

# Changes in mortality due to major alcohol-related diseases in four Nordic countries, France and Germany between 1980 and 2009: a comparative age–period–cohort analysis

Ludwig Kraus<sup>1,2</sup>, Ståle Østhus<sup>3</sup>, Ellen J. Amundsen<sup>3</sup>, Daniela Piontek<sup>2</sup>, Janne Härkönen<sup>4,5</sup>, Stéphane Legleye<sup>6,7,8</sup>, Kim Bloomfield<sup>9</sup>, Pia Mäkelä<sup>4</sup>, Jonas Landberg<sup>10,11</sup> & Jukka Törrönen<sup>1</sup>

Centre for Social Research on Alcohol and Drugs (SoRAD), Stockholm University, Stockholm, Sweden,<sup>1</sup> IFT Institut für Therapieforchung, München, Germany,<sup>2</sup> The Norwegian Institute for Alcohol and Drug Research (SIRUS), Oslo, Norway,<sup>3</sup> The National Institute for Health and Welfare (THL), Helsinki, Finland,<sup>4</sup> The Finnish Foundation for Alcohol Studies, Helsinki, Finland,<sup>5</sup> Institut national des études démographiques (INED), Paris, France,<sup>6</sup> INSERM, U669 Paris, France,<sup>7</sup> University Paris-Sud and University Paris Descartes, UMR-S0669 Paris, France,<sup>8</sup> Centre for Alcohol and Drug Research, Aarhus University, Copenhagen, Denmark,<sup>9</sup> The Swedish Council for Information on Alcohol and Other Drugs (CAN), Stockholm, Sweden<sup>10</sup> and Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden<sup>11</sup>

## ABSTRACT

**Aims** To investigate age, period and cohort effects on time trends of alcohol-related mortality in countries with different drinking habits and alcohol policies. **Design and setting** Age–period–cohort (APC) analyses on alcohol-related mortality were conducted in Denmark, Finland, Norway, Sweden, France and Germany. **Participants** Cases included alcohol-related deaths in the age range 20–84 years between 1980 and 2009. **Measurements** Mortality data were taken from national causes of death registries and covered the ICD codes alcoholic psychosis, alcohol use disorders, alcoholic liver disease and toxic effect of alcohol. **Findings** In all countries changes across age, period and cohort were found to be significant for both genders [effect value with confidence interval (CI) shown in Supporting information, Table S1]. Period effects pointed to an increase in alcohol-related mortality in Denmark, Finland and Germany and a slightly decreasing trend in Sweden, while in Norway an inverse U-shaped curve and in France a U-shaped curve was found. Compared with the cohorts born before 1960, the risk of alcohol-related mortality declined substantially in cohorts born in the 1960s and later. Pairwise between-country comparisons revealed more statistically significant differences for period ( $P < 0.001$  for all 15 comparisons by gender) than for age [ $P < 0.001$  in seven (men) and four (women) of 15 comparisons] or cohort [ $P < 0.01$  in two (men) and three (women) of 15 comparisons]. **Conclusions** Strong period effects suggest that temporal changes in alcohol-related mortality in Denmark, Finland, Norway, Sweden, France and Germany between 1980 and 2009 were related to secular differences affecting the whole population and that these effects differed across countries.

**Keywords** Age–period–cohort analysis, alcohol-related mortality, trends.

Correspondence to: Professor Dr Ludwig Kraus, Centre for Social Research on Alcohol and Drugs, SoRAD, Stockholm University, SE-106 91 Stockholm, Sweden/IFT Institute for Therapy Research, Munich, Germany. E-mail: kraus@ift.de

Submitted 10 November 2014; initial review completed 16 January 2015; final version accepted 13 May 2015

## INTRODUCTION

Alcohol consumption is a leading risk factor for the burden of disease world-wide. In 2010 alcohol was estimated to account for 2.7 million deaths and 3.9% of all disability-adjusted life years (DALYs), thus ranking fifth among 67 risk factors and risk factor clusters [1]. Most recently, the net burden caused by alcohol consumption in the European Union among the population aged 15–84

years was estimated to be one in seven deaths in males and one in 14 deaths in women [2].

Changes in per-capita alcohol consumption and drinking patterns in particular will influence both beneficial and detrimental disease outcomes via the mediating mechanisms of (1) toxic and beneficial biological effects on the organism, (2) intoxication and (3) dependence [3]. In Europe and elsewhere, investigations of survey and sales data have clearly documented changes in alcohol consumption

over time [4–8]. While aggregated trend data have been used extensively to study the link between consumption and various alcohol-related causes of mortality [9–11], less is known about the underlying mechanisms influencing the observed temporal changes.

For the identification of specific sources of variation in trend data, the time-sensitive factors age and cohort need to be considered simultaneously and time modelled independently of these influences. Research on decomposing temporal changes in alcohol consumption suggests that in addition to general effects such as social and political influences, trends may be affected by biological, psychological and behavioural changes over the life-course as well as by the behaviour of individuals who share the same historical experience [12–15]. Due to the strong link between alcohol consumption and mortality [16], changes in mortality are thus assumed to be: (1) subject to general physiological and socio-biological effects of alcohol on the organism over the life-course (age effect), (2) influenced by alcohol policies as well as general economic growth or developments in health care, conditions which impact the whole population (period effect), and (3) affected by the commonalities of individuals who are born in the same period, share the same education and socialization to a large extent, and have experienced the same historical events and social changes (cohort effects).

Research assessing age, period and cohort (APC) effects on trends of alcohol-related mortality or other alcohol-related harm is scarce. A Swedish study found the period effect of non-accident alcohol-related mortality between 1969 and 2002 to mainly follow the increasing observed trend in alcohol consumption [17]. The authors reported a strong cohort effect, suggesting that restrictive alcohol policies had a stronger effect on the mortality of those cohorts that were younger at the time that such policies were put into effect. When comparing liver cirrhosis mortality in four European regions between 1970 and 1989, Corrao and colleagues [18] found that the period effects generally followed the observed trend of the age-standardized mortality rates and per-capita consumption. Unfortunately, differences between countries were not tested statistically and were based solely on descriptive analyses.

