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Alcohol Dependence, Co-occurring Conditions and Attributable Burden

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Abstract

Aims: Alcohol dependence is associated with high rates of co-occurring disorders which impact health-related quality of life (HRQoL) and add to the cost-of-illness. This study investigated the burden of alcohol dependence and associated co-occurring conditions on health and productivity.

Methods: A cross-sectional survey was conducted in eight European countries. Physicians (Psychiatrists and General Practitioners) completed patient record forms, which included assessment of co-occurring conditions, and patients completed matching self-completion forms. Drinking risk level (DRL) was calculated and the relationship between DRL, co-occurring conditions, work productivity, hospitalisations and rehabilitation stays was explored.

Results: Data were collected for 2979 alcohol-dependent patients (mean age 48.8 ± 13.6 years; 70% male). In total, 77% of patients suffered from moderate-to-severe co-occurring psychiatric and/or somatic conditions. High DRL was significantly associated with depression, greater work productivity losses, increased hospitalisations and rehabilitation stays. Co-occurring conditions were significantly associated with poorer HRQoL and decreased work productivity, with a statistical trend towards an increased frequency of rehabilitation stays.

Conclusions: Alcohol-dependent patients manifest high rates of co-occurring psychiatric and somatic conditions, which are associated with impaired work productivity and HRQoL. The continued burden of illness observed in these already-diagnosed patients suggests an unmet need in both primary and secondary care.

INTRODUCTION

According to the World Health Organization (WHO), Europe is the heaviest drinking region in the world (World Health Organization, 2014), with more than 11 million people in the age group 18–64 being alcohol dependent in the EU alone (Rehm *et al.*, 2015b). Alcohol consumption imposes a significant burden on the overall public health of Europe (World Health Organization, 2012; Shield *et al.*, 2012). Alcohol is a causal factor for >200 different types of diseases and conditions as defined in ICD-10, including injuries, mental and behavioural disorders, cancers and cardiovascular diseases (Rehm *et al.*, 2010). In Europe alone, this burden of mortality and disease associated with alcohol consumption has been estimated at over €155 billion per year (Rehm *et al.*, 2012).

For most alcohol-related conditions, alcohol increases the risk of experiencing these consequences in a dose-dependent manner, with higher alcohol consumption corresponding to a greater risk (Anderson and Baumberg, 2006; Rehm *et al.*, 2010; Nutt and Rehm, 2014). The differing levels of risk related to alcohol consumption are reflected in

the WHO criteria of risk of acute problems, which specifies definitions for low, medium, high and very high drinking risk levels (DRLs) (World Health Organization, 2000). In alcohol use disorders, and in particular alcohol dependence, the risk of experiencing consequences from alcohol use is significantly increased due to high levels of consumption (Hasin *et al.*, 2007). In fact, a high preponderance of co-occurring somatic and psychiatric conditions is the norm, rather than the exception in alcohol dependence where up to two-thirds of individuals will have a lifetime co-occurring disorder (Regier *et al.*, 1990; Davidson and Ritson, 1993; Schuckit *et al.*, 1997; Hasin *et al.*, 2007). Diminished social, occupational and psychological functioning are also common (Samokhvalov *et al.*, 2010), as are poor health-related quality of life (HRQoL) (Foster *et al.*, 1999; Rehm *et al.*, 2014), an increased risk of premature mortality (Roerecke and Rehm, 2013), and work-related problems (Leggat and Smith, 2009; Bacharach *et al.*, 2010; World Health Organization, 2011).

Studies have shown that absenteeism is two to three times higher for employees with drug and alcohol problems than for other employees (Leggat and Smith, 2009) and that the frequency of heavy episodic drinking is positively correlated with the number of absent days recorded (Bacharach *et al.*, 2010), which is not surprising given that alcohol dependence is characterized by heavy episodic drinking. Furthermore, a Spanish study indicated a causal relationship between increased alcohol consumption, morbidity and hospitalisations (Gual *et al.*, 1999), while in the USA, a large survey reported that alcohol dependence was significantly associated with multiple physical and psychological disorders (Hasin *et al.*, 2007). Such problems are costly, both to the individual and society: Hospitalisations are the main driver of direct costs of alcohol dependence in Europe, which are estimated at €24 billion annually (Olesen *et al.*, 2012), and although data specific to alcohol dependence and productivity are scarce, a review of national costing studies in Europe estimates that lost productivity due to alcohol-attributable absenteeism and unemployment costs €9–€19 billion and €6–€23 billion, respectively (Anderson and Baumberg, 2006), with overall indirect costs of alcohol dependence estimated at €38 billion (Olesen *et al.*, 2012).

Despite the high rate of co-occurrence between alcohol dependence and somatic and psychiatric conditions, questions remain regarding if co-occurring conditions in alcohol dependence are associated with more hospitalisations and occupational difficulties. As such, and in addition to examining the profiles of alcohol-dependent patients with co-occurring somatic and psychiatric conditions, this study sought to examine the potential association between the experience of co-occurring conditions, high risk drinking, and impact on work life and hospitalisations in the largest (to the authors' knowledge), multi-national European sample of alcohol-dependent patients conducted to date.

MATERIALS AND METHODS

Study design

A large multinational, cross-sectional survey was conducted amongst treating physicians and their consulting patients, collecting both qualitative and quantitative data from eight European countries (Czech Republic, Denmark, Finland, Greece, Ireland, Portugal, Slovenia and Switzerland) from June 2013 to January 2014.

