Title page

Who receives treatment for alcohol use disorders in the European Union? A cross-sectional representative study in primary and specialized health care

Running title: Prediction of treatment for alcohol use disorders

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Abstract

Background Alcohol use disorders (AUDs) are highly prevalent in Europe, but only a minority of those affected receive treatment. It is therefore important to identify factors that predict treatment in order to reframe strategies aimed at improving treatment rates.

Methods Representative cross-sectional study with patients aged 18-64 from primary health care (PC, six European countries, N=8,476, data collection 01/13 – 01/14) and from specialized health care (SC, eight European countries, N=1,762, data collection 01/13 – 03/14). For descriptive purposes six groups were distinguished, based on type of DSM-IV AUD and treatment setting. Treatment status (yes/no) for any treatment (model 1), and for SC treatment (model 2) were main outcome measures in logistic regression models.

Results AUDs were prevalent in PC (12-month prevalence: 11.8%; 95% confidence interval (CI):11.2-12.5%), with 17.6% receiving current treatment (95% CI: 15.3-19.9%). There were clear differences between the six groups regarding key variables from all five predictor domains.
Prediction of any treatment (model 1) or SC treatment (model 2) was successful with high overall accuracy (both models: 95%), sufficient sensitivity (model 1: 79%/ model 2: 76%) and high specificity (both models: 98%). The most predictive single variables were daily drinking level, anxiety, severity of mental distress, and number of inpatient nights during the last 6 months.

Conclusions Variables from four domains were highly predictive in identifying treatment for AUD, with SC treatment groups showing very high levels of social disintegration, drinking, comorbidity and functional losses. Earlier intervention and formal treatment for AUD in PC should be implemented to reduce these high levels of adverse outcomes.

Key words Alcohol use disorder, Alcohol dependence, Treatment, Specialized care, Primary care, Europe

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1. Introduction

Treatment of alcohol use disorders (AUDs) is one of the biggest challenges for mental health. On the one hand, AUDs are among the most prevalent mental disorders in the European Union (EU) with an estimated 23 million people affected in 2010 [1, 2], with high associated disability [3, 4] and standardized mortality ratios (SMR; a ratio quantifying the increase or decrease in mortality of a specific group – people with AUD in treatment – compared to the general population of same sex and age [5]) around 10 for young adults [6]. Overall, AUDs have the second highest burden of disease of all mental disorders after depression, the highest in men [1]. On the other hand, treatment rates have been low – in fact the lowest of all major mental disorders [7] – with about 10% in Europe during the past decade [8-10].

Different explanations for the low treatment rate for AUDs have been brought forward. Based on a large-scale study by the World Health Organization, Üstün and Sartorius [11] claimed that primary care physicians (GPs) do not recognize mental disorders, and therefore neither treat nor refer them to specialized health care (SC). Stigmatization of AUDs may be another reason for the low treatment rate, as it was found to be higher than stigmatization for other mental disorders in general population studies [12], and may be a barrier for people affected to enter treatment [13-15]. A third main reason concerns the perceived need of medical treatment by affected people, who may prefer to deal with the problem by themselves [16, 17], and may only seek help if they "hit bottom" [18, 19]. Even EU treatment systems with their reliance on SC predominently for severely affected people [20] seem to reflect similar thinking. In this sense, the low treatment rate could be explained as a continuum of severity of AUDs, where only the most problematic forms (i.e., severe alcohol dependence (AD) according to ICD-10 [21] or DSM-IV [22], or AUDs above a certain criteria threshold in DSM 5 [23]) are seen in need of formal treatment, whereas the less severe forms would take care of themselves by natural recovery/auto-remission [24, 25]. Severity could be in part characterized by comorbidity (both somatic and mental;

[26-30]), functionality losses (for the impact of functionality limitations on treatment seeking see [30-32]), or social disintegration [19, 28].

Two recent large-scale representative epidemiological samples in primary and specialized health care in six and eight EU countries, respectively, offered a unique opportunity to further investigate AUDs and treatment pathways, for the primary health care sample and for the specialized health care sample). First, it was established that GPs could identify AD and AUD with the exception of younger cases [33], thus not corroborating the first explanation above. Second, we wanted to examine the role of social disintegration, drinking behaviour, co-morbidities and functionality in receiving treatment. The main hypothesis tested predictability of any or SC treatment with indicators from these predictor classes.