Comparisons of the effects of APC on trends in alcohol-related mortality across countries that have different drinking patterns, alcohol policies and economic developments can help to clarify the influence of these different factors and may be used for predicting alcohol-related mortality. In the present study we applied an APC analysis to trends in alcohol-related mortality in countries with differing alcohol policies and drinking cultures: the Nordic countries of Denmark, Finland, Norway and Sweden as well as the central European countries of France and Germany. The study aimed to (1) explain changes in alcohol-related mortality by modelling the independent effects of age, period

and cohort by country and (2) compare APC effects across countries with differing alcohol policies and drinking cultures. In addition, a descriptive comparison between trends in per-capita consumption and alcohol-related mortality was conducted.

## METHODS

### Data sources

Data on alcohol-related mortality came from the national cause of death registers in Denmark, Finland, France, Germany, Norway and Sweden, for the period 1980–2009. Alcohol-related death was defined as death due to alcoholic psychosis, alcohol use disorders, alcoholic liver disease and toxic effect of alcohol as the underlying (primary) cause of death. Diagnoses were based on the International Classification of Diseases (ICD-8: 291, 303, 571.0, 980; ICD-9: 291, 303, 305.0, 571.0–571.3, 980; ICD-10: F10, K70, T51, X45, X65 and Y15). Of these diagnoses, alcoholic psychosis was a rare cause of death, and the majority of deaths were due to alcohol use disorders and alcoholic liver disease. The periods for use of the ICD versions 8, 9 and 10 differed across the six countries, but overlapped to a large extent (ICD-9 introduced: Finland: 1987; France and Germany: 1980; Norway: 1986; Sweden: 1987; ICD-10 introduced: Denmark: 1994, from ICD-8 to ICD-10; Finland and Norway: 1996; France: 2000; Germany: 1998; Sweden: 1997). Other alcohol-related causes of deaths (e.g. injuries with alcohol intoxication as a contributory cause) were excluded due to validity and comparability problems.

The at-risk population for each country was taken from the Human Mortality Database (HMD) [19]. Estimates of the population exposed to the risk of death were based on annual (1 January) population estimates, with a small correction for the dates of deaths during the interval. Data on recorded adult per-capita consumption for 1961 to 2010 was obtained from the Global Information System on Alcohol and Health [8]. In this system, recorded per-capita (15+) consumption of pure alcohol comes from three sources (in order of priority): government statistics; country-specific alcohol industry statistics and the Food and Agriculture Organization of the United Nations' statistical database.

### Statistical analyses

The number of alcohol-attributable deaths was summarized by sex in 5-year period and age groups, resulting in 13 5-year age groups (20–24, ..., 80–84 years), six time-points (1980–84, ..., 2005–09) and 18 5-year birth cohorts born in 1900–05 up to 1980–84. Cases of death younger than 20 years (too few deaths) or older than 84 years (questionable reliability) were excluded. When no

deaths occurred in a specific age group by time cell, the number of deaths was set to '1'. This substitution was necessary in 13 of 936 cells (males: one cell in Denmark and two cells in Norway; females: three cells in Denmark and Sweden and four cells in Norway). In order to demonstrate overall temporal trends in alcohol-related mortality in each country, the number of deaths was aggregated into three age groups (20–34, 35–54 and 55–84 years) and divided by the population at risk obtained from the HMD, and expressed as a rate per 100 000.

Estimation of the effects of APCs is complicated by the exact linear dependency among the three variables (period – age = cohort), resulting in non-unique regression estimates that cannot be interpreted [20]. For obtaining independent effect estimates of APC, the Intrinsic Estimation model (IE) proposed by Yang, Fu & Land [21,22] was used. Instead of making any prior assumptions about how the dimensions of the data space can be reduced (for example, assuming that the age effect is the same for two age categories – a solution which has been common in epidemiology), the IE estimator reduces the number of dimensions in the data based on principal components analysis. In each stratum (gender, country) incidence rate ratios were calculated, for which the reference group for each variable (age, period, cohort) is the mean for that variable; e.g. for cohorts, the mean value across all cohorts. Model effects between countries were tested by ordinary  $\chi^2$  statistics. To test differences in age effects, the test statistic  $S_{ij} = \sum (a_{ik} - a_{jk})^2$  was applied for all countries  $i$  and  $j$ , where  $a_{ik}$  and  $a_{jk}$  represent the estimated parameters in age category  $k$  in country  $i$  and  $j$  [23]. The distribution of  $S_{ij}$  was simulated by re-sampling all  $a_k$  1000 times from a normal distribution with the estimated mean and standard error values, assuming  $a_{ik}$  and  $a_{jk}$  to be independent for all  $i$  and  $j$ .  $S_{ij}$  divided by its variance is  $\chi^2$  distributed, with the number of degrees of freedom equal to the number of age categories. Tests for differences in period and cohort effects were carried out in the same way. All models were stratified by gender using Stata/SE version 12.1 (StataCorp LP, College Station, TX, USA).

## RESULTS

### Sample description

Summary statistics for the number of alcohol-related deaths and the total and age-specific rates per 100 000 population for all six countries from 1980 to 2009 are displayed in Table 1. Mortality rates were consistently higher in males than females and highest in France, followed by Finland, Denmark and Germany, and lowest in Sweden and Norway. The rates show an increasing time trend for both genders in Denmark and Finland; a declining trend in males after a peak in 1985–89 and somewhat stable rates among females in Norway; a decreasing trend among males and, after an

increase of rates up to 1990–94, also a decreasing trend in females in Sweden; decreasing rates in both genders in France; and a general increase in both genders followed by a decline after a peak in 1995–99 in Germany.