Physician and patient recruitment criteria

A convenience sample of 368 physicians actively involved in the care of patients with alcohol dependence was identified from public lists of healthcare professionals by local fieldwork teams. Physicians were screened against predefined inclusion criteria: either psychiatrists or primary care physicians (PCPs), with 2–40 years of experience, and could be hospital-based, office-based, or both. Specialists were required to see a minimum of 15 patients with any condition per week, and PCPs were required to see at least 40. No required minimum was stipulated for the number of alcohol-dependent patients seen. Each physician included up to a maximum of 10 consecutive patients consulting with a current diagnosis of alcohol dependence. No other patient selection criteria were applied.

Assessments

Physicians completed patient record forms (PRFs) detailing the patient's demographics, disease symptoms and severity, patient-management strategies, treatment history and reasons for treatment decisions. These patients were then invited to answer a self-report questionnaire (patient self-completion [PSC]) related to their symptoms, expectations and health status. Patients who gave informed consent completed the PSC forms voluntarily and independently of their physician immediately after consultation and returned it in a sealed envelope. All responses were anonymized to preserve patient confidentiality and to avoid bias during data collection and analysis. Of 2979 patients for whom a PRF was completed, 1808 matching PSCs were collected.

The Alcohol Use Disorders Identification Test (AUDIT), a 10-item self-reported screening tool, was included within the study (Babor *et al.*, 2001). The AUDIT was developed by the WHO as a simple screening tool to detect the early signs of hazardous and harmful drinking and identify probable alcohol dependence (Saunders *et al.*, 1993a,b). Given that patients in this study had already received a diagnosis of alcohol dependence, the WHO DRLs were considered the most appropriate method for classifying disease severity in the present analyses (see 'statistical analysis' section for details of how the DRLs were defined).

PSCs also included validated patient-reported outcome (PRO) instruments, including the EuroQol-5 dimensions-5 level (EQ-5D-5L), Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) and the Work Productivity and Activity Impairment Questionnaire (WPAI). The EQ-5D-5L is a standardized measure of health status which provides a simple, generic measure of health (EuroQol, 2013). This short questionnaire was chosen to limit the burden of the overall study to the participants (given the other information that was being collected as part of this study) and also because it has been used extensively in quality of life research (EuroQol, 2013) as well as to support product reimbursement across Europe. The EQ-5D descriptive system assesses impact of disease on mobility, self-care and usual activities, as well as levels of pain/discomfort and anxiety/depression, with responses scored on a five-point scale (with a higher score indicating better quality of life). The EQ visual analogue scale (EQ VAS) records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints (on a scale of 0–100) are labelled 'Best imaginable health state' (score: 100) and 'Worst imaginable health state' (score: 0) (EuroQol, 2013).

The Q-LES-Q-SF is a generic measure designed to detect enjoyment and satisfaction in various areas of daily functioning (Endicott *et al.*, 1993). The Q-LES-Q-SF is a 16-item tool that evaluates overall physical health, mood, work, household and leisure activities, social and family relationships, daily functioning, sexual life, economic status, overall well-being and medications. Responses are scored on a five-point scale ('not at all or never' to 'frequently or all the time'), with higher scores indicating greater life enjoyment and satisfaction (Stevanovic, 2011).

The WPAI is a generic, six-item tool validated for the measurement of impairment in work and daily activities (Reilly *et al.*, 1993). The WPAI evaluates employment status, absenteeism from work, impairment while at work and impairment in regular daily activities. Respondents estimate the number of hours worked and the number of hours missed from work for health reasons during the last 7 days. The extent to which health problems affect respondents' work and daily activities is also recorded using a ten-point scale (Reilly *et al.*, 1993).

The survey was performed according to the regulations and practice of the market research governing bodies the European Society for Opinion and Marketing Research (ESOMAR) and European Pharmaceutical Market Research Association (EphMRA) (European Society for Opinion and Market Research, 2007; European Pharmaceutical Market Research Association, 2014). Local regulations were also adhered to, where appropriate. In Slovenia, study materials were reviewed and approved by an independent Slovenian research ethics committee (National Medical Ethics Committee, 22/08/13).

Statistical analysis

Data were aggregated and analysed at a European level. Data from individual patients were not reported. Where there were missing values for particular variables, analysis was performed on only the patients who answered. Patients were classified based on the presence of co-occurring moderate-to-severe conditions (to capture conditions that had a meaningful impact on patients) as reported by the physician: psychiatric only, if they had a minimum of one psychiatric condition and no somatic condition ($n = 343$); somatic only if they had a minimum of one somatic condition and no psychiatric conditions ($n = 182$); and somatic and psychiatric if they possessed at least one psychiatric and one somatic condition ($n = 494$). A fourth category encompassed patients in whom co-occurring conditions were absent or mild in severity ($n = 277$). Only patients with both PRF and PSC data were included within each group to enable analysis of variables from both sources. Since the current paper sought to examine associations between continued drinking in alcohol dependence and a number of health and psychosocial variables, patients who screened as currently abstinent in either the PSC or AUDIT were excluded from the analysis.

An analysis was performed to identify those patients with a 'high drinking risk level' (HDRL; including those in the 'high' and 'very high' WHO groups), medium risk and low risk drinking level (defined in the WHO guidelines (World Health Organization, 2000)), using answers to question two of the country-specific AUDIT questionnaire. While the AUDIT assumes that a standard drink is equivalent to 10 mg of alcohol, adjustments were made to account for country-specific variations, where necessary.

