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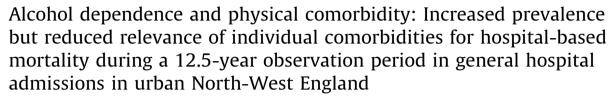
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#### Original article





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#### ABSTRACT

*Purpose*: Alcohol dependence (AD) is associated with an increase in physical comorbidities. The effects of these diseases on general hospital-based mortality are unclear. Consequently, we conducted a mortality study in which we investigated if the burden of physical comorbidities and their relevance on general hospital-based mortality differs between individuals with and without AD during a 12.5-year observation period in general hospital admissions.

Methods: During 1 January 2000 and 30 June 2012, 23,371 individuals with AD were admitted at least once to seven General Manchester Hospitals. Their physical comorbidities with a prevalence  $\geq 1\%$  were compared to those of 233,710 randomly selected hospital controls, group-matched for age and gender (regardless of primary admission diagnosis or specialized treatments). Physical comorbidities that increased the risk of hospital-based mortality (but not outside of the hospital) during the observation period were identified using multiple logistic regression analyses.

Results: Hospital-based mortality rates were 20.4% in the AD sample and 8.3% in the control sample. Individuals with AD compared to controls had a higher burden of physical comorbidities, i.e. alcoholic liver and pancreatic diseases, diseases of the conducting airways, neurological and circulatory diseases, diseases of the upper gastrointestinal tract, renal diseases, cellulitis, iron deficiency anemia, fracture neck of femur, and peripheral vascular disease. In contrast, coronary heart related diseases, risk factors of cardiovascular disease, diverticular disease and cataracts were less frequent in individuals with AD than in controls. Thirty-two individual physical comorbidities contributed to the prediction of hospital-based mortality in univariate analyses in the AD sample; alcoholic liver disease (33.7%), hypertension (16.9%), chronic obstructive pulmonary disease (14.1%), and pneumonia (13.3%) were the most frequent diagnoses in deceased individuals with AD. Multiple forward logistic regression analysis, accounting for possible associations of diseases, identified twenty-three physical comorbidities contributing to hospital-based mortality in individuals with AD. However, all these comorbidities had an equal or even lower impact on hospital-based mortality than in the comparison sample.

Conclusion: The excess of in-hospital deaths in general hospitals in individuals with AD is due to an increase of multiple physical comorbidities, even though individual diseases have an equal or even reduced impact on general hospital-based mortality in individuals with AD compared to controls.

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#### 1. Introduction

Alcohol dependence (AD) is a chronic, often progressive psychiatric disorder characterized by a pattern of physiological, behavioral, and cognitive phenomena in which alcohol consumption takes on an excess priority [11]. AD usually starts early in life and affects about 5.4% of individuals in the general population aged between 15 and 64 years, contributing to 3.8% of all global deaths [28,38,47]. Alcohol consumption can have protective or detrimental effects on different physiological functions: low levels of alcohol consumption, especially wine, may protect against some cardiovascular diseases (CVDs) and cancers. In contrast, binge

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drinking causes the opposite effect. Dose-response relationships between alcohol consumption and physiological functions may be linear or accelerated, i.e. the more alcohol is consumed over time, the more the risk for atrial fibrillation increases; but the risk for liver cirrhosis increases more rapidly with heavier alcohol consumption [12,34,39,71]. All in all, physical morbidity risks related to more than sixty medical conditions tend to increase over time with the amount of alcohol consumption (and the proportion of wine intake relative to total alcohol intake) [10.45]. In a crosssectional European sample that included 315 treatment seeking individuals with alcohol use disorder with a mean age of 45.8 years, more than 60% had at least one comorbid physical disease that required medical treatment [21]. It is said that up to 70% of the premature all-cause mortality of alcohol use disorders is caused by physical comorbidity [16,38]. Physical disease related mortality risk factors of longstanding alcohol excess that usually become prevalent in later stages of AD are strongly related to alcoholic liver cirrhosis, chronic alcoholic pancreatitis, hypertension, and stroke. In particular, alcoholic liver disease (ALD) and alcoholic pancreatic disease, circulatory and respiratory diseases represent increased risks of fatal complications [8,17,25,42,46,47,65]. AD is also strongly associated to cancers of the mouth, oesophagus, and larynx, but less so with cancers of the colon, rectum, breast, and primary liver cancer [10].

Most individuals with AD receive care from their general practitioner, where they represent a fifth of the caseload [60]. However, we know of no representative study that has identified the physical diseases that are associated with general hospital-based mortality in individuals with AD. Consequently, the relevance of physical comorbidities on general hospital-based mortality in individuals with AD in comparison to individuals without AD needs further investigation. The knowledge of specific physical diseases that are risk factors for general hospital-based mortality in individuals with AD may help towards reducing avoidable excess mortality.

