DOSE-RESPONSE RELATION BETWEEN VOLUME OF DRINKING AND ALCOHOL-RELATED DISEASES IN MALE GENERAL HOSPITAL INPATIENTS

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Abstract — Aims: Previous studies investigating dose-response relations between volume of drinking and diseases have focused on single diseases only. Until now, the relation between the drinking volume and the risk of having any alcohol-attributable disease is largely unknown. The aim of the present study is to investigate to what extent is the risk of diseases with different alcohol-attributable fractions (AAFs) predicted by daily alcohol consumption (>120 g, 61–120 g vs 31–60 g). Methods: The sample consisted of 805 inpatients classified as at-risk drinking, aged 18–64 years bailing from four general hospitals in North-eastern Germany. Inpatients were classified into three groups (AAF = 1, AAF < 1, AAF = 0). Group differences regarding alcohol-related variables, smoking, and demographics were analysed. A multinomial logistic regression analysis was conducted to predict the risk of diseases with AAF = 1 and AAF < 1. Results: In our sample, 26.6% of the inpatients showed a disease with AAF = 1, while 20.2% had a disease with AAF < 1. Inpatients consuming >120 g, and inpatients consuming 61–120 g revealed significantly higher odds for diseases with AAF = 1 compared to inpatients consuming 31–60 g (OR = 6.30, CI = 3.55–11.26; OR = 2.91, CI = 1.64–5.13). Regarding diseases with AAF < 1, inpatients consuming >120 g revealed significantly higher odds compared to the inpatients consuming 31–60 g (OR = 1.97, CI = 1.15–3.37). Conclusions: A dose-response relation between the level of the drinking volume and the risk of diseases with AAF = 1 was found in this sample of inpatients from the general hospitals.

INTRODUCTION

Alcohol consumption has been attributed to more than 60 medical conditions (Rehm et al., 2003a). Although many studies focus on alcohol-related mortality (Britton et al., 2003), little is known about alcohol-related diseases among the consumers who are still alive. In the past, research on alcohol-related health consequences has investigated dose-response relations between alcohol consumption and the risk of specific alcohol-related diseases. For example, a meta-analysis revealed a twofold increased risk of cirrhosis of the liver, a 24–31% increased risk of cancers of the pharynx and larynx, and a 40–70% increased risk of breast cancer for persons with a daily alcohol consumption of approximately 20 g compared to abstainers (Anderson et al., 1993). Another meta-analysis explored the association between alcohol consumption and the risk of 14 major alcohol-related neoplasms, non-neoplastic diseases, and injuries (Corrao et al., 2004). It revealed that the risk of cancer of the oral cavity, esophagus and larynx, hypertension, liver cirrhosis, chronic pancreatitis, as well as injuries and violence, significantly increased with the amount of alcohol consumed starting from a daily consumption of 25 g compared to light consumption.

Alcohol consumption increases the craving for smoking in cigarette smokers and vice versa (Burton and Tiffany, 1997). Synergistic effects between alcohol consumption and tobacco smoking have been reported in several studies. For example, the two habits have a synergistic effect on the risk of oesophageal cancer among moderately exposed individuals (Castellsague et al., 1999).

Diseases may be classified according to their alcohol-attributable fractions (AAFs) into two groups (Rehm et al., 2006b): (i) Diseases wholly attributable to alcohol by definition (AAF = 1), e.g. alcoholic neuropathy and alcoholic gastritis, and (ii) diseases partially attributable to alcohol (AAF < 1), e.g. malignant neoplasms and cardiovascular diseases. AAFs have been defined as the proportion by which disease cases, injury events, or deaths would be reduced if alcohol use and misuse were eliminated among the population (Shultz et al., 1991). Little is known about alcohol-attributable diseases among the general hospital inpatients. In general hospitals, inpatients with alcohol-related diseases seem to constitute a large proportion of the inpatients. In one hospital for example, 21% (29.3% of the men and 9.4% of the women) of the inpatients were found to have an alcohol-related disease (Gerke et al., 1997).