Chi-squared tests were used for categorical variables; ANOVA was performed to identify any differences between groups. Additionally, regression analysis (linear, negative binomial, logistic and ordered logistic) was used to model the relationship between co-occurring condition groupings and the result of each of the PRO instruments, frequency of hospital visits or rehabilitation stays, work productivity, and DRL. Regression analyses adjusted for age, gender, and time since diagnosis and treatment status.

RESULTS

Across all eight countries, a total of 2979 PRFs were collected, with 1660 for whom DRL was assessed (Table 1). DRL was available only for this number of patients due to the voluntary nature of completion of this form.

Patient demographics and clinical characteristics

As noted in Table 1, the average age of the sample was 48.8 ± 13.6 years, 69.7% were male, and 29.6% were unemployed. The average AUDIT score across patients was 20.3. Examining current drinking behaviours according to the WHO drinking risk levels, over one-third of patients (33.8%) were currently drinking at a high DRL.

Patients who completed a PSC (including providing information on their drinking levels) and who were not abstinent ($n = 1373$) did not differ significantly in descriptive patient population demographics from the overall PRF population ($n = 2979$): there were no significant differences in descriptive patient population demographics such as age or gender across countries (Table 1).

Associations between co-occurring conditions and clinical factors

The experience of moderate to severe co-occurring conditions was common in the alcohol-dependent population. Overall, 77% of the alcohol-dependent population suffered from at least one co-occurring moderate to severe condition. The most common co-occurring conditions included anxiety disorders (47.7%), sleep disorders (43.7%), depression (43.1%), hepatological problems (38.4%) and gastrointestinal issues (32.2%). Overall, it was found that 37% of patients ($n = 510$) had both somatic and psychiatric co-occurring conditions, 27% had psychiatric conditions ($n = 373$) only and 13% experienced co-occurring somatic conditions only ($n = 177$). In the remaining 23% of patients, co-occurring conditions were either absent or mild in severity.

Drinking risk level and co-occurring conditions

Table 2 illustrates both the frequency and the spread of individual co-occurring conditions across the WHO DRLs. The odds of patients with a high DRL having co-occurring depression were significantly higher than patients in the low DRL group (OR: 1.41; 95% CI: 1.02–1.93) while the medium DRL group were 44% less likely to have alcohol-related dementia than the low DRL group (OR: 0.56; 95% CI: 0.34–0.91).

Diagnosing physician and co-occurring conditions

We further sought to examine the relationship between co-occurring somatic or psychiatric conditions and type of physician who diagnosed the patients' alcohol dependence. Using primary care physicians ($n = 642$) as the reference group, we calculated odds ratios for each co-occurring condition in the specialist group ($n = 483$). We found that the odds of a patient having depression were 71% higher or a sleep disorder 69% higher in those diagnosed with alcohol dependence by a specialist. Regarding somatic conditions, we found that the odds of having a cardiovascular disease were 39% higher or diabetes 44% higher in those diagnosed with alcohol dependence by a primary care physician. The odds of a patient having neuropathy or bipolar disorder were higher when diagnosed by a different healthcare professional (Table 3).

Time since diagnosis and co-occurring conditions

Patients who had been diagnosed with alcohol dependence for at least 3 years had significant associations with the experience of often chronic and disabling diseases, including diabetes (OR: 2.69; 95% CI: 1.68–4.31), neuropathy (OR: 1.68; 95% CI: 1.05–2.69), cardiovascular disease (OR: 1.83; 95% CI: 1.23–2.73) and liver disease (OR: 1.45; 95% CI: 1.02–2.05) (Table 4). Significant associations between longer time since diagnosis and alcohol-related dementia (OR: 2.36; 95% CI:

Table 1. Demographic and clinical characteristics of patients with alcohol dependence

Variable	All patients 8EU (*n* = 2979)	Drinking risk assessed (*n* = 1660)	Drinking risk assessed and not abstinent (*n* = 1373)
Demographics			
Age			
Mean (± SD), years	48.77 (13.60)	48.35 (12.64)	48.30 (12.89)
Gender			
Male	2073 (69.66)	1137 (68.49)	954 (69.48)
BMI, mean (± SD)			
Male	26.18 (4.89)	26.50 (5.13)	26.63 (5.37)
Female	24.17 (5.24)	24.35 (5.23)	24.47 (5.30)
Marital status			
Single	774 (26.53)	443 (27.38)	377 (28.18)
Relationship	1264 (43.32)	714 (44.13)	584 (43.65)
Divorced/separated/widowed	880 (30.16)	461 (28.49)	377 (28.18)
Work status			
Employed	1191 (41.05)	744 (46.27)	608 (45.75)
Unemployed	859 (29.61)	444 (27.61)	371 (27.92)
Other (retired/student/homemaker)	851 (29.33)	420 (26.12)	350 (26.34)
Clinical characteristics			
Drinking risk level			
Abstinent		287 (17.29)	0 (0.00)
Low		389 (23.43)	389 (28.33)
Medium		423 (25.48)	423 (30.81)
High		561 (33.80)	561 (40.86)
AUDIT score			
Mean (± SD)	20.33 (9.45)	20.31 (9.39)	20.86 (9.00)
WPAI scores			
Absenteeism mean (± SD)	11.09 (25.90)	10.34 (24.57)	12.15 (26.11)
Presenteeism mean (± SD)	20.81 (22.34)	21.28 (22.44)	24.40 (22.65)
Work productivity loss mean (± SD)	22.83 (25.46)	23.34 (25.50)	27.19 (25.63)
Q-LES-Q-SF			
Mean (± SD)	52.37 (19.12)	52.24 (19.07)	49.52 (17.65)
EQ-5D utility			
Mean (± SD)	0.74 (0.23)	0.74 (0.23)	0.72 (0.23)
EQ-5D VAS			
Mean (± SD)	67.99 (20.06)	67.92 (19.96)	66.61 (19.82)

All items are *n* (%) unless otherwise noted.

