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Temporal Changes in Alcohol-Related Morbidity and Mortality in Germany

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Key Words

Morbidity · Mortality · Alcohol · Epidemiology · Trends

Abstract

Aims: Trends in morbidity and mortality, fully or partially attributable to alcohol, for adults aged 18–64 were assessed for Germany. **Methods:** The underestimation of population exposure was corrected by triangulating survey data with per capita consumption. Alcohol-attributable fractions by sex and two age groups were estimated for major disease categories causally linked to alcohol. Absolute numbers, population rates and proportions relative to all hospitalizations and deaths were calculated. **Results:** Trends of 100% alcohol-attributable morbidity and mortality over thirteen and eighteen years, respectively, show an increase in rates of hospitalizations and a decrease in mortality rates. Comparisons of alcohol-attributable morbidity including diseases partially caused by alcohol revealed an increase in hospitalization rates between 2006 and 2012. The proportion of alcohol-attributable hospitalizations remained constant. Rates

of alcohol-attributable mortality and the proportion among all deaths decreased. **Conclusions:** The increasing trend in mortality due to alcohol until the mid-1990s has reversed. The constant proportion of all hospitalizations that were attributable to alcohol indicates that factors such as improved treatment and easier health care access may have influenced the general increase in all-cause morbidity. To further reduce alcohol-related mortality, efforts in reducing consumption and increasing treatment utilization are needed.

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Introduction

Alcohol is one of the leading avoidable risk factors for hospitalization and premature mortality worldwide. Estimates from the 2010 Global Burden of Disease and Injury study indicate that alcohol consumption ranks fifth among 67 risk factors and risk factor clusters accounting for 2.7 million deaths and 3.9% of all disability adjusted life years (DALYs) [1]. A recent study on the size and bur-

den of mental disorders of the brain in Europe reported that in 2011 mental disorders contributed 26.6% to the all-cause burden. Alcohol disorders were among the most disabling diseases and were estimated at 3.4% ranking seventh in the prevalence of disorders of the brain in Europe [2]. Alcohol consumption is not only a risk factor for the physical, psychological, and social well-being of consumers but also a risk factor for others, particularly family members [3], friends, acquaintances, and sometimes even to unknown others [4].

In Germany, alcohol is by far the most widely used psychoactive substance. Recent survey data from 2012 suggest that only one in ten individuals aged 18–64 refrained from alcohol use in the past 12 months [5]. Excessive drinking operationalized as more than 60 g of ethanol per day at least once in the last 30 days was reported by 20.6% of men and 6.6% of women. Moreover, DSM-IV alcohol use disorders were estimated at 6.5% (dependence 3.4%, abuse 3.1%), resulting in 3.4 million 18–64 year-olds being negatively affected by alcohol use. While abuse is mostly associated with disabling effects that manifest themselves in neglect of social roles or functional problems in everyday life [6], alcohol dependence (AD) is regarded a major health risk contributing as much as 74% to the estimated overall net burden of mortality [7]. The social burden and the economic costs from alcohol consumption in Germany are immense [8], with costs amounting to 32.5 billion EUR in 2010 borne by the society [9].

Although there is up-to-date knowledge available in Germany on the size and burden of disease from alcohol consumption [7, 8, 10], information on changes in alcohol-related hospitalization and mortality is scarce. A study based on all fully alcohol-attributable deaths revealed an increase in rates per 100,000 population from 12 cases in 1980 to 21 in the mid-1990s with rates decreasing thereafter to 18 in 2005 [11]. And Nolte and colleagues [12] comparing mortality fully and partially attributable to alcohol in East and West Germany between 1992 and 1997 reported an increase in mortality rates in the West but not in the East, while the proportion of all deaths that were fully or partially attributable to alcohol increased in both parts of Germany.