2. Methods

2.1. Sampling procedures

Both study samples were cross-sectional: first, we sampled 8,476 primary health care (PC) patients from 358 GPs across six European countries (patient response rate: 82.2%; GP response rate: 43.6%) between January 2013 and January 2014 (see also [34, 35]. Representativeness was achieved regionally in countries with more than 40 million inhabitants (Germany: Saxony and Berlin, Italy: Friuli-Venezia Giulia and Tuscany, Poland: Łódź and Podkarpackie provinces, Spain: Catalonia), and nationally in smaller countries (Hungary, Latvia). Second, 1,767 patients from various SC settings were sampled across eight European countries between January 2013 and March 2014 (patient response rate: 82.73%; institutional response rate: 62.5%; see Web Table 1 for an overview; see [36] for details). Patients receiving SC for AUDs were recruited from the same regions and countries of the PC sample with the exception of Poland (provinces: Pomorskie, Warmińsko-Mazurskie, Dolnośląskie, Podlaskie, Podkarpackie,

Małopolskie); Austria (one region Carinthia) and France (whole country) were added. Both samples were restricted to patients aged 18-64.

Selection of PC patients was carried out randomly on one day or consecutive days. GPs filled in a short questionnaire about all patients for the next day if prior appointment was made or on the same day if GP visits were mostly spontaneous. For the patient interview, we contacted all patients in Hungary and Spain and drew subsamples of those being assessed by their GP in all remaining countries, with different probabilities based on GP's answers about alcohol consumption and problems (undersampling abstainers, oversampling AUD cases). Most SC patients were also selected by presence on a given day. In Poland, admission to the SC facility in a given time period comprised study participation.

2.2. Instruments

In addition to socio-demographic assessment including measures of social disintegration [37] (unemployment, not being married, low socio-economic status (SES)), we assessed somatic (hypertension, liver problems) and mental comorbidity (anxiety, depression) both via GP (PC sample only) and interview. We used the Composite International Diagnostic Interview [38] to establish 12-month diagnoses of AUDs according to the DSM-IV [22] and DSM-5 [23]; and to assess current drinking levels. Further, the Kessler Psychological Distress Scale (K10 [39]) determined the extent of experienced mental distress, and the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0 [40, 41]) assessed the degree of functionality losses in different life domains. Custom-made items were applied to gain information on current or lifetime treatments; and on somatic and mental co-morbidities of SC patients. All patient interviews were conducted after written consent was given. Compensation for being interviewed was offered in some countries.

Independently from and in addition to the patient interview, all PC patients were assessed by their treating GPs using a brief form. The form comprised questions on socio-demographics, general health

and assessed past and current alcohol use and alcohol-related problems and possible treatment of the patient as perceived by the GP.

One of the main outcome variable in this study – treatment access by PC patients – was derived by a combination of GP assessment and patient interview. GPs provided very basic treatment information (distinguishing only between psychosocial and/or pharmacological AD interventions), whereas the patients themselves disclosed more details about the type of treatment received (e.g. counselling, pharmacotherapy) and the kind of health professional involved (e.g. GP, psychotherapist, psychiatrist). Our definition of professional treatment included group therapies led by health professionals, but excluded mere social support (e.g. from family, friends) or interventions from non-health professionals such as herbalists and priests.

Patients from the SC sample received a variety of interventions – depending on the type of setting they were recruited from. Most patients were treated in inpatient clinics (53.6%), followed by outpatient centers (32.8%). The remaining patients received interventions by GPs, psychiatrists or were in self-help groups. Large country-specific differences regarding treatment settings were prevalent, for more details, see Rehm et al., 2015[36].

For descriptive purposes, the following six exclusive subgroups were created: PC patients without AUD; alcohol abuse (AA; without concurrent AD) in PC without treatment; AD in PC without treatment; AUD in PC with treatment (mainly for AD); AUD in SC with at most 3 DSM-5 criteria; and AUD in SC with at least 4 DSM-5 criteria. All AUD diagnoses (AD, AA) were determined by GP and/or CIDI in the PC sample, while the SC patients' were diagnosed with CIDI only.

We have excluded current abstainers or very light drinkers from the five groups with AUD in analyses concerning alcohol measures, as they did not reflect the original drinking level associated with AUDs. In

total, 336 women (39.9%) and 461 men (22.7%) were excluded due to less than 10g daily alcohol use or missing values in this variable.

2.3. Statistical Analysis

Descriptive analyses on means, proportions and their uncertainty were carried out for Tables 1, 2 and 3 and for Web Tables 2 and 3. For linear trends reported, we carried out sex-specific linear and logistic regressions, for continuous and dichotomous outcomes respectively, including age and country as further predictors. Linear trends were carried out as we hypothesized increasing levels of problems with increasing severity of AUDs.

