data with likelihood ratio tests. Because of the observations for the extreme cohorts were less complete, we limited our graphs to cohorts born between 1900 and 1980. All data analyses were performed using R 3.2.5 in R studio 0.99.451.

# 3.3. Results

# 3.3.1. Descriptive results

Age-standardised liver cirrhosis mortality rates—higher for men than for women and at different levels for the different countries—seem to exhibit different patterns over time across the analysed countries (Figure 3.1). In Austria, Italy, Spain and Sweden the decline in liver cirrhosis mortality rates started around 1975, whereas in Hungary in the 1990s and only very recently in Finland.

Examining the age-specific graphs (see Figure S3.2) reveals that for some populations the agespecific period patterns are clearly parallel (i.e., Italian men), which suggests the predominance of period effects; whereas in other populations (i.e., Polish and Dutch women) different period patterns can be observed for different age groups, which suggests the predominance of cohort effects.



**Figure 3.1.** Age-standardised liver cirrhosis mortality rate in 8 European countries, ages 15-94, 1950-2011, by sex

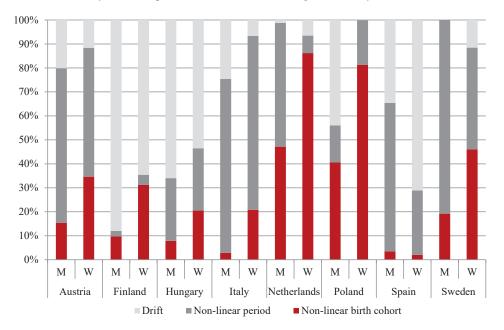
#### 3.3.2. APC modelling: the contribution of birth cohorts

Birth cohorts made statistically significantly contributions to the fit of the liver cirrhosis mortality model (p-values < 0.01), as compared with the AP models. These contributions were larger for women (unweighted average of 38.8%) than for men (unweighted average of 17.4%) in all countries except in Spain, and differed across countries (Figure 3.2). The contributions of birth cohorts were larger than the contributions of period and drift effects for Dutch and Polish women. In addition, the contributions of birth cohorts exceeded 20% for women in all of the other analysed countries except Spain. The APC models for all country-sex combinations provided a good fit to the data (p-values > 0.05).

#### 3.3.3. APC modelling: the effects of age, period, and birth cohort

Liver cirrhosis mortality rates increased with age for men until around ages 60-75 in all countries except Italy, where they kept increasing along the analysed age groups (Figure 3.3). Liver cirrhosis mortality generally peaked at slightly older ages for women than for men. In Hungary, however, the pattern among women looked similar to that of men, while in Italy no

decline was observed. Compared to the reference category (age 50), age effects were largest for women and in the Southern European countries.



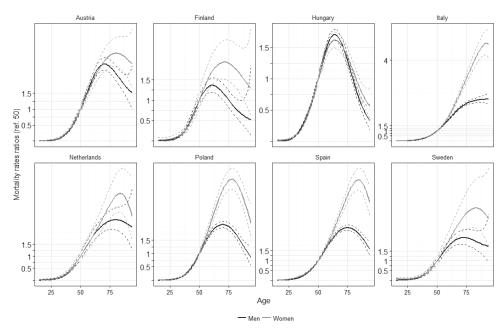
**Figure 3.2.** Contribution to the deviance reduction between models A and APC of liver cirrhosis mortality in 8 European countries 1950-2011, ages 15-94, by sex<sup>a,b,c</sup>

- a. M and W refer to men and women, respectively.
- b. Comparison between AP and APC models p-value (likelihood ratio test): p-values<0.01 in all countries and sexes.
- $c. \quad Comparison of the APC models to the data (likelihood ratio test): p-values > 0.05 in all countries and sexes.$

The period effects (including drift) logically showed the same pattern as the age-standardised liver cirrhosis mortality trends described above (see Figure S3.1).

Overall, the non-linear birth cohort patterns were statistically different across countries and between sex (Table 3.1). Although sex-differences were found in Italy, Spain and Hungary (p-values < 0.001), they were insignificant in all other analysed countries (p-values > 0.999). Birth cohort patterns were statistically different between all pairs of countries except for Netherlands-Finland (p-value = 0.932) and Netherlands-Austria (p-value > 0.999). The graphs of the birth cohort effects (Figure 3.4) suggest that the statistical difference in cohort patterns between most countries, and between sexes in some countries, is mostly due to differences in timing. Mortality started to decline for birth cohorts born around the 1940s and 1950s in Sweden and Finland,

and for cohorts born around the 1960s in Spain and Hungary. In Italy (men) and in Poland the onset of the decline was five to 10 years later.



**Figure 3.3.** Estimated age effects of liver cirrhosis mortality in 8 European countries, 1950-2011, by sex<sup>a</sup>

a. Dotted lines illustrate the 95% confidence intervals.

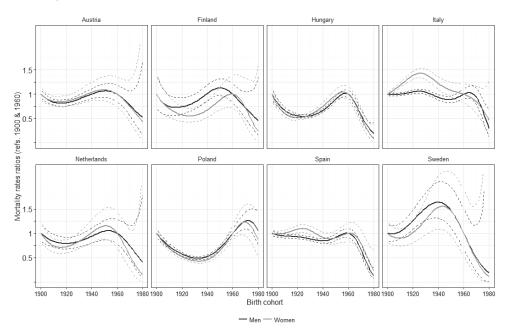
**Table 3.1**. Tests for cohort effects differences<sup>a</sup> by sex (in each country)<sup>b</sup> and between countries<sup>c</sup> in liver cirrhosis mortality (p-values)

|             | Sex     | Austria | Finland | Hungary | Italy   | Netherlands | Poland  | Spain  | Sweden |
|-------------|---------|---------|---------|---------|---------|-------------|---------|--------|--------|
| Austria     | >0.999  |         |         |         |         |             |         |        |        |
| Finland     | >0.999  | < 0.001 |         |         |         |             |         |        |        |
| Hungary     | < 0.001 | < 0.001 | 0.018   |         |         |             |         |        |        |
| Italy       | < 0.001 | < 0.001 | <0.001  | <0.001  |         |             |         |        |        |
| Netherlands | >0.999  | >0.999  | 0.932   | <0.001  | < 0.001 |             |         |        |        |
| Poland      | >0.999  | < 0.001 | <0.001  | <0.001  | < 0.001 | < 0.001     |         |        |        |
| Spain       | < 0.001 | < 0.001 | <0.001  | <0.001  | < 0.001 | < 0.001     | < 0.001 |        |        |
| Sweden      | >0.999  | < 0.001 | <0.001  | <0.001  | <0.001  | <0.001      | <0.001  | <0.001 |        |

a. For the grouped data of 8 countries the p-values for both sex and country differences were <0.001.

b. Likelihood ratio test for sex-specific cohort effects in each country.

c. Likelihood ratio test for country-specific cohort effects between pairs of countries.



**Figure 3.4.** Estimated non-linear birth cohort effects of liver cirrhosis mortality in 8 European countries, 1950-2011<sup>a</sup>

a. Dotted lines illustrate the 95% confidence intervals.

#### 3.4. Discussion

# 3.4.1. Summary of results

Birth cohorts contributed significantly to liver cirrhosis mortality trends in all eight European countries studied, and for both sexes. The relative contributions of birth cohorts differed across countries, and were larger for women than for men. The observed cohort patterns were statistically different between all, but two, country pairs. Sex differences in the patterns existed overall, but not in the majority of countries. Visual inspection of birth cohort patterns reveals that birth cohorts at higher risk of liver cirrhosis mortality were born around 1935-1949 in Sweden and Finland, around 1950 in Austria and the Netherlands, and around 1960 or later in the other analysed countries.

#### 3.4.2. Evaluation of data and methods

In all of the APC analyses an important methodological issue that arose was the treatment of the identification problem (birth cohort = period - age). Like previous demographic (Janssen et

al., 2005) and epidemiological studies (Bijlsma et al., 2012; Dhillon et al., 2011), we applied the standard Clayton and Schifflers approach (Clayton & Schifflers, 1987a,b) because it detects drift, or the co-linear pattern of period and cohort. Using this approach enabled us to identify cohort effects that could not be ascribed to period, although the total cohort effect was underestimated when the share of drift was large. However, because the contribution of drift for many countries (the Netherlands, Austria, Finland, Sweden, and Poland) appears to have been relatively small, our estimated cohort effects—and, consequently, age and period effects as well—are likely close to the real effects.

In our analyses, we compare countries across different European regions. Instead, we could have considered countries as nested in regions, which enables the comparison of cohort trends between regions by modelling country-level random effects and fixed-effect regional indicators (Brown & Prescott, 2006). We focus on the comparison of individual countries because it was as yet unknown to what extent cohort trends between individual countries within a region differ. Indeed, the evidence generated by this study (significant differences between pairs of countries within each region), indicates important within-regional variation. Therefore, we recommend that if a hierarchical (i.e. country-level random effect) approach is taken, more than two countries per region are selected so that regional effects can be precisely estimated despite potentially large within-regional variation.

In assessing the long-term trends in alcohol-related mortality in several European countries, we used liver cirrhosis mortality as a proxy, as was done in previous studies (Leon & McCambridge, 2006; Munoz-Perez & Nizard, 1999; Ramstedt, 2001; Ramstedt, 2007; Zatonski et al., 2010), which enabled us to avoid having to cope with International Classification of Diseases (ICD) revisions for more specific causes of death. Note, however, that liver cirrhosis mortality is a good indicator of alcohol-related chronic diseases, but not of acute conditions. Yet because most of mortality attributed to alcohol is from chronic diseases (i.e., Rehm et al., 2007; Rey et al., 2010), this is unlikely to have affected the results much. Furthermore, although viral hepatitis (Schuppan & Afdhal, 2008) and, to a lesser extent, obesity (i.e., Ioannou et al., 2003) are risk factors that sometimes accompany liver cirrhosis, their low prevalence (viral hepatitis) (Esteban et al., 2008) and different patterns over time (general increase in obesity) (OECD, 2012) suggest that they were of minimal importance. At the population level, liver cirrhosis mortality trends over calendar time generally seem to follow the patterns of per capita alcohol consumption in most European countries (Ramstedt, 2001; Ramstedt, 2007), which

indicates that alcohol was both the main contributor to and the driver of liver cirrhosis mortality trends (Zatonski et al., 2010).

# 3.4.3. Comparison of results with previous APC studies on alcohol-related mortality

Our birth cohort patterns estimates are directly comparable to those of two studies that assessed mortality from a few major diseases attributed to alcohol in Sweden (Rosén & Haglund, 2006) and in the Nordic countries, Germany, and France (Kraus et al., 2015). The birth cohort patterns we observed appear to be similar to the birth cohort patterns in alcohol-attributable mortality found in previous studies for Finland and Sweden, which again supports the use of liver cirrhosis mortality as a proxy for alcohol-related mortality. By including countries with different alcohol consumption levels, patterns and trends, we were able to observe important timing differences between and across countries in the birth cohort effects on liver cirrhosis mortality. Unlike for alcohol-related period trends, Sweden and Finland are forerunners in the cohort decline in alcohol-attributable mortality, whereas Poland seem to lag behind.

Our formal assessment of the actual contributions of birth cohorts to liver cirrhosis mortality trends by country, which was not done before, provided us with additional information about the relative importance of cohort and period patterns.

# 3.4.4. Explanation of results

We observed potential differences between the sexes and across countries in the contributions of birth cohorts to the liver cirrhosis mortality trends. Although different contributions of drift can affect the comparison of the contributions of birth cohorts, we can be certain that the cohort contributions in Poland and the Netherlands were larger for women than for men. These potential sex and country differences in the contributions of birth cohorts can be linked to differences between the sexes and countries in the abruptness of changes in alcohol consumption over time, and subsequent changes in alcohol-attributable mortality over calendar time versus cohort. For example, the small contributions of birth cohorts to liver cirrhosis mortality that we observed in Italy and Spain can be linked to the rapid decline in alcohol consumption over calendar time in those countries (World Health Organization. 2014). This is reflected in the clear bell-shaped curve in liver cirrhosis mortality across all age groups (Figure 3.1), and, more importantly, for the separate age groups (Figure S3.2), which could indicate that the economic factors and policy changes have affected drinking behaviour of the population more equally. Similarly, in Hungary the rapid changes in liver cirrhosis mortality over calendar

time (Figure 3.1) are well reflected in a relatively low contribution of birth cohorts as compared to period (Figure 3.2). For the Netherlands and Poland, on the other hand, the period changes in liver cirrhosis mortality were much less pronounced and varied for the different age groups (see Figure S3.2), which made room for larger contributions of the birth cohort dimension relative to the period dimension. Because women tend to drink less than men (Popova et al., 2007), variation in alcohol consumption over calendar time due to contextual effects (such as policy and cultural changes) is likely to have been smaller as well. Indeed, our results showed more level period trends in liver cirrhosis mortality for women than for men, combined with less parallel age-specific trends for women; which again resulted in cohort effects making stronger contributions for women than for men.

Birth cohort effects are larger when changes in mortality over time are observed for a few, rather than for all age groups. As young drinkers are expected to be more prone to change their drinking behaviour than older drinkers with well-established patterns (Kraus et al., 2015), they may be more likely to alter their patterns not only in response to changes in alcohol policy, but also to changes in levels of social awareness of alcohol damage. Therefore, it is plausible that changes of this kind have affected the drinking behaviour of the younger age groups in particular, and therefore resulted in cohort effects.

The observed differences in the timing of the increase and the subsequent decline in the risk of dying from liver cirrhosis for the subsequent cohorts—which occurred earlier in Sweden and later in Poland—seem to be very much in line with the assumption that economic progress led to contextual changes, especially for young people. Indeed, positive changes in alcohol policies and increased social awareness of alcohol damage generally occurred earlier in more economically advanced countries than in less economically advanced countries (Österberg & Karlsson, 2002). This hypothesis is also in line with the existing literature for Sweden, as the early peak in the cohort pattern has been linked to alcohol policies and social awareness (Kraus et al., 2015; Rosén & Haglund, 2006).

The birth cohorts at higher risk of liver cirrhosis mortality can also be linked with countryspecific alcohol consumption when those generations were young adults. In most Southern European countries, the decline in alcohol consumption started around 1975 (World Health Organization. 2014), and was mostly driven by economic factors and policy changes (Gual & Colom, 1997). This is in line with our observation for Spain that cohorts born around 1960 (aged around 15 in 1975) had higher risk of liver cirrhosis mortality. Similar links between the observed patterns for liver cirrhosis mortality and alcohol consumption can be made for Austria and the Netherlands, as alcohol consumption started to moderately decline in the late 1970s while the cohorts at higher risk of liver cirrhosis mortality were born in the 1950s. In Finland, by contrast, alcohol consumption did not decline during the 20<sup>th</sup> century (World Health Organization. 2014); however a decline in cohort liver cirrhosis mortality for birth cohorts born after 1950 could be observed. The cohorts at higher risk of liver cirrhosis mortality in Finland were adolescents and younger adults between the mid-1960s and the mid-1970s, when a dramatic increase in alcohol consumption in the country occurred (from 2.5 to 6.5 litres per person per year) in response to changes in alcohol policies (Karlsson & Österberg, 2002). For Poland and Hungary information about consumption levels is less reliable because of a large share of underreported home-made alcohol consumption (Popova et al., 2007), which tends to be more toxic (Szucs et al., 2005); however, the late peak in the cohort pattern certainly is in line with the observation that the change in context (and decline in alcohol sales data) occurred later in these countries than in most of the other analysed countries.

Further research should assess whether the decline in alcohol-related mortality risks along generational lines will continue for younger generations, given that in some European countries binge drinking has increased among recent generations (Harkonen & Mäkelä, 2011; OECD, 2015).

# 3.4.5. Conclusions

Overall, the inclusion of the birth cohort dimension significantly adds to our ability to describe and understand alcohol-attributable mortality trends in Europe. We observed clear differences across countries and between the sexes in the effects of birth cohorts on liver cirrhosis mortality trends, which could be linked to differences in the abruptness of changes in alcohol consumption over time. Also, differences in the timing of the birth cohorts experiencing smaller risks than their predecessors showed, with Sweden as a forerunner and Poland lagging behind all other analysed countries.

The cohort dimension should not be ignored in future studies, as it can not only provide information to health policy-makers about the age-specific impact of their health policies and other contextual changes; it can also provide information about which birth cohorts are at elevated risk of alcohol-attributable mortality, and will therefore affect future mortality levels.

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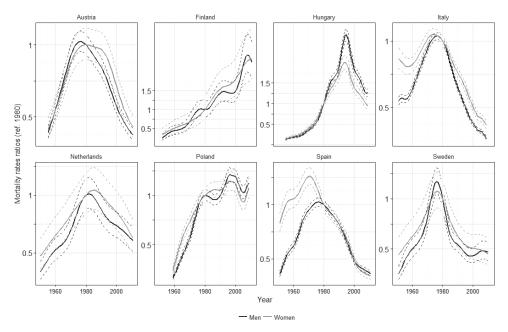
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| Country     | Age   | Period               | Birth Cohorts   |
|-------------|-------|----------------------|-----------------|
| Austria     | 15-94 | 1955-2011            | 1860/61-1995/96 |
| Finland     | 15-94 | 1952-2011            | 1857/58-1995/96 |
| Hungary     | 15-94 | 1955-2009            | 1860/61-1993/94 |
| Italy       | 15-94 | 1951-2003, 2006-2009 | 1856/57-1993/94 |
| Netherlands | 15-94 | 1950-2011            | 1855/56-1995/96 |
| Poland      | 15-94 | 1959-1996, 1999-2009 | 1864/65-1993/94 |
| Spain       | 15-94 | 1951-2011            | 1856/57-1995/96 |
| Sweden      | 15-94 | 1951-2010            | 1856/57-1994/95 |

# **Supporting Information**

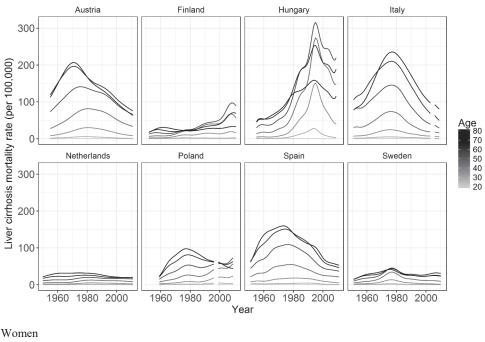
| Table S3.1. Age, p | eriod, and birth | cohorts included | d in the analy | sis by | country |
|--------------------|------------------|------------------|----------------|--------|---------|
|                    |                  |                  |                |        |         |

**Figure S3.1.** Estimated period effects (including drift) of liver cirrhosis mortality in 8 European countries, 1950-2011, by sex<sup>a</sup>

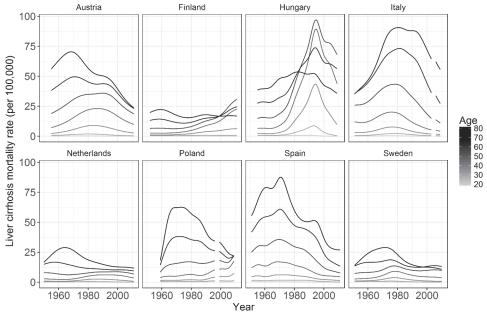


a. Dotted lines illustrate the 95% confidence intervals.

Men



# Figure S3.2. Age-period<sup>a</sup> liver cirrhosis mortality by country and sex (1950-2011)



For selected ages: 20, 30, ..., 80. a.

| 81

3

# **Chapter 4**

The contribution of alcohol to the East-West life expectancy gap in Europe from 1990 onward

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# Abstract

Background: Central and Eastern European (CEE) countries have lower life expectancies and higher alcohol-attributable mortality than Western European countries. We examine the contribution of alcohol consumption to mortality across Europe, and specifically to the East-West life expectancy gap from 1990 onward.

Methods: We retrieved alcohol-attributable mortality rates (GBD Study 2013) and all-cause mortality rates (Human Mortality Database) by age and sex for nine CEE countries and for the EU-15 countries. We assessed country-specific potential gains in life expectancy (PGLE) by eliminating alcohol-attributable mortality using associated single decrement life tables. We decomposed the life expectancy differences between each CEE country and the EU-15 population-weighted average for 1990-2012/13 into alcohol-attributable and non-alcohol-attributable mortality.

