

# BMJ Open Multimorbidity, psychoactive substance use and psychological distress among acute medically ill patients: a cross-sectional study

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## ABSTRACT

**Background** In order to target the complex health needs of patients with multimorbidity using psychoactive substances, knowledge regarding the association between substance use and multimorbidity in an acute setting is needed.

**Aims** Examine psychoactive substance use patterns among acute medically ill patients, and determine the association between multimorbidity and substance use, and psychological distress.

**Design** Cross-sectional study.

**Setting and participants** 2874 acute medically ill patients admitted to a medical emergency department in Oslo, Norway.

**Measurements** Primary outcome: multimorbidity recorded by the presence of  $\geq 2$  International Classification of Diseases 10th revision—physical and/or mental health conditions per patient, extracted from medical records. Predictor variables: self-reported data on age, sex, occupational status, psychological distress (Hopkins Symptom Check List-5), alcohol use (Alcohol Use Disorder Identification Test-4) and results from blood samples on psychoactive medicinal and illicit drugs.

**Findings** Of all patients, 57.2% had multimorbidity. Of these, 62.6% reported psychological distress, 85.5% consumed either alcohol, medicinal and/or illicit drugs and 64.4% combined alcohol with psychoactive medicinal drugs. Patients with risky alcohol use were more likely to have multimorbidity compared with patients with low-risk alcohol use (OR 1.53; 95% CI 1.05 to 2.24). Patients using psychoactive medicinal drugs were more likely to have multimorbidity compared with non-users (OR 1.34; 95% CI 1.07 to 1.67).

**Conclusion** Multimorbidity was associated with psychoactive medicinal drug and risky alcohol use, and psychological distress. Substance use was widespread, with alcohol and psychoactive medicinal drugs most frequently combined. Monitoring substance use among multimorbid patients is necessary to develop tailored treatments, and reduce burden on the healthcare system.

## INTRODUCTION

Patients with multimorbidity—two or more disorders—are more likely to use multiple

## Strengths and limitations of this study

- This is one of few studies examining multimorbidity ( $\geq 2$  physical/mental conditions) in relation to psychoactive substance use and psychological distress in acute secondary healthcare settings—a primary contact point for many non-treatment seeking patients.
- The study showed the need for monitoring of psychoactive substance use in the disease management of patients with multimorbidity, in order to improve the adherence to treatment and its outcomes, and reduce burden on the healthcare system.
- The study combines data from objective blood samples and self-reported questionnaires on psychoactive substances, and uses objective medical records on the health conditions.
- To reflect a more realistic daily clinical practice, acute diseases and other signs and symptoms were included in the definition of multimorbidity; this might have inflated the prevalence of multimorbidity.
- This study design was not able to distinguish between medical and non-medical use of psychoactive prescription drugs.

prescribed medications, live more years of life with disability and die prematurely.<sup>1,2</sup> As such, multimorbidity exacts a great toll on the healthcare system.<sup>3</sup> Psychoactive substance use leads to adverse health effects, influences existing disorders and complicates disease management in patients with multimorbidity.<sup>4</sup> Therefore, psychoactive substance use among patients with multimorbidity should be addressed in both epidemiological research and in healthcare settings, for example, when developing effective interventions and adequate care for people with multimorbidity. Depression, anxiety, alcohol use—and illicit drug use—disorders are causing the highest proportions of disability-adjusted life-years worldwide.<sup>5</sup> Substance use

disorders (SUDs) often co-occur with other medical disorders and are associated with psychological conditions such as depression and anxiety.<sup>6</sup> Hence, it is important to examine the mental state of multimorbid patients using psychoactive substances. A combination of alcohol, psychoactive medicinal and illicit drugs might lead to detrimental health outcomes<sup>7</sup>; including an elevated risk of overdose when opioids are used in combination with other central nervous system (CNS) depressants, such as benzodiazepines and alcohol,<sup>8</sup> and increased adverse effects of stimulants such as cocaine when combined with alcohol, particularly on the cardiovascular and cerebrovascular systems.<sup>8–10</sup>