Data on alcohol consumption from self-reports indicate a declining trend in the average volume of alcohol consumption in men and an increase in frequency of heavy drinking to intoxication particularly among women since 1995. During the same time, the prevalence of alcohol dependence increased in both genders [13]. On the other hand, data on aggregated per capita consump-

tion show a general decrease in consumption since a peak of 17.2 l of ethanol in the population aged 15+ in 1976. Between 1990 (14.9 l) and 2011 (11.0 l) a further decline of about 4 l of ethanol was reported (Global Information System on Alcohol and Health (GISAH)). Thus, due to the strong link between consumption and alcohol-related diseases, changes in hospitalization and mortality due to alcohol-related diseases and disease conditions are expected [14, 15].

While disease conditions that are fully attributable to alcohol such as alcohol psychosis or alcoholic liver disease can, on a yearly basis, be taken from routine statistics, disease conditions, where alcohol is only a component cause, need to be estimated by alcohol-attributable fractions (AAF). The present study thus aimed at (1) examining trends of diseases and disease conditions that are fully attributable to alcohol based on data from the hospital discharge register (2000–2012) and the death register (1995–2012), and (2) estimating the burden of hospitalization (morbidity) and death (mortality) of major disease categories fully and partially linked to alcohol for 2006 and 2012. Estimates were based on the methods applied in the Global Burden of Disease study [15, 16] using appropriate age- and gender-specific alcohol exposure data.

Methods

Data Sources

Data on alcohol exposure for the calculation of alcohol-attributable fractions (AAF) were collected from two waves of the cross-sectional German Epidemiological Survey of Substance Abuse (ESA) that have been conducted in 2006 and 2012. Overall, 7,912 (2006) and 9,084 (2012) individuals aged 18–64 participated in the surveys, corresponding to response rates of 44.9 and 53.6%, respectively (for a detailed description of the methods see [13, ESA, 17]).

For estimating alcohol-related morbidity and mortality, annual reports provided by the Federal Statistical Office for the years 2006 and 2012 were used. With regard to mortality, statistics on the cause of death based on death certificates were examined [18, 19]. Morbidity data were taken from statistics on patients discharged from hospital after in-patient treatment [20, 21]. These statistics cover general, psychiatric, psychotherapeutic, neurologic and geriatric hospitals, and maternity as well as prevention and rehabilitation facilities. Both datasets were available by age (5-year age groups from 15 to 64 years), gender, and a four-digit classification according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems [22].

Data on trends of morbidity (2000–2012) and mortality (1995–2012) fully attributable to alcohol were collected from the same sources as described earlier. Mortality statistics from 1995 to 1997

were based on ICD-9, whereas more recent data were based on ICD-10. Hospital discharge data for the observed period was based on ICD-10. In earlier years, ICD-9 records were available only for three-digit codes, impeding comparisons with data before 2000. For calculating population rates of morbidity and mortality, population data on 15–64 year-olds for the years 1995–2012 were collected from the DESTATIS-Online database [23].

Measures

Survey respondents were divided into lifetime abstainers, former drinkers (used alcohol but not within the past 12 months), and current drinkers (used alcohol at least once within the past 12 months). For current drinkers, a standardized quantity-frequency measure for beer, wine/sparkling wine, spirits, alcopops (in 2006 only), and mixed alcoholic beverages (in 2012 only) was used to calculate the average daily intake (in grams of ethanol). In addition, for estimating injuries and ischemic heart disease attributable to alcohol, data on the prevalence and frequency of episodic heavy drinking were used (online suppl. appendix B; for all online suppl. material, see www.karger.com/doi/10.1159/000381672). Episodic heavy drinking was defined as average daily ethanol intake of at least 48 g for women and 60 g for men.

Disease conditions that are causally attributable to alcohol consumption were obtained from the Comparative Risk Assessment for alcohol within the 2005 Global Burden of Disease (GBD) study [15]; the same list was used in the 2010 GBD study and the 2014 Global Status Report on Alcohol and Health by the World Health Organization [24]. An overview is given by ICD-10 code in online supplementary appendix C. For the vast majority of diseases, a detrimental effect of alcohol use was assumed. In addition, diseases for which moderate consumption of alcohol can have a beneficial effect were also considered. The number of cases and deaths that are, by definition, fully attributable to alcohol were directly included in the calculations of alcohol-related morbidity and mortality. For diseases and deaths that are not fully attributable to alcohol, alcohol-attributable fractions (AAF) were estimated and applied to respective morbidity and mortality data [25]. An AAF represents the estimated proportion of cases and deaths that may be attributed to alcohol, that is, that would disappear should no alcohol have been consumed.

