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Direktor: Prof. Dr. Dr. Tobias Kurth

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Methodological Challenges in Observational Studies: Measuring Socio-Economic Status and Alcohol Consumption

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Dr. phil. Ulrike Grittner
geboren in Potsdam

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Dekan: Prof. Dr. med. Axel R. Pries

1. **Gutachter: Prof. Dr. Hajo Zeeb**
2. **Gutachter: Prof. Dr. Peter Schlattmann**

Content

“all *methodologies, even the most obvious ones, have their limits”*

Paul K. Feyerabend. Against Method: Outline of an Anarchist Theory of Knowledge (1975), pg 32

1. INTRODUCTION

This habilitation treatise gives an overview of three methodological challenges often encountered in epidemiological research. The first part of this treatise describes these issues in detail and puts them into the context of alcohol-related epidemiological research questions. The second part consists of facsimiles of original research reports, which answer these research questions using various datasets. The final part provides an overall discussion and summary.

1.1 Methodological Challenges and Possible Solutions

1.1.1 Challenge 1: Measuring Socio-Economic Status

Socio-economic status (SES) is often defined as an individual's or group's economic and social standing in relation to other individuals or groups within a society (American Psychological Association 2016). The concept of SES assumes a hierarchical, structured society. Higher SES indicates a higher probability of access to resources such as money, material goods, power, reputation, and healthcare, and to cultural, educational or leisure time activities (Oakes and Rossi 2003). However, up to date there is no standard definition of SES, although most definitions are based on information about highest educational achievement, net income, and occupation.

Measuring SES in health sciences is essential for the following reasons:

- It renders the description and understanding of the structure and level of stratification in or between societies possible.
- It helps understanding the dynamics in the structure of societies over time.
- It allows studying SES in relation to health related behaviour, morbidity, and mortality.
- It allows adjustment for possible confounding of SES and by doing so, avoiding misinterpretations of research results.

Different operationalisations of SES and their advantages and disadvantages have been discussed (see for example Braveman et al. 2005).

An operationalised SES measure should

- be easy to measure in all or most participants of a study,
- be internationally comparable (at least for international studies),
- be transparent in the assumptions made to construct it,
- reflect the hierarchical structure within a society with regard to resources, power and privileges.

Analysing the association between SES and health-related outcomes, the causal path way is often not easily determined and results have to be interpreted with caution. Health outcomes in SES strata might differ due to differences in health-related behaviours or due to differences in resources even if behaviour is similar. For example, people in lower SES groups live in noisier and more polluted city regions due to lower resources and therefore have worse health outcomes than people in higher SES groups. In the majority of cases, both phenomena (behavioural and resource differences) will be present at the same time.

Established Indices and international classification systems of countries' SES

Besides measuring SES on the level of individuals or groups, it is also of interest to measure the SES of whole countries or their economic position in relation to other countries. Two proposed measures for doing so are the per capita **gross national income (GNI)** (OECD 2016a) or the **gross domestic product (GDP)** (OECD 2016b). GDP and GNI are highly related but not interchangeable measures of a country's economic power. GDP is the market value of all services and goods within the borders of a nation, GNI adds to this the income obtained abroad by the citizens. To have a measure for economic power comparable across countries, the World Bank provides for example **purchasing power parity (PPP)** (World Bank 2016a). It is the GNI converted to international dollars using PPP rates. "An international dollar has the same purchasing power as an U.S. dollar has in the United States" of America (World Health Organization 2016).

Another country level SES characteristic measures the spread of economic resources between the individuals of a society for example given by **the Gini coefficient** (Gini

1912). It quantifies the extent to which a distribution of values of a specific measure deviates from a uniform distribution, and as such degree of inequality in a country's income distribution. The Gini coefficient ranges from 0 to 1 (or is expressed as percentage and maximized at 100%): a value of 0 means total equality, i.e. all individuals have the same income, and 1 refers to total inequality; i.e. one individual has the whole income. Countries like e.g. Norway have low values of inequality with a Gini coefficient of 25.9% (value from 2012, World Bank 2016b), whereas other countries such as South Africa have high values with 63.4% (value from 2011, World Bank 2016b). In 2011, Germany had a Gini coefficient of 30.1% (World Bank 2016b), the USA had 2013 a value of 41.1% (World Bank 2016b).

Established Indices and international classification systems of individual SES

In the following section, different operationalisations of individual SES using single indicators are presented, such as education, occupation, income, or combined summary indices as e.g. the Winkler-Index (Winkler & Stolzenberg 1999). All indicators are discussed in light of the points mentioned earlier (see 1.1.1). For single indicators here the focus is on international classification systems, which are important when analysing individual's data from different countries.

Education. One prominent indicator for SES on the individual level is the **highest educational achievement**. An easy way of measuring and comparing different levels of education is to quantify the **years of schooling,** assuming that more years of schooling indicate a higher educational achievement.

Another approach is to use an international classification system like the **International Standard Classification of Education (ISCED)** 2011 (UNESCO Institute for Statistics 2012). ISCED 2011 is the product of an international agreement, formally adopted by the General Conference of UNESCO Member States and a revision of the ISCED 1997. It classifies education based on levels and fields of education (general vs. vocational education or academic vs. professional education). In this scheme, there are nine different main categories and many subcategories. Those nine main categories are as follows: (0) early childhood education, (1) primary education, (2) lower secondary education, (3) upper secondary education, (4) post-secondary non-tertiary education,

(5) short-cycle tertiary education, (6) Bachelor's or equivalent level, (7) Master's or equivalent level, (8) Doctoral or equivalent level. Revised mappings of the national education systems of different countries are not yet available for the ISCED 2011 but only for the ISCED 1997 (United Nations Educational, Scientific Cultural Organization 2006).

The **Comparative Analysis of Social Mobility in Industrial Nations (CASMIN**) classification system is an older version of another international education classification system (König et al. 1988). It is similar to the ISCED with 3 major categories (elementary / primary education, secondary education, tertiary education) and more detailed sub-categories resulting altogether into 9 categories: (1a) inadequately completed general education, (1b) general elementary education, (1c) basic vocational qualification/general elementary education and vocational education, (2a) intermediate vocational qualification / intermediate general qualification and vocational qualification, (2b) intermediate general qualification, (2c_gen) general maturity certificate, (2c_voc) vocational maturity certificate / general maturity certificate and vocational qualification, (3a) lower tertiary education, (3b) higher tertiary education) (König et al. 1988).