### APC effects within countries

The model predictions for APC effects by country are depicted in Figs 1–3. The IE analyses of mortality show effects for all three indicators. In all countries changes across age, time and cohort were found to be significant for both genders ( $P < 0.001$ ). As expected, the age effect increased up to age 60–64 years and decreased thereafter. In all countries the risk curves are somewhat similar, with males and females showing the same pattern. Risks of mortality in Finland and Germany peaked at a slightly earlier age (55–59 years). The period effects point to an increasing trend in Denmark and Finland over the entire period, and up to 1995 in Germany. A slightly decreasing trend is found in Sweden, whereas time trends in Norway and France are less pronounced, with rates showing an inverse U-shaped curve in the former and a U-shaped curve in the latter country. Finally, strong cohort effects can be seen in all countries.

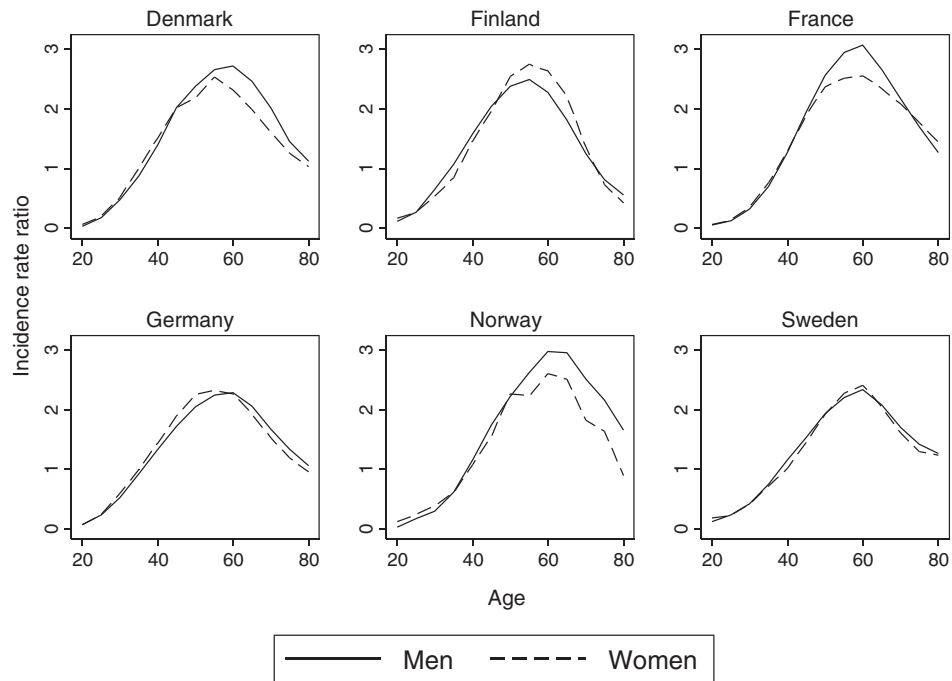
There are some country differences, but the general pattern is that, compared to cohorts born up through the 1950s, the risk curves showed a strong decrease in alcohol-related mortality starting with cohorts born in the 1960s, indicating a lower risk than average for younger cohorts. Gender differences can be seen in older generations in most countries with female mortality risk increasing before decreasing in the post-war generations. The country-specific cohort findings show that the risk of mortality in Finland declined somewhat in later cohorts compared to Norway and Sweden, and compared to males the risk increased more strongly in females in Denmark (1910–40), Finland (1920–95) and Norway (1910 and 1935). However, clear gender differences can be observed only in France, where the risk of female alcohol-related mortality followed the general pattern, while the mortality risk of males declined consistently from older to younger cohorts (see Supporting information, Table S1 for the estimated incidence rate ratios, 95% confidence intervals and  $P$ -values for male and female alcohol-attributable mortality rates 1980–2009 by country).

### Between-country differences in APC effects

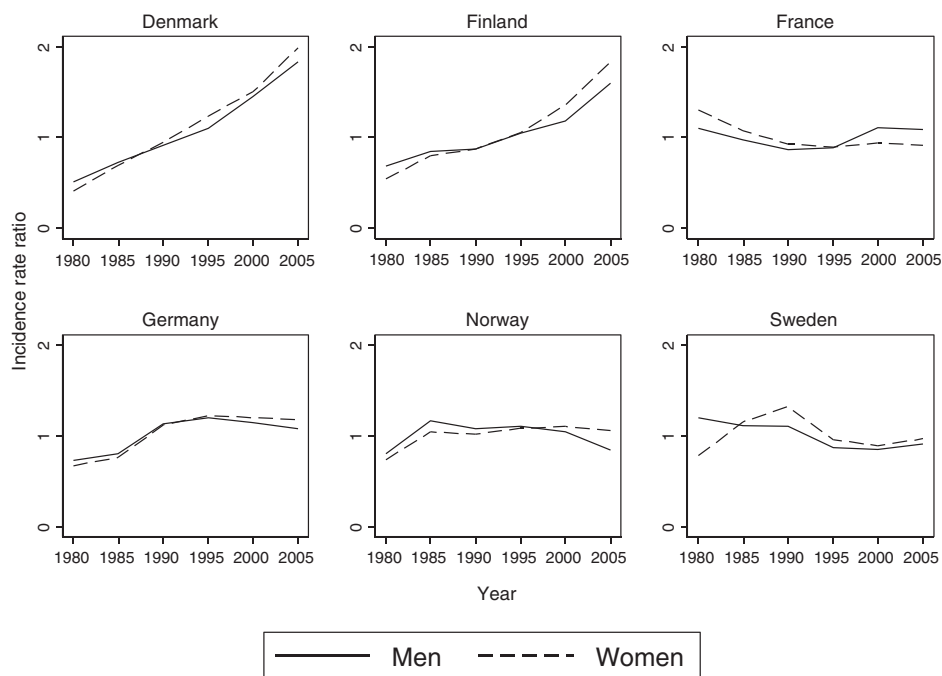
Between-country differences in period effects were statistically significant for all comparisons and for both genders ( $P < 0.001$ ). Between-country differences in age effects were found for some but not all countries, and the results did not follow any discernible pattern (Table 2). Country differences in cohort effects were significantly different in only a few comparisons (Germany versus Finland and

Table 1 Alcohol-related deaths by country and age group: *n* and rate per 100 000 people (20–84 years) in parentheses.