Statistical Analyses

AAFs were calculated using the etiological fraction methodology [26] as outlined in detail in online supplementary appendix B. First, survey data on alcohol consumption were statistically weighted to represent the general population of Germany in 2006 and 2012. In order to adjust the undercoverage of total consumption in the population, data on average daily alcohol intake were triangulated with data on adult per capita consumption as obtained from GISAH [27] (online suppl. appendix A). Second, a gamma distribution was used to model data on alcohol consumption continuously [16]. The shape and scale parameters of the gamma distribution were calculated from the mean and standard deviation of the triangulated consumption data [28]. Finally, the gamma distribution was integrated and gender- and disease-specific AAFs were estimated (online suppl. appendix B).

Risk relations for alcohol were deduced from recent meta-analyses [28]. The upper boundary of the integral was capped at 150 g to ensure that relative risk functions are used only in the range in which they have been defined. Finally, AAFs were multiplied with

morbidity and mortality data to obtain estimates for the number of hospital cases and deaths that were in part attributable to alcohol consumption. All analyses were stratified by age (15–34, 35–64 years) and gender. Results are presented as absolute numbers and rates per 100,000 population. Assumptions about consumption in age groups not covered by the survey were taken from European results of the GBD.

Total morbidity and mortality for disease conditions fully attributable to alcohol were calculated in crude rates per 100,000 population for the years 1995–2012. ICD-10 code K85.2 was introduced in the German hospitalization statistics in 2006. This code was excluded in trends of total morbidity. ICD-10 codes G31.2, K85.2 and K86.0 had no corresponding code in ICD-9. For comparative reasons these codes were excluded in trends of total mortality. In Germany, causes X45 (accidental poisoning by and exposure to alcohol), X65 (intentional self-poisoning by and exposure to alcohol), and Y15 (poisoning by and exposure to alcohol, undetermined intent) are included in T51.0 and T51.9. These codes are not separately listed. Trends were calculated for total alcohol-attributable morbidity and mortality, and in addition separately for mental behavioral disorders due to use of alcohol (F10 in ICD-10; 291, 303, 305.0 in ICD-9), alcohol dependence (F10.2 in ICD-10; 303 in ICD-9), and alcoholic liver disease (K70 in ICD-10; 571.0–571.3 in ICD-9). Because death due to alcohol intoxication (F10.0 in ICD-10) is rare, F10.0 was included only as a separate trend in the analysis of morbidity. Data were stratified by age (15–34, 35–64 years) and gender.

The survey data on alcohol consumption were analyzed using the Stata 12.1 SE software package, taking the complex sampling design of the ESA study into account (StataCorp LP, College Station, Tex., USA). AAFs and corresponding confidence intervals were calculated using the statistical software package R version 2.11.1 [29].

Results

Trends in Rates of Morbidity and Mortality Fully Attributable to Alcohol: 1995/2000–2012

In figures 1 and 2, trends in morbidity fully attributable to alcohol for both genders expressed in number of hospitalizations and number of deaths per 100,000 population (15–64 years) are shown. Rates of hospitalizations of men exceeded those of women by a factor of 3.2 in 2000 and 2.7 in 2012. Between 2000 and 2012 rates of total 100% alcohol-attributable morbidity in men and women increased by 16 and 38%, respectively. The rates of hospitalizations due to alcohol dependence (F10.2) for men remained almost constant, while rates for women slightly increased. Overall, gender-specific trends of total and F10.2 rates of hospitalizations showed a larger increase in women compared to men (fig. 1). On average, F10 diagnoses contributed 88% in men and 90% in women to total hospitalizations with almost no variation over time. Conversely, between 2000 and 2012, the share of

Fig. 1. Trends of the number of hospitalizations per 100,000 (15–64 years) fully attributable to alcohol by gender: 2000–2012. All data based on ICD-10.

Fig. 2. Trends of the number of deaths per 100,000 (15–64 years) fully attributable to alcohol by gender: 1995–2012. Data 1995–1997: ICD-9; 1998–2012: ICD-10.