These substance groups are highly prevalent in acute care settings<sup>11 12</sup> and are, therefore, important to consider in the management of multimorbid patients presented to for example, emergency departments (EDs). The intersection between multimorbidity and substance use is growing with the growing ageing population, as shown in the increasing age of people in opioid treatment in many countries.<sup>13</sup> Subsequently, older adults should be screened for substance use, since multimorbidity is more prevalent in this group.<sup>14</sup>

Research on multimorbidity is usually conducted in general populations and primary care settings, and pertains to older patient populations.<sup>14–16</sup> Alcohol, psychoactive medicinal and illicit substance use have been shown to be associated mostly with individual diseases and not with co-occurring diseases; there is a scarcity of reports examining the association between multimorbidity and all three substance groups in the same study population; the majority of the evidence on substance use and health outcomes including mortality pertains to alcohol and tobacco.<sup>17–19</sup> Individual studies have explored alcohol as a risk factor for multimorbidity with mixed results,<sup>18–21</sup> others demonstrate an association of multimorbidity and polypharmacy (use of multiple medications in a single individual).<sup>22</sup> However, data on the association of multimorbidity and illicit drug use are scant.<sup>15</sup> Moreover, there is a paucity of reports focusing solely on multimorbidity in relation to psychoactive substance use and psychological distress.<sup>15</sup> Studies using patient-reported diseases have shown to be biased in the disease measurement compared with those using administrative hospital data.<sup>23</sup>

### Study aims

Our aims were to (1) examine the distribution of psychoactive substance use patterns among patients with multimorbidity of age  $\geq 18$  years presented to an ED and (2) determine the association between multimorbidity and psychological distress, and substance use including alcohol, illicit and psychoactive medicinal drugs.

## METHODS

### Study design and participants

This study uses data from a cross-sectional observational study conducted from November 2016 to December

2017, and the study design of the data gathering has been previously described in detail.<sup>24</sup> In brief, the study site was Lovisenberg Diaconal Hospital in Oslo, where all patients having acute medical disorders from the defined hospital catchment area are presented to. The hospital has a catchment area comprising four inner city boroughs with low life-expectancy—and income rates compared with the rest of Norway.<sup>25</sup> Patients admitted to the medical wards (acute medically ill patients aged  $\geq 18$ ) of the ED were recruited to the study.<sup>24</sup>

### Patient and public involvement statement

No patients nor any other members of the public were involved in the design, conduct or reporting of this study. Informed written consent was obtained from all participants.

### Data collection

In addition to self-reported data and data from the blood samples presented in our previous studies,<sup>24 26</sup> for this analysis the patients' electronic medical records were systematically reviewed for registration of diagnoses codes according to the 10th revision of the International Classification of Diseases (ICD-10). A limited number of the patients were diagnosed with solely mental and behavioural diseases assigned by F00–F99 ICD-10 diagnostic codes. We chose, however, to include these patients in our study (which are taken into account in the sensitivity analysis), because they represent a complex patient group that poses a challenge to the healthcare system and deserves exploration.

### Measures

Sociodemographic measures such as sex, age (18–35 years, 36–50 years, 51–65 years, 66–80 years,  $>80$  years) and occupational status (economically active, non-economically active and retired) were self-reported.

When multiple outcomes are examined in relation to multimorbidity, the use of disease counts is suggested to be the most adequate manner to measure multimorbidity.<sup>2 27</sup> Therefore, we defined multimorbidity as the presence of two or more medical and/or mental health conditions in one patient. ICD-10 codes of chapter F00–F99 comprising mental and behavioural diseases were defined as mental health conditions, while all other ICD-10 chapters were defined as medical conditions. ICD-10 codes for physical and mental diseases, intoxications, signs and symptoms, abnormal findings and complaints were included. ICD-10 codes for social circumstances, injury and external causes of morbidity and mortality were excluded, that is, patients having only these diagnostic codes were excluded entirely from the dataset.