AUDIT, Alcohol Use Disorders Identification Test; WPAI, Work Productivity and Activity Impairment; Q-LES-Q-SF, Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form; EQ-5D, EuroQol-5 dimension; VAS, visual analogue scale.

1.30–4.29) and injury (OR: 1.77; 95% CI: 1.09–2.87) were also noted (Table 4).

Regression analysis: factors independently associated with co-occurring conditions

The results of a regression analysis to examine factors independently associated with the experience of co-occurring conditions in our alcohol-dependent population sample can be found in Table 5. Factors included current DRL, work productivity as measured by the WPAI, quality of life, overall health status, and hospitalisations or rehabilitation stays over the past year. Using 'none/mild' co-occurring conditions as the reference group, the regression model predicted that presence of co-occurring psychiatric conditions only or a combination of psychiatric and somatic conditions was associated with work productivity losses, presenteeism and absenteeism. As expected, we found an inverse relationship with HRQoL and health status (as measured by the EQ-5D) for all co-occurring condition groupings. While the percentage of variance accounted for by these factors was, overall, not robust, the results suggest an overall low HRQoL and health status in the alcohol-dependent population with greater work disability seen in those with either co-occurring psychiatric or psychiatric plus somatic conditions.

Impact of alcohol dependence on hospitalisation and work productivity

Patients who were hospitalised for alcohol dependence had an average length of stay of 24.3 days (based on physician-reported length of stay in hospital for a patient's most recent hospitalisation within the last 12 months). In addition, the mean rehabilitation stay was 37.5 days (based on last completed stay in rehabilitation within the last 12 months). Higher DRL suggested a greater impact on hospitalisations and rehabilitation stays and work productivity. 15.15% of patients with high DRL were hospitalised in the last 12 months, compared to 8.23% of patients in the low DRL group (*P* = 0.004) (Fig. 1). The same trend was seen in relation to rehabilitation stays, with almost double the proportion of patients in the high DRL group requiring a rehabilitation stay compared to patients in the low DRL group (*P* = 0.086).

The same trend was seen for a higher DRL suggesting increased work impairment (Fig. 2). Patients with a high DRL had an overall work productivity loss of 32.49%, compared with a 19.96%

Table 2. Specific co-occurring conditions in relation to drinking risk level

Variable	Total (n = 1660)	Abstinent (n = 287)	Low DRL (n = 389)		Medium DRL (n = 423)		High DRL (n = 561)	
	n (%)	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Hepatological (liver disease)	638 (38.43)	69 (24.04)	178 (45.76)	Ref.	167 (39.48)	0.77 (0.56–1.06)	224 (39.93)	0.79 (0.56–1.11)
GI issues (pancreatitis, stomach problems)	534 (32.17)	64 (22.30)	125 (32.13)	Ref.	164 (38.77)	1.34 (0.98–1.83)	181 (32.26)	1.01 (0.73–1.39)
Cardiovascular disease	322 (19.40)	35 (12.20)	95 (24.42)	Ref.	85 (20.09)	0.78 (0.54–1.13)	107 (19.07)	0.73 (0.50–1.06)
Injury	154 (9.28)	13 (4.53)	46 (11.83)	Ref.	39 (9.22)	0.76 (0.48–1.20)	56 (9.98)	0.83 (0.52–1.32)
Obesity	288 (17.35)	36 (12.54)	72 (18.51)	Ref.	89 (21.04)	1.17 (0.83–1.66)	91 (16.22)	0.85 (0.59–1.22)
Underweight (BMI below 20)	132 (7.95)	16 (5.57)	27 (6.94)	Ref.	38 (8.98)	1.32 (0.81–2.15)	51 (9.09)	1.34 (0.79–2.28)
Neuropathy	221 (13.31)	23 (8.01)	58 (14.91)	Ref.	53 (12.53)	0.82 (0.56–1.20)	87 (15.51)	1.05 (0.68–1.63)
Anaemia	136 (8.19)	18 (6.27)	32 (8.23)	Ref.	37 (8.75)	1.07 (0.60–1.92)	49 (8.73)	1.07 (0.61–1.86)
Diabetes	219 (13.19)	23 (8.01)	60 (15.42)	Ref.	69 (16.31)	1.07 (0.63–1.81)	67 (11.94)	0.74 (0.44–1.25)
Alcohol-related dementia	171 (10.30)	17 (5.92)	54 (13.88)	Ref.	35 (8.27)	0.56* (0.34–0.91)	65 (11.59)	0.81 (0.53–1.25)
Depression	716 (43.13)	106 (36.93)	154 (39.59)	Ref.	187 (44.21)	1.21 (0.90–1.63)	269 (47.95)	1.41* (1.02–1.93)
Anxiety	791 (47.65)	116 (40.42)	183 (47.04)	Ref.	202 (47.75)	1.03 (0.75–1.41)	290 (51.69)	1.20 (0.89–1.63)
Bipolar disorders	89 (5.36)	18 (6.27)	28 (7.20)	Ref.	20 (4.73)	0.64 (0.32–1.29)	23 (4.10)	0.55 (0.27–1.14)
Sleep disorders	726 (43.73)	101 (35.19)	169 (43.44)	Ref.	200 (47.28)	1.17 (0.85–1.60)	256 (45.63)	1.09 (0.81–1.48)

Base for the analysis by drinking risk level excludes abstinent patients.