	Males						Females					
	1980–84	1985–89	1990–94	1995–99	2000–04	2005–09	1980–84	1985–89	1990–94	1995–99	2000–04	2005–09
<b>Denmark</b>												
20–34	90 (3.1)	126 (4.2)	94 (3.1)	60 (2.0)	42 (1.5)	47 (1.9)	27 (1.0)	39 (1.4)	19 (0.7)	29 (1.0)	17 (0.6)	19 (0.8)
35–54	639 (20.0)	983 (28.2)	1391 (37.6)	1677 (43.3)	1975 (50.4)	2021 (51.4)	200 (6.4)	359 (10.6)	553 (15.4)	666 (17.7)	647 (17.0)	667 (17.4)
55–84	737 (26.5)	1081 (39.1)	1390 (50.4)	1827 (64.0)	2709 (85.0)	3712 (106.2)	174 (5.1)	337 (10.0)	493 (14.7)	716 (21.2)	1022 (28.3)	1401 (36.5)
Total	1466 (16.5)	2190 (23.9)	2875 (30.4)	3564 (36.4)	4726 (45.6)	5780 (53.2)	401 (4.2)	735 (7.3)	1065 (10.3)	1411 (13.3)	1686 (15.3)	2087 (18.2)
<b>Finland</b>												
20–34	305 (9.8)	271 (9.2)	185 (6.7)	181 (7.0)	195 (7.8)	168 (6.7)	62 (2.1)	46 (1.6)	40 (1.5)	39 (1.6)	35 (1.5)	36 (1.5)
35–54	1288 (42.2)	1758 (51.1)	2018 (53.7)	2578 (65.1)	2685 (67.9)	2912 (78.4)	183 (6.1)	325 (9.7)	427 (11.7)	596 (15.5)	714 (18.5)	813 (22.4)
55–84	915 (44.0)	1302 (58.0)	1434 (60.1)	1776 (68.8)	2320 (78.3)	3781 (109.0)	184 (5.9)	311 (9.5)	346 (10.4)	430 (12.6)	705 (19.1)	1155 (28.2)
Total	2508 (32.0)	3331 (39.4)	3637 (40.2)	4535 (47.0)	5200 (51.3)	6861 (64.7)	429 (4.7)	682 (7.0)	813 (7.9)	1065 (9.9)	1454 (13.0)	2004 (17.4)
<b>France</b>												
20–34	1484 (4.6)	1298 (4.0)	1282 (4.0)	970 (3.1)	742 (2.5)	930 (3.2)	819 (2.6)	604 (1.9)	467 (1.5)	371 (1.2)	178 (0.6)	172 (0.6)
35–54	19451 (60.6)	15374 (44.6)	13296 (35.8)	14370 (35.8)	19791 (46.9)	18099 (42.7)	8370 (26.6)	6444 (19.0)	5620 (15.3)	5882 (14.5)	6627 (15.4)	5417 (12.4)
55–84	42178 (162.3)	34143 (123.5)	27375 (94.0)	25685 (85.5)	29700 (90.8)	29867 (80.8)	14503 (42.6)	12192 (34.3)	10471 (28.6)	9748 (26.3)	10160 (25.5)	10687 (24.1)
Total	63113 (75.8)	50815 (57.3)	41953 (44.6)	41025 (41.5)	50233 (46.8)	48896 (42.2)	23692 (23.9)	19240 (18.4)	16558 (15.1)	16001 (14.0)	16965 (13.8)	16276 (12.4)
<b>Germany</b>												
20–34	2110 (4.7)	2203 (4.6)	3033 (6.0)	2238 (4.8)	1186 (2.9)	738 (2.0)	625 (1.5)	614 (1.3)	883 (1.9)	625 (1.4)	318 (0.8)	210 (0.6)
35–54	16782 (31.6)	18358 (34.0)	25653 (45.7)	24538 (42.4)	23111 (36.4)	19984 (30.6)	4834 (9.3)	5562 (10.6)	8273 (15.3)	8037 (14.4)	7570 (12.3)	6571 (10.4)
55–84	13018 (36.3)	16401 (43.2)	26524 (62.8)	33395 (69.1)	33147 (64.1)	31420 (56.5)	5029 (8.6)	6093 (10.4)	9414 (15.9)	11683 (18.8)	11705 (18.5)	11297 (17.3)
Total	31910 (24.2)	36962 (27.3)	55210 (38.2)	60171 (38.8)	57444 (34.5)	52142 (29.7)	10488 (6.5)	12269 (7.5)	18570 (11.0)	20345 (11.5)	19593 (10.5)	18078 (9.4)
<b>Norway</b>												
20–34	37 (1.6)	52 (2.1)	24 (0.9)	16 (0.6)	11 (0.5)	7 (0.3)	13 (0.6)	14 (0.6)	12 (0.5)	6 (0.3)	6 (0.3)	5 (0.2)
35–54	314 (13.7)	556 (21.7)	534 (18.7)	569 (18.3)	509 (15.6)	298 (8.7)	90 (4.0)	131 (5.3)	138 (5.1)	157 (5.3)	139 (4.4)	100 (3.1)
55–84	729 (31.1)	948 (40.8)	883 (39.1)	900 (39.7)	882 (35.7)	814 (29.7)	146 (5.2)	216 (7.7)	211 (7.7)	229 (8.4)	251 (8.9)	264 (8.8)
Total	1080 (15.4)	1556 (21.6)	1441 (19.6)	1485 (19.5)	1402 (17.3)	1119 (12.9)	249 (3.3)	361 (4.5)	361 (4.4)	392 (4.7)	396 (4.5)	369 (4.0)
<b>Sweden</b>												
20–34	286 (6.4)	138 (3.1)	92 (2.0)	55 (1.2)	38 (0.9)	27 (0.6)	60 (1.4)	47 (1.1)	24 (0.5)	13 (0.3)	11 (0.3)	21 (0.5)
35–54	1797 (34.6)	1672 (29.7)	1638 (27.3)	1311 (21.2)	1064 (17.1)	828 (13.2)	359 (7.1)	406 (7.5)	427 (7.4)	365 (6.1)	299 (5.0)	257 (4.2)
55–84	2046 (39.5)	2177 (42.4)	2338 (46.2)	1853 (35.6)	1972 (34.6)	2279 (37.0)	383 (6.3)	756 (12.5)	935 (15.6)	617 (10.2)	595 (9.3)	665 (9.9)
Total	4129 (26.8)	3987 (25.1)	4068 (25.1)	3219 (19.3)	3074 (17.5)	3134 (16.9)	802 (4.9)	1209 (7.0)	1386 (7.8)	995 (5.5)	905 (4.8)	943 (4.9)