There are three main advantages of operationalising SES with education. First, it is easy to measure. Second, it is almost always available for most participants of a study. And third, a hierarchy of different educational achievements can often be derived without additional assumptions, as hierarchy is inherent in most educational systems where a certificate from a lower level program is needed to enter the next level of education. The number of years of schooling is often used in international studies, as it is much easier to handle than a re-categorisation of educational achievements into classification systems like CASMIN or ISCED. The main advantages of these classification systems are, that they define comparable important steps for every system, for example the achievement of a vocational qualification or a university degree, and that they are therefore more informative with regard to contents of educational achievements than the number of years of schooling.

Occupation. The International Labour Organization provides a classification scheme for occupations: the **International Standard Classification of Occupations (ISCO)** The newest version was adopted in 2007 and is called ISCO-08 (International Labour Organization 2008). There are 10 main groups for occupations, divided into several subgroups. Those main groups are: (0) managers, (1) professionals, (2) technicians and associate professionals, (3) clerical support workers, (4) service and sales workers, (5) skilled agricultural, forestry and fishery workers, (7) craft and related trade workers, (8) plant and machine operators, and assemblers, (9) elementary occupations, (9) armed forces occupations (International Labour Organization 2008). Within the ISCO scheme, there is no strict hierarchical order of occupations, as it is solely a classification of occupations without socio-economic assignment. It is much more complicated to define a hierarchical structure related to the relative prestige or socio-economic position for occupation than for education or income. To solve this problem, Ganzeboom et al. (1992) developed an **International Socio-Economic Index of Occupational Status (ISEI**), based on additional information on education and income for more than 70,000 full-time employed men from 16 countries. They used an optimal scaling procedure resulting in a hierarchical system with a continuous scale for occupational prestige at its core. Although the ISEI uses additional information to derive a hierarchical scale for occupational categories, it is not a combined index. Lampert et al. (2013) showed that for Germany, the ISEI only moderately correlates with income (0.37) and education (0.59).

Income. Income is another single indicator for SES. Different kinds of income measure are household net income, personal income, equivalent income. Equivalent income is a weighted personal income based on household net income and household structure. However, participants often consider asking information about income too sensitive, and therefore these variables often suffer from many missing values. Education and income are associated, but Braveman et al. (2005) showed for the USA that the correlation between education and income is not very strong (Spearman correlation coefficient below 0.5), and that both variables can be used in the same multiple regression model without causing problems of collinearity.

Combined Indices. Combined indices have the advantage of aggregating information form several dimensions into one single dimension. In Germany a prominent combined index for measuring individual SES is the **Winkler-Index** (Winkler & Stolzenberg 1999). It combines information on education, income (monthly household net income), and occupation. Each of these three dimensions is classified on an ordinal scale from 1 to 7, and their sum score (ranging from 3 to 21) is the Winkler-Index.
For the analysis of socio-economic differences in health status and related dimensions in Germany, Lampert et al. (2013) modified the Winkler-Index to use the new Index for the regular representative German health surveys. Lampert et al.'s index also uses all three single dimensions ranging from 1 to 7, but with more fine-grained non-integer values between 1 and 7 to allow higher differentiation. The three dimension get then equal weights in the sum. Individual education is coded according to the CASMIN score, occupation classification according to the ISEI Index (Ganzeboom et al. 1992), and income and occupation are coded on the household level.

Using single indicators or combined indices, especially for occupation, two main assumptions are made. First, we assume a hierarchy between different categories. Often this problem is solved by comparing the typical income level of specific occupational categories. However, this approach does not account for potential status inconsistencies. These inconsistencies are present if for example people with a high level of education have a low income. Second, we assume that all indicators provide information on a single dimension. This assumption is not always true.

1.1.2 Challenge 2: Clustered Data

In medical, social, public health, or psychological research, observations are often not strictly dependent or strictly independent from each other. A typical example are multicentre studies, where patients in one centre are potentially more similar to each other than to other centres' patients – due to similarities in their characteristics or the therapies, or both. Similarly, the same holds for multinational studies or longitudinal studies. In the latter, repeated measurements of an individual are dependent, but independent of other individual's measurements. This kind of data is referred to as

clustered or hierarchical data. Multilevel analysis (Snijders & Bosker 1999) was developed in order to provide special statistical tools to appropriately account for the included dependencies. Its main characteristics are the following. First, it identifies the variance in the outcome related to each level or cluster of data. Second, it evaluates the association of individual or group characteristics with the outcome at the appropriate levels. This method has been described under various names such as hierarchical models (Raudenbush & Bryk 2002), random effects models (Dunson 2008), and mixed models (Verbeke & Molenberghs 2000; Zuur et al. 2009). The aim of multilevel modelling is to combine the regression equations (statistical models) from several levels into one, and to incorporate covariates at appropriate levels. This means, that the models for lower levels (e.g. the individual level) are combined with models for higher levels (such as hospitals). Additional adjustment is performed for similarities of the lower level units belonging to the same higher level. Therefore one can make overall inferences about relationships between lower level as well as higher-level characteristics and the outcome of interest. For further reading and a simple introduction see Grittner & Bloomfield 2013. Population average modelling that uses generalised estimating equations (GEE) is another statistical approach that is prominent and often used for handling clustered or longitudinal data (Liang & Zeger 1986, Ziegler 2011). GEE models are extension of generalised linear models (GLM) by accounting for clustered or correlated data. Insofar they are similar to multilevel models. But while GEE models provide population mean outcome values as a function of covariates given dependent or clustered data, multilevel models model outcomes conditional on the characteristics of each cluster as a function of the covariates. That means, if it is only important to account for clustering, GEE models are sufficient but multilevel models can also be used. However, if inference on cluster characteristics is of interest, mixed models have to be used. GEE are not able to provide answers with regard to inference on the cluster level or cross level interactions. There has been a discussion of which of both approaches gives more reliable or stable estimates (see e.g. Hubbard et al. 2010, Subramanian & O'Malley 2010).