F10.2 in F10 diagnoses constantly declined from 51 to 43% in men and from 49 to 42% in women, indicating a larger share of other diagnoses than alcohol dependence. A major contribution of the observed changes came from treatment of acute intoxication (F10.0) with rates increasing more than twofold in both genders between 2000 and 2012.

Total 100% alcohol-attributable mortality rates in men decreased between 1995 and 2012 from 37 to 25 cases, and in women from 12 to 8 cases per 100,000 population, indicating a reduction of one third in both genders. In parallel, mortality rates due to alcohol dependence decreased by 38 and 33% for men and women, respectively (fig. 2). In contrast to morbidity, the majority (87% in men and 88% in women) of deaths diagnosed as F10 were contributed by alcohol dependence, while the average share of F10 (291, 303, 305.0 in ICD-9) in total 100% alcohol-attributable mortality was 35% in men and 27% in women with almost no variation over time. The major contribution to mortality was due to alcoholic liver disease accounting on average for 57% of deaths in men and 67% of deaths in women. Mortality rates due to alcoholic liver cirrhosis decreased in a similar manner to the other 100% alcohol-attributable causes of death.

Alcohol-Attributable Morbidity and Mortality Fully or Partially Attributable to Alcohol: 2006–2012

Tables 1 and 2 summarize hospitalizations and deaths due to disease conditions fully or partially attributable to alcohol. Although the rates of net alcohol-attributable hospitalizations increased between 2006 and 2012, the proportion relative to total morbidity remained constant with 5.1% in both years. However, while the proportion of all net hospitalizations in men slightly decreased, the proportion among women slightly increased (table 1). The death rates as well as the proportion of alcohol-attributable deaths to all deaths declined in both genders (table 2). Interestingly, the decrease in alcohol-attributable mortality between 2006 and 2012 could be observed in all disease categories. Changes in hospitalization, however, differed by disease category. While the number of alcohol-related cancer as well as diseases in the category ‘other 100% alcohol-attributable diseases’ declined, the number of all other disease categories increased in the observed time period. Close inspection of changes within single codes in the ‘other’ category revealed that the reduction in this category was due to a significant change in coding with F10.0 being prioritized over T51 in 2012 compared to 2006 (data not shown and available on request).

Discussion

Overall, trends of 100% alcohol-attributable morbidity and mortality over thirteen and eighteen years, respectively, show an increase in rates of hospitalizations and a decrease in rates of mortality. The increase in rates of alcohol-related hospitalization in women (+38%) was larger than in men (+16%), while mortality rates decreased almost at the same extent in both genders (–32% in men and –33% in women). Comparisons of estimated alcohol-attributable morbidity including diseases not fully attributable to alcohol between 2006 and 2012 revealed an increase in rates per 100,000 population. However, relative to total morbidity there were no changes in alcohol-related hospitalization. Alcohol-attributable mortality decreased between 2006 and 2012 both in terms of rates and relative to all deaths.

As expected, in line with the literature [30–33] a strong link between alcohol consumption and mortality could be observed in Germany. Assuming that mortality lagged behind consumption [34], reductions in per capita consumption since the late 1970s corresponded with a declining trend in 100% alcohol-attributable mortality in the last two decades. The observed decreasing trend in per capita consumption was supported by consumption data obtained from self-reported surveys both in adolescents [35] and the general population [36]. The declining trend in mortality fully attributable to alcohol was corroborated by estimates that included diseases that were partially attributable to alcohol for 2006 and 2012. The observed trends were in line with earlier research. The reversal of the increasing trend in mortality fully attributable to alcohol since the mid-1990s [11] was found to continue until recently. Similarly, the increase in mortality rates and the proportion of all deaths that were attributable to alcohol when including deaths partially caused by alcohol in the 1990s [12] were found to have reversed as well.