DRL, drinking risk level; GI, gastrointestinal.

*$P < 0.05$.

Table 3. Specific co-occurring conditions split by physician that first diagnosed alcohol dependence

Variable	Total (n = 1290)	PCP (n = 642)		Psychiatrist (n = 483)		Other (n = 165)[a]	
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Hepatological (liver disease)	536 (41.55)	282 (43.93)	Ref.	175 (36.23)	0.73 (0.52–1.01)	79 (47.88)	1.17 (0.77–1.78)
GI issues (pancreatitis, stomach problems)	448 (34.73)	229 (35.67)	Ref.	151 (31.26)	0.82 (0.58–1.16)	68 (41.21)	1.26 (0.80–2.01)
Cardiovascular disease	274 (21.24)	152 (23.68)	Ref.	77 (15.94)	0.61* (0.43–0.86)	45 (27.27)	1.21 (0.76–1.93)
Injury	133 (10.31)	62 (9.66)	Ref.	52 (10.77)	1.13 (0.67–1.91)	19 (11.52)	1.22 (0.68–2.17)
Obesity	238 (18.45)	125 (19.47)	Ref.	78 (16.15)	0.80 (0.58–1.10)	35 (21.21)	1.11 (0.71–1.74)
Underweight (BMI below 20)	113 (8.76)	57 (8.88)	Ref.	40 (8.28)	0.93 (0.59–1.46)	16 (9.70)	1.10 (0.62–1.95)
Neuropathy	192 (14.88)	90 (14.02)	Ref.	65 (13.46)	0.95 (0.61–1.49)	37 (22.42)	1.77* (1.08–2.90)
Anaemia	113 (8.76)	59 (9.19)	Ref.	35 (7.25)	0.77 (0.49–1.23)	19 (11.52)	1.29 (0.76–2.18)
Diabetes	190 (14.73)	108 (16.82)	Ref.	49 (10.14)	0.56* (0.36–0.87)	33 (20.00)	1.24 (0.69–2.21)
Alcohol-related dementia	142 (11.01)	71 (11.06)	Ref.	45 (9.32)	0.83 (0.53–1.28)	26 (15.76)	1.50 (0.87–2.59)
Depression	580 (44.96)	253 (39.41)	Ref.	254 (52.59)	1.71* (1.27–2.30)	73 (44.24)	1.22 (0.80–1.85)
Anxiety	636 (49.30)	276 (42.99)	Ref.	279 (57.76)	1.81 (1.35–2.44)	81 (49.09)	1.28 (0.81–2.01)
Bipolar disorders	65 (5.04)	24 (3.74)	Ref.	28 (5.80)	1.58 (0.89–2.81)	13 (7.88)	2.20* (1.12–4.34)
Sleep disorders	589 (45.66)	254 (39.56)	Ref.	254 (52.59)	1.69* (1.25–2.29)	81 (49.09)	1.47 (0.99–2.20)

Base excludes abstinent.

GI, gastrointestinal; PCP, primary care physician.

[a]Other includes gastrologists/hepatologists (n = 46), addiction specialists (n = 32), other specialists not specified (n = 43) and other healthcare professionals (n = 44).

*$P < 0.05$.

overall work productivity impairment for patients who were in the low DRL group.

DISCUSSION

The current study is one of the largest to examine a multi-national population of clinically diagnosed alcohol-dependent patients to date. The average AUDIT score in our sample was 20.3, illustrating that, on average, our sample still suffered significantly from alcohol use as a score of 20 or more indicates probable alcohol dependence (Babor *et al.*, 2001). The fact that our patient sample had been clinically diagnosed with alcohol dependence yet had such high AUDIT scores suggests that treatment strategies available at the time of the study may be insufficient to reduce symptoms.

Further, our results show that alcohol dependence is associated with a high preponderance of both co-occurring somatic and psychiatric conditions, similar to rates noted in previous studies of individuals with alcohol dependence (Regier *et al.*, 1990; Schuckit *et al.*,