Previous studies on alcohol-related diseases contain several limitations: Firstly, only specific alcohol-related diseases were considered in the single studies (e.g. Anderson et al., 1993). Secondly, data was limited to one general hospital only (e.g. Gerke et al., 1997) or to one special ward, such as emergency rooms (e.g. McDonald et al., 2004). Thirdly, alcohol-related mortality was not as well investigated as alcohol-related morbidity (e.g. Britton and McPherson, 2001; Rehm et al., 2006a). Fourthly, the majority of studies on alcohol-related health consequences were based on older database using ICD-9 coding for medical conditions (e.g. Rehm et al., 2003b). Lastly, the volume of drinking was often categorized using non-evidence-based threshold values (e.g. Boffetta et al., 2006).
To our knowledge, there is no study providing data on alcohol-related diseases in the general hospitals from an entire geographical region encompassing the following conditions: (i) focusing on any alcohol-related diseases; (ii) comprising more than one general hospital and more than one ward; (iii) using ICD-10 coding for disease conditions; and (iv) categorizing alcohol consumption using evidence-based threshold values.

The aim of the present study is to provide data on alcohol-related diseases in a general hospital inpatient population with alcohol-related problems from one region of Germany and to investigate dose-response relations between the volume of drinking and alcohol-attributable diseases.

METHOD
Sample recruitment
Data for this study was collected as part of the intervention study 'Early Intervention in General Hospitals' (NCT 00423904, conducted by the Research Collaboration on Early Substance Use Intervention, EARLINT) between 28 April 2002 and 30 June 2004 at four general hospitals in Mecklenburg-Western Pomerania, Germany. These four hospitals provide medical care for the 198,745 inhabitants in the entire geographical region (Statistisches Landesamt, 2005). A total of 29 wards, including internal medicine, surgical medicine, dermatology, orthopedics as well as ear, nose, and throat units were included. The recruitment is described in more detail elsewhere (Freyer et al., 2007).

All inpatients between 18 and 64 years, with a minimum stay of 24 h were screened using the German Adaptation of the Alcohol Use Disorder Identification Test (AUDIT, Saunders et al., 1993) and the Luebeck Alcohol Screening Test (LAST, Rumpf et al., 1997) with cut-off values of eight and two, respectively. Patients meeting one or both of these cut-off values were considered to be screening positive. A positive screening result was obtained for 2337 inpatients and they were asked to further participate in the study. Those giving informed consent were then assessed using the M-CIDI (B¨uhringer et al., 2002). The number of drinking years was calculated on the basis of the age of the onset of the highest age and its volume percentage. Frequency was assessed using five categories: almost daily, 3–4 times a week, 1–2 times a week, 1–3 times a month, and less than once a month.

Alcohol consumption was assessed using the quantity-frequency questions of the M-CIDI. Quantity was assessed using the standard drinks. Standard drinks were converted into grams of pure alcohol, based on the type of the beverage and its volume percentage. Frequency was assessed using five categories: almost daily, 3–4 times a week, 1–2 times a week, 1–3 times a month, and less than once a month. A quantity-frequency-index was computed using the mean of frequency and alcohol consumption within past 12 months.

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To classify inpatients into three groups of AAFs, all general hospitals provided one routine principal diagnosis and one secondary diagnosis for each inpatient. The diagnoses were based on ICD-10 (World Health Organization, 1992). Hospital diagnoses were missing for 41 inpatients which led to the exclusion of these cases from the final sample (N = 805). Classification of the hospital diagnoses was done according to their relation to alcohol following the approach of Rehm et al. (2006a). ICD-10 codes indicating diseases 100% attributable to alcohol by definition (e.g. alcoholic gastritis), were assigned an AAF of 1. ICD-10 codes indicating diseases partially attributable to alcohol (e.g. esophageal cancer) were assigned an AAF of less than 1 (AAF < 1). Diseases with no causal relation to alcohol or diseases, where alcohol was found to have a preventive effect (e.g. diabetes mellitus) were assigned AAF = 0.