Results: In 2012/13, the PGLE for men and women were, respectively, 2.15 and 1.00 years in the CEE region and 0.90 and 0.44 years in the EU-15 region. The contribution of alcohol to the East-West gap in life expectancy was largest among men in Russia (2.88 years (Uncertainty intervals (UI): 1.57-4.06)), Belarus (3.70 years (UI: 1.75-5.45)), and Ukraine (2.47 years (UI: 0.90-3.88)). The relative contributions increased in most of the countries between 1990 and 2005 (on average, from 17.0% to 25.4% for men, and from 14.7% to 22.5% for women), and declined thereafter (20.2% for men and 20.5% for women in 2012/13).

Conclusions: Alcohol contributed substantially to the East-West life expectancy gap in Europe, and to its increase (1990-2005) and decline (2005 onward). Diminishing alcohol consumption in CEE countries to Western European levels can contribute to mortality convergence across Europe.

Keywords: Alcohol, life expectancy, East-West gap, mortality, Europe

## 4.1. Introduction

Levels of alcohol consumption are higher in Europe than elsewhere in the world (World Health Organization, 2014), and excess alcohol consumption is the third-leading cause of premature death in the EU (Mladovsky et al.,2009). Both alcohol prevalence and alcohol-attributable mortality levels differ substantially across Europe, with Eastern European countries experiencing higher levels of alcohol-attributable mortality than Western European countries (Franco, 2015; Rehm et al., 2011; World Health Organization, 2013; World Health Organization, 2014). Eastern European countries also perform worse than Western European countries in terms of overall mortality and life expectancy, with countries in the East having lower life expectancies and more irregular trends than countries in the West (Leon, 2011; Zatoński, 2008). The marked East-West differences in both alcohol-attributable mortality (e.g. Rehm et al., 2011) and life expectancy (e.g. Leon, 2011) suggest that alcohol contributes substantially to life expectancy differentials. Understanding the potential contribution of alcohol to the East-West life expectancy gap, and how it might be changing over time, is important for informing health policies aimed at reducing inequalities in mortality between countries.

Most of the previous research on the East-West mortality gap was based on analyses of broad groups of diseases (e.g. Meslé et al., 2002; Vallin & Meslé, 2004; Vallin, 2013; Zaridze et al., 2009; Zatoński, 2008), and showed that cardiovascular diseases and injuries were the main contributors to this life expectancy gap (Bobak et al., 2016; Meslé et al., 2002; Powles et al., 2005; Vallin, 2013; Zatoński, 2008). Because mortality from cardiovascular diseases and injuries is closely related to alcohol consumption in Eastern Europe (Bobak et al., 2016; Britton & McKee, 2000; Leon et al., 2010; Pridemore, 2016), several authors have postulated that alcohol is one of the main drivers of mortality and mortality differences across Europe (e.g. Anderson & Baumberg. 2006; Karanikolos et al., 2012; Leon et al., 1997; Meslé et al., 2002; Shkolnikov et al., 2001; Shkolnikov et al., 1998; Shkolnikov et al., 2004).

The actual impact of alcohol on life expectancy levels and trends has been assessed in few countries (e.g. Jasilionis et al., 2011; Martikainen et al., 2014), and only once on East-West life expectancy levels (Zatoński, 2008). This study by Zatoński estimated that in 2002 the contribution of alcohol to the life expectancy differences between the old and the new EU countries ranged from between 3% and 33% among men and between -8% and 22% among women (Zatoński, 2008).

However, for non-EU countries the size of this gap remains unknown. When studying alcoholattributable mortality across Europe, it is essential that Russia and other former Soviet countries are included, because relative to the EU countries, these countries have lower life expectancy levels and more irregular life expectancy trends (Leon, 2011), riskier drinking patterns (Popova et al., 2007), and higher levels of alcohol-related mortality (Leon et al., 2007).

In addition, it is unknown how the contribution of alcohol to East-West differences in life expectancy levels has developed in recent years. This is particularly interesting because of the East-West country-specific differences in life expectancy trends. Whereas life expectancy levels have gradually increased in Western Europe, in Eastern Europe they actually declined or stagnated from 1986 onwards. Increases reoccurred in central European countries around 1990, in the Baltic states in 1995 (Leon, 2011), but in the other former Soviet countries from 2005 onwards (Rechel et al., 2013). This has led to divergence in mortality until 2005, followed by convergence (Muszyńska & Janssen, 2016). In this context, examining the relative importance of alcohol may provide insights into the determinants of mortality disparities across Europe.

Our aim is to examine the impact of alcohol consumption on mortality in 24 European countries, and its contribution to the East-West life expectancy gap from 1990 onward.

## 4.2. Data and Methods

## 4.2.1. Settings

We studied the EU-15 countries as representative of Western Europe, and nine Central and Eastern European (CEE) countries: Belarus, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Russia, and Ukraine.

## 4.2.2. Data

Alcohol-attributable mortality rates, with their corresponding 95% uncertainty intervals (UI), were retrieved from the Global Burden of Disease Study 2013 (GBD) by country, five-year age group (up until 80+), sex, and year (1990, 1995, 2000, 2005, 2010, and 2013) (GBD 2013 Risk Factors Collaborators et al., 2015; Global Burden of Disease Study 2013, 2016). The GBD estimates include deaths due to causes wholly-attributable to alcohol and they estimated the proportions of deaths due to causes partly-related to alcohol using alcohol prevalence and dose-specific relative risks (for further detail, see Agardh et al., 2016; GBD 2013 Risk Factors Collaborators et al., 2015).

All-cause mortality data by country, year, and five-year age group were retrieved from the Human Mortality Database (HMD) (HMD, 2016). We used 2012 all-cause mortality data (data for 2013 were not available for all countries) and 2013 alcohol-attributable mortality data to obtain results for 2012/13.

#### 4.2.3. Methods

The analyses were performed separately by sex, using five-year age group data (up to 110+). We applied the alcohol-attributable death rate for 80+ to the age groups from age 80 onward.

Life expectancies at birth were calculated for each country using standard life table techniques (Preston et al., 2000). To visualize the geographical differences, we mapped life expectancies at birth and age-standardized alcohol-attributable mortality for European countries for 2012 and 2013, respectively.

To estimate the contribution of alcohol to life expectancy in each individual country in 2012/2013, we applied associated single decrement life tables (ASDLT) (Preston et al., 2000) to non-alcohol-attributable mortality obtained by subtracting alcohol-attributable mortality from all-cause mortality. Comparing life expectancies at birth from the ASDLT with the original life expectancies at birth, we obtained potential gains in life expectancy (PGLE) by eliminating alcohol-attributable mortality.

To estimate the East-West life expectancy gap by year, we calculated an average life expectancy for Western Europe using the total death counts and exposures from EU-15 countries, and subtracted from these population-weighted averages the life expectancies of each individual CEE country.

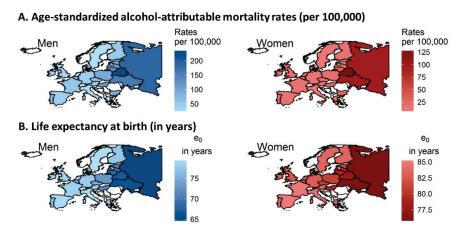
To estimate the contribution of alcohol to the East-West life expectancy gap, we used the decomposition technique by Andreev et al. (2002). This involved 1) decomposing the differences in life expectancy into the contribution of each age-specific group (Andreev et al., 2002), 2) decomposing these age-specific contributions into the contribution of alcohol-attributable mortality and the contribution of non-alcohol-attributable mortality by multiplying the age-specific contributions by the relative importance of alcohol to total mortality differences in each age group, and 3) summing up the age-specific contributions of alcohol- and non-alcohol attributable mortality. The upper and lower 95% uncertainty intervals (UI) were obtained using the 95% UI data from CEE countries. All of the data analyses were performed using R 3.2.4 (R Core Team (2016)) in R studio 0.99.893 (RStudio Team, 2015).

# 4.3. Results

# 4.3.1. Descriptive results

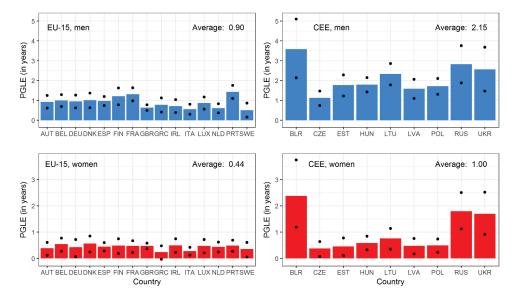
Across Europe, the age-standardized alcohol-attributable mortality rates were higher for men than for women. For both men and women, these rates were higher in most of the CEE countries than in the Western European countries in 2013 (Figure 4.1A). This pattern persisted over the period 1990-2013 (Table S4.1). Life expectancies in 2012 displayed the same patterns (but inversed), and all of the Western European countries had higher life expectancy levels than the CEE countries (Figure 4.1B) across the period 1990-2012 (Figure S4.1).

**Figure 4.1.** Age-standardized alcohol-attributable mortality (per 100,000) in Europe in 2013 (A) and life expectancy at birth (e0) in Europe in 2012 (B), by country and sex



In 2012/2013 in Western Europe, the average PGLE after alcohol-attributable mortality was eliminated was 0.90 years among men, ranging from 0.51 years (UI: 0.16-0.86) in Sweden to 1.43 years (UI: 1.10-1.76) in Portugal (Figure 4.2). Among women in Western Europe, the average PGLE was 0.44 years, ranging from 0.24 years (UI: -0.03-0.47) in Greece to 0.57 years (UI: 0.24-0.85) in Denmark. Among men in Eastern Europe, the average PGLE was 2.15 years, ranging from 1.13 years (UI: 0.75-1.47) in the Czech Republic to 3.59 years (UI: 2.14-5.10) in Belarus. The average PGLE among Eastern European women was 1.00 years, ranging from 0.38 years (UI: 0.07-0.64) to 2.38 years (UI: 1.19-3.75). Over the period 1990-2012/13, the PGLE were generally higher in the CEE countries than in the Western European countries (Tables S4.2 and S4.3).

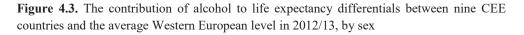
**Figure 4.2**. Potential gains in life expectancy (PGLE) by eliminating alcohol-attributable mortality in 2012/13, by country and sex

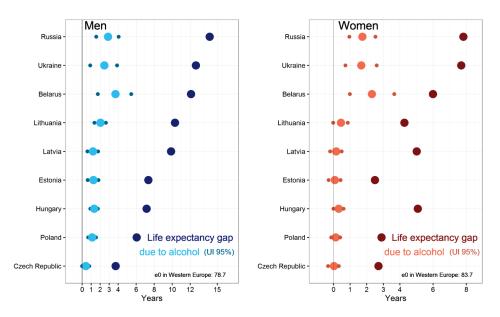


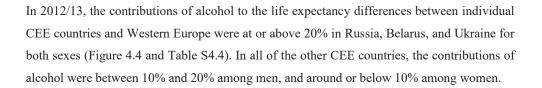
a. Black dots represent the upper and lower bounds of the uncertainty interval (UI).

b. Country abbreviations: Austria (AUT), Belgium (BEL), Germany (DEU), Denmark (DNK), Spain (ESP), Finland (FIN), France (FRA), United Kingdom (GBR), Greece (GRC), Ireland (IRL), Italy (ITA), Luxembourg (LUX), Netherlands (NLD), Portugal (PRT), Sweden (SWE), Belarus (BLR), Czech Republic (CZE), Estonia (EST), Hungary (HUN), Lithuania (LTU), Latvia (LVA), Poland (POL), Russia (RUS), and Ukraine (UKR).

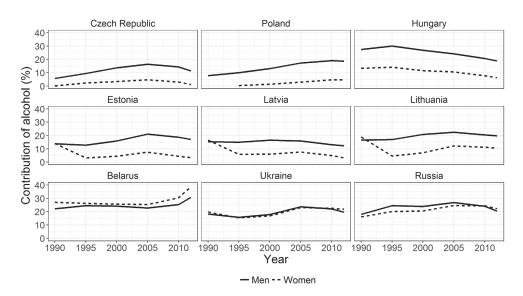
In 2013 the sizes of the life expectancy gaps between Eastern European countries and the average Western European level (78.7 years among men, 83.7 years among women) ranged from almost four to 15 years among men and from 2.5 to eight years among women (Figure 4.3). The contribution of alcohol to the East-West difference in life expectancy was greater in Russia, Belarus, and Ukraine than in any of the other countries (Figure 4.3). Among men, it was 3.70 years (UI: 1.75-5.45) in Belarus, 2.88 years (UI: 1.57-4.06) in Russia, and 2.47 years (UI: 0.90-3.88) in Ukraine. The average across the other analyzed countries (the Czech Republic, Estonia, Hungary, Latvia, Lithuania, and Poland) was smaller, but still positive at 1.23 years. Among women, the gap was 2.14 years (UI: 1.01-3.24) in Belarus, 1.74 years (UI: 0.95-2.53) in Russia, and 1.67 years (UI: 0.62-2.60) in Ukraine.







The relative contributions of alcohol to the life expectancy gap increased between 1990 and 2005 from 17.0% to 25.4% among men and from 14.7% to 22.5% among women (population-weighted averages). Increases in the contributions of alcohol were observed in most of the countries over the period 1990-2005, except in Belarus and Hungary. Since 2005 the contribution of alcohol to life expectancy differences has been (slightly) declining in all of the CEE countries, except in Belarus and Poland, in 2012/13 the average contribution across the CEE countries had reached 20.2% among men and 20.5% among women.



**Figure 4.4.** The relative contribution of alcohol to the life expectancy gap between individual CEE countries and the average Western European level over time (1990-2012/13), by sex

#### 4.4. Discussion

#### 4.4.1. Summary of results

In 2012/2013, the impact of alcohol on life expectancy was substantial, and was greater in the CEE countries (2.15 and 1.00 years of PGLE for men and women, respectively) than in the Western European countries (0.90 and 0.44 years). This impact differed greatly within the CEE region, and was largest among men in Belarus, Russia, and Ukraine. In most of the CEE countries, the relative contribution of alcohol to the East-West gap in life expectancy increased between 1990 and 2005 (on average, from 17.0 to 25.4% among men and from 14.7% to 22.5% among women), but declined thereafter, falling to 20.2% among men and 20.5% among women in 2012/13. Recently, the relative contribution of alcohol among men has been relatively similar across the countries, whereas among women it has been larger in Belarus, Russia, and Ukraine.

# 4.4.2. Evaluation of data

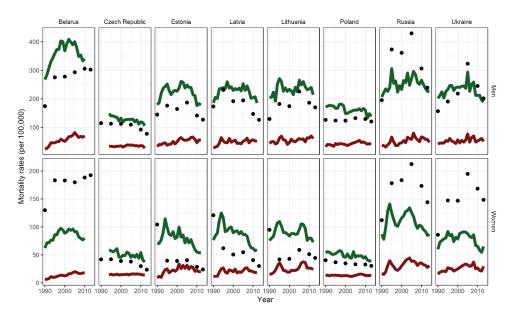
The study used harmonized, uniformly calculated, and comparable mortality data across countries from the Human Mortality Database (HMD) (Barbieri et al., 2015). The data on deaths were nearly complete for all of the countries under study. To ensure the accuracy and consistency of the data, the HMD adjusted the raw population data for the CEE countries (Wilmoth et al., 2007).

The estimation of alcohol-attributable mortality is a challenge for researchers, as death certificates provide information on the so-called "underlying cause of death" (e.g., heart disease, cancer, or a digestive disease), but not on conditions underlying the occurrence of disease and injuries, such us excessive alcohol consumption. We have carefully considered different approaches for estimating alcohol-attributable mortality. In addition to using the Global Burden of Disease (GBD) approach, we considered two cause-of-death approaches: an approach that only takes into account the main diseases that are wholly attributed to alcohol consumption, as well as liver cirrhosis; and the Health for All-Database (HFA-DB) approach. The first method clearly underestimates alcohol-attributable mortality (Figure 4.5), because much of the impact of alcohol on health and mortality outcomes is channeled through diseases and injuries that are not caused solely by alcohol (Corrao et al., 1999). The HFA-DB approach is based on strong assumptions, such as that all external deaths are due to alcohol. Meanwhile, the GBD estimates include both deaths due to conditions that are wholly attributable to alcohol and a share of deaths due to conditions that are partly attributable to alcohol.

The estimation of alcohol-attributable mortality from diseases that are partly attributable to alcohol depends on the quality of alcohol prevalence data and on the relative risks used (e.g. Guerin et al., 2013; Rey & Jougla, 2014). Alcohol prevalence was estimated by the GBD using alcohol consumption per capita data, adjusted for unrecorded consumption (using a correction factor from WHO); and country survey data that provide information on the distribution of alcohol consumption according to sex and age (GBD 2013 Risk Factors Collaborators et al., 2015). Although this approach is sophisticated, and that enormous efforts have been made by Rehm and colleagues, the use of different sources of data for different countries and over time—which vary in their levels of completeness and accuracy—may have influenced our results. Thus, the GBD estimates are less reliable in countries with large shares of unreported alcohol consumption (Russia, Ukraine and Belarus), because of the inherent uncertainty of unrecorded alcohol consumption estimates.

In terms of the RRs, it should be noted that the GBD used Russian sex-specific RRs (Zaridze et al., 2009) for the most important causes of death partly attributable to alcohol for Russia, Belarus, and Ukraine; for all of the estimations from 1990 to 2013 (GBD 2013 Risk Factors Collaborators et al., 2015); and for the Baltic states in 1990 (Max Griswold, personal communication, August 13, 2016). This was done to account for differences in the risk of dying from alcohol-related causes of death (Zaridze et al., 2009).

**Figure 4.5.** Comparison of age-standardized alcohol-attributable mortality rates between the GBD estimates (black dots), conditions wholly attributable to alcohol and liver cirrhosis (dark red line), and estimates using the HFADB definition (dark green line)<sup>1</sup>, for selected CEE countries over time (1990-2012/2013)<sup>2</sup>



1. Different approaches to estimating alcohol-attributable mortality exist. These can be divided into cause-of deathapproaches and attributable fraction approaches. Examples of cause-of-death approaches are those that include the main diseases wholly attributable to alcohol consumption and liver cirrhosis (F10, K70-K76, X45); and the Health for All-Database (HFA-DB) approach, which includes cancers of the esophagus and larynx, alcohol dependence syndrome, liver cirrhosis, and all external causes (C15, C32, F10, K70-76, V00-Y99). The GBD estimates include both the share of deaths due to conditions wholly attributable to alcohol and the share of deaths due to conditions partly attributable to alcohol using alcohol prevalence data, cause-specific mortality, and dose-specific relative risks. Because the first method clearly underestimates alcohol-attributable mortality, whereas the second is based on strong assumptions (e.g., that all external deaths are due to alcohol), we used the GBD estimates for this article.

#### 2. Data for Hungary were not available.

Source: Own elaboration based on data from the Global Burden of Disease 2013 Study and from the Human Causeof-death Database (<u>http://www.causesofdeath.org/</u>).

However, Russian-specific RR have several important limitations, as already discussed by Shield and Rehm (2015). Additional analysis in which we compared the GBD estimates with cause-specific alcohol-attributable mortality approaches (Figure 4.5) revealed that the GBD estimates for women—but not for men—are much higher in Russia, Belarus and Ukraine from 1990 to 2013. In addition, trends for women in Baltic states revealed high and unlikely differences between 1990 and 1995. Especially among women in the countries where Russian-

specific RR were applied we, therefore, should be cautious about the estimates. Overall time trends seem only affected for Baltic states in 1990-95.

# 4.4.3. Comparison of results

The only previous study that formally assessed the contribution of alcohol to life expectancy differences across European countries found that in 2002 the contribution of alcohol to the differences between new and the old EU countries (ages 20-64) was 25% among men and 6% among women (Zatoński, 2008). Our all-age are similar for men (weighted average of 22.1% in 2000 and 25.4% in 2005), but higher for women (18.2% and 22.5%). Differences in mortality at ages above 65 have limited impact on the overall contribution to life expectancy differences across countries. Therefore, we do not expect the use of different age groups to have a big influence, although we recognize our results may be slightly higher because of the use of all age groups. Moreover, both studies used similar methods to estimate alcohol-attributable mortality, except that we used more recent attributable fractions. A main difference is that we included Russia, Ukraine and Belarus, where levels of alcohol-attributable mortality are especially high for women.