1.1.3 Challenge 3: Missing Values

Another common problem in epidemiology or medical research are missing values, which typically occur because of non-response or drop out. Analysing only the complete observations in study or survey data might lead to biased results and underestimation of standard errors. Therefore, estimation and imputation of missing values prior to data analysis are often preferable. However, it is important to classify the type of missing in the data. We distinguish three main types of missing data mechanisms (Little & Rubin 2014):

1. Missing completely at random (MCAR)
2. Missing at random (MAR)
3. Missing not at random (MNAR)

MCAR is present if missing data are not associated to other observed or unobserved measures relevant to the study. In this case, the analysis of complete observations only results in unbiased parameter estimates, but at the cost of lower power and precision. In reality, however, MCAR rarely holds. MAR refers to a setting where the missing of data can be explained with observed variables. An example is to have missing data in income being more likely in middle aged people, i.e. missing is related to age, but not the actual income level. It cannot be tested analytically whether data are MCAR or MAR, but only argued upon based on assumptions. MNAR is a situation where the probability of missing is related to the value of the missing data itself. An example here is that people with overweight participating in a survey, are more likely not to report their weight than people with normal weight. Most currently available imputation methods assume MAR to hold. The estimation of values for replacing missing data is

subsequently carried out by using both, the observed data of the variables with missing data, and the observed data of other variables that might be related to the missing data. Heckman modelling is an approach that accounts for MNAR (Heckman 1979, for a short explanation of Heckman modelling see 2.5).

Multiple imputation methods are in general preferred over single imputation methods, as they correctly reflect the uncertainty about the true value. This is done by imputing the missing data m times, resulting in m different complete datasets. Each of these m datasets is subsequently analysed with regard to the research question,

resulting in m different estimates for the parameters of interest. These are in a final step combined into one estimate with the method first introduced by Rubin (1987). The final estimate is simply the mean of the estimates in the imputed data sets. The variance of this estimate is calculated with the formula: $\sigma = \sigma_w + (1 + \frac{1}{m})\sigma_b$.

With σ_w being the within imputation variance, calculated as the mean of the variances of the m imputations: $\sigma_w = \frac{1}{m}\sum_{i=1}^{m} \hat{\sigma}_i$, and σ_b is the between imputation variance, calculated with this formula: $\sigma_b = \frac{1}{m-1}\sum_{i=1}^{m}(\hat{e}_i - \bar{e})^2$; where $\hat{e}_i$ is the estimate of the ith imputed data set and $\bar{e}$ is the mean of this estimate over the m imputed data sets (Rubin 1987).

1.2 Examples of How to Face these Challenges in Alcohol Epidemiology

The three methodological challenges given in section 1.1. (measuring SES, clustered data, and missing data) will be discussed in relation to alcohol research. Each results in a relevant public health research question in the field of alcohol research, which is subsequently addressed in the papers.

1.2.1 SES and Alcohol Consumption or Alcohol-Related Problems in a Multinational Survey

One focus in alcohol research is the analysis of the association between SES and alcohol consumption, as well as the identification of alcohol related consequences and problems to specify most vulnerable groups who are potential targets for preventive strategies. In international surveys information on all three single indicators, i.e. education, income, and occupation, is often not available for all countries and participants. Therefore, we were limited to use education as indicator for SES for the analysis of all study countries within the GENACIS (Gender, Alcohol and Culture - An International Study) project in one analysis model (see below section 2.2 and 2.3 for project details). For Germany, we performed a separate analysis using all three single indicators, combined into a single index created via optimal scaling. Optimal scaling is a nonlinear principle component analysis with the possibility of using variables with different scales in parallel (Joliffe 2002). No further a priori assumptions

about the hierarchical order of, for example, occupational categories are necessary. Based on this method it is also possible to derive a more-dimensional index. The German dataset was well suitable for the use of dimensional scaling, as it was a large, representative, and high-quality study, and thought as an example for further studies in Germany or other countries.

For large international studies like the GENACIS study, which included epidemiological data on alcohol consumption of more than 30 countries, it is essential to account for the clustering of the data, as participants belong to different countries. Therefore, we used multilevel models and could analyse overall effects over all countries, as well as identify countries with deviating patterns of consumption or alcohol-related problems (see 2.2 and 2.3).

1.2.2 Measuring Changes in Alcohol Consumption over Time

Analysing panel data, multilevel models are suitable since they account for clustering of different measures within one participant. Additionally, these models can easily handle unbalanced data, a common problem in longitudinal research resulting from the fact that not all participants responded at all time points. Therefore, we also used multilevel models for analysing panel data of alcohol consumption in Denmark (see 2.4).

1.2.3 Attrition in Longitudinal Measures of Alcohol Consumption

After alcohol tax reduction in 2003 and higher import allowance in Denmark, alcohol researchers expected higher consumption levels in Denmark. Astonishingly, no raise in consumption was noticed in cross sectional and panel data (see 2.4). Since missing values can distort results and might yield to an underestimation or overestimation of probable changes in longitudinal data analysis, we explored different missing value imputation methods for longitudinal data, using simulated data, and analysed the Danish alcohol tax study data again after multiple imputation of missing values (see 2.5).

1.3 Data Collections

For the three research questions stated above, we used three different datasets. These are introduced in the following paragraphs.

1.3.1 Survey on the Consumption of Psychoactive Substances in the German Adult Population 2000

Since 1980, the German National Survey on the Use of Psychoactive Substances has been conducted every two to five years. The target group is the 18 to 59 year old adult population. In 2000, the overall response rate was 45.5%, resulting in 8,139 participants (for details of the study see Kraus & Augustin 2001). Participants were randomly selected based on data from the residents' registration offices. Selection was done according to number of inhabitants in different regions. It was a postal survey with further phone inquiries in case of inconsistencies. Data were weighted according to age, sex, and region to account for non-response. The questionnaire asked about consumption of illegal drugs, alcohol, medications, and tobacco. Additionally, information about socio-demographic characteristics, leisure time activities, general health status, pathological gaming, and the financial situation was collected.