Measures
Alcohol consumption was assessed using the quantity-frequency questions of the M-CIDI. Quantity was assessed using the standard drinks. Standard drinks were converted into grams of pure alcohol, based on the type of the beverage and its volume percentage. Frequency was assessed using five categories: almost daily, 3–4 times a week, 1–2 times a week, 1–3 times a month, and less than once a month. A quantity-frequency-index was computed using the mean of the frequency categories. The mean alcohol consumption was categorized into three groups: >120, 61–120, and 31–60 g (Bühringer et al., 2002). The number of drinking years was calculated on the basis of the age of the onset of the highest lifetime alcohol consumption provided by the M-CIDI.

Smoking status was assessed on the basis of two conditions. First, inpatients were asked whether they had ever smoked about 100 or more cigarettes (yes/no). If so, they were asked ‘Do you currently smoke?’ with four response categories (yes; daily; yes, occasionally; no, for less than 6 months; no, for more than 6 months). Additionally, the mean number of cigarettes smoked per day was obtained.

The following demographics were assessed: age, having one intimate partner, having own children, employment status, and school education.

Data analysis
Descriptive statistics and a multinomial logistic regression analysis were conducted using SPSS 14.0 (SPSS Inc., Chicago, IL). For the effect size estimate we used Cramer’s
RESULTS

Sample description
As depicted in Table 1, 26.6% of the inpatients had a disease with AAF = 1 and 20.2% had a disease with AAF < 1. Among the inpatients, 31.4% consumed >120 g, 34.4% consumed 61–120 g, and 34.2% consumed 31–60 g pure alcohol per day. The rate of the current smokers was 71.8%.

Characteristics of the AAF groups
The three AAF groups differed significantly in terms of alcohol-related variables, smoking, and demographics (Table 2). Compared to inpatients with diseases with AAF < 1 and AAF = 0, inpatients with diseases with AAF = 1 had the highest daily alcohol consumption, the highest proportion of inpatients who consumed >120 g per day and the highest proportion of current smokers. Compared to inpatients with AAF = 0, those with AAF = 1 smoked a higher number of cigarettes per day. Regarding cigarettes smoked per day, inpatients with AAF < 1 did not differ from those with AAF = 0. Inpatients with AAF < 1 were older and had a higher number of drinking years compared to inpatients with AAF = 1, but also compared to inpatients with AAF = 0. In our database, almost all medical conditions according to the classification of Rehm et al. (2006a) were found. Diseases not found in our database include certain forms of cancer (e.g. cancer of the lip), alcoholic cardiomyopathy, and ICD-10 codes starting with X, Y, or Z representing unintentional injuries. Regarding the single disease categories, the mean daily alcohol consumption ranged between 94.26 g (cerebrovascular diseases) and 127.39 g (diabetes mellitus).

Multinomial regression analysis
Inpatients consuming >120 g and inpatients consuming 61–120 g showed higher odds for diseases with AAF = 1 compared to inpatients consuming 31–60 g. Regarding diseases with AAF < 1, inpatients consuming >120 g showed increased odds compared to inpatients consuming 31–60 g (Table 3).

DISCUSSION
The three main findings of the study are: Firstly, 46.8% of all male inpatients admitted to the participating wards, and with a daily alcohol consumption of more than 30 g had a disease attributable to alcohol. Secondly, the data revealed a dose-response relation between the amount of alcohol consumed and the degree of AAF. Thirdly, an extremely high proportion of current smokers was found among the inpatients with alcohol-related problems.