# 4.4.4. Discussion of results

Our findings for 2012/13 that alcohol had a greater impact on life expectancy in the CEE countries than in the Western European countries, and that alcohol therefore made a positive contribution to the East-West differences in life expectancy, are likely related to the demonstrable East-West differences in alcohol consumption. In 2010, the recorded levels of alcohol consumption were higher in CEE than in Western Europe (Figure S4.2). In addition, Eastern European countries had higher shares of unreported consumption and riskier drinking patterns (Mäkelä et al., 2006; Popova et al., 2007; World Health Organization, 2014). Both the total amounts of alcohol consumed and the binge drinking prevalence levels are especially high among men, and in Russia, Belarus, and Ukraine (World Health Organization, 2014).

The increase in the relative contribution of alcohol to the East-West life expectancy gap until 2005 might in principle have occurred because the East-West gap in life expectancy itself decreased. However, this gap increased until 2005 (Mackenbach, 2013). Therefore, the increasing contribution is likely to be linked to trends in alcohol consumption.

In the 1990s and the early 2000s, alcohol consumption increased in the former Soviet republics (e.g. Grigoriev & Andreev, 2015; World Health Organization, 2014). For example, the recorded

levels of pure alcohol consumption per person per year in Russia increased from around eight liters in 1990 to around 11 liters in 1995 and to 12 liters in 2006 (Grigoriev & Andreev, 2015), and similar increases are observed for unrecorded alcohol consumption in the early 1990s and 2000s (Moskalewicz & Österberg, 2016; Nemtsov, 2002). This rise in alcohol consumption in the early 1990s likely occurred because the anti-alcohol measures implemented by Gorbachev were phased out during a severe health and socioeconomic crisis. In that context, alcohol consumption kept increasing in most former Soviet republics until around mid-2000. In Central Europe, the socioeconomic and health circumstances were much more favorable, and alcohol consumption stagnated in Czech Republic and Poland in the 1990s, whereas it kept moderately declining in Western Europe (World Health Organization, 2014).

From around 2005 onward, the relative contribution of alcohol to the East-West life expectancy gap declined. This development occurred in the context of overall mortality convergence (Muszyńska & Janssen, 2016) and a decline in alcohol consumption in the CEE region. Between 2007 and 2010 pure alcohol consumption per capita dropped in all of the CEE countries analyzed, except in Belarus. Especially in in Russia, Latvia, Estonia, and Hungary these declines were marked, e.g. at or above 10% (HFA-DB).

These recent declines in alcohol consumption can partly be linked to the implementation starting in the mid-2000s of a range of policies that have proven successful in tackling alcohol abuse: alcohol tax increases in Estonia (2008), Latvia (2006, 2009), Lithuania (2008, 2009) (Jasilionis et al., 2011), and Ukraine (2009) (Krasovsky, 2016); the enactment of a federal law regulating the production and sale of ethyl alcohol in Russia (2005) (Grigoriev & Andreev, 2015; Neufeld & Rehm, 2013); and the adoption of the third program of alcoholism prevention in Belarus (2011) (Grigoriev & Andreev, 2015). Alcohol-related policies cannot be the only factor though. That is, in some CEE countries (such as Russia and Belarus) the decline in alcohol consumption had started before these policies were implemented (Grigoriev & Andreev, 2015). In addition, the economic crisis of 2008 might have affected alcohol consumption. According to studies conducted in Ukraine and the Baltic states, the recession may have contributed to declines to alcohol consumption and attributable mortality, because alcohol became less affordable (Moskalewicz & Österberg, 2016). However, a recent review showed that economic crises can affect alcohol consumption in many different ways (De Goeij et al., 2015). More research is needed to completely unravel the causes behind the recent declines in alcohol consumption in CEE countries.

## 4.5. Conclusion

Despite some important data limitations, we showed that alcohol consumption contributed substantially to the East-West life expectancy gap in Europe, especially among those populations characterized by riskier patterns of drinking: namely, men in Russia, Belarus, and Ukraine. Furthermore, alcohol contributed to both the diverging (1990-2005) and the converging (2005 onwards) mortality trends in Europe. The implementation of alcohol-related policies in the CEE countries may have contributed to the recent convergence in mortality. The further development of preventive alcohol policies is needed to ensure that life expectancy levels further increase in the CEE countries and become more equal across Europe.

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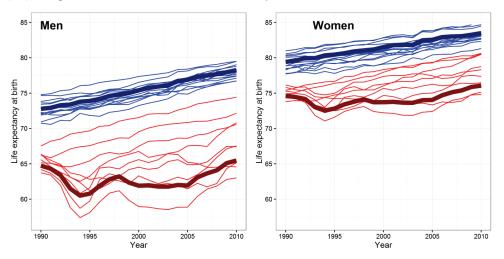
# Supporting information

| Men            |       |       |       |       |       |       | Wom  | en    |       |       |       |       |
|----------------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|-------|-------|
| <u></u>        | 1990  | 1995  | 2000  | 2005  | 2010  | 2013  | 1990 | 1995  | 2000  | 2005  | 2010  | 2013  |
| Belarus        | 139.4 | 218.6 | 220.1 | 231.0 | 240.2 | 238.0 | 85.0 | 120.2 | 120.7 | 119.4 | 124.6 | 127.1 |
| Czech Republic | 88.0  | 87.3  | 87.5  | 85.0  | 70.9  | 59.4  | 27.4 | 27.9  | 26.3  | 25.6  | 20.3  | 16.1  |
| Estonia        | 114.8 | 141.1 | 130.9 | 147.0 | 110.0 | 98.5  | 67.8 | 28.4  | 28.4  | 29.4  | 20.5  | 17.1  |
| Hungary        | 216.0 | 228.7 | 188.4 | 170.0 | 133.8 | 114.8 | 66.1 | 63.1  | 52.0  | 46.4  | 35.2  | 29.4  |
| Latvia         | 137.5 | 184.2 | 152.4 | 153.4 | 115.5 | 99.0  | 78.3 | 41.7  | 34.7  | 38.0  | 28.2  | 20.8  |
| Lithuania      | 103.4 | 146.3 | 139.3 | 179.8 | 147.4 | 134.6 | 62.8 | 30.5  | 30.9  | 42.3  | 36.7  | 31.8  |
| Poland         | 98.4  | 96.8  | 96.4  | 102.7 | 100.1 | 93.4  | 26.3 | 24.3  | 23.5  | 22.6  | 22.3  | 20.6  |
| Russia         | 156.4 | 299.5 | 288.7 | 342.7 | 243.9 | 190.3 | 74.8 | 121.3 | 124.5 | 145.7 | 118.0 | 97.3  |
| Ukraine        | 124.4 | 151.7 | 172.3 | 255.5 | 193.0 | 159.3 | 82.5 | 97.2  | 97.6  | 131.2 | 112.2 | 98.4  |
| Austria        | 90.3  | 81.0  | 72.9  | 65.8  | 50.4  | 41.0  | 34.0 | 30.2  | 28.5  | 23.2  | 17.0  | 14.4  |
| Austria        | 90.5  | 81.0  | 12.9  | 03.8  | 50.4  | 41.0  | 54.0 | 30.2  | 28.3  | 23.2  | 17.0  | 14.4  |
| Belgium        | 55.5  | 56.6  | 56.4  | 52.0  | 49.2  | 45.0  | 26.4 | 25.8  | 24.6  | 23.5  | 22.6  | 20.9  |
| Denmark        | 46.0  | 52.0  | 58.3  | 61.4  | 54.2  | 45.6  | 32.5 | 33.7  | 32.7  | 31.1  | 26.2  | 23.0  |
| Finland        | 60.5  | 52.0  | 56.6  | 64.0  | 57.2  | 50.8  | 24.1 | 19.3  | 20.5  | 22.8  | 19.9  | 17.2  |
| France         | 93.8  | 84.2  | 75.6  | 66.0  | 60.9  | 55.8  | 24.9 | 22.4  | 20.4  | 18.1  | 17.2  | 15.8  |
| Germany        | 58.1  | 57.1  | 53.9  | 48.7  | 47.4  | 43.1  | 21.1 | 19.8  | 20.3  | 18.5  | 18.1  | 16.2  |
| Greece         | 56.0  | 46.9  | 43.3  | 39.7  | 37.3  | 35.1  | 18.9 | 15.7  | 14.4  | 12.5  | 10.1  | 9.5   |
| Ireland        | 34.3  | 40.3  | 45.8  | 39.7  | 35.0  | 31.0  | 25.7 | 29.1  | 28.8  | 25.0  | 21.3  | 19.2  |
| Italy          | 62.9  | 51.0  | 42.1  | 34.0  | 27.2  | 23.6  | 25.0 | 20.7  | 16.6  | 13.3  | 11.0  | 10.2  |
| Luxembourg     | 66.8  | 64.9  | 64.7  | 59.6  | 44.7  | 38.4  | 28.0 | 24.7  | 26.2  | 23.3  | 20.1  | 17.8  |
| Netherlands    | 34.8  | 36.2  | 39.5  | 34.9  | 31.6  | 30.0  | 20.9 | 20.6  | 22.3  | 19.9  | 17.4  | 17.6  |
| Portugal       | 123.9 | 109.4 | 95.2  | 84.9  | 72.6  | 68.7  | 40.6 | 34.1  | 29.3  | 24.8  | 20.3  | 18.7  |
| Spain          | 86.2  | 72.3  | 65.1  | 58.5  | 46.7  | 43.8  | 30.4 | 24.7  | 21.3  | 19.0  | 16.7  | 15.6  |
| Sweden         | 25.3  | 22.1  | 22.3  | 24.2  | 23.1  | 21.2  | 19.0 | 16.1  | 15.6  | 15.7  | 14.3  | 13.6  |
| UK             | 26.2  | 26.6  | 31.8  | 35.5  | 32.7  | 27.2  | 26.4 | 23.1  | 24.0  | 24.4  | 21.3  | 18.5  |

**Table S4.1.** Age-standardized alcohol-attributable mortality rates (per 100,000) in European countries, 1990-2013, by sex

Source: GBD Study 2013.

**Figure S4.1.** Life expectancy at birth (e0) in Western (EU-15) (blue) and Central and Eastern (red) European countries, over time, 1990-2012, by sex



a. Bold lines illustrate the weighted averages for the Western and the Central and Eastern regions.

|         | Austria | Belgium | Denmark | Finland | France | Germany | Greece | Ireland | Italy | Luxembourg | Netherlands | Portugal | Spain | Sweden | United<br>Kinødom | EU-15 |
|---------|---------|---------|---------|---------|--------|---------|--------|---------|-------|------------|-------------|----------|-------|--------|-------------------|-------|
| Men     |         |         |         |         |        |         |        |         |       |            |             |          |       |        |                   |       |
| 1990    | 1.68    | 1.07    | 0.96    | 1.20    | 1.82   | 1.15    | 1.07   | 0.60    | 1.16  | 1.21       | 0.59        | 2.13     | 1.60  | 0.58   | 0.53              | 1.18  |
| 1995    | 1.57    | 1.12    | 1.04    | 1.10    | 1.69   | 1.18    | 0.91   | 0.72    | 1.00  | 1.17       | 0.61        | 1.95     | 1.39  | 0.51   | 0.56              | 1.13  |
| 2000    | 1.47    | 1.14    | 1.17    | 1.22    | 1.58   | 1.13    | 0.83   | 0.87    | 0.88  | 1.21       | 0.68        | 1.75     | 1.30  | 0.52   | 0.68              | 1.09  |
| 2005    | 1.39    | 1.10    | 1.27    | 1.45    | 1.45   | 1.04    | 0.83   | 0.85    | 0.75  | 1.21       | 0.65        | 1.63     | 1.19  | 0.56   | 0.79              | 1.04  |
| 2010    | 1.11    | 1.08    | 1.15    | 1.33    | 1.41   | 1.03    | 0.83   | 0.80    | 0.63  | 0.95       | 0.63        | 1.47     | 1.02  | 0.55   | 0.76              | 0.97  |
| 2012/13 | 0.93    | 1.00    | 1.01    | 1.21    | 1.31   | 0.95    | 0.78   | 0.71    | 0.56  | 0.87       | 0.61        | 1.43     | 0.97  | 0.51   | 0.64              | 0.89  |
| Women   |         |         |         |         |        |         |        |         |       |            |             |          |       |        |                   |       |
| 1990    | 0.74    | 0.61    | 0.72    | 0.55    | 0.64   | 0.51    | 0.39   | 0.50    | 0.57  | 0.62       | 0.47        | 0.85     | 0.70  | 0.45   | 0.55              | 0.57  |
| 1995    | 0.70    | 0.61    | 0.72    | 0.47    | 0.60   | 0.50    | 0.33   | 0.57    | 0.50  | 0.58       | 0.46        | 0.76     | 0.60  | 0.39   | 0.50              | 0.53  |
| 2000    | 0.68    | 0.59    | 0.72    | 0.52    | 0.56   | 0.52    | 0.31   | 0.59    | 0.42  | 0.62       | 0.50        | 0.67     | 0.54  | 0.39   | 0.54              | 0.52  |
| 2005    | 0.58    | 0.58    | 0.72    | 0.62    | 0.51   | 0.48    | 0.29   | 0.59    | 0.35  | 0.58       | 0.47        | 0.59     | 0.49  | 0.40   | 0.58              | 0.49  |
| 2010    | 0.45    | 0.59    | 0.63    | 0.56    | 0.51   | 0.47    | 0.25   | 0.54    | 0.30  | 0.53       | 0.43        | 0.52     | 0.47  | 0.37   | 0.54              | 0.46  |
| 2012/13 | 0.38    | 0.54    | 0.57    | 0.48    | 0.47   | 0.43    | 0.24   | 0.49    | 0.28  | 0.47       | 0.44        | 0.48     | 0.44  | 0.35   | 0.47              | 0.42  |

**Table S4.2.** Potential gains in life expectancy by eliminating alcohol-attributable mortality in Western European countries, over time (1990-2012/13), by sex

**Table S4.3.** Potential gains in life expectancy by eliminating alcohol-attributable mortality in

 CEE countries over time (1990-2012/13), by sex

| Men     | Belarus | Czech<br>Renublic | Estonia | Hungary | Lithuania | Latvia | Poland | Russia | Ukraine | CEE  |
|---------|---------|-------------------|---------|---------|-----------|--------|--------|--------|---------|------|
| 1990    | 2.28    | 1.17              | 1.87    | 2.74    | 1.94      | 2.02   | 1.37   | 2.28   | 2.10    | 2.09 |
| 1995    | 3.05    | 1.28              | 2.00    | 3.04    | 2.33      | 2.33   | 1.43   | 3.68   | 2.34    | 2.99 |
| 2000    | 3.10    | 1.39              | 2.10    | 2.65    | 2.42      | 2.24   | 1.55   | 3.65   | 2.60    | 3.02 |
| 2005    | 3.11    | 1.45              | 2.42    | 2.44    | 2.91      | 2.18   | 1.76   | 4.17   | 3.42    | 3.52 |
| 2010    | 3.28    | 1.31              | 1.95    | 2.05    | 2.50      | 1.79   | 1.81   | 3.43   | 2.91    | 2.95 |
| 2012/13 | 3.59    | 1.13              | 1.78    | 1.79    | 2.34      | 1.60   | 1.72   | 2.82   | 2.56    | 2.50 |
| Women   |         |                   |         |         |           |        |        |        |         |      |
| 1990    | 1.43    | 0.45              | 1.03    | 1.11    | 1.10      | 1.18   | 0.45   | 1.20   | 1.27    | 1.08 |
| 1995    | 1.85    | 0.50              | 0.59    | 1.13    | 0.66      | 0.79   | 0.44   | 1.87   | 1.38    | 1.47 |
| 2000    | 1.88    | 0.52              | 0.63    | 0.96    | 0.71      | 0.71   | 0.47   | 1.93   | 1.46    | 1.51 |
| 2005    | 1.95    | 0.54              | 0.71    | 0.88    | 0.96      | 0.79   | 0.50   | 2.39   | 2.07    | 1.90 |
| 2010    | 2.16    | 0.46              | 0.52    | 0.70    | 0.86      | 0.62   | 0.52   | 2.09   | 1.85    | 1.68 |
| 2012/13 | 2.38    | 0.38              | 0.45    | 0.59    | 0.76      | 0.48   | 0.49   | 1.79   | 1.69    | 1.46 |