General aims and research questions of the survey. This survey provides representative estimates of the consumption of drugs, alcohol, medications, and tobacco in the German general population in 2000, as well as consumption related dependencies and consequences. Because this is a regularly repeated survey in Germany, information on long-term consumption trends is available. Additionally this survey was used within the international GENACIS project as German data set on alcohol consumption.

Funding and support. The survey was funded by the German Federal Ministry of Health.

Aims and research questions addressed.

1. We used this study to demonstrate how an empirically based two-dimensional socio-economic status indicator can be constructed using information about education, income, and occupation, without any assumptions about hierarchy of occupational categories (see chapter 2.1).

2. We compared the new SES index to the Winkler-Index.
3. We addressed the question how socio-economic status according to the new SES index and alcohol consumption are related in Germany.

1.3.2 GENACIS - Gender, Alcohol and Culture - An International Study

The GENACIS study is a large international collaboration collecting epidemiological data on alcohol consumption from different cultures (for details of the study see Wilsnack et al. 2009). The study combines general population surveys on drinking behaviour in 38 countries; including 17 European countries (Austria, Czech Republic, Denmark, Finland, France, Germany, Great Britain, Hungary, Iceland, Ireland, Isle of Man, Italy, Netherlands, Norway, Spain, Sweden, Switzerland), 7 North American countries (Belize, Canada, Costa Rica, Dominican Republic, Mexico, Nicaragua, United States of America), 5 South American countries (Argentina, Brazil, Guyana, Peru, Uruguay), 5 Asian countries (India, Israel, Japan, Kazakhstan, Sri Lanka), 2 African countries (Nigeria, Uganda), Australia, and New Zealand. Most data come from national surveys, some from regional surveys (www.genacis.org).

General aims and research questions of the survey. One main research question of this study is how gender differences in alcohol consumption vary across different cultures and countries. Other research questions within GENACIS include

- the description of culture-, age-, and sex-specific drinking pattern and alcohol-related consequences;
- the question of how alcohol consumption and alcohol-related consequences are associated with socio-economic conditions, social status, and social roles;
- how drinking is related to physical and social contexts;
- how drinking is linked to various types of harmful behaviour or violence;
- how informal social pressures to control drinking vary between countries.

Funding and support. GENACIS is an international project, affiliated with the Kettil Bruun Society for Social and Epidemiological Research on Alcohol, and coordinated by partners in the USA (University of North Dakota, the Alcohol Research Group in

California, the Public Health Institute in California), Canada (the Centre for Addiction and Mental Health in Toronto), Denmark (the Aarhus University), Australia (the University of Melbourne), and Switzerland (the Swiss Institute for the Prevention of Alcohol and Drug Problems) (www.genacis.org). The U.S. National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institutes of Health (NIH) supported parts of the project (Grant Numbers R21 AA012941 and R01 AA015775, Sharon C. Wilsnack as principal investigator). Additionally the study was supported by the Quality of Life and Management of Living Resources Programme of the European Commission (Concerted Action QLG4-CT-2001-0196, Kim Bloomfield, coordinator), the World Health Organization (Isidore Obot, coordinator), the Pan American Health Organization (Maristela Monteiro, coordinator), the German Federal Ministry of Health, and Swiss national funds. Individual country surveys have been supported by government agencies and other national sources. Gerhard Gmel from the Swiss Institute for the Prevention of Alcohol and Drug Problems in Lausanne was the data coordinator. A second funding period was supported by the U.S. National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute of Health (NIH) (2007-2012, Grant Number: R01 AA015775).

Aims and research questions addressed. The papers being part of this habilitation treatise addressed and analysed the following research questions within the GENACIS study:

1. How is SES related to alcohol consumption in 33 study countries, and which country-level-characteristics are related to country specific differences in consumption? (chapter 2.2)
2. How is SES related to alcohol-related consequences in 25 countries? Which role do country-level-characteristics play with regard to the prevalence of alcohol-related consequences? (chapter 2.3)

1.3.3 The Nordic Tax Study

"Effects of major changes in alcohol availability", or short "Nordic tax study", is a study conducted collaboratively by researchers from Denmark, Finland, and Sweden. The main research question for this study was how lower pricing and higher availability of alcohol affects alcohol consumption in Denmark, Finland, and southern Sweden,

after an alcohol tax reduction and higher private alcohol import allowance, which took place in Denmark and Finland in 2003-2004. The research was carried out at the Unit of Health Promotion Research of the University of Southern Denmark, Esbjerg, the Alcohol and Drug Research Group of the National Research and Development Centre for Welfare and Health (STAKES), Helsinki, and the Centre for Social Research on Alcohol and Drugs of the Stockholm University.

The survey used longitudinal and repeated cross-sectional population surveys from 2003, 2004, 2005, and 2006. In these surveys, information on beverage specific alcohol consumption, private alcohol import behaviour, and alcohol-related consequences were collected. Additionally, routinely collected registry data on recorded and unrecorded alcohol consumption, alcohol-related hospitalisation, morbidity and mortality, as well as police statistics on handling of drunkenness were assessed.

General aims and research questions of the survey. In 2003 and 2004, taxes on alcoholic beverages were reduced in Denmark and Finland, and quantitative quotas on private alcohol import from other European Union countries were abolished (Grittner et al. 2013). Because of these policy changes, cheaper alcohol was easier available in Denmark, Finland, and Sweden. The study tested the effects of these changes and its related changes in alcohol consumption and alcohol-related consequences in Denmark, Finland, and southern Sweden (see e.g. Room et al. 2013, Bloomfield et al. 2009, Bloomfield et al. 2010).

Funding and support. The study was supported by the Joint Committee for Nordic Research Councils for the Humanities and the Social Sciences (NOS-HS, project 20071), and the U.S. National Institute on Alcohol Abuse and Alcoholism (NIAAA) (R01 AA014879). For Sweden, Systembolaget financed parts of the study. For Denmark, the Danish Medical Research Council (contract no. 22-02-374), as well as the Danish Health Insurance Fund (journal nos. 2003B195, 2004B195, 2005B093) supported the data collection.

Aims and research questions addressed.

1. How did alcohol consumption in Denmark change over the four-year study period (Chapter 2.4)? Linear mixed models were used to analyse the panel data.