**Figure 1** Age effects in alcohol-related mortality by gender for Denmark, Finland, France, Germany, Norway and Sweden



**Figure 2** Period effects in alcohol-related mortality by gender for Denmark, Finland, France, Germany, Norway and Sweden

Germany versus France ( $P < 0.001$ ) for men; Norway versus Denmark ( $P < 0.01$ ), Finland versus Denmark and Germany versus France ( $P < 0.001$ ) for women).

#### Mortality and per-capita consumption

With regard to per-capita consumption, general trends between 1961 and 2010 showed a decrease (age 15+

or older) in Denmark (after a peak in 1983 and a stable phase until 1996 from 12.3 to 10.4 l), France (from 26.0 to 11.1 l) and Germany (after a peak in 1976 from 17.2 to 11.2 l) and an increase in Finland (from 2.9 to 9.7 l), Norway (from 3.7 to 6.6 l) and Sweden (from 6.0 to 7.3 l). While per-capita consumption in the 1960s varied considerably across these countries, with intake in France and Germany being many times higher than



**Figure 3** Cohort effects in alcohol-related mortality by gender for Denmark, Finland, France, Germany, Norway and Sweden

**Table 2** Between-country differences in age, period and cohort effects. Tests based on simulated standard errors.

	Men			Women		
	Age effect $\chi^2_{(13)}$	Period effect $\chi^2_{(6)}$	Cohort effect $\chi^2_{(18)}$	Age effect $\chi^2_{(13)}$	Period effect $\chi^2_{(6)}$	Cohort effect $\chi^2_{(18)}$
Finland–Denmark	15.0	6470.9**	5.0	12.3	18983.0**	52.0**
France–Denmark	13.4	548.7**	3.9	19.2	208.4**	4.4
Germany–Denmark	6.1	710.0**	3.5	8.6	234.7**	4.2
Norway–Denmark	242.2**	1302.9**	7.7	182.0**	578.6**	35.2*
Sweden–Denmark	12.4	5446.8**	25.5	8.6	5380.0**	16.9
France–Finland	124.8**	1166.1**	11.0	25.1	267.9**	17.8
Germany–Finland	105.7**	1689.2**	35.1*	24.0	377.5**	13.1
Norway–Finland	9.9	663.8**	2.3	56.2**	400.8**	6.0
Sweden–Finland	1081.4**	47 422.5**	26.4	144.2**	7898.8**	4.2
Germany–France	23128.9**	576 056.3**	393.9**	34 054.8**	556 069.1**	295.3**
Norway–France	5.5	267.6**	2.0	4.6	81.1**	1.7
Sweden–France	65.5**	1536.6**	14.3	20.3	362.0**	3.1
Norway–Germany	5.8	327.7**	0.8	6.3	125.5**	1.8
Sweden–Germany	54.0**	1434.3**	21.4	24.9	459.6**	1.5
Sweden–Norway	5.1	709.5**	2.5	14.6	538.8**	22.1

\* $P < 0.01$ ; \*\* $P < 0.001$ .

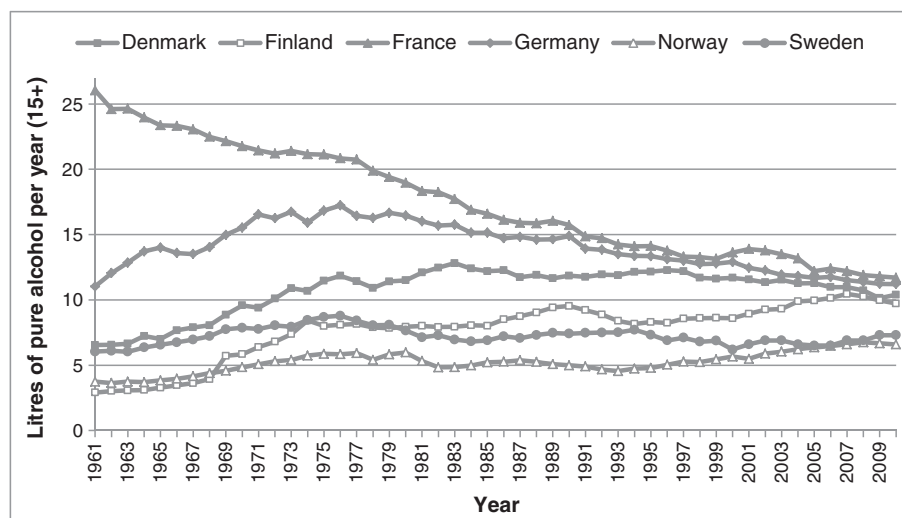
in the Nordic countries, by 2010 differences were less pronounced (see Fig. 4).

## DISCUSSION

The present study has demonstrated that trends in alcohol-attributable mortality in Denmark, Finland, France, Germany, Norway and Sweden clearly differ. Although

the estimated age and cohort effects were somewhat similar across countries, between-country differences in period effects were relatively strong, suggesting that country-specific macro-shocks affected all age groups and cohorts simultaneously in the respective countries. Thus, the main finding of our study is that after controlling for age and cohort, period effects show the strongest influence on trends of alcohol-attributable mortality in all countries.