Contrary to mortality, rates of hospital admissions related to diseases fully attributable to alcohol have increased over the last thirteen years. When considering diseases partially attributable to alcohol, estimates for 2006 and 2012 support this trend. Rates of net alcohol-attributable hospitalizations increased by 11%. The largest increase was observed in the diagnosis of mental and behavioral disorders (F10). This increase seems to be mainly driven by an increase in hospitalizations due to acute alcohol intoxication (F10.0). One reason may be an increased sensitivity to alcohol-related problems, which consequently leads to more visits to health care professionals and more hospital admissions. Evidence for such a mechanism

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^a A15–A19, B20–B24, B90; ^b C00–C15, C18, C20, C22, C32, C50 (female); ^c F10; ^d G40, G41; ^e I11–I13, I47–I49, I60–I62, I63–I67 (male), I69.0, I69.2, I69.3 (male); ^f K29.2, K70, K85, K86; ^g Q86.0; ^h V01–V98, W00–W52, W65–W99, X00–X19, X30–X33, X40–X58 (except X45), X60–Y09 (except X65), Y85.0, Y87.0, Y87.1; ⁱ E24.4, E52, G31.2, G62.1, G72.1, I42.6, O35.4, P04.3, R78.0, T51.0, T51.9; ^j E11–E14, I20–I25, I63–I67 (female), I69.3 (female).

Some limitations of the present study need to be discussed. (1) Information concerning the cause of death is prone to inaccuracies and considerable degrees of error [40, 41]. While we have no way to improve the official statistics on the cause of death, cases above the age of 64 were excluded because of evidence questioning the reliability of deaths certificates in older age [42]. Moreover, relative risks of risk factors such as alcohol tend to converge to 1 with older age [43], and using the current methodology based on meta-analyses would not result in unbiased estimates of the impact of alcohol. (2) Hospital morbidity statistics, particularly diagnoses related to alcohol dependence, are known to be underreported due to physicians' inability in detecting [44] or physicians' tendency not to report such disorders [45]. Since there is no evidence for systematic changes in detecting and reporting F10.2 over time, trends will not be affected. (3) Unfortunately, aspects of harms to others (e.g. a drunk driver being responsible for an injury or death of persons who have not consumed alcohol) could not be included in the analysis. Incidents such as accidents involving passengers, other drivers or pedestrians, or alcohol-attributable

violence have recently been shown to contribute a large proportion to the burden of alcohol-related injuries [4]. (4) There are a number of limitations linked to the used RR and AAF analysis for partially attributable outcomes: this includes the assumption of no lag-time, which is unrealistic especially for cancer, where it takes 20 years between exposure and disease incidence [46, in general 47]. Also, the use of risk relations from global meta-analyses may introduce some error. While such risks have been shown to be relatively constant for more biological relationships (e.g. alcohol and breast cancer [48]), more variation can be expected for outcomes like injuries, which depend on a multitude of social factors (e.g. traffic injury will depend on road safety, average mileage per population or drinking driving countermeasures [49]). (5) Exposure data for triangulation and calculation of AAFs (age range 18–64 years) did not perfectly match morbidity and mortality statistics that were in the age range 15–64 years. Unfortunately, hospitalization and death records were available only in 5-year age groups. Instead of using the age range 20–64 years we decided to apply the analysis to 15–64 year-olds. For mortality, this may be justified by the fact that alcohol-related death below age 18 is fairly rare. For morbidity, the number of alcohol-attributable hospitalizations may be slightly overestimated. The bias, however, applies to both years and comparisons will not be affected. (6) Exposure to EHD in the population was based on the same threshold of five or more alcoholic drinks per day for men and women, whereas AAFs for ischemic heart disease were estimated using gender-specific thresholds of 48 and 60 g of ethanol per day for women and men, respectively. This approach was chosen to enhance comparability with earlier studies on alcohol-related morbidity and mortality. Moreover, because of lack of information on differential undercoverage, the approach of triangulation assumes a constant undercoverage in different population segments [28]. Finally, alcohol-related hospitalizations and deaths were not standardized by age. The observed trends may thus in part be due to shifts in the age structure of the German population in the observed periods. Relative risks for diseases and deaths attributable to alcohol were available only by two age groups, precluding an age-adjusted calculation of AAFs. However, no major changes in the age distribution occurred between 2006 and 2012.