2. What are the results of analysing change in consumption if multiple imputation of missing values was be used (Chapter 2.5)? How do different methods of missing value imputation differ? To answer these questions, the Danish panel data, as well as simulated data were used.

2 SCIENTIFIC PAPERS

2.1 The Construction of an Empirically Based Social Status Index

Motivation for this study stems from the problem of operationalising socio-economic status (SES) if an association between SES and alcohol consumption is to be analysed. SES is commonly operationalised by using one of the single indicators education (highest educational achievement), occupation, or income, or as a summary score by combining information on these indicators. These approaches imply assumptions about the explanatory value of a chosen indicator. In this study, we created a gender specific metric SES-indicator for Germany by combing information on education, occupation, and income. For the construction method that we, no further assumptions about the hierarchical order of educational or occupational categories were necessary.

Paper 1: Grittner, U., Bloomfield, K., Kramer, S., Kuntsche, S., Gmel, G. (2006) Die Konstruktion eines empirisch bestimmten Sozialschichtindexes mittels optimaler Skalierung am Beispiel von Deutschland. *Das Gesundheitswesen*. 68. S.116-122. DOI: 10.1055/s-2005-858999

Aims.

- To construct a new gender- and country specific empirically based social status index for Germany.
- To compare this index with the Winkler-Index.
- To analyse the association between the new SES-Index and drinking pattern in Germany.

Data. Data came from a national representative postal survey on use of drugs and psychoactive substances of adults in Germany from 2000 (Kraus & Augustin 2001). Because we focused on people in the working age, we used only information of participants from 25 to 59 years old. This resulted in a dataset with information on 7,001 individuals. Regular risky single occasion drinking (RSOD, drinking 5 or more drinks on one occasion more often than once a month) was defined as the outcome. To account for non-response and to ensure representability, data were weighted according to sex, age, and regional distributions of the general population in Germany.

Methods. We constructed a new empirical SES index based on information about occupation, education, and income by using optimal scaling (a categorical principal component analysis).

Results. The optimal scaling resulted in a two-dimensional solution. The first dimension corresponded to the levels of education, occupation, and income, and explains 60% of the variance in education, occupation and income. In contrast, the second dimension reflected inconsistencies with regard to education and income, i.e. it scored higher for those with middle education but high income, or low for those with high education but low income. As the second dimension explains 25% of the variance, one quarter of differences in education, occupation and income were explained by income differences that do not correspond to differences in education or occupation. The first dimension was highly correlated with the Winkler-Index (Pearson's correlation coefficient r=0.86) showing that it measures SES differences similarly to the Winkler-Index. The second dimension was not correlated to the Winkler Index (Pearson's correlation coefficient r=0.10), demonstrating that existing inconsistencies between the three single indicators are not reflected by the Winkler-Index. Interestingly, differences in drinking behaviour were not only related to differences in the first but also the second dimension. With regard to the first dimension, RSOD was more prevalent in lower status groups (low education, low occupational status, low income) than in higher SES groups. Around 31.5% of men in the lowest quartile of the first SES dimension compared to 22.7% of men in the highest SES quartile of the first dimension were regular RSO drinkers; for women prevalence was 6.5% for the lowest quartile compared to 5.8% for those in the highest quartile. With regard to the second dimension, those with higher income but lower education had a higher prevalence of RSOD than those with higher education but lower income. For men /women prevalence in the highest quartile of the second SES dimension was 31.6%/ 7.9% compared to 27.9%/6.1% for the lowest quartile.

Conclusion. SES based on levels of education, occupation, and income is a complex construct, and can therefore not be reflected by a one-dimensional scale in all circumstances. Using a two-dimensional SES score, health relevant behaviour reflected by regular RSOD differed with regard to both dimensions.

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2.2 Alcohol Consumption and Social Inequality in 33 Countries

The first paper showed that SES is a complex construct even if only using information about education, occupation, and income. In large international studies, we often lack high-quality and complete data and information on even these three indicators. The first paper also showed that education alone is strongly related to the first dimension of the presented two-dimensional SES index, explaining most of the variation in SES represented by all three indicators. We used education as SES indicator since it was available for most participants in many study countries. We analysed the relation between SES and alcohol consumption in 33 countries in the GENACIS study:

Paper 2: **Grittner, U**., Kuntsche, S., Gmel, G., & Bloomfield, K. (2013). Alcohol consumption and social inequality at the individual and country levels—results from an international study. *The European Journal of Public Health*, *23*(2), 332-339. DOI: 10.1093/eurpub/cks044

Aims.

- To examine the relation between SES and alcohol consumption in 33 countries.
- To test whether SES-related differences in alcohol consumption are similar between countries
- To analyse whether country-level characteristics, such as economic power, are related to alcohol consumption after adjusting for individual characteristics.

Data. The data comprised information of 101,525 individuals in 33 countries of the GENACIS project (www.genacis.org). In 22 countries, data came from national representative survey samples. Regional data were available in 11 additional countries (see Table 1 in Paper 2). Only data from participants of age range 25 to 69 years were used for this study. Data were collected between 1993 and 2007. Respondents were on average 44 years old, 45.4% of the respondents were male. As an estimate of individual SES we used the educational level of the respondents, measured by years of schooling, and recoded into three categories (low: ≤10 years of education; middle: >10 years and <13 years of education; high: ≥13 years of education, or Bachelor, Master or PhD). The

variables drinking status (respondents were coded as drinker if they drank any alcohol within the last 12 months) and monthly RSOD (drinking 60 or more grams of pure alcohol on one occasion, equivalent to 5 or more drinks) served as indicators for alcohol use. Additionally, the GNI per capita as a measure of a country's economic power, as well as the Gini coefficient as indicator of inequality in the income distribution within a country, were used. The gender gap index was included as a measure for gender equity within a country.

Methods. Data were analysed without adjustment using meta-analysis methods, and with adjustment using multilevel logistic regression models (random intercept models) to account for the nested data structure of individual measures nested within countries. In the multiple multilevel regression models individual characteristics (age, a squared age term to test curvilinear relation between age and outcome, education), country level variables (GNI, Gini coefficient, Gender Gap index), and cross-level interactions were tested.