Psychological distress the past 14 days was assessed by patient-reported anxiety and depression by Hopkins Symptom Checklist 5 (SCL-5).<sup>28</sup> SCL-5 is used as a dichotomised variable with a cut-off score  $>2$  being the positive outcome (a valid predictor of psychological distress)

and <2 being the negative outcome (no psychological distress).<sup>28</sup>

Blood samples provided by patients were analysed for the most commonly prescribed psychoactive medicinal drugs including analgesics and CNS depressants (15 different medicinal drugs including tramadol, opioids, benzodiazepines and z-hypnotics) and illicit drugs including stimulants (amphetamines, cocaine, **3,4-Methylenedioxymethamphetamine** (MDMA)), heroin and cannabis (**Tetrahydrocannabinol** (THC)).<sup>29</sup> Compared with alcohol screening questionnaires, which correlate well with blood samples,<sup>30</sup> drug screening questionnaires have shown to be less sensitive in detection of drug use compared with biological sample tests.<sup>31</sup> Hence, psychoactive medicinal and illicit drugs detected in blood were used as dichotomised variables, with the positive outcome being at least one drug found in the blood sample of each patient and the negative outcome being no drugs detected.

Self-reported alcohol use the past year was measured by Alcohol Use Disorder Identification Test 4 (AUDIT-4).<sup>24</sup> The total score ranges from 0 to 16. We categorised AUDIT-4 scores into five categories including abstainers: (1) abstinence (scores 0), (2) low-risk drinking (scores 1–3), (3) alcohol use in excess of low-risk guidelines (scores 4–6), (4) hazardous drinking (scores 7–8), (5) risky alcohol use and possible alcohol dependence (scores  $\geq 9$ ).<sup>24 32</sup> Ideally, the reference group should have been teetotalers, although several concerns are related to this group.<sup>33</sup> However, due to the under-representativeness of this group the group of low-risk drinkers is used as a reference in our study.

### Statistical analyses

Differences in mean number of health conditions between men and women, illicit drug use and psychological distress were analysed using t-test. Differences in mean number of health conditions across age groups, occupational status groups, psychoactive medicinal drug use and alcohol use patterns were analysed with one-way **analysis of variance** (ANOVA). The **chi-squared** ( $\chi^2$ ) test was used to measure differences in prevalence of multimorbidity between variables.

Subsequently, we assessed the prevalence of all three substance groups used individually and in combination with each other among single diseased and multimorbid patients by using  $\chi^2$  test.

Binary logistic regression was employed to examine the likelihood of being multimorbid based on predictor variables. Total number of observations was reported for each variable in the tables to indicate missing data, and cases with any missing data were excluded from the logistic regression analysis.

The level of significance was  $p < 0.05$  for all statistical tests.

All statistical analyses were performed using R software V.4.0.3.

### Sensitivity analysis

In addition to the main analysis described above, we conducted a sensitivity analysis to test whether the association between multimorbidity and substance use and/or psychological distress was influenced by the inclusion of mental and behavioural diagnoses (F00–F99 codes).

The sensitivity analysis was conducted rerunning the logistic regression where all F00–F99 codes were excluded (they were set to not count in the outcome variable) and we were left analysing only medical multimorbidity ( $\geq 2$  medical conditions only per patient). The group of patients having any of the F00–F99 codes in either the index diagnoses or secondary diagnoses comprised 250 patients in total. Of these, 51 (1.9% of the total study sample of 2725 patients) patients diagnosed with solely F00–F99 codes were excluded from the model, while the remaining 199 patients (7.4% of the study sample) with physical diagnoses in addition to the F00–F99 codes were not excluded from the analysis, but ended up having one disorder (diagnostic code) less.