Our findings support data from a different German study which showed that 13.4% of all inpatients of a general hospital were treated because of definitely alcohol-related problems, and 39.1% were treated due to possibly alcohol-attributable diseases (Gerke et al., 1997). However, the study by Gerke et al. (1997) was limited to one hospital and this study suffered from not using international standards for the definition of alcohol-attributable diseases. Results from earlier studies demonstrating a dose-response relation between the volume of drinking and the risk of specific alcohol-related diseases (e.g. Anderson et al., 1995; Bondy et al., 1999; Corrao et al., 1999, 2004) were supported by our study. Our findings reveal that compared to inpatients consuming 31–60 g, the chances of having a disease with AAF = 1 was three times higher for inpatients consuming 61–120 g and six times higher for inpatients consuming >120 g. Moreover, inpatients consuming >120 g were twice as likely to have a disease with AAF < 1 than those inpatients consuming 31–60 g.
DRINKING AND ALCOHOL-RELATED DISEASES

Table 2. Sociodemographic and alcohol-related characteristics of the sample based on groups with different alcohol-attributable fractions of hospital diagnoses

<table>
<thead>
<tr>
<th>Variables</th>
<th>AAF = 1</th>
<th>AAF &lt; 1</th>
<th>AAF = 0</th>
<th>F(χ²) 1 (df)</th>
<th>P</th>
<th>f²/Φ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age M (SD)</td>
<td>214</td>
<td>163</td>
<td>428</td>
<td>12.45 (2)</td>
<td>&lt;0.001</td>
<td>0.18</td>
</tr>
<tr>
<td>Gram alcohol per day (SD)</td>
<td>214</td>
<td>163</td>
<td>428</td>
<td>10.239 (4)</td>
<td>&lt;0.001</td>
<td>0.25</td>
</tr>
<tr>
<td>Daily alcohol consumption (%)</td>
<td>&gt; 120 g</td>
<td>120</td>
<td>120</td>
<td>82</td>
<td>19.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>61–120 g</td>
<td>65</td>
<td>65</td>
<td>158</td>
<td>36.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31–60 g</td>
<td>29</td>
<td>29</td>
<td>188</td>
<td>43.9</td>
<td></td>
</tr>
<tr>
<td>Drinking years M (SD)</td>
<td>212</td>
<td>162</td>
<td>427</td>
<td>8.88 (2)</td>
<td>&lt;0.001</td>
<td>0.14</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td>Current</td>
<td>169</td>
<td>264</td>
<td>41</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>occasionally</td>
<td>10</td>
<td>26</td>
<td>26</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Former</td>
<td>14</td>
<td>95</td>
<td>95</td>
<td>22.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>19</td>
<td>41</td>
<td>41</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Cigarettes per day (SD)</td>
<td>178</td>
<td>103</td>
<td>288</td>
<td>7.08 (2)</td>
<td>&lt;0.001</td>
<td>0.14</td>
</tr>
<tr>
<td>Has intimate partner (%) yes</td>
<td>91</td>
<td>62.6</td>
<td>253</td>
<td>15.91 (2)</td>
<td>&lt;0.001</td>
<td>0.14</td>
</tr>
<tr>
<td>Has own children (%) yes</td>
<td>138</td>
<td>128</td>
<td>281</td>
<td>9.48 (2)</td>
<td>&lt;0.001</td>
<td>0.11</td>
</tr>
<tr>
<td>Employment status (%)</td>
<td>Job-seeking</td>
<td>138</td>
<td>45.3</td>
<td>41</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Full- or half-time</td>
<td>42</td>
<td>25.6</td>
<td>266</td>
<td>39.5</td>
<td></td>
</tr>
<tr>
<td>Others (e.g., retired, housewives)</td>
<td>30</td>
<td>25.6</td>
<td>166</td>
<td>21.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>School education (%)</td>
<td>&lt;10 years</td>
<td>105</td>
<td>40.6</td>
<td>167</td>
<td>39.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10–11 years</td>
<td>92</td>
<td>43.8</td>
<td>190</td>
<td>45.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;11 years</td>
<td>14</td>
<td>15.6</td>
<td>62</td>
<td>14.8</td>
<td></td>
</tr>
</tbody>
</table>