Two different models (1a and 2a) to predict treatment included sociodemographic variables (age, sex, country); indicators for social disintegration (unemployment, marriage/cohabitating status, low SES), somatic comorbidity (liver problems), mental comorbidities (depression, anxiety, mental distress), functionality losses (disability days, inpatient nights) and alcohol consumption patterns (daily ethanol intake) as independent variables in logistic regressions. The first model predicted any treatment, i.e. all cases in AUD treatment (one PC group and both SC groups) vs. untreated cases and patients without AUD, while the second model predicted SC treatment only (see Web Table 4 and 5). Both models excluded current abstainers and very light drinkers but included also cases from countries where only SC samples were assessed (Austria and France). Subsequently, the strongest predictor of each domain (social disintegration, mental and somatic comorbidity, functionality loss, and alcohol) was determined in each model (via largest effect size) and entered into two additional models, predicting the same outcome (1b: any treatment; 2b: specialized treatment). In order to test for heterogeneity on the identified predictors between the included countries, we ran the same logits for each country separately and entered the log odds of each independent variable of the five domains into respective meta analyses. The resulting forest plots are included in the Web Appendix (Web Figures 1-10) and report I^2 as the measure of heterogeneity [42]. The same procedure was repeated separately by sex.

All analyses took sampling design into consideration and were conducted with STATA 12.0 [43]. More detailed information on sampling techniques and other methodological aspects are published elsewhere [33, 35]. Ethical approval was obtained in all countries.

3. Results

3.1. Prevalence of AUD and proportion receiving treatment

Prevalence of AUD was high (overall 12-month prevalence: 11.8%, 95% confidence interval (CI): 11.2-12.5%; men 19.9%, 95% CI: 18.6-21.2%; women 6.5%, 95% CI: 5.8-7.1%; for details see Table 1), with AD being the more prevalent disease. Current treatment rates were low (overall 17.6%, 95% CI: 15.3-19.9%; men 19.1%, 95% CI: 16.2-22.1%; women 14.5%, 95% CI: 10.7-18.2%), with even lower rates for lifetime treatment before the current episode indicating that for many patients this was the first treatment episode.

- Insert **Table 1** about here -

3.2. Socio-demographic indicators

Web Table 2a and 2b give the most important socio-demographic indicators for women and men, respectively. Social disintegration was related to the diagnostic and treatment status: the indicators of marriage, unemployment, and SES below average show clear trends that differentiate people between the six groups with SC showing the highest rate of disintegration. For age, no clear trend emerged, but AUD cases in treatment were older (46.5 years, standard deviation (SD): 10.2 years) than their counterparts not in treatment (42.8 years, SD: 14.6 years; Scheffé test: $t=6.94$, $p<.001$)

3.3. Alcohol consumption and related measures

In Table 2, alcohol consumption measures are presented across all subgroups. Linear trends were observable for all measures, i.e. with SC treatment samples showing the highest level of drinking, followed by patients in PC in AUD treatment, untreated AD cases, untreated AA cases, and PC patients without AUD showing the lowest level of drinking. To give one example about the spread: chronic heavy

drinking patterns (at least 100g alcohol daily) were present in more than every second SC patient with at least four DSM-5 AUD criteria (57.6%, 95% CI: 54.6-60.6%;), compared to 0.3% (95% CI: 0.2-0.5%) in the general population without AUD. The former group consistently showed the highest values in all alcohol measures.

- Insert **Table 2** about here -

3.4. Somatic and mental comorbidity

For both somatic and mental comorbidity we see a gradient for the groups examined. For somatic comorbidity, this is true for hypertension and liver problems, but with some unexpected results for SC (Table 3). In interpreting these results, the different sources should be taken into consideration: SC results were self-reports, whereas the results for PC were based on GP judgement.

For mental comorbidity, i.e., depression, anxiety and severe mental distress, as measured with K10 (see Table 3), the gradient was significant but less pronounced compared to drinking indicators. As an example, take the K10 summary measure: the respective proportions with marked mental distress, as defined by reaching the threshold of 21 points on a scale ranging 0-40 (for the threshold: [44]), rose from 5.2% (95% CI: 4.7-5.7%) among the PC patients without AUD to 42.4% (95% CI: 39.6-45.2%) among the most severe patients receiving SC.

- Insert **Table 3** about here -

3.5. Functionality losses

The degree of functionality losses, as measured by the extent of disability in various life domains, also increased along the groups defined (see Web Table 3 and Figure 1). On average, PC patients (general population) could not carry out usual activities on 1.3 days (SD: 4.6 days) within the past month due to any health condition, compared to the most severely affected SC patients with 4.9 days (SD: 8.1 days) in

the same time period; the other groups were in between. Similar differences between groups were reported for number of inpatient nights during the past six months.