| Country         Year         e0 gap         Alcohol contr.         e0 gap         Alcohol contr.           1990         6.54         1.45 (0.25-2.50)         22.1%         3.61         0.98 (0.23-1.76)         26.3%           Belarus         2000         12.10         2.92 (1.29-4.36)         24.1%         6.83         1.75 (0.72-2.80)         25.6%           2010         13.68         3.46 (1.78-4.92)         25.3%         7.02         2.14 (1.01-3.24)         30.5%           2012/13         12.09         3.70 (1.75-5.45)         30.6%         5.99         2.31 (0.99-3.66)         38.6%           1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           2012/13         2.09         3.70 (1.75-5.45)         30.6%         3.79         0.09 (-0.31-0.44)         2.3%           Czech         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.87         0.63 (0.06-1.27)         14.0%  |             |         | Men    |                   |       | Women  |                    |       |
|--|-------------|---------|--------|-------------------|-------|--------|--------------------|-------|
| Belarus         1995         11.11         2.72 (1.30-3.95)         24.5%         6.24         1.64 (0.65-2.64)         26.3%           2000         12.10         2.92 (1.29-4.36)         24.1%         6.83         1.75 (0.72-2.80)         25.6%           2010         13.68         3.46 (1.78-4.92)         22.3%         7.54         1.90 (0.85-2.97)         25.2%           2012         13.209         3.70 (1.75-5.45)         30.6%         5.99         2.31 (0.99-3.66)         38.6%           1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           Czech         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           Republic         2000         3.84         0.55 (0.13-0.39)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         7.5%           2010         7.45         1.39 (0.75-1.39)         18.7%         2.024 (-0.19-0.64)         4.5%  | Country     | Year    | e0 gap | Alcohol contr.    |       | e0 gap | Alcohol contr.     |       |
| Belarus         2000         12.10         2.92 (1.29-4.36)         24.1%         6.83         1.75 (0.72-2.80)         25.6%           2015         14.14         3.21 (1.49-4.67)         22.7%         7.54         1.90 (0.85-2.97)         25.2%           2010         13.68         3.46 (1.78-4.92)         25.3%         7.02         2.14 (1.01-3.24)         30.5%           2012/13         12.09         3.70 (1.75-5.45)         30.6%         5.99         2.31 (0.99-3.66)         38.6%           1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           1995         4.24         0.40 (-0.12-0.86)         9.4%         3.79         0.09 (-0.27-0.35)         3.4%           Republic         2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           2010         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         3.3% </td <td></td> <td>1990</td> <td>6.54</td> <td>1.45 (0.25-2.50)</td> <td>22.1%</td> <td>3.61</td> <td>0.98 (0.23-1.76)</td> <td>27.0%</td>   |             | 1990    | 6.54   | 1.45 (0.25-2.50)  | 22.1% | 3.61   | 0.98 (0.23-1.76)   | 27.0% |
| Betarus         2005         14.14         3.21 (1.49-4.67)         22.7%         7.54         1.90 (0.85-2.97)         25.2%           2010         13.68         3.46 (1.78-4.92)         25.3%         7.02         2.14 (1.01-3.24)         30.5%           2012/13         12.09         3.70 (1.75-5.45)         30.6%         5.99         2.31 (0.99.3.66)         38.6%           1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           1995         4.24         0.40 (-0.12-0.86)         9.4%         3.79         0.09 (-0.31-0.44)         2.3%           Czech         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           Republic         2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.21-0.62)         3.2%           Estonia         2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-01-6.02)         3.2%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.05         0.03 (   |             | 1995    | 11.11  | 2.72 (1.30-3.95)  | 24.5% | 6.24   | 1.64 (0.65-2.64)   | 26.3% |
| 2005         14.14         3.21         (1.49-4.67)         22.7%         7.54         1.90         (0.85-2.97)         25.2%           2010         13.68         3.46         (1.78-4.92)         25.3%         7.02         2.14         (1.01-3.24)         30.5%           2012/13         12.09         3.70         (1.75-5.45)         30.6%         5.99         2.31         (0.99-3.66)         38.6%           1995         4.24         0.40 (-0.12-0.86)         9.4%         3.79         0.09 (-0.31-0.44)         2.3%           Czech         2005         3.95         0.64         (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           20110         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           2005         9.36         1.97 (1.20-2.61)         21.0%         4.27         0.32 (-0.15-0.72)         7.5%           2010         7.45         1.39 (0.75-1.93)         18.7%   | Dolomic     | 2000    | 12.10  | 2.92 (1.29-4.36)  | 24.1% | 6.83   | 1.75 (0.72-2.80)   | 25.6% |
| 2012/13         12.09         3.70 (1.75-5.45)         30.6%         5.99         2.31 (0.99-3.66)         38.6%           1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           1995         4.24         0.40 (-0.12-0.86)         9.4%         3.79         0.09 (-0.31-0.44)         2.3%           Czech         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           Republic         2015         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5% <td>Delatus</td> <td>2005</td> <td>14.14</td> <td>3.21 (1.49-4.67)</td> <td>22.7%</td> <td>7.54</td> <td>1.90 (0.85-2.97)</td> <td>25.2%</td>  | Delatus     | 2005    | 14.14  | 3.21 (1.49-4.67)  | 22.7% | 7.54   | 1.90 (0.85-2.97)   | 25.2% |
| Image: Czech         1990         5.26         0.30 (-0.25-0.79)         5.7%         4.02         0.00 (-0.38-0.34)         0.1%           Republic         2000         3.86         0.52 (0.05-0.95)         13.6%         3.79         0.09 (-0.31-0.44)         2.3%           2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.064 (0.0-1.27)         14.0%           1995         12.30         1.56 (0.79-2.34)         12.7%         6.11         0.19 (-0.21-0.62)         3.2%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.33)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2010         7.44         2.10 (1.63-2.52)         27.4%         5.62         0.75 (0.37-1.14)         13.3% <td></td> <td>2010</td> <td>13.68</td> <td>3.46 (1.78-4.92)</td> <td>25.3%</td> <td>7.02</td> <td>2.14 (1.01-3.24)</td> <td>30.5%</td>  |             | 2010    | 13.68  | 3.46 (1.78-4.92)  | 25.3% | 7.02   | 2.14 (1.01-3.24)   | 30.5% |
| Image: Czech         1995         4.24         0.40 (-0.12-0.86)         9.4%         3.79         0.09 (-0.31-0.44)         2.3%           Czech         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           Republic         2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2012/13         7.36         1.26 (0.62-1.82)         7.1%         2.50         0.08 (-0.29-0.43)         3.3%           Hungary         2000         7.92         2.12 (1.64-2.57)         26.8%         5.47  |             | 2012/13 | 12.09  | 3.70 (1.75-5.45)  | 30.6% | 5.99   | 2.31 (0.99-3.66)   | 38.6% |
| Czech<br>Republic         2000         3.86         0.52 (0.05-0.95)         13.6%         3.18         0.11 (-0.27-0.45)         3.4%           2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           1995         12.30         1.56 (0.79-2.34)         12.7%         6.11         0.19 (-0.21-0.62)         3.2%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2012/13         7.36         1.26 (0.62-1.82)         17.1%         2.50         0.08 (-0.29-0.43)         3.3%           1990         7.64         2.10 (1.63-2.57)         26.8%         5.47         0.63 (0.25-1.01)         11.5%   |             | 1990    | 5.26   | 0.30 (-0.25-0.79) | 5.7%  | 4.02   | 0.00 (-0.38-0.34)  | 0.1%  |
| Republic         2005         3.95         0.64 (0.21-1.03)         16.3%         3.27         0.15 (-0.21-0.46)         4.6%           2010         3.84         0.55 (0.13-0.93)         14.3%         2.85         0.09 (-0.27-0.39)         3.0%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2012/13         7.36         1.26 (0.62-1.82)         17.1%         2.50         0.08 (-0.29-0.43)         3.3%           Hungary         2000         7.92         2.12 (1.64-2.57)         26.8%         5.47         0.63 (0.25-1.01)         11.5%           2010         7.68         1.59 (1.15-2.43)         24.1%         5.47         0.58 (0.23-0.94)         10.6% <td></td> <td>1995</td> <td>4.24</td> <td>0.40 (-0.12-0.86)</td> <td>9.4%</td> <td>3.79</td> <td>0.09 (-0.31-0.44)</td> <td>2.3%</td>   |             | 1995    | 4.24   | 0.40 (-0.12-0.86) | 9.4%  | 3.79   | 0.09 (-0.31-0.44)  | 2.3%  |
| 2010         3.84         0.63 (0.11 1.02)         10.0 %         20.11         0.00 (0.27.0.3)         10.3%           2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           1995         12.30         1.56 (0.79-2.34)         12.7%         6.11         0.19 (-0.21-0.62)         3.2%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           20110         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.08 (-0.29-0.43)         3.3%           2012/13         7.36         1.26 (0.62-1.82)         17.1%         2.50         0.08 (0.25-0.48)         4.5%           2010         7.64         2.10 (1.63-2.52)         27.4%         5.62         0.75 (0.37-1.14)         13.3%           1995         8.48         2.54 (2.01-3.02)         30.0%         5.72         0.81 (0.41-1.21)         14.1%           2010         7.6   | Czech       | 2000    | 3.86   | 0.52 (0.05-0.95)  | 13.6% | 3.18   | 0.11 (-0.27-0.45)  | 3.4%  |
| 2012/13         3.72         0.42 (0.00-0.79)         11.3%         2.71         0.03 (-0.33-0.32)         1.1%           1990         8.12         1.12 (0.07-2.15)         13.8%         4.52         0.63 (0.06-1.27)         14.0%           1995         12.30         1.56 (0.79-2.34)         12.7%         6.11         0.19 (-0.21-0.62)         3.2%           2000         9.81         1.57 (0.78-2.27)         15.9%         5.22         0.24 (-0.19-0.64)         4.5%           2005         9.36         1.97 (1.20-2.61)         21.0%         4.27         0.32 (-0.15-0.72)         7.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2012/13         7.36         1.26 (0.62-1.82)         17.1%         2.50         0.08 (-0.29-0.43)         3.3%           1990         7.64         2.10 (1.63-2.52)         27.4%         5.62         0.75 (0.37-1.14)         13.3%           1995         8.48         2.54 (2.01-3.02)         30.0%         5.72         0.81 (0.41-1.21)         14.1%           Hungary         2000         7.92         2.12 (1.64-2.57)         26.8%         5.47         0.63 (0.25-1.01)         11.5%           2   | Republic    | 2005    | 3.95   | 0.64 (0.21-1.03)  | 16.3% | 3.27   | 0.15 (-0.21-0.46)  | 4.6%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 2010    | 3.84   | 0.55 (0.13-0.93)  | 14.3% | 2.85   | 0.09 (-0.27-0.39)  | 3.0%  |
| $ \begin{array}{c} \mbox{Estonia} & 1995 & 12.30 & 1.56 \ (0.79-2.34) & 12.7\% & 6.11 & 0.19 \ (-0.21-0.62) & 3.2\% \\ 2000 & 9.81 & 1.57 \ (0.78-2.27) & 15.9\% & 5.22 & 0.24 \ (-0.19-0.64) & 4.5\% \\ 2005 & 9.36 & 1.97 \ (1.20-2.61) & 21.0\% & 4.27 & 0.32 \ (-0.15-0.72) & 7.5\% \\ 2010 & 7.45 & 1.39 \ (0.75-1.93) & 18.7\% & 2.95 & 0.13 \ (-0.25-0.48) & 4.5\% \\ 2012/13 & 7.36 & 1.26 \ (0.62-1.82) & 17.1\% & 2.50 & 0.08 \ (-0.29-0.43) & 3.3\% \\ \hline & 2012/13 & 7.36 & 1.26 \ (0.62-1.82) & 17.1\% & 2.50 & 0.08 \ (-0.29-0.43) & 3.3\% \\ \hline & 1990 & 7.64 & 2.10 \ (1.63-2.52) & 27.4\% & 5.62 & 0.75 \ (0.37-1.14) & 13.3\% \\ \hline & 1995 & 8.48 & 2.54 \ (2.01-3.02) & 30.0\% & 5.72 & 0.81 \ (0.41-1.21) & 14.1\% \\ \hline & 2000 & 7.92 & 2.12 \ (1.64-2.57) & 26.8\% & 5.47 & 0.63 \ (0.25-1.01) & 11.5\% \\ \hline & 2010 & 7.68 & 1.59 \ (1.15-2.01) & 20.7\% & 5.17 & 0.40 \ (0.09-0.74) & 7.7\% \\ \hline & 2012/13 & 7.16 & 1.34 \ (0.92-1.75) & 18.8\% & 5.08 & 0.31 \ (0.09-0.74) & 7.7\% \\ \hline & 2012/13 & 7.16 & 1.34 \ (0.92-1.75) & 18.8\% & 5.08 & 0.31 \ (0.09-0.74) & 7.7\% \\ \hline & 2012/13 & 7.16 & 1.34 \ (0.92-1.75) & 18.8\% & 5.08 & 0.31 \ (0.09-0.74) & 7.7\% \\ \hline & 2012/13 & 7.16 & 1.34 \ (0.92-2.58) & 17.0\% & 5.48 & 0.25 \ (-0.23-0.64) & 4.6\% \\ \hline & 1990 & 6.65 & 1.80 \ (1.07-2.44) & 20.8\% & 4.13 & 0.29 \ (-0.16-0.67) & 7.0\% \\ \hline & 2010 & 10.72 & 2.19 \ (1.51-2.78) & 20.4\% & 4.74 & 0.53 \ (0.05-0.96) & 11.3\% \\ \hline & 2010 & 10.72 & 2.19 \ (1.51-2.78) & 20.4\% & 4.74 & 0.53 \ (0.05-0.96) & 11.3\% \\ \hline & 2012/13 & 10.31 & 2.04 \ (1.36-2.64) & 19.7\% & 4.27 & 0.45 \ (-0.02-0.86) & 10.5\% \\ \hline & 1990 & 8.61 & 1.31 \ (0.27-2.32) & 15.3\% & 4.89 & 0.81 \ (0.24-1.38) & 16.5\% \\ \hline & 2010 & 10.83 & 1.42 \ (0.77-1.97) & 13.1\% & 6.11 & 0.30 \ (-0.11-0.67) & 4.9\% \\ \hline & 2012/13 & 9.88 & 1.21 \ (0.59-1.77) & 12.3\% & 5.01 & 0.16 \ (-0.21-0.49) & 3.2\% \\ \hline & 1990 & 6.52 & 0.51 \ (-0.02-1.01) & 7.8\% & 4.13 & -0.02 \ (-0.34-0.29) & -0.6\% \\ \hline & 1995 & 6.33 & 0.63 \ (0.12-1.10) & 10.0\% & 4.05 & 0.01 \ (-0.31-0.31) & 0.3\% \\ \hline & Poland \end{array}$ |             | 2012/13 | 3.72   | 0.42 (0.00-0.79)  | 11.3% | 2.71   | 0.03 (-0.33-0.32)  | 1.1%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 1990    | 8.12   | 1.12 (0.07-2.15)  | 13.8% | 4.52   | 0.63 (0.06-1.27)   | 14.0% |
| Estonia         2005         9.36         1.97 (1.20-2.61)         21.0%         4.27         0.32 (-0.15-0.72)         7.5%           2010         7.45         1.39 (0.75-1.93)         18.7%         2.95         0.13 (-0.25-0.48)         4.5%           2012/13         7.36         1.26 (0.62-1.82)         17.1%         2.50         0.08 (-0.29-0.43)         3.3%           1990         7.64         2.10 (1.63-2.52)         27.4%         5.62         0.75 (0.37-1.14)         13.3%           1995         8.48         2.54 (2.01-3.02)         30.0%         5.72         0.81 (0.41-1.21)         14.1%           2000         7.92         2.12 (1.64-2.57)         26.8%         5.47         0.63 (0.25-1.01)         11.5%           2010         7.68         1.59 (1.15-2.01)         20.7%         5.17         0.40 (0.09-0.74)         7.7%           2012/13         7.16         1.34 (0.92-1.75)         18.8%         5.08         0.31 (0.00-0.61)         6.1%           1990         6.40         1.06 (0.04-2.04)         16.6%         3.26         0.62 (0.00-1.28)         19.0%           1995         10.66         1.81 (0.93-2.58)         17.0%         5.48         0.25 (-0.23-0.64)         4.6%           200   |             | 1995    | 12.30  | 1.56 (0.79-2.34)  | 12.7% | 6.11   | 0.19 (-0.21-0.62)  | 3.2%  |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   | Estania     | 2000    | 9.81   | 1.57 (0.78-2.27)  | 15.9% | 5.22   | 0.24 (-0.19-0.64)  | 4.5%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  | Estonia     | 2005    | 9.36   | 1.97 (1.20-2.61)  | 21.0% | 4.27   | 0.32 (-0.15-0.72)  | 7.5%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 2010    | 7.45   | 1.39 (0.75-1.93)  | 18.7% | 2.95   | 0.13 (-0.25-0.48)  | 4.5%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 2012/13 | 7.36   | 1.26 (0.62-1.82)  | 17.1% | 2.50   | 0.08 (-0.29-0.43)  | 3.3%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 1990    | 7.64   | 2.10 (1.63-2.52)  | 27.4% | 5.62   | 0.75 (0.37-1.14)   | 13.3% |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 1995    | 8.48   | 2.54 (2.01-3.02)  | 30.0% | 5.72   | 0.81 (0.41-1.21)   | 14.1% |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  | Uungory     | 2000    | 7.92   | 2.12 (1.64-2.57)  | 26.8% | 5.47   | 0.63 (0.25-1.01)   | 11.5% |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  | Thungary    | 2005    | 8.28   | 2.00 (1.55-2.43)  | 24.1% | 5.47   | 0.58 (0.23-0.94)   | 10.6% |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   |             | 2010    | 7.68   | 1.59 (1.15-2.01)  | 20.7% | 5.17   | 0.40 (0.09-0.74)   | 7.7%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 2012/13 | 7.16   | 1.34 (0.92-1.75)  | 18.8% | 5.08   | 0.31 (0.00-0.61)   | 6.1%  |
| $ \begin{array}{c c c c c c c c c c c c c c c c c c c $  |             | 1990    | 6.40   | 1.06 (0.04-2.04)  | 16.6% | 3.26   | 0.62 (0.00-1.28)   | 19.0% |
| Lithuana200511.682.63 (1.84-3.30)22.5%5.100.62 (0.11-1.08)12.1%201010.722.19 (1.51-2.78)20.4%4.740.53 (0.05-0.96)11.3%2012/1310.312.04 (1.36-2.64)19.7%4.270.45 (-0.02-0.86)10.5%19908.611.31 (0.27-2.32)15.3%4.890.81 (0.24-1.38)16.5%199514.172.11 (1.23-2.97)14.9%7.770.46 (-0.02-0.90)5.9%200010.881.80 (0.99-2.48)16.5%5.830.35 (-0.09-0.75)5.9%200512.011.91 (1.14-2.56)15.9%6.290.48 (0.02-0.89)7.6%201010.831.42 (0.77-1.97)13.1%6.110.30 (-0.11-0.67)4.9%2012/139.881.21 (0.59-1.77)12.3%5.010.16 (-0.21-0.49)3.2%19906.520.51 (-0.02-1.01)7.8%4.13-0.02 (-0.34-0.29)-0.6%19956.330.63 (0.12-1.10)10.0%4.050.01 (-0.31-0.31)0.3%Poland20005.870.77 (0.30-1.19)13.1%3.560.05 (-0.24-0.32)1.3%  |             | 1995    | 10.66  | 1.81 (0.93-2.58)  | 17.0% | 5.48   | 0.25 (-0.23-0.64)  | 4.6%  |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   | Lithuania   | 2000    | 8.65   | 1.80 (1.07-2.44)  | 20.8% | 4.13   | 0.29 (-0.16-0.67)  | 7.0%  |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   | Littituaina | 2005    | 11.68  | 2.63 (1.84-3.30)  | 22.5% | 5.10   | 0.62 (0.11-1.08)   | 12.1% |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   |             | 2010    | 10.72  | 2.19 (1.51-2.78)  | 20.4% | 4.74   | 0.53 (0.05-0.96)   | 11.3% |
| $ \begin{array}{c ccccccccccccccccccccccccccccccccccc$   |             | 2012/13 | 10.31  | 2.04 (1.36-2.64)  | 19.7% | 4.27   | 0.45 (-0.02-0.86)  | 10.5% |
| Latvia         2000         10.88         1.80 (0.99-2.48)         16.5%         5.83         0.35 (-0.09-0.75)         5.9%           2005         12.01         1.91 (1.14-2.56)         15.9%         6.29         0.48 (0.02-0.89)         7.6%           2010         10.83         1.42 (0.77-1.97)         13.1%         6.11         0.30 (-0.11-0.67)         4.9%           2012/13         9.88         1.21 (0.59-1.77)         12.3%         5.01         0.16 (-0.21-0.49)         3.2%           1990         6.52         0.51 (-0.02-1.01)         7.8%         4.13         -0.02 (-0.34-0.29)         -0.6%           1995         6.33         0.63 (0.12-1.10)         10.0%         4.05         0.01 (-0.31-0.31)         0.3%           Poland         2000         5.87         0.77 (0.30-1.19)         13.1%         3.56         0.05 (-0.24-0.32)         1.3%  |             | 1990    | 8.61   | 1.31 (0.27-2.32)  | 15.3% | 4.89   | 0.81 (0.24-1.38)   | 16.5% |
| Latvia         2005         12.01         1.91 (1.14-2.56)         15.9%         6.29         0.48 (0.02-0.89)         7.6%           2010         10.83         1.42 (0.77-1.97)         13.1%         6.11         0.30 (-0.11-0.67)         4.9%           2012/13         9.88         1.21 (0.59-1.77)         12.3%         5.01         0.16 (-0.21-0.49)         3.2%           1990         6.52         0.51 (-0.02-1.01)         7.8%         4.13         -0.02 (-0.34-0.29)         -0.6%           1995         6.33         0.63 (0.12-1.10)         10.0%         4.05         0.01 (-0.31-0.31)         0.3%           Poland         2000         5.87         0.77 (0.30-1.19)         13.1%         3.56         0.05 (-0.24-0.32)         1.3%  |             | 1995    | 14.17  | 2.11 (1.23-2.97)  | 14.9% | 7.77   | 0.46 (-0.02-0.90)  | 5.9%  |
| $\begin{array}{c ccccccccccccccccccccccccccccccccccc$  | Latvia      | 2000    | 10.88  | 1.80 (0.99-2.48)  | 16.5% | 5.83   | 0.35 (-0.09-0.75)  | 5.9%  |
| 2012/13         9.88         1.21 (0.59-1.77)         12.3%         5.01         0.16 (-0.21-0.49)         3.2%           1990         6.52         0.51 (-0.02-1.01)         7.8%         4.13         -0.02 (-0.34-0.29)         -0.6%           1995         6.33         0.63 (0.12-1.10)         10.0%         4.05         0.01 (-0.31-0.31)         0.3%           Poland         2000         5.87         0.77 (0.30-1.19)         13.1%         3.56         0.05 (-0.24-0.32)         1.3%  | Latvia      | 2005    | 12.01  | 1.91 (1.14-2.56)  | 15.9% | 6.29   | 0.48 (0.02-0.89)   | 7.6%  |
| 1990         6.52         0.51 (-0.02-1.01)         7.8%         4.13         -0.02 (-0.34-0.29)         -0.6%           1995         6.33         0.63 (0.12-1.10)         10.0%         4.05         0.01 (-0.31-0.31)         0.3%           Poland         2000         5.87         0.77 (0.30-1.19)         13.1%         3.56         0.05 (-0.24-0.32)         1.3%  |             | 2010    | 10.83  | 1.42 (0.77-1.97)  | 13.1% | 6.11   | 0.30 (-0.11-0.67)  | 4.9%  |
| 1995         6.33         0.63 (0.12-1.10)         10.0%         4.05         0.01 (-0.31-0.31)         0.3%           Poland         2000         5.87         0.77 (0.30-1.19)         13.1%         3.56         0.05 (-0.24-0.32)         1.3%   |             | 2012/13 | 9.88   | 1.21 (0.59-1.77)  | 12.3% | 5.01   | 0.16 (-0.21-0.49)  | 3.2%  |
| Poland 2000 5.87 0.77 (0.30-1.19) 13.1% 3.56 0.05 (-0.24-0.32) 1.3%  |             | 1990    | 6.52   | 0.51 (-0.02-1.01) | 7.8%  | 4.13   | -0.02 (-0.34-0.29) | -0.6% |
| Poland   |             | 1995    | 6.33   | 0.63 (0.12-1.10)  | 10.0% | 4.05   | 0.01 (-0.31-0.31)  | 0.3%  |
|  | Poland      | 2000    | 5.87   | 0.77 (0.30-1.19)  | 13.1% | 3.56   | 0.05 (-0.24-0.32)  | 1.3%  |
|  | i oidilu    | 2005    | 6.04   | 1.04 (0.58-1.44)  | 17.3% | 3.19   | 0.09 (-0.18-0.36)  | 2.9%  |
| 2010 6.10 <b>1.16 (0.70-1.55) 19.0%</b> 3.02 0.14 (-0.14-0.40) 4.7%  |             | 2010    | 6.10   | 1.16 (0.70-1.55)  | 19.0% | 3.02   | 0.14 (-0.14-0.40)  | 4.7%  |
| <u>2012/13 6.06</u> <b>1.13 (0.67-1.55) 18.6%</b> 2.89 0.14 (-0.14-0.40) 4.7%  |             | 2012/13 | 6.06   | 1.13 (0.67-1.55)  | 18.6% | 2.89   | 0.14 (-0.14-0.40)  | 4.7%  |