Table 4. Specific co-occurring conditions in relation to time since diagnosis

Variable	Total ($n = 1060$)	<12 months ($n = 358$)		13–36 months ($n = 185$)		>36 months ($n = 517$)	
	n (%)	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Hepatological (liver disease)	445 (41.98)	136 (37.99)	Ref.	66 (35.68)	0.91 (0.63–1.29)	243 (47.00)	1.45* (1.02–2.05)
GI issues (pancreatitis, stomach problems)	353 (33.30)	112 (31.28)	Ref.	60 (32.43)	1.05 (0.69–1.61)	181 (35.01)	1.18 (0.83–1.69)
Cardiovascular disease	217 (20.47)	54 (15.08)	Ref.	36 (19.46)	1.36 (0.83–2.24)	127 (24.56)	1.83* (1.23–2.73)
Injury	108 (10.19)	26 (7.26)	Ref.	19 (10.27)	1.46 (0.79–2.69)	63 (12.19)	1.77* (1.09–2.87)
Obesity	190 (17.92)	64 (17.88)	Ref.	30 (16.22)	0.89 (0.55–1.43)	96 (18.57)	1.05 (0.75–1.47)
Underweight (BMI below 20)	85 (8.02)	22 (6.15)	Ref.	17 (9.19)	1.55 (0.77–3.09)	46 (8.90)	1.49 (0.85–2.62)
Neuropathy	150 (14.15)	38 (10.61)	Ref.	26 (14.05)	1.38 (0.83–2.28)	86 (16.63)	1.68* (1.05–2.69)
Anaemia	92 (8.68)	33 (9.22)	Ref.	13 (7.03)	0.74 (0.38–1.48)	46 (8.90)	0.96 (0.58–1.61)
Diabetes	148 (13.96)	31 (8.66)	Ref.	12 (6.49)	0.73 (0.37–1.45)	105 (20.31)	2.69* (1.68–4.31)
Alcohol-related dementia	119 (11.23)	24 (6.70)	Ref.	20 (10.81)	1.69 (0.82–3.49)	75 (14.51)	2.36* (1.30–4.29)
Depression	465 (43.87)	146 (40.78)	Ref.	89 (48.11)	1.35 (0.92–1.98)	230 (44.49)	1.16 (0.83–1.62)
Anxiety	528 (49.81)	171 (47.77)	Ref.	100 (54.05)	1.29 (0.88–1.89)	257 (49.71)	1.08 (0.77–1.51)
Bipolar disorders	53 (5.00)	13 (3.63)	Ref.	6 (3.24)	0.89 (0.31–2.55)	34 (6.58)	1.87 (0.91–3.83)
Sleep disorders	493 (46.51)	167 (46.65)	Ref.	78 (42.16)	0.83 (0.58–1.20)	248 (47.97)	1.05 (0.76–1.47)

Base excludes abstinent patients.

GI, gastrointestinal.

*$P < 0.05$.

Table 5. Regression analysis of factors independently associated with co-occurring conditions

Variable	None/mild ($n = 340$)	Somatic only ($n = 231$)	Psychiatric only ($n = 315$)	Psychiatric + somatic ($n = 487$)	Regression	R-squared
Drinking risk level	Ref.	1.17 (0.80 to 1.72)	1.24 (0.85 to 1.83)	1.28 (0.91 to 1.82)	OL	0.04
WPAI scores						
Absenteeism	Ref.	10.23 (−2.57 to 23.02)	9.92* (1.95 to 17.90)	5.37 (−1.39 to 12.12)	O	0.05
Presenteeism	Ref.	5.55 (−2.23 to 13.33)	8.61* (2.21 to 15.01)	8.12* (1.78 to 14.46)	O	0.09
Work productivity loss	Ref.	8.94 (−0.93 to 18.82)	12.81* (4.89 to 20.74)	10.63* (2.85 to 18.41)	O	0.12
Q-LES-Q-SF	Ref.	−4.81* (−8.65 to −0.97)	−8.38* (−12.33 to −4.43)	−11.81* (−15.48 to −8.14)	O	0.09
EQ-5D utility	Ref.	−0.06* (−0.1 to −0.02)	−0.13* (−0.17 to −0.08)	−0.17* (−0.21 to −0.13)	O	0.13
EQ-5D VAS	Ref.	−7.10* (−10.94 to −3.25)	−7.79* (−10.71 to −4.88)	−13.70* (−17.04 to −10.36)	O	0.15
Hospitalisations	Ref.	1.01 (0.6 to 1.69)	0.85 (0.51 to 1.42)	1.13 (0.68 to 1.86)	N	0.04
Rehab stays	Ref.	0.33 (0.1 to 1.16)	0.43 (0.14 to 1.36)	0.42 (0.15 to 1.18)	N	0.06
Presence of caregiver	Ref.	1.54 (0.87 to 2.7)	2.23* (1.25 to 3.96)	1.99* (1.16 to 3.41)	L	0.02

Base excludes abstinent patients.

Covariates adjusted for: age, gender, time since diagnosis and whether treated.

All items are coefficient (95% CI) except Drinking Risk Level & Caregiver (odds ratio (95% CI)), Hospitalisations & Rehab stays (incidence rate ratio (95% CI)).

Regression: OL = ordered logistic, O = linear, N = negative binomial, L = logistic.

WPAI, Work Productivity and Activity Impairment; Q-LES-Q-SF, Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form; EQ-5D, EuroQol-5 dimension; VAS: Visual Analogue Scale.

*$P < 0.05$

1997; Hasin *et al.*, 2007). In fact, ~77% of patients examined in this study were found to have moderate-to-severe somatic and/or psychiatric co-occurring conditions. The presence of co-occurring conditions was associated with decreased work productivity and increased frequency of hospitalisation. These results reflect findings from previous studies both in terms of physical and psychological disorders (Hasin *et al.*, 2007), as well as the link between increased alcohol consumption, and morbidity and hospitalisations (Gual *et al.*, 1999). These findings highlight the importance of considering patient morbidities when making treatment and management decisions, and the impact that both somatic and psychiatric conditions can have not only on the patient (in terms of their HRQoL) but also on the healthcare

system (number of rehabilitation stays) and wider society (in terms of lost work productivity).