Notes: acontinuous variables, b categorical variables, Φ > 0.071 small effect, Φ > 0.212 medium effect, Φ > 0.354 large effect, f > 0.10 small effect, f > 0.25 medium effect, f > 0.40 large effect. Schefte-Test show AAF = 1 < AAF < 1 < AAF = 0. Schefte-Test show AAF = 1 > AAF < 1 > AAF = 0. Schefte-Test show AAF = 1 > AAF = 0. Due to skewed data, the variable was log transformed for analysis.

Table 3. Multinomial regression analysis (N = 747)

<table>
<thead>
<tr>
<th></th>
<th>AAF = 1</th>
<th>AAF &lt; 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95%)</td>
<td>OR (95%)</td>
</tr>
<tr>
<td>&gt;120 g (SD)</td>
<td>Ref.</td>
<td>6.30</td>
</tr>
<tr>
<td></td>
<td>3.55–11.26</td>
<td>1.97</td>
</tr>
<tr>
<td>61–120 g (SD)</td>
<td>Ref.</td>
<td>2.91</td>
</tr>
<tr>
<td></td>
<td>1.64–5.13</td>
<td>0.95</td>
</tr>
<tr>
<td>31–60 g (SD)</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

Notes: Adjusted for age, intimate partner, children, employment status, school education, number of drinking years, smoking status, and hospital. OR, odds ratio; CI, confidence interval; Ref., reference group or category.

The proportion of current smokers was extremely high in this sample of male inpatients with alcohol-related problems compared to the proportion of current smokers in the general population. This finding is in accordance with extremely high proportions of daily smokers found among persons who are at-risk drinking (John et al., 2003a), and also among alcohol dependent persons (Daepen et al., 2000). Inpatients with AAF = 1 had a higher proportion of current smokers and were heavier smokers than the inpatients with AAF < 1, or AAF = 0. However, inpatients with AAF < 1 and those with AAF = 0 did not differ regarding smoking. Smoking may have added to diseases less than 100% attributable to alcohol, but also to those not attributable to alcohol (e.g. lung cancer). Several studies reported co-occurrence of diseases attributable to alcohol consumption and smoking (e.g. John et al., 2003b). Thus, it might be possible that the inpatients in our sample who are severely affected by diseases resulting from problematic drinking, could also be suffering from a tobacco-attributable disease, e.g. cancers of the trachea, bronchus and lung, or arteriosclerosis.

The present study adds new information on the following aspects: (i) A reduction in the sample selection bias by including four general hospitals representing a variety of wards of a mixed rural and urban region. (ii) Any alcohol-related diseases associated with inpatient hospital treatment in the study region were included. (iii) ICD-10 codes for disease conditions were used. (d) Alcohol consumption was assessed using evidence-based drinking categories.

A few limitations of the study should be considered. Firstly, our analyses are based on the principal diagnosis and on one secondary diagnosis only. As additional secondary diagnoses may be questionable. We cannot rule out that diagnoses were biased because of economic considerations of inpatient care. Thirdly, according to Rehm’s et al. (2006a) classification of diseases attributable to alcohol, the ICD-10 codes starting with X, Y, or Z representing unintentional
injuries did not appear in our database. Instead, unintentional injuries received codes starting with S and T, which were not classified by Rehm et al. (2006a). Thus, unintentional injuries were assigned AAF = 0, which may have led to an underestimation of diseases with AAF < 1. Fourthly, as we recruited inpatients with alcohol problems only, we did not have informed consent to obtain hospital diagnoses of inpatients with moderate alcohol consumption, or from the abstainers. Fifthly, women were excluded from our analyses.

We conclude that alcohol-related diseases are highly prevalent among male general hospital inpatients with alcohol-related problems, and that there is a dose-response relation between the volume of drinking and risk of diseases with AAF = 1.

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