**Table S4.4.** The contribution of alcohol to life expectancy differentials between Eastern European countries and Western Europe (in years), over time (1990-2012/13), by sex

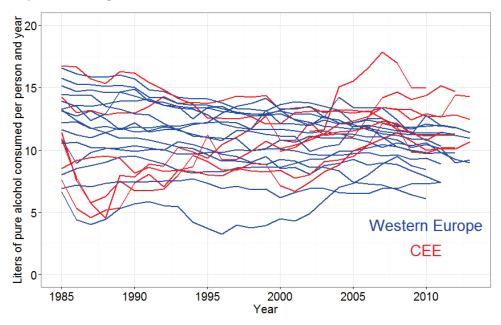
|         |         | Men    |                  |       | Women  |                  |       |
|---------|---------|--------|------------------|-------|--------|------------------|-------|
| Country | Year    | e0 gap | Alcohol contr.   |       | e0 gap | Alcohol contr.   |       |
|         | 1990    | 9.05   | 1.62 (0.70-2.48) | 17.9% | 5.10   | 0.82 (0.36-1.38) | 16.0% |
|         | 1995    | 15.79  | 3.87 (2.46-5.08) | 24.5% | 8.85   | 1.77 (1.06-2.49) | 20.0% |
| Russia  | 2000    | 16.44  | 3.92 (2.42-5.2)  | 23.9% | 9.29   | 1.90 (1.14-2.66) | 20.5% |
| Kussia  | 2005    | 18.02  | 4.83 (3.24-6.27) | 26.8% | 10.14  | 2.50 (1.61-3.37) | 24.6% |
|         | 2010    | 15.25  | 3.67 (2.27-4.98) | 24.0% | 8.67   | 2.11 (1.27-2.93) | 24.3% |
|         | 2012/13 | 14.16  | 2.88 (1.57-4.06) | 20.3% | 7.83   | 1.74 (0.95-2.53) | 22.2% |
|         | 1990    | 7.19   | 1.31 (0.13-2.41) | 18.2% | 4.51   | 0.89 (0.27-1.59) | 19.7% |
|         | 1995    | 12.70  | 1.99 (0.63-3.26) | 15.7% | 7.94   | 1.22 (0.49-1.98) | 15.4% |
| Ukraine | 2000    | 13.33  | 2.38 (0.87-3.73) | 17.9% | 8.00   | 1.35 (0.56-2.14) | 16.8% |
| Ukraine | 2005    | 15.43  | 3.64 (1.98-5.11) | 23.6% | 9.21   | 2.13 (1.17-3.08) | 23.1% |
|         | 2010    | 13.10  | 2.88 (1.31-4.24) | 22.0% | 8.35   | 1.88 (0.94-2.77) | 22.5% |
|         | 2012/13 | 12.63  | 2.47 (0.90-3.88) | 19.5% | 7.70   | 1.67 (0.72-2.60) | 21.7% |

# Table S4.4. (continued)

Note: Life expectancy among men in Western Europe was 72.8, 73.9, 75.5, 76.9, and 78.3 in 1990, 1995, 2000, 2005, and 2010, respectively; while for the corresponding years life expectancy was 79.4, 80.5, 81.5, 82.5, 83.5 among women.

Abbreviations: Belarus (BLR), Czech Republic (CZE), Estonia (EST), Hungary (HUN), Lithuania (LTU), Latvia (LVA), Poland (POL), Russia (RUS), Ukraine (UKR), and the population-weighted average of the Central and Eastern European (CEE) countries.

**Figure S4.2.** Recorded per capita consumption in liters of pure alcohol per adult (aged 15+) and year in 24 European countries<sup>1</sup>, 1985-2013



<sup>1</sup> We included the Western and the CEE countries analyzed in the paper. Western Europe: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and United Kingdom. CEE: Belarus, the Czech Republic, Estonia, Hungary, Lithuania, Latvia, Poland, Russia, and Ukraine.

Source: Own elaboration based on data from World Health Organization's Global Information System on Alcohol and Health (GISAH) (<u>http://www.who.int/gho/alcohol/en/</u>).

4

# **Chapter 5**

Alcohol and gender gaps in life expectancy in eight Central and Eastern European countries

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# Abstract

*Background*: Gender differences in life expectancy have been traditionally large in Central and Eastern Europe (CEE), and alcohol has been hypothesized to be one of its main determinants. We examined the role of alcohol in gender differences in life expectancy in Estonia, Lithuania, Latvia, Moldova, Poland, Romania, Russia, and Ukraine , and changes in this role from 1965 until 2012.

*Methods*: We decomposed the gender differences in life expectancy at birth (LE) into alcoholand non-alcohol-related mortality. We examined causes of death wholly attributable to alcohol over the whole period, and estimated from 1990 onwards additional alcohol-attributable mortality by using alcohol-attributable fractions from the Global Burden of Disease study.

*Results*: In the eight CEE countries, women's advantage in LE relative to men increased from 7.3 years on average in 1965 to 10.0 years on average in 2012. All alcohol-attributable mortality contributed 1.9 years on average (UI: 1.2-2.5) (18.8%) to the gender differences from 1990 to 2012. Its relative contribution increased in most countries until around 2005, and declined thereafter, resulting in a contribution of at least 15% in 2012. The absolute contribution of alcohol to the LE gender gap was strongly correlated with the overall LE gender differences (Pearson's r > 0.75), except in Poland and Estonia.

*Conclusions*: Despite recent declines, the contribution of sex differences in excessive alcohol consumption to the LE gender gap is substantial, and should not be neglected. Tackling gender differences in alcohol consumption and alcohol-attributable mortality would contribute to further progress in reducing mortality.

Keywords: alcohol, mortality, alcohol harm, cause-specific mortality, gender gap

## 5.1. Introduction

Around the world, women live longer than men. Gender differences in life expectancy are especially large in Central and Eastern Europe (CEE); in several CEE countries, the life expectancy (LE) gender gap exceeds 10 years (Rochelle et al., 2015). These substantial gender inequalities are attributable far less to biological factors (Luy & Wegner-Siegmundt, 2015) than to behavioural factors (Aboulghar et al., 2016; Luy & Wegner-Siegmundt, 2015; Rogers et al., 2010). It is therefore important to study these factors in depth to support the formulation of health policies aimed at reducing health and gender equalities.

It has been argued that the gender gap in alcohol consumption (Bobrova et al., 2010; Popova et al., 2007) is an important contributor to gender differences in health and mortality (Aboulghar et al., 2016). Especially among middle-aged men in CEE countries, alcohol consumption is highly prevalent, binge drinking is common, and men are more likely than women to prefer vodka and other beverages with very high levels of ethanol (Bobrova et al., 2010; Minagawa, 2013; Pomerleau et al., 2008; World Health Organization, 2014). These patterns have resulted in large gender differences in mortality from causes of death strongly linked to excessive alcohol consumption and binge drinking; i.e., cardiovascular and external causes, especially at working ages (McKee & Shkolnikov, 2001; Weidner & Cain, 2003).

Despite the important role alcohol appears to play in the mortality gender gaps in CEE countries, to our knowledge only one existing study has examined the impact of alcohol on gender gaps in life expectancy in CEE countries. McCartney et al. (2011) found that alcohol explained about 20-30% of the gender gap in mortality in Eastern Europe in 2003-2005. However, they used a very broad definition of alcohol-attributable mortality, defining all external deaths as alcohol-related deaths, and including very few causes of death from diseases partly attributable to alcohol use. Moreover, they only studied the importance of alcohol at one point in time.

Life expectancy trends have varied markedly between men and women and across CEE countries in recent decades, leading to an overall pattern of divergence (Leon, 2011). Alcohol consumption in these countries also fluctuated over time (Moskalewicz & Österberg, 2016; World Health Organization, 2014), and its impact on mortality in CEE region has been recognized in several studies (e.g. Aburto & van Raalte, 2017; Meslé et al., 2002; Shkolnikov et al., 2001)). It is therefore essential to study the varying contributions of alcohol to the gender gaps in life expectancy in different CEE countries and different periods of time.

# Aim

To examine the role of alcohol in gender differences in life expectancy in Central and Eastern Europe, and changes in this role over time.

# 5.2. Methods

# 5.2.1. Setting

We studied gender-specific national populations from Central and Eastern European (CEE) countries for which recent long-term time series of cause-specific mortality data were available: namely, Estonia, Lithuania, Latvia, Moldova, Poland, Romania, Russia, and Ukraine. For most countries, we were able to study the 1965-2012 period. For some countries, longer time series data were available and were used (1955-2014). For Romania, only data from 1980 onwards were available.

We assessed the gender differences in life expectancy at birth (LE), and examined the contribution of i) causes of death wholly and partly related to alcohol over the whole period, and ii) alcohol-attributable mortality from 1990 onwards.

# 5.2.2. Data

Cause-specific and all-cause mortality data were retrieved by gender, age (0, 1-4, 5-9, ..., 85+) and year from the Human Cause of Death Database (HCD) (HCD, n.d.). The HCD is a recent open-source project that offers harmonised data on reconstructed long-term trends in cause-specific mortality.

We distinguished two different groups of alcohol-related causes of death by selecting the diseases related to alcohol from a recent review by Rehm and colleagues (Rehm & Imtiaz, 2016). The first group included causes of death wholly attributable to alcohol (mental and behavioural disorders due to alcohol use, alcohol liver disease, and poisoning by exposure to alcohol; F10, K70, and X45, respectively). The second group included causes partly attributable to alcohol-related cancers, epilepsy, pancreatitis, non-alcoholic cirrhosis, tuberculosis, transport accidents, and other external causes (Table 5.1). Finally, the remaining causes were considered not attributable to alcohol.

| Alcohol | Group of causes                                 | Causes of death  | ICD-10 code             |
|---------|---|--|-------------------------|
| Wholly  | Wholly attributable<br>to alcohol               | Mental and behavioural disorders due to alcohol use      | F10                     |
|         |   | Alcoholic liver disease                                  | K70                     |
|         |   | Accidental poisoning by and exposure to alcohol          | X45                     |
|         | IHD or stroke                                   | Ischemic heart disease                                   | 120-125                 |
|         |   | Cerebrovascular disease                                  | I60-I69, G45            |
|         | Transport accidents                             | Transport accidents                                      | V01-V99                 |
|         | Other non-external<br>alcohol-related<br>causes | Colon and rectum cancer                                  | C18-C21                 |
|         |   | Oesophageal cancer                                       | C15                     |
|         |   | Larynx cancer  | C32                     |
|         |   | Lip and oral cavity cancer                               | C00-C14                 |
|         |   | Epilepsy   | G40-G41                 |
|         |   | Pancreatitis   | K85-K86                 |
|         |   | Non-alcoholic cirrhosis and other chronic liver diseases | K71-K76                 |
|         |   | Tuberculosis   | A12-A19,<br>B90         |
| Partly  | Other external<br>alcohol-related<br>causes     | Other external causes                                    | W00-Y98<br>(except X45) |
| No      | Remaining causes                                | Remaining causes   | All other codes         |

Table 5.1. Selected causes of death wholly, partly, and not attributable to alcohol

We estimated from 1990 onwards alcohol-attributable mortality by summing the mortality wholly and partly attributable to alcohol. Mortality partly attributable to alcohol was obtained by multiplying the country, year, gender, and age-specific mortality rates from causes of death partly attributable to alcohol (see Table S5.1) by the corresponding alcohol-attributable fractions. The country-, year-, gender-, age-, and cause-specific alcohol-attributable fractions (and their 95% uncertainty intervals) were obtained from the Global Burden of Disease (GBD) Study 2013 for the years 1990, 1995, 2000, 2005, 2010, and 2013 (GBD 2013 Risk Factors Collaborators et al., 2015; Global Burden of Disease Study 2013, 2016). By linear interpolation we obtained the alcohol-attributable fractions for the years in between (data available online: https://osf.io/av958/).

# 5.2.3. Analysis

Life expectancies (LE) were estimated for each country, year, and gender using standard life table techniques (Preston et al., 2000). We applied a standard decomposition technique (Andreev et al., 2002) to the gender differences in LE to obtain the contribution of i) the different causes of death, and ii) alcohol-attributable mortality versus non-alcohol-attributable mortality. This decomposition technique involved decomposing the differences in the LE gender gap into the contribution of each specific age group, estimating the cause-specific contribution for each age group, and summing up the age-specific contributions for each country-year combination. We used the Pearson's correlation coefficient (r) to assess the correlation between the absolute contribution of alcohol and the differences in the LE gender gap.

All of the data analyses were performed using R 3.4.0 (R Core Team, 2016) in R studio 1.00.44 (RStudio Team, 2015).

# 5.3. Results

# 5.3.1. LE gender differences and trends in these differences

In the eight CEE countries studied in 1965, life expectancy at birth (LE) was, on average, 7.3 years higher for women than for men (Figure 5.1). In 2012, the female advantage was even larger, at 10.0 years. In five countries, this gap surpassed 12 years at some point in time. The LE gender gap ranged from 4.6 years in Moldova to 9.4 years in Russia in 1965, and from 7.4 years in Romania to 12.0 years in Russia in 2012.

These LE gender differences gradually increased until the early 1990s, except during the Gorbachev period (1984-1987) in the former Soviet republics. In most CEE countries, the largest LE gender gap occurred in the mid-1990s and the mid-2000s. From around 2005 onwards, the LE gender gap generally declined, but remained at a high level. In the non-post-Soviet states, the LE gender gap either stayed relatively stable (Romania) or slowly declined (Poland) from the 1990s onwards.

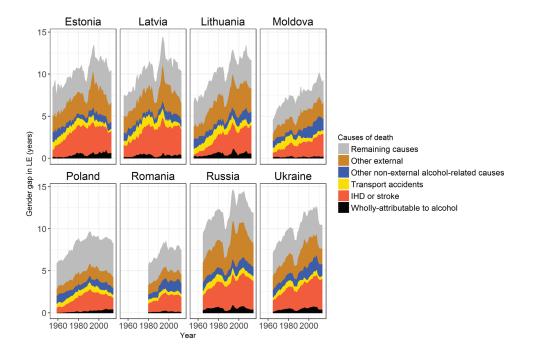
# 5.3.2. Contribution of alcohol-related causes of death to gender differences in LE

In all available country-years analysed from 1955 to 2014, the causes of death wholly attributable to alcohol (mental and behavioural disorders due to alcohol use, alcohol-induced

liver disease, and poisoning by exposure to alcohol) explained between 1.1% and 10.3% of the LE gender gap (4% on average).

The causes of death partly related to alcohol explained, on average, 64% of the gender gap in LE. These causes, which included IHD, strokes, and external causes, were also the main contributors to increases over time in the LE gender gap. However, the contribution of alcohol to causes of death partly related to alcohol – and, consequently, the overall contribution of alcohol-attributable mortality – can only be ascertained for the period from 1990 onwards.

**Figure 5.1**. The contribution of causes of death wholly and partly related to alcohol to gender differences in life expectancy at birth (LE) in 8 CEE countries, 1955-2014<sup>b</sup>



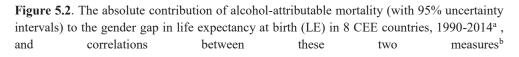
- a. See Table 5.1 for further details on causes of death partly related to alcohol.
- Data availability by country: Estonia: 1955-2012; Latvia and Lithuania: 1956-2012, Moldova 1965-2014;
   Poland: 1959-2014; Romania: 1980-2012; Russia: 1965-2014; Ukraine: 1965-2013.

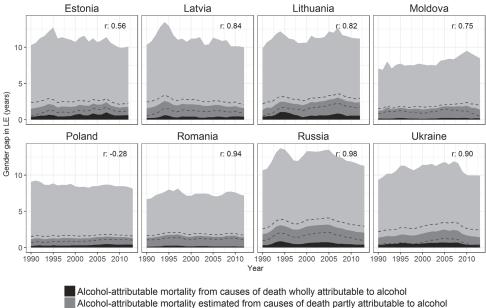
## 5.3.3. Contribution of alcohol-attributable mortality to gender differences in LE

Overall, alcohol-attributable mortality (deaths wholly attributable to mortality plus estimates of alcohol-attributable mortality from causes of death partly related to alcohol) contributed 1.9 years on average (UI: 1.2-2.5) (18.8%) to the LE gender gap between 1990 and 2012 (Figure

5.2, Table 5.2). The contribution of alcohol to the LE gender gap exceeded 15% in all eight countries in 2012, and in 173 out of 188 country-years analysed between 1990 and 2012. The relative contribution of alcohol to the gender gap in LE ranged from 12.7% (UI: 7.6-16.8%) in Poland in 1990 to 24.1% (UI: 18.2-28.6%) in Lithuania in 2007.

Visual inspection of the time trends in the relative contribution of alcohol to the LE gender gap revealed that in most countries, the gap increased until around 2005, and declined thereafter (Table 5.2). Exceptions were Latvia and Romania, where the relative contribution of alcohol to the LE gender gap changed little between 1990 and 2012; and Poland, where it increased throughout the period. Visual inspection of the trends in the LE gender gap and in alcohol-attributable mortality revealed that these trends evolved parallel to one another in most CEE countries (r > 0.75), except in Poland and Estonia (Figure 5.2).