Overall, an increasing trend in alcohol-attributable morbidity and a decreasing trend in alcohol-attributable mortality were observed in Germany. Based on the evidence of a strong link between alcohol consumption and alcohol-related mortality, further reductions in alcohol

use will impact on the future trend. There is also growing evidence on the positive effects of treatment utilization on mortality [7, 50, 51]. In Germany, alcohol dependence was estimated to contribute 74% of the estimated overall net burden of mortality and an increase of alcohol-dependent individuals in addiction treatment by 40% was estimated to result in a reduction of alcohol-related mortality by up to 13% in men and up to 11% in women [7]. Conversely, an increase in treatment utilization will inevitably raise morbidity figures. Thus, while mortality mirrors consumption trends with a likely lag of about 20 years [52], trends in hospitalization seem to be less driven by consumption per se. The almost constant proportion of the share of alcohol-attributable hospitalizations in total morbidity indicates that the increase of alcohol-attributable inpatient treatment did not exceed the rise in treatment of other diseases.

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Declaration of Interests

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References

- 1 Lim SS, Vos T, Flaxman AD, 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;380:2224–2260.
- 2 Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jonsson B, Olesen J, Allgulander C, Alonso J, Faravelli C, Fratiglioni L, Jennum P, Lieb R, Maercker A, Van Os J, Preisig M, Salvador-Carulla L, Simon R, Steinhausen HC: The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol* 2011;21:655–679.
- 3 Nutt DJ, King LA, Phillips LD: Drug harms in the UK: a multicriteria decision analysis. *Lancet* 2010;376:1558–1565.
- 4 Laslett AM, Room R, Ferris J, Wilkinson C, Livingston M, Mugavin J: Surveying the range and magnitude of alcohol's harm to others in Australia. *Addiction* 2011;106:1603–1611.