**Figure 4** Recorded per-capita consumption in litres pure alcohol for Denmark, Finland, France, Germany, Norway and Sweden from 1961 to 2010

The congruence between the estimated period effects (Fig. 2) and the observed population-standardized trends across countries (Table 1) must be discussed in light of the similarities in age and cohort effects. First, the age effects are not unexpected: the increasing risk of alcohol-related mortality with age has a physiological explanation. The highest mortality risk in the life-course in all countries was found to be between ages 55 and 64 years. The operationalization of mortality (i.e. diagnoses) used in our study represents mainly the chronic effects of long-term alcohol use. Keeping in mind that liver cirrhosis or alcohol dependence develops only after drinking excessively over a long period, the increasing rates with age reflect the long-term toxic effects of excessive drinking on the organism.

Secondly, with the exception of males in France, a general pattern of declining mortality in cohorts born after World War II was found in all countries. This was observed independently of whether alcohol-related mortality in general had increased, as in Finland and Denmark, or decreased, as in France, Germany and Sweden. The consistency of this pattern is somewhat surprising, as these countries have large differences in their drinking habits, with more regular drinking styles in France and Germany compared to more intoxication-orientated drinking in the Nordic countries [24]. One explanation could be that other factors may have played a more influential role than alcohol intake *per se*. Cohorts born into the prospering economies of post-war Europe have enjoyed increasingly good nutrition, healthy life-styles and responsive health-care systems and may have profited from these developments more than earlier cohorts. Consequently, the lower risk of mortality in younger cohorts may have only slightly dampened the period effect in countries where mortality was generally increasing. In contrast, in countries with

declining mortality the cohort effect may have merely contributed to the general decreasing trend.

Nevertheless, APC analyses on trends in mean alcohol intake in Germany support the relationship between cohort-specific alcohol consumption and mortality [13]. Cohort effects suggest that individuals born in the 1960s and 1970s have had a lower mean alcohol volume than older cohorts. Our findings are also in line with the literature that suggests that changes in drinking patterns impact mortality caused by acute rather than chronic disease conditions [3]. For instance, although cohort effects have been reported with regard to increases in the frequency of heavy drinking episodes in cohorts born after World War II in Finland and Germany [13,15], our results indicate that alcohol-related mortality due to chronic diseases has decreased in these cohorts.

The period effects may be interpreted as secular influences that impact on alcohol-related mortality in all strata of the population simultaneously; for instance, through changes in country-specific alcohol policies, per-capita alcohol consumption, drinking patterns or through general societal-level changes such as increasing prosperity. The majority of alcohol-attributable deaths in the present study consists of chronic disease conditions: approximately 90% of all deaths in this study were due to alcohol dependence (AD) or alcoholic liver cirrhosis. When modelling the impact of AD on alcohol-related mortality burden, Rehm and colleagues [2] found that AD contributed to 71% of the total alcohol-related mortality. Furthermore, meta-analyses offer convincing evidence that risk of liver cirrhosis continuously increases with increasing volume of alcohol consumption [25–27]. Although the present approach is not able to test statistically the association between trends in per-capita consumption and alcohol-

related mortality, one may speculate on the descriptive comparisons.

When comparing changes in consumption and mortality, the possibility of time lags needs to be considered [16,17,28]. The occurrence of time lags in chronic effects of alcohol depends on the extent of an increase in consumption among light drinkers (long delay) as well as among heavy drinkers who are already suffering serious consequences such as liver damage (short delay). In Finland, for instance, changes in consumption due to alcohol reforms in 1960s and 1970s and due to tax cuts in 2004 were reported to be associated strongly with changes in liver cirrhosis mortality in the same year, indicating changes among those with pre-existing liver damage [15,29–31]. However, in countries with increasing per-capita consumption and increasing alcohol-related mortality, short- and long-term effects on mortality cannot be distinguished. Per-capita consumption in Denmark increased from 6.5 l in 1961 to 12.8 l in 1983 and did not begin to fall until after 1996, and this is reflected in an increase in mortality in the last 30 years. Denmark is known for its liberal alcohol policy, and a sales monopoly has never been implemented. No age limit for alcohol purchases existed between 1970 and 1998, when a legal purchasing age was re-introduced [32]. Conversely, in countries with varying consumption a time lag between consumption and mortality can be observed. The increase in consumption in Norway in the 1960s and 1970s may be seen as affecting the increase in mortality in the 1980s. The stabilization and even decrease in consumption between 1980 and the mid-1990s may have decreased mortality in the 2000s. Similarly, after a large increase in consumption in the 1960s and early 1970s in Sweden, a more restrictive alcohol policy was introduced in the late 1970s and 1980s with the abolishment of medium-strength beer from grocery stores [33]. This may have led to the high mortality rates, as observed in the 1980s and early 1990s followed by lower mortality rates in the late 1990s and 2000s. The effects of the increase in consumption in the 1990s up to 2004 in Sweden as well as the increase since the mid-1990s in Norway may not yet be observable. More importantly, mortality after 1990 may mirror the German reunification and the higher mortality in the former German Democratic Republic may have increased mortality in the 1990s despite the general downward consumption trend.

As effective treatments for heavy drinkers have been demonstrated to have significant potential in reducing mortality [2], it has been argued that increasing the numbers of heavy drinkers in alcohol treatment will contribute to a decline in alcohol-related mortality. Findings of short-term effects of treatment on liver cirrhosis mortality support this hypothesis [34]. Although the possible positive effects on mortality due to changes in treatment cannot

be teased out in our analyses, reports of somewhat low alcohol treatment utilization, ranging between 4 and 15% in our study countries [2,35], suggest that such effects may be weak.