Results. In most countries, more subjects with higher SES were current drinkers compared to respondents with lower SES. Men with lower SES were more often regular RSO (risky single occasion) drinkers compared to men with higher SES. Heterogeneity with regard to this finding was higher for countries with lower economic power compared to countries with higher economic power. Women with higher SES in countries with lower economic power were more likely to engage in regular RSOD compared to women with low SES. In most countries with higher economic power, the opposite was true. But heterogeneity in findings was large with mixed findings in both, countries with lower and in countries with higher economic power.

Conclusion. In most countries, risky drinking but also abstention were more prevalent in lower SES strata. In lower income countries, women with higher SES are more often regular RSO drinkers than women with lower SES.

Grittner, U., Kuntsche, S., Gmel, G., & Bloomfield, K. (2013). Alcohol consumption and social inequality at the individual and country levels—results from an international study. The European Journal of Public Health, 23(2), 332-339. DOI: 10.1093/eurpub/cks044

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2.3 Alcohol-Related Consequences and Social Inequality in 25 Countries

Paper 2 analysed how SES is related to drinking behaviour in 33 countries. Another research question within the GENACIS project was whether negative consequences of potentially harmful behaviour differ in their relation to social and health-related consequences and problems between SES groups, even in the case of similar behaviour. Using again data from the GENACIS study, we analysed how SES was related to alcohol-related consequences in 25 countries:

Paper 3: **Grittner, U**., Kuntsche, S., Graham, K., & Bloomfield, K. (2012). Social Inequalities and Gender Differences in the Experience of Alcohol-Related Problems. *Alcohol and Alcoholism, 47*, 597-605. DOI: 10.1093/alcalc/ags040

Aims.

- To examine the relation between SES and alcohol-related consequences in 25 countries.
- To analyse whether there are differences between people with different SES in alcohol-related consequences after controlling for alcohol consumption, i.e. whether subjects with lower SES report more often problems, even if they drink in the same manner with regard to consumption level and pattern of drinking.
- To test whether SES-related differences in alcohol-related consequences are similar in different countries.
- To analyse whether country-level characteristics, such as economic power, are associated with alcohol-related problems after adjusting for individual characteristics.

Data. Survey data information from more than 42,000 individuals in 25 countries participating in the GENACIS project were used (www.genacis.org). In 16 of these countries, data were derived from national representative surveys. Regional data were available for 9 additional countries, (Table 1 in Grittner et al. 2012). We used only data from respondents of age 25 to 69 years, and from respondents who consumed any alcohol within the last 12 months before the survey. Data were collected between 1997 and 2007. Highest educational achievement served as measure of individual SES.

Questions on alcohol-related consequences were based on the AUDIT (The Alcohol Use Disorders Identification Test, Babor et al. 1989), and were coded as 1, if the consequence occurred within the last 12 months or 0 if not. We used a set of five questions reflecting internal consequences (see Babor et al. 1989):

- Did you have a feeling of guilt or remorse after drinking?
- Have you been unable to remember what happened the night before because you had been drinking?
- Have you failed to do what was normally expected from you because of drinking?
- Have you found that you were not able to stop drinking once you started?
- Did you need a first drink in the morning to get yourself going after a heavy drinking session?

and another set of eight questions reflecting external and social consequences (see Babor et al. 1989):

- Did your drinking had harmful effects on your finances / your housework or chores around the house / your work, studies or employment / your marriage or intimate relationship / family relationships including children / friendships and social life?
- Have you or someone else been injured because of your drinking?
- Did you get into a fight while drinking?

To control for alcohol consumption, we used a drinking pattern variable to distinguish between four different groups of alcohol consumers (Grittner et al. 2012):

(1) moderate drinkers: no monthly RSO drinkers and no heavy drinkers (≤10/20 g of pure alcohol per day for women/men);

(2) heavy drinkers (>10/20 g of pure alcohol for women/men on average per day);

(3) (at least) monthly RSO drinkers; and

(4) both: heavy drinkers and monthly RSO drinkers.

At the country level, we used GNI (gross national income per capita) as measure of economic power of a country, the Gini coefficient as measure of income disparity, and the Gender gap index as measure for gender equity.

Methods. We calculated country- and sex-specific age-adjusted odds ratios of reporting one of the above internal or external problems and consequences within the last 12 months for middle and higher educated vs. lower educated people within a meta-analysis framework. Additionally, we used multilevel logistic regression models to account for individuals being nested within countries. Regression models were adjusted for drinking pattern, and we additionally tested whether country-level characteristics were associated with the relation between SES and alcohol related consequences.

Results. More subjects with lower SES report alcohol-related negative consequences compared to respondents with higher SES, even after adjustment for drinking pattern and age. This was more pronounced for external consequences (such as harmful effects on finances, social and family relationships, injuries and fights) than for internal consequences (e.g. dependence). For men external consequences were more prevalent in countries with lower economic power than for men in countries with higher economic power. Other country-level characteristics such as gender gap index and Gini coefficient were not significantly associated with alcohol-related consequences.

Conclusion. The load of alcohol related negative consequences is higher for those from lower SES groups, even if people drink in the same manner in different SES groups. This might reflect a lack of resources potentially helpful in finding ways to avoid negative consequences.

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2.4 Changes in Alcohol Consumption in Denmark during a Time of Increased Availability

Paper 2 and 3 analysed the association between SES and alcohol consumption, using cross-sectional data of more than 20 countries. The following study analysed changes in consumption in Denmark based on cross-sectional and panel data on alcohol consumption over a period of 4 years between 2003 and 2006. During this period, alcohol availability increased due to a lowering in taxes on spirits and an increase in travellers' alcohol import quotas. (Mäkelä et al. 2008).

Paper 4: **Grittner, U**., Gustafsson, N. K., & Bloomfield, K. (2009). Changes in alcohol consumption in Denmark after the tax reduction on spirits. *European Addiction Research*, *15*(4), 216-223. DOI:10.1159/000239415

Aims.

- To test the hypothesis whether there was an increase in alcohol consumption in Denmark over the long-term, and whether younger consumers were especially affected by stronger increases in alcohol consumption, after higher availability of cheaper alcohol.