As stated earlier in this manuscript, hospitalisations are the main driver of direct costs of alcohol dependence in Europe (Olesen *et al.*, 2012) and therefore comprise a critical component to consider in the management of these patients. In this study, the mean length of stay across all severities was 24.3 days in the last 12 months. This is substantially longer than the 0.70 nights in the last 6 months (95% CI: 0.61–0.79 nights) reported separately among people without alcohol use disorders (study description in Rehm *et al.* (2015a,b); data on hospitalization not yet published (Rehm *et al.*, 2015a)). The study by Rehm *et al.* was a large, representative study in primary health care

was conducted in six European countries among a participant sample of a similar average age to the present study (N = 9098 patients, average age = 44.2 years; 95% CI = 44.0–44.6 years). In our study, however, length of stay was only calculated for hospitalised patients, limiting the comparability of these figures.

The current study also revealed a higher number of hospitalisations among patients with a high DRL and further suggests a potential

Fig. 1. Hospitalisations and rehabilitations in relation to different drinking risk levels. DRL, drinking risk level.

unmet need for the treatment of these patients. It has been suggested that many alcohol-attributable costs may be avoidable, especially considering the potential effective treatments available which make only a minor contribution to the direct cost burden of European alcohol dependence (Mohapatra *et al.*, 2010; Laramee *et al.*, 2013).

Furthermore, the high level of lost productivity noted by patients in this study is likely to be costly for society, particularly in light of the recent data which estimates that lost-productivity costs associated with alcohol dependence could be up to €38 billion (Anderson and Baumberg, 2006; Olesen *et al.*, 2012).

The results of the present study identify a population of alcohol-dependent patients burdened by co-occurring conditions, even after having been diagnosed for a long duration of time. The fact that patients who had been diagnosed with alcohol dependence for at least 3 years had significant associations with the experience of often chronic and disabling diseases suggests that the burden of alcohol dependence extends well beyond the initial diagnosis of the disorder. A reduction of alcohol consumption in these patients may offer a significant target for improved health status, improved productivity and potential long-term cost-savings. This has been suggested in a previously published economic evaluation which showed that reduction in the proportion of patients drinking harmful amounts of alcohol was associated with lower costs and higher quality adjusted life years (QALYs) (Barbosa *et al.*, 2010).

Limitations of the current study include the potential for sampling bias, since the sample was not fully randomised. Despite this potential limitation, however, there were no significant differences in descriptive population demographics between countries. The high rate of patients currently being treated in this study (72%) may be subject to consultation-based population bias; patients refusing treatment are less likely to be captured in the study. Treated patients were at different stages of the treatment pathway at the time of the survey and therefore treatment was not considered in the statistical analyses. Furthermore, the cross-sectional nature of this study does not allow cause-and-effect relationships to be drawn. As with any study regarding alcohol dependence, the high level of undiagnosed alcohol dependence in the population limits the generalisability of the sample to the
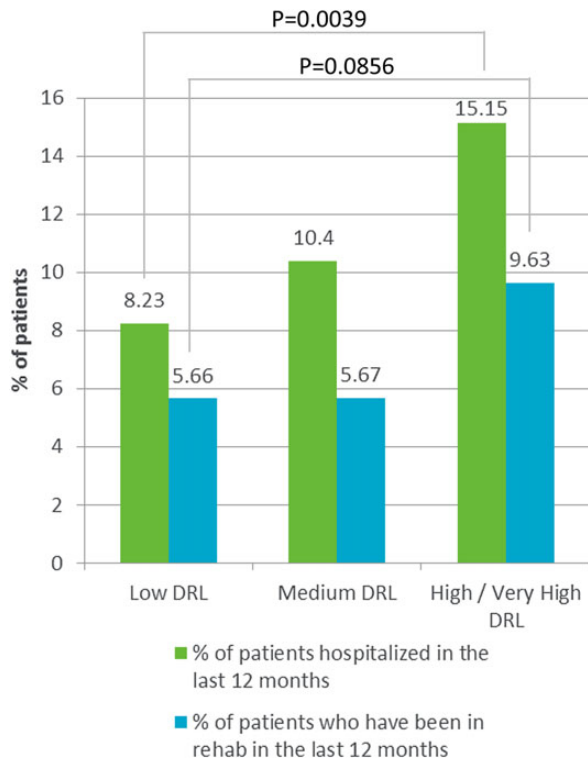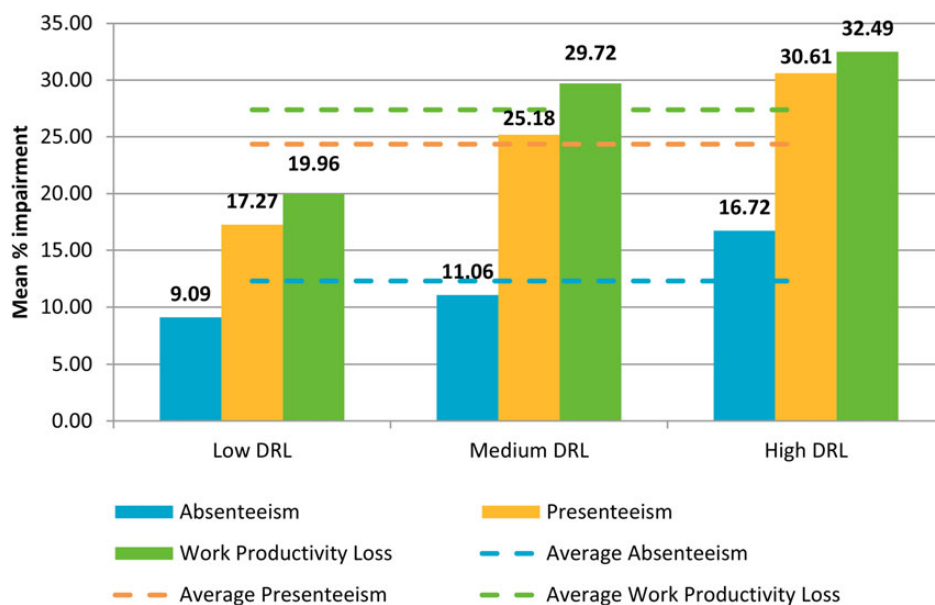