One limitation of our study is the analysis of only 100% alcohol-attributable causes of death. Although estimates including all types of alcohol-attributable death following the method of the Global Burden of Disease study [1,3] could have been provided, the breakdown of estimates by time, age and gender would not have been possible. However, the disease codes selected in the present study cover the majority of all deaths fully attributable to alcohol and are also likely to be a good indicator for other chronic alcohol-induced causes. In a recent German study on mortality among 15–64-year-olds it was found that the diagnoses F10, K70 and T51 contributed to more than 90% to all deaths fully attributable to alcohol, and that this rate remained constant across the study period of 1995 to 2012 [36]. It should be acknowledged, however, that the acute effects, especially of more occasional drinking, i.e. injuries and violence, are not well captured by our measure, which means that we may have missed the impact of drinking particularly on young people. Secondly, combining numbers of deaths into 5-year age and cohort groups reduced the variability of deaths over time, but this was necessary in order to avoid empty cells and had no effect on the age and cohort estimates as tested in sensitivity analyses (data available on request). However, this resulted in only six time-points, reducing the variability over time. Thirdly, changes in diagnostic codes from ICD-8 to versions 9 and 10 may have systematically affected the trends. This effect would appear in the period trends. Close inspection of the data, however, did not reveal systematic changes after the implementation of the different versions. Fourthly, having not taken unrecorded consumption into account may have obscured the association between time trends in per-capita consumption and mortality, particularly in the Nordic countries. Estimates for 2005 indicate higher proportions of unrecorded consumption in Denmark (15%) Finland (22%), Norway (20%) and Sweden (35%) than in Germany (8%) and France (3%) [37]. Fifthly, due to combining cohorts from different study years, the estimated effects for cohorts at the edge of the spectrum are less reliable and should be interpreted with caution. Finally, there exist various approaches to APC analysis, all of which are controversial and debated [38–40]. To justify APC analysis we followed the procedure recommended by Yang & Land [41]. We conducted descriptive data analyses using graphics and tested whether the data were sufficiently well described by any single- or two-factor model for which there is no identification problem. As all three dimensions were found operative, we applied three-factor APC models. Although the constraints imbedded in IE cannot be tested, inspections revealed that the estimates of the coefficients



were quite close to descriptive plots of the 'true models' (data available on request).

As suggested by Skog [42], Norström [43] and more recently by others [44], per-capita alcohol consumption seems to be a reliable indicator of heavy drinking in the population, and consequently alcohol-related problems generally follow per-capita consumption. Our results support this association suggesting that in the last 30 years changes in alcohol-related mortality have been influenced most strongly by period effects. Furthermore, although cohort variation in the risk of mortality contributed to population changes, such effects seemed to have had only a marginal influence on the observed trends.

### Declaration of interests

Ludwig Kraus and Daniela Piontek declare having received a grant from Lundbeck GmbH for a research project unrelated to this project.

### Acknowledgements

Funding of the project was provided by the Nordic Centre for Welfare and Social Issues. Janne Härkönen was funded by the Academy of Finland (Project no. 137685). Stéphane Legleye would like to thank Mireille Eb, from CepiDC, INSERM, France.

### References

- Lim S. S., Vos T., Flaxman A. D., Danaei G., Shibuya K., Adair-Rohani H. *et al.* A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**: 2224–60.
- Rehm J., Shield K. D., Rehm M. X., Gmel G., Frick U. Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. *Eur Neuropsychopharmacol* 2013; **23**: 89–97.
- Rehm J., Baliunas D., Borges G. L., Graham K., Irving H., Kehoe T. *et al.* The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction* 2010; **105**: 817–43.
- Hibell B., Guttormsson U., Ahlström S., Balakireva O., Bjarnason T., Kokkevi A. *et al.* The 2011 ESPAD Report. Substance Use Among Students in 36 European Countries. Stockholm: The Swedish Council for Information on Alcohol and other Drugs (CAN), The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Council of Europe, Co-operation Group to Combat Drug Abuse and Illicit Trafficking in Drugs (Pompidou Group); 2012.
- Leifman H. Trends in population drinking. In: Norström T., editor. *Alcohol in Postwar Europe: Consumption, Drinking Patterns, Consequences and Policy Responses in 15 European Countries*. Stockholm: Almqvist & Wiksell; 2002, pp. 49–81.
- Kraus L., Pabst A., Piontek D., Gomes de Matos E. Substanzkonsum und substanzbezogene Störungen: Trends in Deutschland 1980–2012 [Substance use and substance use disorders: trends in Germany 1980–2012]. *Sucht* 2013; **59**: 333–45.
- Mäkelä P., Tigerstedt T., Mustonen H. The Finnish drinking culture: change and continuity in the past 40 years. *Drug Alcohol Rev* 2012; **31**: 831–40.
- World Health Organization. *World Health Organization's Global Information System on Alcohol and Health (GISAH)*; 2014. Available at: <http://apps.who.int/gho/data/node.main.GISAH> (accessed 8 June 2015).
- Leifman H., Romelsjö A. The effect of changes in alcohol consumption on mortality and admissions with alcohol-related diagnoses in Stockholm County—a time-series analysis. *Addiction* 1997; **92**: 1523–36.
- Norström T. The impact of per capita consumption on Swedish cirrhosis mortality. *Br J Addict* 1987; **82**: 67–75.
- Ramstedt M. Per capita alcohol consumption and liver cirrhosis mortality in 14 European countries. *Addiction* 2001; **96**: S19–33.
- Kerr W. C., Greenfield T. K., Bond J., Ye Y., Rehm J. Age-period-cohort modelling of alcohol volume and heavy drinking days in the US National Alcohol Surveys: divergence in younger and older adult trends. *Addiction* 2009; **104**: 27–37.
- Pabst A., Kraus L., Piontek D., Müller S. Age, period, and cohort effects on time trends in alcohol consumption in the German adult population. *Sucht* 2010; **56**: 349–59.
- Meng Y., Holmes J., Hill-McManus D., Brennan A., Meier P. S. Trend analysis and modelling of gender-specific age, period and birth cohort effects on alcohol abstinence and consumption level for drinkers in Great Britain using the General Lifestyle Survey 1984–2009. *Addiction* 2014; **109**: 206–15.
- Härkönen J. T., Mäkelä P. Age, period and cohort analysis of light and binge drinking in Finland, 1968–2008. *Alcohol Alcohol* 2011; **46**: 349–56.
- Rehm J., Baliunas D., Borges G. L., Graham K., Irving H., Kehoe T. *et al.* The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction* 2010; **105**: 817–843.
- Rosen M., Haglund B. Trends in alcohol-related mortality in Sweden 1969–2002: an age-period-cohort analysis. *Addiction* 2006; **101**: 835–40.
- Corrao G., Ferrari P., Zambon A., Torchio P., Arico S., Decarli A. Trends of liver cirrhosis mortality in Europe, 1970–1989: age-period-cohort analysis and changing alcohol consumption. *Int J Epidemiol* 1997; **26**: 100–9.
- Human Mortality Database, University of California, Berkeley (USA), Max Planck Institute for Demographic Research (Germany). Available at: [www.mortality.org](http://www.mortality.org) or [www.humanmortality.de](http://www.humanmortality.de). 2013 (accessed 25 August 2013).
- Mason W., Fienberg S. E. *Cohort Analysis in Social Research: Beyond the Identification Problem*. New York: Springer; 1985.
- Yang Y., Fu W. J., Land K. C. A methodological comparison of age-period-cohort models: the intrinsic estimator and conventional generalized linear models. *Sociol Methodol* 2004; **34**: 75–110.
- Yang Y. Trends in U.S. adult chronic disease mortality, 1960–1999: age, period, and cohort variations. *Demography* 2008; **45**: 387–416.
- Aalen O. O., Farewell V. T., De Angelis D., Day N. E., Gill O. N. A Markov model for HIV disease progression including the effect of HIV diagnosis and treatment: application to AIDS prediction in England and Wales. *Stat Med* 1997; **16**: 2191–210.
- Room R., Mäkelä K. Typologies of the cultural position of drinking. *J Stud Alcohol* 2000; **61**: 475–83.