Data. The data were derived from a national representative survey of the Danish general population. For this study, longitudinal samples and, independently, repeated cross-sectional samples were used. In 2003, 1,771 participants were interviewed. For the panel data, respondents were re-interviewed in 2004, 2005, and 2006. Additional cross-sectional samples were interviewed in 2004, 2005, and 2006 with sample sizes of around 900 participants per wave. We restricted the age range to 16–69 years in order to ensure comparability to the surveys in Finland and Sweden. Cross-sectional data were weighted according to age, sex, and regional distributions in the Danish general population.

Methods. The intervention effect and the univariate linear trend for the panel data were tested based on multilevel models. The different time points formed the lower level, which were nested in the individuals, forming a second level. We used a model

with random intercept and random slope (for time). To analyse changes in consumption in the cross-sectional samples, we used linear regression models with the survey year as an independent variable (Rehm & Arminger 1996). The amount of change in consumption in centilitres of pure alcohol per day was re-calculated from the coefficient for time from the model for log-transformed consumption. The panel data were additionally analysed using multivariable multilevel models. In sensitivity analyses, the same models were applied after multiple imputation for missing values. Additionally alcohol private import levels from last trip abroad were analysed

Results. Despite higher availability after a tax reduction on spirits and an increased import allowance, consumption levels in Denmark did not increase over the study period from 2003 to 2006, but even slightly decreased. Separate analysis for men and women revealed that in men decrease was minor and not statistically significant, while decrease of alcohol consumption in women was more pronounced. For women the interaction of time and age was significant in the panel data, meaning that young women decreased consumption levels more than older women. Results of the analysis of the import levels also show that there was no increase but a decrease for most respondents especially in the last wave.

Conclusion. The finding of no increase in consumption was unexpected, as higher availability of alcohol has often be shown to lead to higher consumption levels. One explanation for this result could be that Denmark, with its high alcohol consumption levels, has already reached a 'saturation' level.

Grittner, U., Gustafsson, N. K., & Bloomfield, K. (2009). Changes in alcohol consumption in Denmark after the tax reduction on spirits. European Addiction Research, 15(4), 216-223. DOI:10.1159/000239415

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2.5 Methods for Missing Value Imputation at the Example of Longitudinal Measures of Alcohol Consumption

Missing data can be a problem in cross-sectional studies, but are especially a point of concern in longitudinal data, where missing data occur due to drop-outs or due to missed interim surveys. This problem is not limited to alcohol research, and might lead to a loss of power and biased results. One strategy to overcome this problem is the imputation of missing values. The study was driven by the surprising observation of decreased alcohol consumption in Denmark and other Northern countries, in the face of increased availability during the study period. Several methods for imputation of missing values were compared, where two main aspects have to be considered: first, the type of the missing data mechanism (missing completely at random (MCAR), missing at random (MAR), missing not at random MNAR)), and second, the general strategy applying single or multiple imputation. As multiple imputation has been shown to be much more reliable than single imputation, we discussed four different multiple imputation methods and used only one flawed strategy of single imputation of last value carried forward for comparison.

Paper 5: Grittner, U., Gmel, G., Ripatti, S., Bloomfield, K., & Wicki, M. (2011). Missing value imputation in longitudinal measures of alcohol consumption. *International journal of methods in psychiatric research*, *20*(1), 50-61. DOI:10.1002/mpr.330

Aims.

- To compare methods of missing value imputation when measuring longitudinally alcohol consumption.
- To evaluate the best method of imputation with a simulation study.
- To analyse how alcohol consumption in Denmark changed from 2003 to 2006, after imputation of missing values.

Data. For this study, we simulated data to assess how induced missing values will be estimated by different imputation methods. Additionally we used data from a Danish national longitudinal alcohol survey including (yearly waves from 2003 to 2006) and 1,771 participants at baseline, and more than 50% missing data at the last wave. The

survey data are part of the "Nordic tax study" (see 1.3.3). Details of the survey were reported elsewhere (Mäkelä et al. 2008, Grittner et al. 2009).

Methods. Five different methods were discussed

1) Last value carried forward (LVCF): It was often criticized for the strong assumption of no change from the last measure to the time point with missing value, which often does not hold (see e.g. Horton & Kleinman 2007, Carpenter et al. 2004). If changes over time are studied, the extent of average change will be underestimated. This method is a single imputation method and therefore does not account for the uncertainty regarding the imputed value.
2) Hot-deck (Siddique & Belin 2008): Random draws from subsets of comparable cases are imputed for missing data. This and all following methods are examples of multiple imputations.
3) Heckman modelling (Heckman 1979): It accounts for missing not at random (MNAR) by estimating the probability of missing dependent on the characteristics of the participants with and without missing values. Imputation of missing values subsequently depends on the probability of missing.
4) Multivariate imputation by chained equations (MICE) (van Buuren & Oudshorn 1999): In this iterative approach, values for imputation will be generated variable wise and regression based, using the other variables as independent variables.
5) Bayesian inference and Markov chain Monte Carlo methods (Lunn et al. 2000): Bayesian inference derives the posterior distribution of the parameters and unobserved (missing) data by using Markov chain Monte Carlo methods. We used non-informative priors.

Missing value imputation was carried out for drinking status (current drinking or abstention during the last 12 months), and volume of pure alcohol on average per day (log-transformed). For the prediction of values, available information on drinking status and volume, as well as frequency of drinking, frequency of RSOD and socio-demographic variables were used. For all methods, except for LVCF, predictive mean matching (Rubin 1987) was used to overcome the problem of back-transformation of log-transformed volume measures.

For the simulation, data of 634 individuals with complete data formed the starting point, where we subsequently created missing values with similar missing patterns as in the original data in this subset.

For all methods, proportion of abstainers (and 95% confidence intervals [CI]), median and mean volume (95%CI) of drinking were calculated. Using the simulated data, the volume of daily alcohol consumption of those with virtually induced missing values were compared to the true values for every method. If the mean difference of daily alcohol volume was lower than 0.6 on the log scale (corresponding to 0.8 grams of pure alcohol per day), the method was classified as precise with regard to reliability of imputations. Additionally we explored whether the bias in estimates after imputation was different in different consumption groups.