#### 1.1. Aim of study

The aim of this study was to investigate – in a representative and non-selected hospital-based sample with a 12.5-year observation period in general hospital admissions – if the prevalences of various physical diseases and their impact on hospital-based

mortality differ between individuals with AD and controls. Four specific hypotheses were tested:

- individuals with AD have a more severe course of disease during the observation period than controls, i.e. individuals with AD compared to controls:
  - are more often admitted as emergencies at their initial hospitalization;
  - have an extended length of hospital stay at their initial hospitalization;
  - have a higher total number of admissions during the observation period;
  - o and have a higher hospital-based mortality rate.
- individuals with AD compared to controls have a higher burden of various physical comorbidities compared with controls;
- these physical comorbidities contribute to an increase of hospital-based mortality in individuals with AD, and in controls;
- the relevance of individual comorbid physical diseases on hospital-based mortality is higher in individuals with AD than in controls

#### 2. Methods

#### 2.1. Sample definitions

The initial sample included all individuals (n = 929,465) who were admitted to hospital for treatment in seven General Manchester Hospitals between January 1, 2000, and June 30, 2012. The study sample consisted of all 23,371 individuals with AD (2.5%) aged 18 years or above who were hospitalized at least once (or repeatedly) for at least 24 hours during this period. Cases were identified by a discharge diagnosis of F10.2x according to ICD-10. The subsample of deceased individuals with AD included all 4765 individuals with AD who had died in any of the seven hospitals; survivors with AD included the remaining 18,606 individuals. The control sample consisted of ten randomly selected non-AD individuals per AD subject admitted to the same hospitals during the same observation period, groupmatched for gender and age ( $\pm$  1 year by date of initial admission; n = 233,710, Table 1), using SPSS version 20.0. The inclusion and

**Table 1**Sociodemographic and clinical characteristics of the initial sample subdivided into AD sample and control sample.

Characteristics	Initial sample					
	AD sample			Control sample		
	All	Deceased	Survivors	All	Deceased	Survivors
Sociodemographic description						
Number, $n$ (%)	23,371 (100)	4765 (20.4) (2)***	18,606 (79.6)	233,710 (100)	19,481 (8.3)	214,229 (91.7)
Mean age, years $\pm$ SD	$\textbf{44.7} \pm \textbf{0.1}$	$54.4 \pm 0.2 \ (1)^{\circ \circ} (2)^{\circ \circ}$	$42.3 \pm 0.1$	$44.7 \pm 0.0$	$62.0 \pm 0.1$	$43.2 \pm 0.0$
Female gender, n (%)	5672 (24.3)	1195 (25.1) (2)***	4477 (24.1)	56,720 (24.3)	3833 (19.7)***	52,887 (24.7)
Marital status, married, $n$ (%)	4230 (18.1)	1078 (22.6) (1) (2)	6152 (16.9)	99,052 (42.4)	9025 (46.3)***	90,027 (42.0)
Caucasian ethnicity, $n$ (%)	19,926 (85.3)***	4205 (88.2) (1) (2)	15,271 (84.5)	178,369 (76.3)	16,533 (84.9)	161,836 (75.5)
South Asian ethnicity, $n$ (%)	386 (1.7)***	54 (1.1) (1) (2)	332 (1.8)	19,637 (8.4)	746 (3.8)	18,891 (8.8)
Afro-Caribbean ethnicity, $n$ (%)	209 (0.9)	26 (0.5) (1) (2)	183 (1.0)	6703 (2.9)	281 (1.4)	6422 (3.0)
Clinical description						
Initial admission (emergency), $n$ (%)	21,127 (90.4)***	4304 (90.3) (1) (2)	16,823 (90.4)	123,180 (52.7)	12,771 (65.6)	110,409 (51.5)
Length of hospital stay at intial	$5.7 \pm 0.1$	$10.7 \pm 0.3 \ (1)^{\circ \circ} (2)^{\circ \circ}$	$4.4 \pm 0.1$	$2.9 \pm 0.0$	$9.5 \pm 0.2$ ***	$2.3 \pm 0.0$
admission during 2000-2012						
Mean number of admissions	15.5***	19.9 (1) (2)	14.4	10.8	17.1***	10.2
Mean duration of observation, days $\pm\text{SD}$	$1745.5\pm7.8$	$881.7 \pm 12.0 (1)$	$1966.7\pm8.6$	$2128.5\pm2.7$	$879.5\pm6.5^{\bullet\bullet\bullet}$	$2242.1\pm2.8$

Stars indicate in the first column sample comparisons between all individuals with AD and all controls, in the second column subsample comparisons (1) between deceased individuals with AD and hospital survivors with AD and (2) between deceased individuals with AD and deceased controls, in the fifth column subsample comparisons between deceased controls and hospital control survivors;  ${}^*P \le 0.05$ ,  ${}^{**}P \le 0.01$ .

 $P \le 0.001$ .

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