Non-alcohol related mortality

- a. Or latest available year: 2012 for Estonia, Latvia, Lithuania, and Romania; 2013 for Ukraine; and 2014 for Poland, Russia, and Ukraine.
- b. Expressed by the Pearson correlation coefficient (r)

**Table 5.2.** The absolute and relative contributions of alcohol-attributable mortality to the gender gap in life expectancy at birth in 8 CEE countries, 1990, 2012, and 1990-2012 (only relative contributions)

|           | 1990          |       | 2012          |       | 1990-2012 |
|-----------|---------------|-------|---------------|-------|-----------|
|           | years         | %     | years         | %     | Trend (%) |
| Estonia   | 1.5 (0.5-2.4) | 14.7% | 1.8 (1.2-2.3) | 17.4% | sim       |
| Latvia    | 1.5 (0.5-2.4) | 15.0% | 1.6 (0.9-2.1) | 16.0% | ~~~~      |
| Lithuania | 1.4 (0.5-2.2) | 13.9% | 2.4 (1.7-3.0) | 21.5% | ~         |
| Moldova   | 1.2 (0.8-1.5) | 17.6% | 1.6 (0.7-2.1) | 18.0% | ~~~~      |
| Poland    | 1.2 (0.7-1.5) | 12.7% | 1.4 (1.1-1.7) | 16.9% | ~~~       |
| Romania   | 1.4 (1.1-1.7) | 20.9% | 1.4 (1.1-1.7) | 19.9% | ~~~       |
| Russia    | 1.9 (1.0-2.6) | 17.7% | 2.1 (1.1-3.0) | 18.6% | $\sim$    |
| Ukraine   | 1.4 (0.4-2.2) | 14.9% | 1.5 (0.3-2.5) | 15.1% | ~         |

## 5.4. Discussion

## 5.4.1. Summary of results

Our study reported estimates of the contribution of alcohol to the gender gap in life expectancy (LE) trends in eight CEE countries. Women's advantage in LE relative to men increased from 7.3 years on average in 1965 to 10.0 years on average in 2012. Causes of death wholly attributable to alcohol explained 0.4 years on average (4.0%) of the LE gender gap over the 1965-2012 period. Alcohol-attributable mortality as a whole accounted for 1.9 years on average of the LE gender gap (1990-2012), and for at least 15% of the LE gender gap in all countries studied in 2012. Overall, the contributions of alcohol to the LE gender gap and to the size of the LE gender gap were highly correlated (r > 0.75), except in Poland and Estonia. The relative contributions of alcohol to the LE gender gap increased in most CEE countries until around 2005, and declined thereafter. However, the contribution of alcohol to the LE gender gap exceeded 15% in 2012 in all analysed countries.

## 5.4.2. Strengths and limitations of the study

Our study provided a very detailed examination of the impact of alcohol on LE gender differences in CEE countries by studying time trends from 1965 to 2012 in eight CEE countries, and by using a method to estimate alcohol-attributable mortality that went beyond merely using (underlying) cause-specific mortality data, as was done in the only previous study on the same topic (McCartney et al., 2011).

In our view, the use of cause-specific mortality in combination with alcohol prevalence data and information on the relationship between alcohol consumption and cause-specific mortality (relative risks) leads to more accurate estimates of total alcohol-attributable mortality than methods that use only underlying cause-of-death mortality data.

The use of the GBD estimates based on alcohol prevalence and relative risks also has some limitations, which have been discussed in detail elsewhere (Agardh et al., 2016; Trias-Llimós et al., 2018). The estimates for Russia and Ukraine in particular should be interpreted with caution. The GBD used Russian-specific relative risks for Russia and Ukraine to account for potential differences in drinking behaviours between these two countries and the other countries for which world-wide relative risks were used (Trias-Llimós et al., 2018). However, the Russian-specific relative risks suffer from several limitations. When we compare the resulting alcohol-attributable mortality levels in Russia and Ukraine with other estimates of alcohol-attributable mortality, the potential for overestimation using this approach becomes apparent, especially for women (Trias-Llimós et al., 2018). If alcohol-attributable mortality among women is overestimated, the sex differences would be smaller, and the contribution of alcohol to the LE gender gap in Russia and Ukraine could be underestimated.

Additionally, some causes of death either wholly or partly related to alcohol could not be included in our estimate of alcohol-attributable mortality because of a lack of mortality data (HCD) or attributable fractions (GBD). In a sensitivity analysis using additional available data on causes of death wholly attributable to alcohol (I426 –alcoholic cardiomyopathy-, G312, K860 and Y15) for Poland, Romania, and Ukraine, we observed that in both 1990 and 2012, the contribution of alcohol to the LE gender gap increased by less than 1% in Romania and Poland, and slightly more in Ukraine (1.4% in 1990; 2.8% in 2012). These findings suggest that the degree of underestimation was small when the causes of death wholly attributable to alcohol were not included; though it was largest in the former Soviet countries where alcoholic

cardiomyopathy was high, especially among men (Leon & Peccholdova, 2017). The causes of death partly attributable to alcohol that could not be included were hypertensive diseases (I10-I15) and cardiac arrhythmias (I47-I49) (Rehm & Imtiaz, 2016). However, because mortality from those causes was relatively low (usually below 2% in most country-years), we expect that not including these causes resulted in only a slight underestimation of the contribution of alcohol to the LE gender gap.

Any comparison between countries and over time of alcohol-related cause-specific mortality may been affected by differences in coding practices (Rahu et al., 2011). Because our goal was to examine the role of alcohol in sex differences in LE we do not expect that differences in coding practices have a notable effect on our results.

Taking the abovementioned data issues into account, we believe that our estimates of the contribution of alcohol-attributable mortality to the LE gender differences are actually rather conservative.

## 5.4.3. Interpretation

The contribution of alcohol-attributable mortality to the LE gender gap exceeded 15% in 2012 in all eight analysed CEE countries. Sex differences in excessive alcohol consumption thus seem to play a substantial role in explaining the LE gender gap. The evidence showing that alcohol consumption levels are higher and alcohol consumption patterns are risker among men than among women of young and working ages has generally been explained by differences in gender roles (Bobrova et al., 2010; Minagawa, 2013), as well as by differences in strategies for coping with stress (Cockerham, 2012; Weidner & Cain, 2003).

Despite the importance of alcohol to the observed LE gender differences, those differences remain very large even after the contribution of alcohol-attributable mortality is excluded. If alcohol-attributable mortality is removed, the LE gender gap still exceeds eight years in Russia, Ukraine, and the Baltic states in 2012, and the peaks in the trends over the study period are less accentuated (i.e., around 1994 in former Soviet countries) (Figure 5.2). These remaining LE gaps are even larger than the current LE gender gaps of between four and seven years observed in the rest of Europe (Liu et al., 2012), and to which the contribution of alcohol tends to be smaller than in the CEE countries (around 0.5 years based on the gender differences in potential gains in LE by eliminating alcohol-attributable mortality) (Trias-Llimós et al., 2018). Since alcohol alone cannot explain why sex differences in mortality are larger in CEE countries than

in other European countries, other factors should be considered when trying to explain the LE gender gap.

Both biological and non-biological factors contribute to LE gender gaps. The main nonbiological factors are unhealthy lifestyles (Janssen & van Poppel, 2015; Luy & Wegner-Siegmundt. 2013; Luy & Wegner-Siegmundt, 2015; Rogers et al., 2010; Waldron, 2000), of which smoking is the most researched. A recent study examined in detail the contributions of smoking, other non-biological factors, and biological factors to the LE gender gap in 53 industrialised countries over the last 50 years (Luy & Wegner-Siegmundt, 2015). For our eight CEE countries, this study found that smoking accounted for an average of 36% (range: 32-43%), biological factors accounted for an average of 14% (range: 12-17%), and other nonbiological factors accounted for an average of 50% (range: 39-55%) of the LE gender gap in 2005/09. Our estimate for the contribution of alcohol in 2012 (15-22%) is close to half of the estimated contribution of smoking, but more than one-third of the estimated contribution of other non-biological factors. Clearly, the role of alcohol should not be neglected when seeking to explain LE gender gaps in CEE countries.

Over the 1990-2012 period, LE gender gaps were strongly correlated with the contribution of alcohol-attributable mortality to those gaps in most CEE countries. Because correlations between the LE gender gap and the contribution to this gap of causes of death wholly attributable to alcohol remained strong over this period for most CEE countries, we can assume that the attributable fraction approaches we applied had only a minor impact on these correlations. Instead, the similarities between the time patterns of and the fluctuations in the contribution of alcohol and the LE gender gap suggest that alcohol indeed influenced the trends in LE sex differences. However, because the time pattern for the contribution of alcohol was less pronounced than the time pattern for the LE sex differences, other determinants of the trends in the LE gender gap should have exhibited similar patterns over time. It therefore appears likely that the overall context, including economic and health conditions, affected several factors (e.g., alcohol, other lifestyles, health care) at the same time.

The contribution of alcohol to the LE gender gap in both absolute and relative terms increased in most former Soviet countries throughout the 1990s, and declined from around 2005 onwards. The increase in the 1990s may have been related to both the end of Gorbachev's anti-alcohol campaign and the severe socioeconomic and health crisis in the early 1990s (Grigoriev & Andreev, 2015; Shkolnikov et al., 2002). The recent declines in the contribution of alcohol to

the LE gender gap (in both absolute and relative terms) could be related to changes in alcohol consumption. Over the last 10 years, alcohol consumption has been gradually declining in most CEE countries, and especially in the former Soviet countries due to the decline of drinking beverages with high levels of ethanol (mainly spirits and unrecorded alcohol) (Moskalewicz & Österberg, 2016; World Health Organization, 2014). This trend is at least partly the result of alcohol policy changes that occurred in most CEE countries from around 2005 onwards (Grigoriev & Andreev, 2015; Jasilionis et al., 2011; Neufeld & Rehm, 2013). Men have likely been affected by these developments more than women for the simple reason that men tend to drink more than women. However, in line with the general convergence in the lifestyle behaviours of men and women as a result of changes in the position of women in society (Waldron, 2000), women in Russia and worldwide have recently started adopting the alcohol consumption behaviours of men (Hinote et al., 2009; Minagawa, 2013; Slade et al., 2016).

## 5.4.4. Conclusions and policy implications

The contribution of alcohol to the life expectancy gender gap in the eight CEE countries studies, accounting for at least 15% in 2012, is notable. The recent declines in the contribution of alcohol to the LE gender gap can be partly explained by declining sex differences in alcohol consumption as a result of successful alcohol policies and changes in the position of women in society.

Tackling gender differences in alcohol consumption and alcohol-attributable mortality would contribute to further progress in reducing mortality, and to gender convergence in life expectancy. However, tackling alcohol alone is not sufficient; other risk factors, and especially smoking, also deserve special attention.

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# Supplementary material

**Table S5.1.** Table of correspondence of alcohol-related causes of death between the Human

 Cause of Death Database (HCD) and the Global Burden of Disease Study 2013 (GBD)

| Cause of death name   | ICD-10<br>codes | HCD names  | GBD names  |
|---|-----------------|--|--|
| Ischemic heart<br>disease   | I20-I25         | Acute myocardial infarction, atherosclerotic cardiovascular diseases and other IHD   | Ischemic heart<br>disease  |
| Cerebrovascular<br>disease  | I60-I69,<br>G45 | Intracranial haemorrhage, cerebral infarction,<br>occlusion and stenosis, other cerebrovascular<br>diseases and sequelae of cerebrovascular<br>disease | Cerebrovascular<br>disease   |
| Transport accidents   | V01-V99         | Transport accidents  | Transport<br>injuries  |
| Colon and rectum cancer   | C18-C21         | Malignant neoplasms of colon, rectum, and anus   | Colon and rectum cancer  |
| Esophaegal cancer   | C15             | Malignant neoplasm of esophagus  | Esophageal cancer  |
| Larynx cancer   | C32             | Malignant neoplasm of larynx   | Larynx cancer  |
| Lip and oral cavity cancer  | C00-C14         | Malignant neoplasms of lip, oral cavity and pharynx  | Lip and oral cavity cancer   |
| Epilepsy  | G40-G41         | Epilepsy   | Epilepsy   |
| Pancreatitis  | K85-K86         | Diseases of pancreas   | Pancreatitis   |
| Non-alcoholic<br>cirrhosis and other<br>chronic liver<br>diseases | K71-K76         | Other cirrhosis of the liver and other diseases of the liver   | Cirrhosis due to<br>hepatitis B,<br>hepatitis C or<br>due to other<br>causes |
| Tuberculosis  | A12-A19,<br>B90 | Iuberculosis   | Tuberculosis   |

Minor issues regarding the linkage between mortality data from the HCD and the GBD are: 1) colon and rectum cancer includes anus cancer in the mortality data, but not in the GBD data; 2) lip and oral cavity cancer includes pharynx cancer in the mortality data, but not in the AF data; and 3) pancreatitis includes diseases of the pancreas in the mortality data, but not in the AF data.

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# **Chapter 6**

Discussion

# 6.1. Objective

The aim of this PhD thesis was to assess past alcohol-attributable mortality trends in Europe and to examine the role of alcohol in overall mortality differences across countries and between men and women.

More specifically, the sub-objectives of this research were:

- to assess past alcohol-attributable mortality trends and the differences in these trends across countries, the sexes, and birth cohorts (= generations); and
- 2) to assess the role of alcohol in overall mortality differences across countries, between the sexes, and over time.

This PhD research is innovative because it combines a comparative and a temporal approach to studying alcohol-attributable mortality trends and their contributions to overall mortality variations. In this study, data by sex from several countries in both Eastern and Western Europe were used, and the birth cohort dimension was included in addition to age and period when examining long-term past mortality trends. This PhD thesis employed a interdisciplinary design in which demographic and epidemiological data were analysed using advanced demographic techniques and modelling.

# 6.2. Summary of results

Previous research on alcohol-attributable mortality at the population level used different techniques to estimate alcohol-attributable mortality. The application of different techniques leads to substantially different results, which have not been compared or discussed in the previous literature. **Chapter 2** compared eight estimates of sex- and age-specific alcohol-attributable mortality in France (2010) and Finland (2013): five estimates using cause-of-death approaches (with one accounting for contributory causes), and three estimates using attributable fraction (AF) approaches. The estimated alcohol-attributable mortality was found to be around twice as high when methods that required detailed data (attributable fraction approaches and the cause-of-death approach, which accounts for contributory causes) were used than when methods that relied on underlying cause-of-death data only were applied. A clear inverse U-shaped age pattern in alcohol-attributable mortality rates –especially for Finland – was found when the approaches that relied on cause-of-death mortality data only were used. Theoretically,

the more detailed approaches used to estimate alcohol-attributable mortality (attributable fraction approaches and approaches that account for both underlying and contributory causes of death) provide more accurate estimates of the overall level of alcohol-related mortality. However, these more detailed approaches all require detailed data of high quality, which may be unavailable for different countries and periods of time.

In **Chapter 3**, the contributions of birth cohorts to liver cirrhosis mortality trends in eight European countries were examined (sub-objective 1). The results confirmed that the inclusion of the birth cohort dimension can improve our understanding of alcohol-attributable mortality trends in Europe. Birth cohorts were found to contribute to the model fit more than the models that included only age and period (calendar time). Additionally, important differences across the eight analysed countries were observed in the birth cohorts at higher risk of liver cirrhosis mortality: namely, the cohorts born between 1935 and 1949 in Sweden and Finland; around 1950 in Austria and the Netherlands; and around 1960 or later in Hungary, Italy, Poland, and Spain.

**Chapters 4 and 5** were devoted to the assessment of the role of alcohol in overall mortality differences over time, across countries, and between the sexes (sub-objective 2).

In **Chapter 4**, the impact of alcohol on mortality and its contribution to the East-West life expectancy gap was investigated. The findings indicated that alcohol had a notable impact on overall life expectancy and on differences in life expectancy between individual Central and Eastern European (CEE) countries and Western Europe. For 2012/13, the potential gains in life expectancy by eliminating alcohol-attributable mortality were found to be 0.90 years for men and 0.44 years for women in the EU-15 countries, and 2.15 years for men and 1.00 years for women in the CEE countries. Furthermore, alcohol was shown to contribute substantially to the East-West life expectancy gap, especially among men and in Russia, Belarus, and Ukraine (around or above 2.5 years in 2012/13). The relative contributions increased in most of the CEE countries between 1990 and 2005 (on average, from 17.0% to 25.4% for men, and from 14.7% to 22.5% for women), and declined thereafter (20.2% for men and 20.5% for women in 2012/13).

In **Chapter 5**, the contribution of alcohol to gender differences in life expectancy in eight CEE countries was analysed. The results showed that the life expectancy advantage of women relative to men increased from 7.3 years on average in 1965 to 10.0 years on average in 2012. Alcohol-attributable mortality contributed 1.9 years on average to these gender differences from

1990 to 2012. The relative contribution of alcohol-attributable mortality increased in most of the analysed countries until around 2005, and declined thereafter, resulting in a contribution of at least 15% in 2012 in all of these countries.

In sum, this PhD thesis showed that past trends in alcohol-attributable mortality in Europe differed considerably across Europe. The results indicated that the levels of alcohol-attributable mortality were higher and the trends in deaths related to alcohol were more irregular in Eastern Europe than elsewhere; but that in recent years, the countries with the highest levels of alcoholattributable mortality have seen moderate declines in deaths linked to alcohol. In addition, the analysis showed that the birth cohorts at highest risk of alcohol-attributable mortality differed across European countries. While alcohol was found to have a large impact on overall mortality levels, important differences were observed across countries and between men and women. The impact of alcohol on mortality was shown to be especially large among men in Central and Eastern Europe (2.15 years of potential gains in life expectancy), but substantial in other European countries as well (e.g., France, Finland). The results indicated that in 2012/13, the average contribution of alcohol to life expectancy differences between individual CEE countries and Western Europe was around 20%; and that in 2012, alcohol contributed at least 15% to the gender gaps in life expectancy in the eight analysed Central and Eastern European countries. The contribution of alcohol to the East-West differences and the gender gap in life expectancy increased up to 2005, but declined thereafter.

Thus, this PhD research clearly highlighted the substantial variation in alcohol-attributable mortality across European countries, between the sexes, and over time (by both calendar year and birth cohort); and the impact of alcohol-attributable mortality on differences in all-cause mortality, particularly between Eastern and Western Europe, but also between men and women.

## 6.3. Reflections on the main findings

## 6.3.1. Variations in levels and trends in alcohol-attributable mortality

The substantial variation in levels of alcohol-attributable mortality observed across Europe are directly related to differences in alcohol consumption, which in turn are related to socioeconomic conditions in addition to differences in drinking cultures across Europe.

For example, the high levels of alcohol-attributable mortality observed among Eastern European men have been linked to the drinking culture in Eastern Europe, which is characterised by particularly risky drinking patterns and high levels of consumption of spirits (e.g., vodka) (e.g., Bobak et al., 2016; Leon et al., 2009; Zaridze et al., 2009). The influence of this culture appears to be particularly relevant for working-aged men. It has, for example, been shown that heavy drinking accounts for around half of the deaths among working-aged men in typical Russian cities (Leon et al., 2007; Zaridze et al., 2009). It has also been suggested that the unfavourable economic conditions and the public health crisis in Eastern Europe after 1975 aggravated this situation, and contributed to increases in both alcohol consumption and alcohol-attributable mortality, especially in the 1990s (Shkolnikov et al., 1998).

The other differences in levels of alcohol-attributable mortality observed across European regions (e.g., Western, Southern) have mainly been linked to differences in drinking culture (Franco. 2015; WHO. 2014). For example, in Southern European countries like France, wine has long been the preferred beverage. Because wine is typically consumed on a daily basis together with meals, overall alcohol consumption levels tend to be high in these countries (Gual & Colom, 1997). In Western Europe, by contrast, beer has long been the preferred beverage. Because beer is mainly consumed outside of mealtimes and on the weekends, overall alcohol consumption levels tended to be lower in these countries (Allamani et al., 2000).

The abovementioned differences between European regions in both levels and patterns of alcohol use have a clear impact on overall mortality differences, and explain both the high levels of and the irregular trends in alcohol-attributable mortality in Eastern Europe (related to drinking patterns), as well as the high levels of alcohol-attributable mortality in Southern Europe in the 1970s and the 1980s (related to the overall volume of alcohol consumed).

Just as alcohol-attributable mortality has been found to be higher among men than among women, gender differences in (excessive) alcohol use have been observed (Mäkelä et al., 2006; Popova et al., 2007). These gender differences have been related in the previous literature to men having a greater propensity than women for taking risks; to behavioural norms that are stricter for women than for men; and to gender-specific ways of coping with stress (Byrnes et al., 1999; Weidner & Cain, 2003). Another important finding related to the temporal dimension was that the birth cohorts at higher risk of liver cirrhosis mortality differed between countries: these cohorts were born around 1935-49 in the Nordic countries and from 1960 onwards in the Southern European and the Central and Eastern European countries. These important differences in the timing of the birth cohorts at higher risk of liver cirrhosis mortality were not identified in previous studies (Kraus et al., 2015; Rosén & Haglund, 2006). These gaps have been explained by differences in the timing of contextual changes related to alcohol, such as

positive changes in alcohol policies and in levels of social awareness of alcohol damage. These shifts occurred earlier in more economically advanced countries (Österberg & Karlsson, 2002), and seem to have affected the behaviour of younger people in particular.