- Insert **Figure 1** about here -

3.6. Identification and treatment seeking

Overall, the six groups almost looked like distinct samples, which could be separated based on the covariates presented. Specifically, treatment status (any vs. no treatment) was correctly predicted of 95.5% of the cases, with a sensitivity of 70.0% and a specificity of 98.4% (positive predictive value: 89.6%; for terminology see [45], see Model 1a, Web Table 4). Inserting the regression weights for members of the other groups did result in the following proportions: primary care patients without AUD: 0.6%; AA without treatment: 5.4%, AD without treatment: 20.4%; AUD in treatment (PC sample): 54.4%; SC sample with at most 3 AUD criteria: 70.3%; SC sample with at least 4 AUD criteria: 86.5% (see Web Table 4). In other words, only 121 additional people of all the persons not in treatment (representing 1.6% of the sample N=7,614) would have qualified for treatment based on this statistical prediction model.

The indicators described above could similarly predict SC treatment vs. all other groups in 95.3% of the cases, with a sensitivity of 76.5%, a specificity of 98.2%, and a positive predictive value of 87.1% (see Model 2a, Web Table 4). Moreover, in the full PC sample excluding non-abstinent patients from the AUD groups, only 137 out of 7,730 would have qualified for SC based on the predictors chosen (1.8%) and most of these (N=76, 55.5%) were identified by the GP as AD.

Strongest predictors (see Web Table 5) in both models were mean daily ethanol intake, anxiety, severe mental distress as measured by K10, number of inpatient nights and sex. We did additional models with one predictor for each of the theoretically hypothesized predictor classes (social disintegration, drinking patterns, somatic comorbidity, mental comorbidity, functionality losses) and could predict almost the

same proportion with treatment status correctly with a much simpler model (see Models 1b and 2b, Web Table 4 and 5).

For the country-specific models (Web Figures 1-30), we found that the effect sizes of indicators of social disintegration (model 1b: unemployment, model 2b: unmarried), somatic comorbidity and inpatient nights (only in model 1b) were homogeneous across the different countries. For the remaining indicators, a more heterogeneous picture between countries was found. The indicator of mental comorbidity (anxiety) was identified as significant predictor in four out of five countries, with varying effect sizes (ORs ranging from 4.09 to 21.44), but not so in Germany. For drinking patterns, statistical heterogeneity was found for both models but all indicators were significant across all observed countries with ORs ranging between 1.03 and 1.09.

The distribution of heterogeneity across the different indicators and countries was similar when separated by sex. The most striking exception to this observation was identified in Hungarian females where being married had a contrary effect compared to patients of the same sex from other countries (OR=0.34, 95% CI: 0.13-0.93). Further, we observed that heterogeneity was more prevalent in females than in males, for instance in liver problems (only among females in model 1b) and inpatient nights only among females in both models). In total, the results can be seen as showing high homogeneity, even though for some indicators the effect sizes varied.

4. Discussion

AUDs were highly prevalent, but only a small proportion received current treatment. We were able to show a marked gradient for all the covariates examined for patients with different severity of AUD, with SC patients showing the highest level of problems. Given this situation, it was not surprising that treatment status could be predicted with high sensitivity and specificity, and relatively homogeneous

across countries. Before we discuss the implications of our research, we would like to discuss limitations.

4.1. Limitations

While both samples were based on representative register-based sampling, more than 55% of all GPs and 37.5[1]% SC settings selected refused participation. This is not surprising given the busy schedule of PC physicians and SC facilities, but we cannot exclude that selected facilities not participating had different characteristics (for general considerations of selection bias see [46]). In light of other GP studies with probabilistic sampling techniques from regional rosters involving personal assessments, our response rate can, however, be considered satisfactorily [47, 48]. This is even more so for the response rate of SC facilities selected. The individual level response rate (i.e., response rate for patients selected) was higher than in current European surveys [49] or in other patients' surveys [50].

Many of our findings are based on self-report and interviews, and the potential bias resulting, while being found relatively low for the standardized instruments used ([41, 51-54]), can never be excluded. However, for hypertension and somatic comorbidity in general, self-reports may be underestimating the true prevalence (e.g., for hypertension see [55]), which could explain the relative low prevalence in SC. The biggest limitation of this study is the cross-sectional nature, which does not allow conclusions about causality [56]. Clearly, longitudinal designs should be used to corroborate key results and conclusions of this study.