Results. The Bayesian approach led to the best estimation of true values according to the simulations, with lowest underestimation of volume measures (0.4 grams lower than the true average). Bias was dependent on consumption level with overestimation for lower levels and underestimation for higher levels for all approaches. The hot-deck approach performed worst with highest overestimation of volume of moderate drinkers (around 5-7 grams of pure alcohol per day) and largest underestimation of high volume drinkers (up to 25 grams per day average underestimation). After imputation and not depending of the imputation method, a decrease in consumption over the four waves was detected, similar as for the complete case analysis.

Conclusion. The Bayesian approach led to the best estimates of missing values. The analysis of the imputed data sets did not change the interpretation of findings of the complete case analysis, meaning that increase of availability of cheaper alcohol in Denmark did not result in higher consumption levels. Overestimation of volume in participants with lower consumption levels and underestimation of volume in those with higher levels might be driven by the heteroscedasticity of consumption levels, where variation in the highest quintile of consumption distribution is much higher than in lower quintiles.

Grittner, U., Gmel, G., Ripatti, S., Bloomfield, K., & Wicki, M. (2011). Missing value imputation in longitudinal measures of alcohol consumption. International Journal of Methods in Psychiatric Research, 20(1), 50-61. DOI:10.1002/mpr.330

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3 DISCUSSION

Several issues have to be taken into account for deriving valid and precise estimates of relationships in public health research. Three of these were discussed in this habilitation treatise, specifically the measurement of SES, the handling of clustered or longitudinal data, as well as the handling of missing data. Methodological considerations on these topics, i.e. on how combined indices like SES indicators could be constructed, how to handle clustered data or missing values, are essential for the analysis and the interpretation of survey data, as well as data from clinical studies. The presented papers offer strategies for handling these problems within the area of alcohol epidemiology, which can however be easily transferred to other areas in public health, epidemiology, or medical research. Important to note is, that how these challenges are faced in specific research areas, has direct implications for results and conclusions of surveys and studies. In chapter 2.1 (Grittner et al. 2006) for example, we have shown that the new empirically derived SES-index for Germany revealed on the second dimension status inconsistencies between income on one side and education and occupation on the other side, which would not have been seen when using a single SES indicator or the Winkler-Index (Winkler & Stolzenberg 1999). This finding was because for some people higher educational achievement was not related to higher income or occupations with higher prestige, or on the other side, because some people with only middle or low education or occupations had high income. Interestingly we could show that alcohol drinking behaviour differentiates not only between groups along the first SES dimension, where education, income and occupational categories are correlated, but also between groups at the second dimension. Here especially those with high income but low educational achievement engage more often in risky drinking patterns than others.

By using forest plots and meta-analytical techniques it was possible to present effect sizes for more than 20 countries at a glance (chapter 2.2 and 2.3). Additionally we combined all country data in a multilevel framework and tested individual and country level characteristics parallel in one regression model (see 2.2 and 2.3, Grittner et al. 2012, Grittner et al. 2013). Therefore in chapter 2.2 it could be shown, that the

association between SES and RSOD is not consistent over the study countries especially for women, and that this association was partly related to economic power of a country: while in most countries with higher economic power, women with lower SES were more often regular RSO drinker, the opposite was true for most countries with lower economic power (Grittner et al. 2013). In chapter 2.3 we showed, that alcohol-related consequences were more prevalent for people with low SES compared to people with higher SES, even after adjustment for individual drinking behaviour within a country. Additionally the analysis revealed that especially for men and alcohol-related external consequences this pattern was also true for country-level SES: in countries with lower economic power more men experienced such consequences compared to men in countries with higher economic power (Grittner et al. 2012).

In chapter 2.4 we analysed alcohol consumption over four years in Denmark using cross-sectional as well as panel data. Our hypothesis was, that consumption will increase due to policy changes (Grittner et al. 2009). However, unexpectedly we found no increase but a slight decrease in alcohol consumption over the four years. Because missing data could be one reason for biased results, we used multiple imputation methods for the panel data to overcome this problem. The result of a slight decrease was confirmed even after multiple imputation of missing values. Since our research group still struggled with this unexpected finding (see e.g. Room et al. 2013), we explored different approaches for handling missing data (Grittner et al. 2011, chapter 2.5 of this treatise) and compared several imputation methods by using simulated data as well as our survey data. These approaches differed with regard to the precision of imputed values, but all approaches lead to the same conclusion of no increase in alcohol consumption in Denmark during 2003 to 2006.

4 SUMMARY

Different methodological challenges in epidemiological studies directed at alcohol research were discussed in this treatise, and strategies to handle these challenges were introduced and explored. First, operationalization of socio-economic status was discussed, and handled in chapter 2.1 by using an empirically derived SES indicator

based on information on education, occupation, and income via using optimal scaling. Second, longitudinal and clustered data on alcohol consumption were analysed in chapters 2.2, 2.3, and 2.4 using multilevel models which account for the clustered data structure, can handle data with missing values better, and allow for testing characteristics on different levels (for example individual level characteristics and country-level characteristics in multinational studies). Third, the problem of how to handle missing values was discussed in chapter 2.5, by comparing different methods of missing value imputation.

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6 APPENDIX

List of Abbreviations

AUDIT	Alcohol Use Disorders Identification Test
CASMIN	Comparative Analysis of Social Mobility in Industrial Nations
GDP	Gross Domestic Product
GEE	Generalised Estimating Equations
GENACIS	Gender, Alcohol and Culture: An International Study
GNI	Gross National Income
ISCED	International Standard Classification of Education
ISCO	International Standard Classification of Occupations
ISEI	International Socio-Economic Index of Occupational Status
LVCF	Last Value Carried Forward
MAR	Missing At Random
MCAR	Missing Completely At Random

MICE	Multivariate Imputation by Chained Equations
MNAR	Missing Not At Random
NIAAA	US National Institute on Alcohol Abuse and Alcoholism
NIH	US National Institutes of Health
PPP	Purchasing Power Parity
RSOD	Risky Single Occasion Drinking
SES	Socio-Economic Status
STAKES	former Finnish National Research and Development Center for Welfare and Health (now THL: National Institute for Health and Welfare)

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Eidesstattliche Erklärung

§ 4 Abs.3 (k) der HabOMed der Charité

Hiermit erkläre ich, dass

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