An important observation is that in recent years, alcohol-attributable mortality has been declining among the countries with the highest levels of alcohol-attributable mortality, and that levels of alcohol-attributable mortality have been converging across Europe (i.e., the differences between countries have become smaller). This trend appears to be a consequence of an overall trend towards convergence across Europe and between men and women in levels of alcohol consumption and in the beverages drinkers prefer (Allamani et al., 2000; Allamani et al., 2014; Bosque-Prous et al., 2015; Gual & Colom, 1997; Slade et al., 2016; WHO. 2014). This convergence has mainly been driven by shifts in alcohol consumption patterns that occurred in different regions and in different periods of time. On the one hand, in the countries with a tradition of drinking wine (i.e., Spain, France, Italy), alcohol consumption levels have fallen from being the highest in Europe in 1975 to hovering around the European average today. This decline has been explained by the decrease in total alcohol consumption, and particularly of wine as a drink that is regularly consumed with meals. As beer has become more popular in Southern Europe, the drinking cultures in these countries have started to converge with those of Western Europe (Gual & Colom, 1997). On the other hand, in the Central European and especially in the Eastern European countries, alcohol consumption seems to have fallen substantially. After increasing for a period of time, levels of alcohol consumption started gradually decreasing from around 2005 or onwards (depending on the country). This decline has been attributed to the implementation of preventive health policies and to moderate changes in the drinking culture (i.e., a shift away from drinking spirits and towards consuming beer) in a context of economic stabilisation (Grigoriev & Andreev, 2015; Neufeld & Rehm, 2013) (see 4.4 for further detail). These improvements benefited the health of men more than of women because men drink more than women, and because women have started drinking more in response to changes in their position in society (Hinote et al., 2009).

# 6.3.2 Role of alcohol in overall mortality levels and variations

For 2012/13, the effect of alcohol on life expectancy was estimated at 0.90 years for men and 0.44 years for women in Western Europe; and at 2.15 years for men and 1.00 years for women in Eastern Europe. The finding that alcohol had a greater impact on overall mortality levels in the CEE countries than in the Western European countries, and among men than among women,

can be directly linked to the abovementioned differences across Europe in the levels of (excessive) alcohol consumption, and in the related levels of alcohol-attributable mortality.

To assess the size of the effect of alcohol on life expectancy, a comparison between the impact of alcohol and of other lifestyle factors (smoking, obesity) is informative. It was estimated that the effect of smoking on life expectancy amounts to 2.38 years for men and 1.00 years for women in Western Europe; and to 3.82 years for men and 0.67 years for women in Eastern Europe (see Vidra et al., submitted). It thus appears that the impact of alcohol has been smaller than that of smoking in Western Europe, but that the impact of alcohol was found to be greater than that of smoking among women in Eastern Europe. Interestingly, the impact of alcohol in Eastern Europe seems to be comparable to that of smoking in Western Europe. It was also shown that in the countries with the lowest alcohol-attributable mortality rates, the potential gains in life expectancy are hardly negligible (e.g., 0.5 years in Sweden among men). Moreover, it was estimated that the impact of alcohol on life expectancy is similar in size to the impact of obesity in most of Western Europe (1.08 years for men and 0.86 years for women), but is clearly greater than the impact of obesity in Eastern Europe (1.44 years for men and 1.16 years for women) (Vidra et al., submitted). Thus, the results of this analysis clearly indicate that the impact of alcohol on mortality vis-à-vis other lifestyle factors has been substantial, especially in Eastern Europe.

In addition, alcohol has been found to explain around three years of the life expectancy gap between the Eastern European countries with the lowest life expectancy levels (Russia and Ukraine) and the Western European countries with the highest life expectancy levels; and, on average, around 20% of the life expectancy gap for the analysed countries and for both men and women. These numbers are somewhat lower than those for smoking, especially among men. For men, the effect of alcohol on the East-West life expectancy gap has been estimated to be between 30% and 50% (Zatoński, 2008). Thus, alcohol can be considered the second-most important determinant after smoking of the East-West life expectancy gap.

The contribution of alcohol to the gender gap in life expectancy also appears to be large. It has been shown that in 2012, alcohol explained at least 15% of this gap in eight selected Central and Eastern European countries. Again, this contribution was found to be smaller than the contribution of smoking, which was estimated to explain, on average, 36% (with a range of 32-43%) of the gender gap in life expectancy for the eight selected CEE countries (Luy & Wegner-

Siegmundt, 2015). Thus, it appears that alcohol can also be considered the second-most important determinant of the sex differences in life expectancy in Eastern Europe.

The decline from around 2005 onwards in the contribution of alcohol to the life expectancy gaps between the East and the West differences and between men and women have mainly been attributed to two recent trends mentioned above: namely, the sharp decline in alcohol consumption in Eastern Europe and the adoption by women of drinking patterns that have traditionally been associated with men. Overall, this convergence in alcohol use across Europe has also benefited from the unifying forces of the creation of one single market, with similar products, brands, marketing and standards.

## 6.4. Reflections on the methodological approach

Overall, the comparative and temporal approaches adopted in this PhD research went one step beyond the approaches used in the previous literature, and provided new knowledge that is comparable across Europe, between the sexes, and over time.

# 6.4.1. Population-level approach

Using population-level data has clear advantages. In particular, analyses based on such data can provide important information about society at large, and are therefore highly relevant for the general public and for public health policy-makers. The population-level approach applied to alcohol-attributable mortality in Europe in this thesis provided important information on the mortality burden of alcohol for several specific countries in Europe, and for its male and female subpopulations. The comparative approach that was used contributed to estimates of countryand sex-specific mortality burdens (relative to those of other countries and the other sex), and provided information on how these burdens evolved over time. It was also found that the alcohol-attributable mortality rates are affected by the share of binge drinkers in a population, as they tend to critically increase the risks of alcohol-attributable mortality. Furthermore, it is generally understood that population-level estimates of, for example, potential gains in life expectancy are relatively easy to interpret for a broader audience. It is important to note, however, that when the country-level approach is used, the results (i.e., the potential gains in life expectancy) should be interpreted as averages of aggregated results, and not as reflecting any particular individual drinking pattern.

## 6.4.2. Estimating alcohol-attributable mortality is not straightforward

A key element of this research was the estimation of population-level alcohol-attributable mortality rates. This estimation is not straightforward because of the complex relationship between alcohol consumption and health outcomes (Rehm et al., 2010; Rehm et al., 2017). Thus, we carefully evaluated different techniques for estimating alcohol-attributable mortality at the population level. The choice of one method over another generally depends on the availability and the accuracy of the data, and on the aim of the study (see 2.5 for further details).

The evaluation conducted in this PhD research showed that the most detailed approaches (attributable fraction approaches, the cause-of-death approach accounting for contributory causes) are theoretically able to provide more accurate estimates of overall alcohol-attributable mortality. However, both approaches require large amounts of data, which are not always available. Thus, these detailed approaches cannot be applied when the aim is to study long-term trends in alcohol-attributable mortality (like in Chapter 3). In such a case, an underlying causeof-death approach is more appropriate. Out of the approaches that are based on underlying causes of death, the Health for All Database method is the least accurate because, as it includes several causes of death which are not wholly attributable to alcohol (i.e. all external deaths). Of the other potential methods, those that rely on at least the main underlying causes of death that are wholly attributable to alcohol (i.e., mental and behavioural disorders due to alcohol, alcoholic liver disease, and accidental poisoning by alcohol) should be preferred. However, it is not possible to use these methods directly to study long-term trends because of coding changes in the International Classification of Deaths (ICD). Thus, for examining long-term trends, the approach that uses liver cirrhosis deaths only seems preferable, as no assumptions are needed to reconstruct mortality data across changes in the ICD. Although the estimates from underlying causes of death are clearly too low, it is unlikely that these estimates inaccurately represent the overall alcohol-attributable mortality trends, as they follow per capita alcohol consumption over time (Ramstedt, 2001) (see also the discussion of Chapter 3).

When the aim is to estimate the total impact of alcohol on mortality (like in Chapters 4 and 5), the more detailed approaches should be considered. In a comparative context, the use of the Global Burden of Disease (GBD) estimates is the only alternative, because detailed mortality data that include both underlying and contributory causes of death are lacking for most countries and most periods of time. The limitations of the used attributable fraction method should, however, be acknowledged. It should also be noted that especially at older ages, the estimates

are sensitive to the data and the assumptions used (see also the discussions of Chapters 2, 4, and 5).

# 6.4.3. Temporal approach: including birth cohort effects

Before this PhD research was conducted, the role of birth cohorts (= generations) in past trends in alcohol-attributable mortality had seldom been formally studied, and the little existing research on this topic did not focus on long-term trends or on Central or Eastern European countries. Cohort effects, in addition to age and period effects, were included in the chapters examining time trends by means of age-period-cohort (APC) modelling.

A main methodological issue that arises in all APC models is the identification problem, as age, period, and birth cohort are linearly dependent (cohort = period – age). Moreover, it is hard to disentangle period and birth cohort effects given that they share a linear term (commonly referred to as drift) (Clayton & Schifflers, 1987a). Thus, it is statistically impossible to accurately disentangle the contributions of period and birth cohorts to the linear trend unless assumptions are made (Holford, 1983). We have opted to use an approach that allows us to include drift within the period dimension, and thus to estimate non-linear cohort effects (Clayton & Schifflers, 1987a; Clayton & Schifflers, 1987b). The application of this approach enabled us to identify pure cohort effects that were not affected by the overall trend over time. Other approaches presented in the literature deal with the linear identification problem in other ways (e.g., Carstensen, 2007; Yang et al., 2004), and generally provide similar results when identifying non-linear birth cohort effects. However, when only the non-linear birth cohort effects are underestimated, especially in cases that have an important linear component (drift) (Janssen & Kunst, 2005).

While conducting our APC analysis had its challenges, the results clearly showed that the birth cohort dimension can play an important role in describing and explaining the alcoholattributable mortality trends in Europe. Related to our analysis, birth cohort analysis was advocated as an important tool for guiding public health interventions (Lazarus & Bromberg, 2017).

## 6.5. Recommendations for future research

Based on the knowledge derived from this thesis, three lines of future research are suggested. Two lines of future research can provide us with a better understanding of the impact of alcohol on mortality: (i) making investments that further improve estimates of alcohol-attributable mortality; and (ii) estimating the future mortality burden of alcohol. The third line of future research is determining the combined – rather than the individual – impact of several unhealthy lifestyles on mortality at the population level.

#### 6.5.1. Improving estimates of alcohol-attributable mortality

Future research should focus on improving the comparability of alcohol-attributable mortality estimates across European populations and over time.

To enhance the quality and the robustness of detailed approaches, more accurate and comparable data are needed so that more detailed approaches can be used to estimate alcoholattributable mortality, and particularly those that require data on age-specific alcohol consumption (attributable fraction approaches) and detailed information on cause-specific mortality (underlying and contributory approaches). The estimates of attributable-fraction approaches could be improved if more accurate and comparable data were available from health surveys on alcohol use between countries and over time, especially if they also included a larger sample of older respondents (see Chapter 2 for further detail). In addition, as new epidemiological evidence on the relationship between alcohol consumption and cause-specific mortality becomes available, the estimates should become more robust. Therefore, regular updates on the relationship between alcohol and mortality will likely be seen as essential in the near future (see Rehm & Imtiaz, 2016; Rehm et al., 2017).

Given the data and methodological limitations that hinder efforts to accurately estimate alcoholattributable mortality across Europe and over time, another potential line of research could focus on the development of indirect methods for estimating alcohol-attributable mortality. It should be noted that indirect techniques have become the benchmark methods for estimating smoking-attributable mortality at the population level (Peto et al., 1992; Preston et al., 2010). However, because of the differential alcohol-related disease-specific patterns across Europe, a flexible method would be needed to obtain robust estimates across countries and over time.

### 6.5.2. Estimating future alcohol-attributable mortality

Another crucial question in the fields of alcohol and health research at the population level is how alcohol-attributable mortality will evolve in the future. Previous studies that provided estimates of future alcohol-attributable mortality are scarce. However, studies by Sheron and colleagues used extrapolation techniques and past time trends from various countries (Sheron et al., 2011; Sheron et al., 2012) to project future trends in United Kingdom and England and Wales; while a more recent study used age-period-cohort models and it kept age and cohort constant over time (Rosén & Haglund, 2018). Given the importance of the cohort dimension in describing past alcohol-attributable mortality trends (Chapter 3), future research could include the already known information on relatively young cohorts in order to project future alcohol-attributable mortality. In some European countries, binge drinking is increasing among the younger birth cohorts (Franco. 2015; Harkonen & Mäkelä, 2011; Pabst et al., 2010). Thus, members of this generation may experience more negative health effects related to alcohol than their older counterparts (Pitkänen et al., 2005). Future research should be undertaken to explore the potential contributions of current and new generations to future trends in alcohol-attributable mortality.

#### 6.5.3. Assessing the combined impact of unhealthy lifestyles

In addition to alcohol consumption, several other lifestyle behaviours are hypothesised to have a large impact on mortality trends. Of these behaviours, smoking has been the most extensively analysed (e.g. Janssen et al., 2015; Janssen et al., 2013; Lindahl-Jacobsen et al., 2016; Renteria et al., 2016). It has been repeatedly shown in the literature that the coexistence of various unhealthy lifestyles could have a cumulative effect on the risk of developing certain diseases and on all-cause mortality (e.g., Loef & Walach, 2012). However, the indirect techniques that are currently used to estimate lifestyle-attributable mortality do not allow us to combine several lifestyles because they pose competing risks. Therefore, it would be convenient to be able to estimate the simultaneous impact of aggregated lifestyles on population-level overall mortality. At the individual level, recent studies based on health survey data have already estimated and quantified the aggregated impact of unhealthy lifestyles on health and mortality outcomes (e.g., Li et al., 2018; Mehta & Myrskylä, 2017; White et al., 2018). However, because of the complexity of individual lifestyle and health outcomes and the lack of detailed data on the combined impact of several lifestyle behaviours on health, the overall impact of lifestyle behaviours at the population level is still unknown. One possible option for obtaining such estimates is to make use of the large population-based cohort datasets that have recently been created.

#### 6.6. General implications for society and recommendations for policy-makers

In this PhD thesis, we showed that (i) alcohol consumption and alcohol-attributable mortality remain high in most European countries, despite recent declines; (ii) important differences in alcohol-attributable mortality exist across countries and between men and women; and (iii)

alcohol has a large impact on overall mortality levels and variations therein. These new findings have important implications. Above all, these results imply that the alcohol problem in Europe clearly deserves further attention from public health policy-makers, and from society at large. In European society, alcohol, unlike smoking, is generally not considered an important risk factor for health. For example, alcohol consumption is broadly accepted in public places and events, but it also has a long history and differential sociocultural roots across Europe (Heath, 1995). Furthermore, the results of this thesis show a clear need and room for additional alcohol-related public health interventions in Europe.

Previous alcohol-related public health policies sought to discourage consumption by, for example, imposing price increases (affordability), placing restrictions on advertising, and setting limits on the availability of alcohol (e.g., limiting the opening hours of shops where alcohol can be sold; establishing age restrictions for buying alcohol) (for further details, see Anderson et al., 2009; Anderson, 2013; Moskalewicz & Österberg, 2016; Wagenaar et al., 2010; WHO. 2010). These previous alcohol-related public health policies have been shown to be effective. There is, for example, evidence that countries with more advertising restrictions have the lowest prevalence of hazardous drinking among middle-aged people (Bosque-Prous et al., 2014). It has also been shown that setting a minimum price for a unit of alcohol can modify alcohol consumption among harmful drinkers, and especially among those from lower socioeconomic classes (Holmes et al., 2014). The introduction of a minimum price on alcohol is currently being considered by several countries. Finally, it is widely known that the density and the opening hours of outlets that sell alcohol are positively associated with alcohol-related harms (Popova et al., 2009). Policy-makers should, however, consider the specific groups being targeted when designing interventions intended to reduce the harmful effects of alcohol over both the short and the long run.

Our findings that both period (e.g., short-term variations) and cohort effects (e.g., long-term variations) are important in understanding alcohol-attributable mortality imply that preventive health policies aimed at reducing the damage to health caused by alcohol should take into account both the short-term and the long-term effects. The short-term effects could be limited by focusing on the groups at higher risk that were also identified in this PhD research (e.g., men, middle-aged people, binge drinkers, certain birth cohorts). The long-term effects could be limited by focusing on younger individuals, as they are still forming the habits that will shape their alcohol consumption patterns, and the associated health consequences, over their adult lives (Raninen et al., 2016).

Preventive health policies should consider the diversity of alcohol consumption patterns across European populations (including socioeconomic, cultural, and gender-specific factors), as the same policies are unlikely to be effective across all subpopulation groups. Furthermore, in addition to these conventional policies, a more extended strategy is needed that also addresses the lack of awareness in society that consuming alcohol poses the same risk to health as smoking tobacco or using other drugs. Therefore, ongoing efforts to inform members of the public about the harmful effects of alcohol on health are required. Greater awareness of how alcohol can damage health could contribute to an overall reduction in alcohol abuse, thereby minimising the damage to health caused by alcohol consumption. One option for encouraging such societal changes is to lower the norms for alcohol consumption in national guidelines in accordance with recent research (Wood et al., 2018), as has recently been done in the UK (Department of Health, 2016). Another option is to include health warning messages in alcohol labelling, as has been done for tobacco products (Hammond, 2011), and as leading experts in the field have suggested (Anderson et al., 2009).

It is likely that the alcohol-related public health interventions outlined above will not only improve overall health, but also reduce health inequalities across Europe.

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## 152 | Engish Summary

### **English summary**

# Alcohol-attributable mortality in Europe: Past trends and their effects on overall mortality variations

Alcohol consumption in Europe is a major public health concern. European countries have the highest levels of alcohol consumption worldwide, and it is well known that drinking alcohol has detrimental effects on health. There are, however, important differences in alcohol consumption levels and drinking patterns across European populations. In particular, Eastern European men have high levels of consumption and a marked tendency to engage in risky drinking behaviour. These distinct patterns of alcohol consumption in European societies could contribute to the large overall differences in mortality across European countries, between the sexes, and over time.

Despite the importance of this issue, there is little detailed research on past trends in alcoholattributable mortality in Europe, and there are even fewer studies that have examined the impact of alcohol on overall mortality differences across Europe.

The main objective of this thesis was to examine past trends in alcohol-attributable mortality in Europe, and their effects on overall mortality differences.

In this PhD research, we used an interdisciplinary approach that took into account both demographic factors like population-level mortality levels and long-term mortality trends, as well as epidemiological factors like the impact of alcohol on mortality. In addition, this PhD research has public health relevance because the analysis was performed comparatively across countries, between the sexes, and over time. For the analysis, we made ample use of newly available demographic and epidemiological data, and of advanced demographic and statistical modelling techniques.

**Chapter 1** presented the background and the objectives of this dissertation, and described the current state-of-the-art of research on overall mortality variations and the role of alcohol consumption in mortality trends.

**Chapter 2** compared the techniques that are currently used to estimate age-specific alcoholattributable mortality at the population level for France (2010) and Finland (2013), for the ages 25-79. Using data on causes of death, alcohol consumption, and the relative risks of mortality at different consumption levels, five cause-of-death approaches (with one accounting for contributory causes) and three attributable fraction (AF) approaches were compared. Detailed approaches (AF and method accounting for contributory causes) provided estimates of alcohol-attributable mortality that were twice as high as the estimates found using underlying cause-of-death approaches. A clear inverse U-shaped age pattern in alcohol-attributable mortality rates was found in the approaches that used cause-of-death mortality data only, especially for Finland. Theoretically, the more detailed provide more accurate estimates of the overall level of alcohol-related mortality. However, these approaches – and especially the attributable fraction approaches – depend heavily on data availability and data quality.