Finally, the differences between SC and treatment at PC levels may be underestimated, as some people who were identified in PC levels may have actually had their reported treatment in SC.

4.2. .Discussion of key results

AUDs were quite prevalent in PC, above twice as high compared to general population surveys [1, 2, 57]. We confirmed that only a minority of people with AUD received treatment, even though our numbers

were higher than the numbers previously reported in the literature [8, 10]. The higher treatment rate in our study may be due to two reasons: contrary to other studies, we assessed treatment status both via GP and via patient, whereas other studies were based on one measurement, only. In particular, it may be, that the GPs included interventions defined based on simple questions or advice about the drinking and control as "treatment" (see [58], for the situation in Germany). Secondly, we had a very wide definition of treatment, including interventions of all health care professionals. Thus, before concluding, that the treatment rate for AUD improved, more detailed studies are necessary.

We could further confirm that receiving treatment was highly predicted by variables from four categories: social disintegration, alcohol consumption levels, somatic and mental co-morbidities, and functionality, which correctly classified almost 96% of all participants' overall treatment status; furthermore, 79% in treatment and 76% of people in SC were correctly predicted. In other words, people with very severe AUD were referred to treatment in general, and to SC treatment in particular, based on these four classes of predictors. But are the algorithms underlying these referrals by GPs, or by the patients themselves, the best possible for the treatment system? The best predictive power could be found for average alcohol consumption and anxiety; these indicators had a very high level in SC patients with an average daily drinking level of 141.1g (95% CI: 135.1-147.0g) and a prevalence of anxiety of 50.3% (95% CI: 47.8-52.9%). It may be questioned if these values do not indicate that treatment in general and SC treatment in particular started too late. The same question arises when the very high proportions of liver problems, depression or losses in functionality are considered.

Even though moralistic approaches to AD tend to consider that patients need to "hit bottom" before they can start a recovery process, early detection of alcohol use/problems has been shown as an important step towards prevention of somatic and psychiatric consequences of chronic alcohol consumption. Early treatment is essential for prevention of alcohol liver disease including liver cirrhosis

as well as for effective treatment of comorbid affective disorders (for example see [59, 60]). However, the data seem to indicate that most treatment at the PC and SC level in Europe is delivered to people with a high level of existing comorbidity.

Consider the following: of all people in AUD treatment, based on the most comprehensive meta-analysis to date, the SMR is 3.38 (95% CI: 2.98-3.84) for men and 4.57 (95% CI: 2.72-7.65) for women [6]. From a public health concern, even more important is the age gradient in SMR in both sexes, in men ranging from over 9-fold for the under 30 year olds to about 2-fold for the over 60 year olds, and in women ranging from almost 14-fold to 3-fold in the same age groups. Based on another meta-analysis, these mortality risks could be considerably reduced, if volume of alcohol consumption were reduced, to about 35% (95% CI: 20-60%) for those who reached abstention and to 61% (95% CI: 39-94%) for those who did not reach abstention but substantially reduced their consumption [61, 62]. In other words: if people with AUD would receive interventions effective in reducing alcohol consumption, a substantial proportion of the mortality associated with AUD could be reduced [9].

4.3. Conclusions

AUDs are prevalent and are associated with high comorbidity and mortality. The data indicate that there may be a non-structured stepped care approach based on drinking level and associated harm. Hence treatment reaches patients after a lot of alcohol-attributable harm has already occurred. To avoid this harm, treatment should be offered much sooner, and GPs need to be thoroughly involved. They have an outstanding role in this by identifying patients at an early stage of AD, before health is more seriously compromised. Many early stage AD (Spithoff & Kahan, 2015), as well as early stage anxiety (Culpepper, 2002), depression (Linde et al., 2015) or hypertension can be treated at the PC level (Alexander, 1998). If not willing to treat by themselves, GPs should refer to SC. A revision of the existing epidemiological models should also be proposed to include PC-centered-analyses in national datasets in addition to the current practice of general population surveys (Manthey et al., in press = current 35).

Moreover, the link between social disintegration and AUD indicates the importance of determinants of health and the importance of an integrated, public health-led, systemic approach [63, 64].

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Contributors

JR, AG and MW conceptualized the APC study and served as PI. All authors except JM and JR served as site PIs and organized and supervised fieldwork, and helped in data cleaning. JM and JR conceptualized the data analyses, helped in data cleaning and quality control, and conducted the quantitative data analyses. JR wrote JR wrote a first draft of the paper, and all authors contributed to and approved of the final version.

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