- 5 Pabst A, Kraus L, Gomes de Matos E, Piontek D: Substanzkonsum und substanzbezogene Störungen in Deutschland im Jahr 2012 [Substance use and substance use disorders in Germany in 2012]. *Sucht* 2013;59:321–331.
- 6 Samokhvalov AV, Popova S, Room R, Ramonas M, Rehm J: Disability associated with alcohol abuse and dependence. *Alcohol Clin Exp Res* 2010;34:1871–1878.
- 7 Rehm J, Rehm M, Shield KD, Gmel G, Frick U, Mann K: Reduzierung alkoholbedingter Mortalität durch Behandlung der Alkoholabhängigkeit [Decrease in alcohol-attributable mortality by treatment of alcohol dependents]. *Sucht* 2014;60:93–105.
- 8 Kraus L, Piontek D, Pabst A, Bühringer G: Alkoholkonsum und alkoholbezogene Mortalität, Morbidität, soziale Probleme und Folgekosten in Deutschland [Alcohol consumption, alcohol-related mortality, morbidity, social problems and costs in Germany]. *Sucht* 2011;57:119–129.
- 9 Effertz T, Mann K: The burden and cost of disorders of the brain in Europe with the inclusion of harmful alcohol use and nicotine addiction. *Eur Neuropsychopharmacol* 2013; 23:742–748.
- 10 Rehm J, Shield KD, Rehm MX, Gmel G, Frick U: Alcohol consumption, alcohol dependence and attributable burden of disease in Europe. Potential gains from effective interventions for alcohol dependence. Toronto, Canada, Centre for Addiction and Mental Health, 2012.
- 11 Rübenach SP: Die Erfassung alkoholbedingter Sterbefälle in der Todesursachenstatistik 1980 bis 2005 [Monitoring of alcohol-related deaths in the German death registry 1980–2005]. *Wirtschaft und Statistik* 2007;3:278–290.
- 12 Nolte E, Britton A, McKee M: Trends in mortality attributable to current alcohol consumption in east and west Germany. *Soc Sci Med* 2003;56:1385–1395.
- 13 Kraus L, Piontek D, Pabst A, Gomes de Matos E: Studiendesign und Methodik des Epidemiologischen Suchtsurveys 2012 [Study design and methodology of the 2012 epidemiological survey of substance abuse]. *Sucht* 2013;59: 309–320.
- 14 Rehm J, Room R, Graham K, Monteiro M, Gmel G, Semplos CT: The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease: an overview. *Addiction* 2003;98:1209–1228.
- 15 Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, Parry CD, Patra J, Popova S, Poznyak V, Roerecke M, Room R, Samokhvalov AV, Taylor B: The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction* 2010;105:817–843.
- 16 Kehoe T, Gmel G, Shield KD, Gmel G, Rehm J: Determining the best population-level alcohol consumption model and its impact on estimates of alcohol-attributable harms. *Popul Health Metr* 2012;10:6.
- 17 Kraus L, Baumeister SE: Studiendesign und Methodik des Epidemiologischen Suchtsurveys 2006 [Study design and methodology of the 2006 epidemiological survey of substance abuse]. *Sucht* 2008;54:S6–S15.
- 18 Statistisches Bundesamt: Ergebnisse der Todesursachenstatistik für Deutschland. Ausführliche 4-stellige ICD-10-Klassifikation 2006. Wiesbaden, Statistisches Bundesamt, 2007.
- 19 Statistisches Bundesamt: Gesundheit. Ergebnisse der Todesursachenstatistik für Deutschland. Ausführliche 4-stellige ICD-10-Klassifikation 2012. Wiesbaden, Statistisches Bundesamt, 2013.
- 20 Statistisches Bundesamt: Gesundheit. Tiefgegliederte Diagnosedaten der Krankenhauspatientinnen und -patienten 2012. Wiesbaden, Statistisches Bundesamt, 2013.
- 21 Statistisches Bundesamt: Tiefgegliederte Diagnosedaten der Krankenhauspatientinnen und -patienten 2006. Wiesbaden, Statistisches Bundesamt, 2008.
- 22 World Health Organization: International classification of diseases and related health problems, 10th revision. Geneva, World Health Organization, 2007.
- 23 Statistisches Bundesamt: GENESIS-Online Datenbank, 2013. <http://www-genesis.destatis.de/genesis/online> (accessed December 18, 2013).
- 24 World Health Organization: Global status report on alcohol and health. Geneva, World Health Organization, 2014.
- 25 Gmel G, Rehm J: Zusammenfassende Gesundheitsmaße von Sterblichkeit und Krankheit: Der steinige Weg zwischen PYLL, YLD, DALY und HALE [Summery measures of public health: the rocky road between PYLL, YLD, DALY and HALE]. *Suchttherapie* 2006;4:143–153.
- 26 Rothman KJ, Greenland S, Lash TL: Modern epidemiology. Philadelphia, Lippincott Williams and Wilkins, 2008.
- 27 World Health Organization: World Health Organization's Global Information System on Alcohol and Health (GISAH), 2014. <http://apps.who.int/gho/data/node.main.GISAH>.
- 28 Rehm J, Kehoe T, Gmel G, Stinson F, Grant B, Gmel G: Statistical modeling of volume of alcohol exposure for epidemiological studies of population health: the US example. *Popul Health Metr* 2010;8:3.
- 29 R Development Core Team: R: A language and environment for statistical computing. Vienna, R Foundation for Statistical Computing, 2011.
- 30 Norström T, Ramstedt M: Mortality and population drinking: a review of the literature. *Drug Alcohol Rev* 2005;24:537–547.
- 31 Ramstedt M: Per capita alcohol consumption and liver cirrhosis mortality in 14 European countries. *Addiction* 2001;96(suppl 1):S19–S33.
- 32 Rehm J, Gmel G: Aggregate time-series regression in the field of alcohol. *Addiction* 2001;96:945–954.
- 33 Ye Y, Kerr WC: Alcohol and liver cirrhosis mortality in the United States: comparison of methods for the analyses of time-series panel data models. *Alcohol Clin Exp Res* 2011;35: 108–115.
- 34 Edwards G, Anderson P, Babor TF, Casswell S, Ferrence R, Giesbrecht N, Godfrey C, Holder HD, Lemmens P, Mäkelä K, Midanik LT, Norström T, Österberg E, Romelsjö A, Room R, Simpura J, Skog OJ: Alcohol policy and the public good. New York, Oxford University Press, 1994.
- 35 Gomes de Matos E, Kraus L, Pabst A, Piontek D: Trends im Substanzkonsum Jugendlicher: Gibt es regionale Unterschiede? [Time trends in adolescent substance use: are there regional differences?]. *Sucht* 2014;60:163–172.
- 36 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;59:333–345.
- 37 Wurdak M, Ihle K, Stürmer M, Dirnberger I, Fischer UC, Funk T, Kraus L, Wolstein J: Indikatoren für das Ausmaß jugendlichen Rauschtrinkens in Bayern [Indicators for measuring the extent of binge drinking among adolescents in Bavaria]. *Sucht* 2013; 59:225–233.
- 38 Kraus L, Hannemann TV, Pabst A, Müller S, Kronthaler F, Gröbl A, Stürmer M, Wolstein J: Stationäre Behandlung von Jugendlichen mit akuter Alkoholintoxikation: Die Spitze des Eisbergs? [Inpatient treatment of adolescents with acute alcohol intoxication: the tip of the iceberg?]. *Gesundheitswesen* 2012;75: 456–464.
- 39 Caldwell JC, Caldwell BK, Caldwell P, McDonald PF, Schindlmayr T: Demographic transition theory. Dordrecht, The Netherlands, Springer, 2006.
- 40 Shojania KG, Burton EC, McDonald KM, Goldman L: Changes in rates of autopsy-detected diagnostic errors over time: a systematic review. *JAMA* 2003;289:2849–2856.
- 41 Nashelsky MB, Lawrence CH: Accuracy of cause of death determination without forensic autopsy examination. *Am J Forensic Med Pathol* 2003;24:313–319.
- 42 Alperovitch A, Bertrand M, Jougle E, Vidal JS, Ducimetière P, Helmer C, Ritchie K, Pavillon G, Tzourio C: Do we really know the cause of death of the very old? Comparison between official mortality statistics and cohort study classification. *Eur J Epidemiol* 2009;24:669–675.
- 43 Ezzati M, Lopez AD, Rodgers A, Murray CJL: Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland, World Health Organization, 2004.