In Chapter 3 of this dissertation, the contributions of birth cohorts to liver cirrhosis mortality trends in eight European countries (Austria, Finland, Hungary, Italy, the Netherlands, Poland, Spain and Sweden) were examined. Birth cohort effects, which are indicative of generational differences in alcohol drinking, have rarely been studied. For this analysis, liver cirrhosis mortality data for the 1950-2011 period were retrieved from the WHO Mortality Database for the national populations aged 15-94; and age-period-cohort models were applied. Birth cohorts were found to contribute to the model fit more than the models that included only age and period (calendar time). Additionally, important differences across the analysed countries were observed in the birth cohorts at higher risk of liver cirrhosis mortality: namely, the cohorts born between 1935 and 1949 in Sweden and Finland; around 1950 in Austria and the Netherlands; and around 1960 or later in Hungary, Italy, Poland and Spain. It appears that these differences can be explained by the timing in contextual changes related to alcohol. Chapters 4 and 5 were devoted to examining the role of alcohol in life expectancy differentials in Europe. In both chapters, age- and sex-specific alcohol-attributable mortality estimates were retrieved from the Global Burden of Disease (GBD) Study 2013, and life table calculations and decomposition techniques were applied.

In **Chapter 4**, the impact of alcohol on mortality and on the difference in life expectancy between East and West Europe was investigated for all ages, and for the years 1990, 1995, 2000, 2005, 2010, and 2012/13. The results indicated that in 2012/2013, the potential gains in life expectancy at birth by eliminating alcohol-attributable mortality were 0.90 years for men and 0.44 years for women in the EU-15 region, and 2.15 years for men and 1.00 years for women in the Central and Eastern European (CEE) region. Furthermore, alcohol was shown to contribute substantially to the East-West life expectancy gap, especially among men in Russia, Belarus, and Ukraine (around or more than 2.5 years in 2012/13). The relative contributions increased in most of the CEE countries between 1990 and 2005 (on average, from 17.0% to

25.4% for men, and from 14.7% to 22.5% for women), and declined thereafter (20.2% for men and 20.5% for women in 2012/13).

In **Chapter 5**, the contribution of alcohol to gender differences in life expectancy at birth in eight CEE countries (Estonia, Lithuania, Latvia, Moldova, Poland, Romania, Russia, and Ukraine) was analysed using, in addition to the GBD data, cause-specific mortality data from the Human Cause-of-Death Database for the 1965-2015 period. The results showed that the life expectancy advantage of women relative to men increased from 7.3 years on average in 1965 to 10.0 years on average in 2012. All alcohol-attributable mortality contributed 1.9 years on average to these gender differences from 1990 to 2012. the relative contribution of alcohol-attributable mortality increased in most of the countries until around 2005, and declined thereafter, resulting in a contribution of at least 15% in 2012 in all of these countries.

Finally, in **Chapter 6**, a summary of the results, an overall discussion of the main results, reflections on the applied approach and methods, and recommendations to future research and policy makers are provided.

Overall, the PhD research uncovered substantial differences in alcohol-attributable mortality in Europe across countries, between the sexes, and over time that had important effects on overall mortality levels and trends. Alcohol-attributable mortality was found to be higher among men than among women, especially in Eastern Europe, where the levels of alcohol-attributable mortality were higher and the trends in deaths related to alcohol were more irregular than in Western Europe. In most of the countries, moderate declines in mortality from alcohol have been observed in recent years. In addition, the analysis showed that the birth cohorts at highest risk of alcohol-attributable mortality differed across European counties. The impact of alcohol on life expectancy was shown to be especially large among men in Eastern Europe, but substantial in other European countries as well. Despite some declines from around 2005 onwards, alcohol-attributable mortality contributed on average around 20% to the life expectancy differences between CEE countries and Western Europe in 2012/13, and at least 15% to the gender differences in life expectancy in the eight selected CEE countries in 2012.

The substantial variation in alcohol-attributable mortality levels observed across Europe could be directly related to differences in drinking cultures across Europe. For example, the striking differences in alcohol-attributable mortality between Eastern and Western Europe may be partly explained by the very large amounts of high-content alcohol beverages consumed (e.g., vodka) and the high prevalence of binge drinking among Eastern European men that characterise Eastern European drinking cultures. The –substantial impact of alcohol on both the East-West life expectancy gap and the gender gap in CEE can be linked entirely to differences in alcohol consumption in Europe The decline in the contribution of alcohol to these East-West differences from around 2005 onwards could be partly attributable to the introduction of preventive public health policies in Eastern Europe during a period of economic and political stability. However, the effects of alcohol on both the life expectancy levels in individual countries and the life expectancy differences between Western and Central and Eastern European countries were still very large in 2012/13.

The comparative and temporal approaches adopted in this PhD research went one step beyond the approaches used in the previous literature, and provided new knowledge on the impact of alcohol on mortality that is comparable across Europe and over time. The inclusion of the birth cohort dimension can improve our understanding of long-term trends in alcohol-attributable mortality. For future research, making investments that further improve estimates of alcohol-attributable mortality, particularly at older ages, would certainly be beneficial. In addition, we recommend the estimation of future alcohol-attributable mortality in order to take into account the birth cohort dimension. To gain a better understanding of the role of alcohol consumption and of other unhealthy lifestyle behaviours (i.e. smoking) in overall mortality levels and variations, research is also needed that examines the combined – rather than the individual – impact of several unhealthy lifestyles on mortality at the population level.

The results of this thesis suggest that introducing public health interventions related to alcohol would not only improve overall health in Europe, but would reduce health inequalities across Europe. Conventional restrictive policies that reduce the availability or raise prices of alcohol should be implemented to limit both the short-term and the long-term effects of alcohol abuse. The short-term effects could be limited by focusing on the groups at higher risk (e.g., men, middle-aged people, and binge drinkers; particularly among the birth cohorts at higher risk). The long-term effects could be limited by focusing on younger individuals as they are still forming their drinking habits. Furthermore, in addition to these conventional policies, a more extended strategy is needed that also addresses the lack of awareness in society that consuming alcohol, like smoking tobacco or using other drugs, poses health risks. Options for encouraging such societal changes include lowering the norms for alcohol consumption in national guidelines in accordance with recent research; and adding health warning messages to alcohol labelling, as has been done for tobacco products.

The alcohol problem in Europe clearly deserves further attention from public health policymakers, and from society at large.

#### Nederlandse samenvatting

## Alcohol-gerelateerde sterfte in Europa: lange-termijn ontwikkelingen en diens effect op totale sterfteverschillen

Alcoholconsumptie in Europa vormt een grote zorg voor de volksgezondheid. Wereldwijd is het alcoholconsumptie niveau het hoogst in Europa en de schadelijke effecten van alcohol op de gezondheid zijn alom bekend. Er bestaan echter belangrijke verschillen in alcoholconsumptie en drinkpatronen binnen Europa. Met name Oost-Europese mannen vertonen hoog en riskant alcohol gebruik. Het hoge alcoholconsumptieniveau en de belangrijke verschillen hierin binnen Europa kunnen mogelijk een belangrijke rol spelen in de waargenomen verschillen in totale sterfte tussen Europese landen, tussen geslachten en over tijd.

Ondanks het grote belang van alcoholconsumptie in Europa, zijn ontwikkelingen in alcoholgerelateerde sterfte in Europa nauwelijks in detail onderzocht en zijn studies naar het effect van alcohol op totale sterfteverschillen in Europa zelfs nog sporadischer.

Dit proefschrift had tot doel om de lange-termijn ontwikkelingen in alcohol-gerelateerde sterfte in Europa en diens effect op verschillen binnen Europa in totale sterfte te onderzoeken.

In deze studie is een interdisciplinaire aanpak op het snijvlak van demografie, epidemiologie en maatschappelijke gezondheid gehanteerd. Het onderzoek is uitgevoerd aan de hand van sterftecijfers op bevolkingsniveau, met een focus op hoe nationale alcohol-gerelateerde sterfte, naar geslacht, zich over tijd ontwikkeld heeft. Daarnaast is specifiek gekeken naar het effect van alcohol op sterfte, maar dan opnieuw op bevolkingsniveau. Door vergelijkbaar onderzoek te doen voor verschillende landen, de beide geslachten en over tijd, heeft de studie relevante resultaten gegenereerd voor de volksgezondheid. Voor de analyse is voornamelijk gebruik gemaakt van recente nieuw beschikbare demografische en epidemiologische data en geavanceerde demografische en statistische modelleringstechnieken.

In **Hoofdstuk 1** is de achtergrond van het onderzoek beschreven en zijn de doelstellingen uiteengezet. Daarnaast is de huidige stand van zaken in het onderzoek naar verschillen in sterfte, alcoholconsumptie en alcohol gerelateerde sterfte beschreven

In **Hoofdstuk 2** zijn de huidige technieken om leeftijdsspecifieke alcohol-gerelateerde sterfte op bevolkingsniveau te berekenen vergeleken voor Frankrijk (2010) en Finland (2013), voor de

leeftijden 25 tot 80. Door gebruik te maken van data over doodsoorzaak specifieke sterfte, alcoholconsumptie en relatieve risico's op sterfte voor verschillende consumptieniveaus zijn zeven benaderingen vergeleken: vijf doodsoorzaakgerelateerde benaderingen (één die rekening houdt met secundaire doodsoorzaken), en drie attributieve fractie benaderingen. De gedetailleerde benaderingen (de attributieve fractie benaderingen en de benadering met secundaire doodsoorzaken) resulteerden in twee keer zo hoge schattingen van alcohol-gerelateerde sterfte als de overige doodsoorzaakgerelateerde benaderingen. De doodsoorzaakgerelateerde benaderingen lieten een duidelijk omgekeerde U-vorm in het leeftijdspatroon van alcohol-gerelateerde sterfte zien, vooral voor Finland. Al met al, leveren de meer gedetailleerde benaderingen theoretisch gezien meer accurate schattingen op van het algehele niveau van alcohol-gerelateerde sterfte. Deze benaderingen, en vooral de attributieve fractie benaderingen, zijn echter sterk afhankelijk van de databeschikbaarheid en -kwaliteit.

In **Hoofdstuk 3** van dit proefschrift is de bijdrage van geboortecohorten op sterfteontwikkelingen in levercirrose in acht Europese landen (Finland, Hongarije, Italië, Nederland, Oostenrijk, Polen, Spanje en Zweden) onderzocht. Geboortecohort effecten, indicatief voor verschillen tussen generaties in alcoholconsumptie, zijn nog zelden bestudeerd. Voor dit doeleinde is data over sterfte aan levercirrose verkregen van de 'WHO Mortality Database' voor de totale nationale bevolkingen in de leeftijd 15 tot 94, voor 1950 tot en met 2011, waarop leeftijd-periode-cohort modellen zijn toegepast. De resultaten laten zien dat het meenemen van geboortecohorten, ten opzichte van het puur meenemen van leeftijd en periode (kalendertijd), de model fit significant verbetert. Daarnaast verschillen landen duidelijk wat betreft het geboortecohort met het hoogste risico op sterfte aan livercirrose. Meer specifiek, de cohorten met een hoger risico op sterfte aan levercirrose zijn in Zweden en Finland geboren tussen 1935-49, in Oostenrijk en Nederland rond 1950, en in Hongarije, Italië, Polen en Spanje rond 1960 of later. Deze verschillen lijken verklaard te kunnen worden door verschillen tussen de landen in de timing van contextuele alcohol-gerelateerde veranderingen.

**Hoofdstukken 4 en 5** zijn toegewijd aan onderzoek naar het effect van alcohol op de verschillen in levensverwachting in Europa. In beide hoofdstukken zijn de leeftijds- en geslacht-specifieke alcohol-gerelateerde sterfte schattingen verkregen van de Global Burden of Disease (GBD) Study 2013. Op deze data zijn zowel sterftetafelberekeningen als decompositie technieken toegepast.

In **Hoofdstuk 4** is het effect van alcohol op totale sterfte en op het verschil in levensverwachting tussen Oost- en West-Europa onderzocht, voor alle leeftijden gezamenlijk en voor de jaren

1990, 1995, 2000, 2005, 2010 en 2012/2013. De resultaten voor 2012/13 laten zien dat de potentiële winst in levensverwachting bij geboorte, door alcohol-gerelateerde sterfte buiten beschouwing te laten, 0,90 en 0,44 jaar betrof voor respectievelijk mannen en vrouwen in de EU-15 regio. Voor Centraal en Oost-Europa (CEE) waren deze getallen respetievelijk 2,15 jaar en 1,00 jaar. Daarnaast bleek alcohol-gerelateerde sterfte substantieel bij te dragen aan het Oost-West verschil in levensverwachting, vooral voor mannen in Rusland, Belarus en Oekraïne waar de bijdrage aan het verschil in 2012/13 rond of boven de 2,5 jaar lag. De relatieve bijdragen namen in de meeste Centraal en Oost Europese landen toe tussen 1990 en 2005 (gemiddeld van 17,0% tot 25,4% voor mannen en van 14,7% tot 22,5% voor vrouwen), om daarna af te nemen tot 20,2% voor mannen en 20,5% voor vrouwen in 2012/13.

In **Hoofdstuk 5** is de rol van alcohol in het verschillen in levensverwachting bij geboorte tussen mannen en vrouwen in acht CEE-landen (Estland, Letland, Litouwen, Moldavië, Oekraïne, Polen, Roemenië en Rusland) onderzocht. Hiervoor is naast de GBD data ook gebruik gemaakt van doodsoorzaakspecifieke data van de 'Human Cause-of-Death Database' voor de periode van 1965 tot en met 2015. De resultaten laten zien dat het voordeel in levensverwachting voor vrouwen ten opzichte van mannen toegenomen is van gemiddeld 7,3 jaar in 1965 tot gemiddeld 10,0 jaar in 2012. Alcohol-gerelateerde sterfte heeft gemiddeld 1,9 jaar bijgedragen aan het verschil in levensverwachting tussen mannen en vrouwen over de periode 1990 tot en met 2012. De relatieve bijdrage van alcohol-gerelateerde sterfte nam in de meeste landen toe tot ongeveer 2005, om vervolgens af te nemen tot een bijdrage van minstens 15% in 2012.

**Hoofdstuk 6** omvat, tot slot, een samenvatting van de resultaten, een discussie van de belangrijkste resultaten, een reflectie op de gehanteerde benadering en methodologie, en aanbevelingen voor verder onderzoek en beleid.

Al met al, demonstreerde dit proefschrift belangrijke verschillen in alcohol-gerelateerde sterfte in Europa tussen landen, geslachten en over tijd, die in belangrijke mate bijdroegen aan (verschillen in) totale sterfteniveaus in Europa.

Alcohol-gerelateerde sterfte was hoger onder mannen dan onder vrouwen, met name in Oost-Europa waar de alcohol-gerelateerde sterfte niveaus het hoogst waren en de trends onregelmatig. Recentelijk, daalde de alcohol-gerelateerde sterfte gematigd in landen met hoge alcohol-gerelateerde sterfte. Daarnaast verschilden landen wat betreft de geboortegeneraties met het hoogste risico op alcohol-gerelateerde sterfte. Het effect van alcohol-gerelateerde sterfte op de levensverwachting bleek niet alleen bijzonder groot onder mannen in Oost-Europa, maar ook substantieel in andere Europese landen. Ondanks dalingen vanaf omstreeks 2005, heeft alcohol-gerelateerde sterfte gemiddeld 20% bijgedragen aan de verschillen in levensverwachting tussen CEE-landen en West-Europa in 2012/13, en minstens 15% aan verschillen in levensverwachting tussen mannen en vrouwen in acht geselecteerde CEE-landen in 2012.

De belangrijke verschillen in alcohol-gerelateerde sterfte in Europa kunnen worden gerelateerd aan verschillen in drinkculturen en sociaaleconomische omstandigheden. Zo, kunnen de opvallende verschillen tussen Oost en West-Europa voor een deel verklaard worden door de hoge consumptie van dranken met een hoog alcoholpercentage (bijvoorbeeld wodka) en de hoge prevalentie van binge drinken onder Oost-Europese mannen, wat kenmerkend is voor de Oost Europese drinkcultuur, maar verergerd werd door de ongunstige economische omstandigheden.

Het geobserveerde substantiële effect van alcohol gerelateerde sterfte op zowel het verschil in levensverwachting tussen Oost en West Europa als op het verschil tussen mannen en vrouwen in CEE-landen, kan één op één gerelateerd worden aan verschillen in alcoholconsumptie in Europa. De recente dalingen in de bijdrage van alcohol aan de Oost-West verschillen in levensverwachting, vanaf omstreeks 2005, kunnen deels toegeschreven worden aan de introductie van preventief gezondheidsbeleid in Oost-Europa, ten tijde van toegenomen economische en politieke stabiliteit. Het effect van alcohol op zowel de levensverwachting in individuele landen als het verschil in levensverwachting tussen Oost en West Europa bleef echter aanzienlijk hoog in 2012/13. Opvallend hierbij is dat, in 2012/2013 het effect van alcohol in Oost-Europa.

De comparatieve en temporele aanpak die toegepast is in dit proefschrift maakte mogelijk om één stap verder te gaan dan eerder onderzoek en leverde nieuwe kennis over het belang van alcohol op sterfteniveaus en -ontwikkelingen op een vergelijkende manier binnen Europa. Het meenemen van de geboortecohort dimensie heeft bijgedragen aan een beter begrip van lange termijn ontwikkelingen in alcohol-gerelateerde sterfte. Voor toekomstig onderzoek, zouden investeringen in het verder verbeteren van berekeningen van alcohol-gerelateerde sterfte, in het bijzonder op oudere leeftijden, nuttig zijn. Daarnaast, raden we onderzoek naar toekomstige alcohol-gerelateerde sterfte aan, daarbij rekening houdend met de geboortecohort dimensie. Voor een beter begrip van de rol van alcohol en ander gezondheidsgedrag (bijvoorbeeld roken) op (verschillen in) totale sterfteniveaus is verder onderzoek nodig naar de gecombineerde in plaats van de individuele bijdrage op bevolkingsniveau hiervan.

De resultaten van dit proefschrift suggereren dat er ruimte is voor alcohol-gerelateerde gezondheidsinterventies die niet alleen de totale gezondheidssituatie in Europa kunnen verbeteren, maar ook de gezondheidsongelijkheden binnen Europa kunnen verkleinen. Daarbij zou het conventionele beleid, door diens impact op de beschikbaarheid of de prijzen van alcohol, moeten worden toegepast om zowel de korte termijn als de lange termijneffecten van alcohol te beperken. De korte-termijn effecten zouden beperkt kunnen worden door te focussen op groepen met een hoger risico op alcohol-gerelateerde sterfte (bijvoorbeeld mannen, mensen op middelbare leeftijd, binge drinkers, binnen bepaalde geboortecohorten). De lange termijneffecten zouden verminderd kunnen worden door te focussen op jonge individuen, omdat ze hun drinkgewoonten nog aan het vormgeven zijn. Daarnaast, is een meer uitgebreide strategie nodig die ook het feit adresseert dat alcohol nog altijd niet gezien wordt door de maatschappij als een even groot risico voor de gezondheid als bijvoorbeeld roken en andere drugs. Mogelijkheden om deze maatschappelijke verandering teweeg te brengen omvatten het verlagen van de norm voor alcoholconsumptie in de nationale richtlijnen en het opnemen van gezondheidswaarschuwingen op verpakkingen zoals bij roken.

Het alcoholprobleem in Europa verdient duidelijk nadere aandacht binnen de samenleving en onder beleidsmakers.

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Sergi Trias Llimós holds a bachelor (llicenciatura) in Economics and a MSc in Population Studies, both from the Autonomous University of Barcelona. He also successfully completed the European Doctoral School of Demography during the academic year 2013-14 at the Warsaw School of Economics and at the Max Planck Institute for Demographic Research. Sergi conducted the research for this dissertation within the VIDI project "Smoking, alcohol and obesity – ingredients for improved robust mortality projections" and (see www.futuremortality.com) led by Prof. Fanny Janssen at the Population Research Centre, Faculty of Spatial Sciences of the University of Groningen, the Netherlands. During his PhD project he spent one month in a research visit abroad at the Max Planck Institute for Demographic Research in Rostock, Germany. After finalizing his PhD thesis he continued as a postdoc researcher within the VIDI research project mentioned above. Sergi is currently a Research Fellow in Epidemiology within "The International Project on Cardiovascular Disease in Russia" (see www.knowyourheart.science) led by Prof. David Leon at the Faculty of Epidemiology & Population Health, London School of Hygiene & Tropical Medicine.