Fig. 2. Work productivity in relation to different drinking risk levels. DRL, drinking risk level.

alcohol-dependent population as a whole. The demography of this population of patients, however, generally coincides with that of other observational cohort studies in alcohol-dependent patients (Stewart *et al.*, 2006; Daeppen *et al.*, 2014). In addition, DRL was assessed by asking patients about the number of drinks per day, which we approximated to the number of grams of alcohol based on the WHO DRL groups. This was judged to be the most feasible approach to collecting these data in a real-world setting, since patients typically will be unaware of their intake of alcohol in grams. It is also recognized that the demographics of the patients in the current study may not be reflective of all alcohol-dependent patients across the EU. Given that the current study includes a diverse sample of nearly 3000 patients from eight European countries, however, and while there may be differences at the local level, the results from the study should be generally applicable across jurisdictions. Furthermore, this study utilised the EQ-5D to measure the health-related quality of life of patients with alcohol dependence. Other scales which could have been considered as a measure of the health-related quality of life are Short-Form 36 (SF-36, a generic measure of health status) or the alcohol-specific AIQoL-9 (Alcohol Index Quality of Life, 9-item questionnaire based on the SF-36 (Malet *et al.*, 2006)), which may have greater sensitivity in alcohol-dependent patients due to the greater number of domains covered in these instruments. Due to the broad objectives of this study, however, the EQ-5D was chosen to limit the burden on the respondents and was deemed appropriate as it is a widely used and accepted questionnaire worldwide. The generic nature of the scores also allows for comparisons between different patient groups (which is of interest when making health policy decisions in Europe), and it has been accepted as an appropriate measure in recent reimbursement decision-making in alcohol dependence (National Institute for Health and Care Excellence, 2014).

Despite these limitations, the current study includes a number of strengths, including data collected from a large sample of eight countries across Europe, covering all major drinking patterns in Europe (Rehm *et al.*, 2012). Real world, evidence-based practice was captured in great breadth and depth, from physicians (both PCPs and specialists) and patients, thereby providing a holistic picture of a disease area. A range of generic validated measures were used, and alcohol consumption was measured with the AUDIT, a WHO recommended screening tool routinely used in real-world clinical practice, and recommended by the Primary Health Care Project on Alcohol (Anderson *et al.*, 2005). Drinking risk levels, as defined by the WHO, were also utilised to reflect the patients' current drinking levels. Further, and whilst current data exist to characterise the alcohol-dependent population in Europe, cohorts have generally derived from patient populations within clinical trials where inclusion/exclusion criteria are strictly defined, restrictive, and often not representative of the people with other psychiatric disorders seeking and receiving treatment in the general population (Zetin and Hoepner, 2007; Okuda *et al.*, 2010; Odlaug *et al.*, 2014). This study utilised direct physician and patient interviews in order to capture data and may be more representative of the treatment-seeking alcohol dependence population.

Future studies

Future longitudinal observational studies will allow causal links to be made, particularly with regard to the effect of treatment on HRQoL and healthcare resource utilisation in alcohol-dependent patients. In addition, further research to understand the specific relationship between health-related quality of life and co-occurring conditions may be warranted, as an inverse relationship between HRQoL and health

status was identified in this study. Whilst this study considered the burden on society in terms of hospitalisations and work productivity, we have not quantified this in terms of economic burden. As highlighted by Laramee *et al.* (2013), there is a lack of data specifically available for the alcohol-dependent population, as costs are often combined with alcohol abuse (Laramee *et al.*, 2013), identifying an area for further research. Furthermore, there are social consequences of drinking which have not been investigated in the present study, and deserve attention.

CONCLUSIONS

The results and conclusions herein are of interest for providers of health care for alcohol-dependent patients and public health officials. These results suggest that patients with alcohol dependence suffer from numerous co-occurring somatic and psychiatric conditions, which are associated with poor HRQoL, impaired work productivity and a high frequency of hospitalisations and rehabilitation stays within a real-world setting. The continued burden of illness observed in these patients—who are already diagnosed with the disorder—suggests an unmet need in care and underscores the substantial complications associated with alcohol dependence (Modesto-Lowe and Kranzler, 1999). Interventions which decrease this burden, improve HRQoL and reduce the direct and indirect cost of illness in patients with alcohol dependence are needed.

CONFLICT OF INTEREST STATEMENT

At the time of submission of this manuscript, the authors had the following potential conflicts of interest: B.L.O. has received research funding from the Trichotillomania Learning Center, consults for H. Lundbeck A/S, and receives royalties from Oxford University Press. A.G. reports grants from the EU and the Spanish Health Ministry, personal fees from H. Lundbeck A/S, Abbvie and D&A Pharma and being a board member for H. Lundbeck A/S and D&A Pharma, all outside the submitted work. J.D., R.P. and J.P. are employees of Adelphi Real World and L.H. is an employee of Adelphi Values. J.R. reports grants from GWT-TUD, NIH, and the EU, personal fees and being a board member (nalmefene) for H. Lundbeck A/S, all outside the submitted work. Other authors have no further conflicts of interest to declare.

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