25. Corrao G., Bagnardi V., Zambon A., Torchio P. Meta-analysis of alcohol intake in relation to risk of liver cirrhosis. *Alcohol Alcohol* 1998; **33**: 381–92.
26. Corrao G., Bagnardi V., Zambon A., La V. C. A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med* 2004; **38**: 613–19.
27. Rehm J., Taylor B., Mohapatra S., Irving H., Baliunas D., Patra J. et al. Alcohol as a risk factor for liver cirrhosis: a systematic review and meta-analysis. *Drug Alcohol Rev* 2010; **29**: 437–5.
28. Norström T., Skog O. J. Alcohol and mortality: methodological and analytical issues in aggregate analyses. *Addiction* 2001; **96**: S5–17.
29. Herttua K., Mäkelä P., Martikainen P. Changes in alcohol-related mortality and its socioeconomic differences after a large reduction in alcohol prices: a natural experiment based on register data. *Am J Epidemiol* 2008; **168**: 1110–18.
30. Mäkelä P., Österberg E. Weakening of one more alcohol control pillar: a review of the effects of the alcohol tax cuts in Finland in 2004. *Addiction* 2009; **104**: 554–63.
31. Room R., Bloomfield K., Gmel G., Grittner U., Gustafsson N. K., Mäkelä P. et al. What happened to alcohol consumption and problems in the Nordic countries when alcohol taxes were decreased and borders opened? *Int J Alcohol Drug Res* 2013; **2**: 77–87.
32. Møller L. Legal restrictions resulted in a reduction of alcohol consumption among young people in Denmark. In: Room R., editor. *The Effects of Nordic Alcohol Policies: Analyses of Changes in Control Systems*. Helsinki: Nordic Council for Alcohol and Drug Research; 2002, pp. 155–66.
33. Ramstedt M. Change and stability? Trends in alcohol consumption, harms and policy: Sweden 1990–2010. *Nordisk Alkohol Nark* 2010; **27**: 409–23.
34. Holder H. D., Parker R. N. Effect of alcoholism treatment on cirrhosis mortality: a 20-year multivariate time series analysis. *Br J Addict* 1992; **87**: 1263–74.
35. Kraus L., Piontek D., Pfeiffer-Gerschel T., Rehm J. Inanspruchnahme gesundheitlicher Versorgung durch Alkoholabhängige [Health care utilization of people with alcohol dependence]. *Suchttherapie* 2014; **15**: 18–26.
36. Kraus L., Pabst A., Piontek D., Gmel G., Shield K. D., Frick H. et al. Temporal changes in alcohol-related morbidity and mortality in Germany. *Eur Addict Res* 2015; **21**: 262–72.
37. World Health Organization. *Global Health Observatory Data Repository*; 2014. Available at: <http://apps.who.int/gho/data/node.main.A1022?lang=en> (accessed 8 June 2015).
38. Kupper L. L., Janis J. M., Karmous A., Greenberg B. G. Statistical age-period-cohort analysis: a review and critique. *J Chronic Dis* 1985; **38**: 811–30.
39. Luo L. Assessing validity and application scope of the intrinsic estimator approach to the age-period-cohort problem. *Demography* 2013; **50**: 1945–67.
40. Luo L. Paradigm shift in age-period-cohort analysis: a response to Yang and Land, O'Brien, Held and Riebler; and Fienberg. *Demography* 2013; **50**: 1985–8.
41. Yang C. Y., Land K. C. Misunderstandings, mischaracterizations, and the problematic choice of a specific instance in which the IE should never be applied. *Demography* 2013; **50**: 1969–71.
42. Skog O.-J. The collectivity of drinking cultures: a theory of the distribution of alcohol consumption. *Br J Addict* 1985; **80**: 83–99.
43. Norström T., Ramstedt M. Mortality and population drinking—a review of the literature. *Drug Alcohol Rev* 2005; **24**: 537–47.
44. Raninen J., Leifman H., Ramstedt M. Who is not drinking less in Sweden? An analysis of the decline in consumption for the period 2004–2011. *Alcohol Alcohol* 2013; **48**: 592–7.

### Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

**Table S1** Estimated incidence rate ratios, 95% confidence intervals and p-values for male and female mortality rates 1980–2009 by country