- 44 Rosón B, Monte R, Gamallo R, Puerta R, Zapatero A, Fernandez-Sola J, Pastor I, Giron JA, Laso J: Prevalence and routine assessment of unhealthy alcohol use in hospitalized patients. *Eur J Intern Med* 2010;21:458–464.
- 45 Rumpf HJ, Bohlmann J, Hill A, Hapke U, John U: Physicians' low detection rates of alcohol dependence or abuse: a matter of methodological shortcomings? *Gen Hosp Psychiatry* 2001;23:133–137.
- 46 Rehm J, Patra J, Popova S: Alcohol drinking cessation and its effect on esophageal and head and neck cancers: a pooled analysis. *Int J Cancer* 2007;121:1132–1137.
- 47 Holmes J, Meier PS, Booth A, Guo Y, Brennan A: The temporal relationship between per capita alcohol consumption and harm: a systematic review of time lag specifications in aggregate time series analyses. *Drug Alcohol Depend* 2012;123:7–14.
- 48 Collaborative Group on Hormonal Factors in Breast Cancer: Alcohol, tobacco and breast cancer – collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer* 2002;87:1234–1245.
- 49 Babor TF, Caetano R, Casswell S, Edwards G, Giesbrecht N, Graham K, Grube J, Hill L, Holder HD, Homel R, Livingston M, Österberg E, Rehm J, Room R, Rossow I: *Alcohol: no ordinary commodity*. Oxford, Oxford University Press, 2010.
- 50 Shield KD, Rehm J, Gmel G, Rehm MX, Al-lamani A: Alcohol consumption, alcohol dependence, and related mortality in Italy in 2004: effects of treatment-based interventions on alcohol dependence. *Subst Abuse Treat Prev Policy* 2013;8:21.
- 51 Rehm J, Shield KD, Rehm MX, 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.
- 52 Rosen M, Haglund B: Trends in alcohol-related mortality in Sweden 1969–2002: an age-period-cohort analysis. *Addiction* 2006;101:835–840.