### RESULTS

A total of 2874 patients were enrolled and after excluding patients with injury as main diagnoses and those with missing ICD-10 diagnoses codes, we ended up with 2725 patients. Of these 1558 (57.2%) were multimorbid. Following the inclusion of covariables (any case with missing data was excluded) the sample size for the complete analysis was 2136. The mean (SD) age was 56 years (20 years) and the mean (SD) number of disorders in the whole population was 2.24 (1.54), with men and women equally represented (**table 1**).

The number of disorders and the proportion of patients with multimorbidity increased significantly with age and was higher for those being non-economically active and retired. Men had a significantly higher number of disorders compared with women (**table 1**). Of the young patients (18–34 years) 35.0% were multimorbid (**table 1**). Of these, 40.3% used alcohol above the recommended guidelines, 12.6% used it hazardously and 8.9% in a risky manner. Prevalence of risky alcohol use was higher among patients aged 35–49 years and 50–64 years (12.7% and 12.1%) and decreased slightly for those aged 65–79 years (8.7%). Of the young multimorbid patients (18–34 years) 14.1% used illicit drugs, 14.1% used psychoactive medicinal drugs and 31.4% reported to have psychological distress. Compared with the young patients,<sup>18–34</sup> among multimorbid patients aged  $\geq 35$  the prevalence of psychological distress decreased with increasing age (for those aged 35–49 years the prevalence was 30.2%; for those 50–64 years it was 26.3%; 65–79 years: 23.9% and for those  $> 80$  years it was 13.8%) while the prevalence of psychoactive medicinal drug use increased substantially with increasing age (for those aged 35–49 years the prevalence was 32.6%; for those 50–64 years it was 45.4%; 65–79 years: 43.8% and for those  $> 80$  years it was 41.2%). Illicit drugs were most prevalent among those aged 35–64

**Table 1** Demography, psychological distress, substance use and multimorbidity

	n (%)	Mean no of disorders (SD) *	Patients with multimorbidity n (%)†
All patients	2725 (100)	2.24 (1.54)	1558 (57.2)
Sex (n=2707)			
Female	1407 (52.0)	2.16 (1.47)	718 (55.2)
Male	1300 (48.0)	2.31 (1.60)	827 (58.8)
Age years (n=2702)			
18–34	568 (21.0)	1.52 (0.88)	199 (35.0)
35–49	445 (16.5)	1.82 (1.26)	200 (44.9)
50–64	618 (22.9)	2.19 (1.56)	355 (57.4)
65–79	742 (27.5)	2.72 (1.73)	516 (69.5)
>80	329 (12.2)	3.03 (1.57)	271 (82.4)
Occupational status (n=2613)			
Active	1242 (47.5)	1.67 (1.07)	502 (40.4)
Retired	990 (37.9)	2.85 (1.71)	734 (74.1)
Non-active	381 (14.6)	2.45 (1.62)	251 (65.9)
Psychological distress (SCL-5) (n=2513)	551 (21.9)	2.41 (1.65)	345 (62.6)
Substance use			
Alcohol use patterns by AUDIT-4 (n=2594)			
Abstinence (score 0)	619 (23.9)	2.61 (1.58)	431 (69.6)
Low-risk drinking (scores 1–3)	867 (33.4)	2.20 (1.52)	487 (56.2)
Alcohol use in excess of low-risk guidelines (scores 4–6)	726 (28.0)	1.95 (1.41)	347 (47.8)
Hazardous drinking (scores 7–8)	183 (7.1)	1.93 (1.35)	89 (48.6)
Risky alcohol use and possible alcohol dependence (scores ≥9)	199 (7.7)	2.46 (1.65)	128 (64.3)
Psychoactive medicinal drugs (n=2477)			
1 psychoactive medicinal drug	461 (18.6)	2.45 (1.60)	302 (65.5)
≥2 psychoactive medicinal drugs	326 (13.2)	2.73 (1.61)	239 (73.3)
Illicit drugs (n=2477)	158 (6.4)	2.23 (1.47)	98 (62.0)
No of disorders (n=2725)			
1	1167 (42.8)		
2	657 (24.1)	–	–
3	430 (15.8)	–	–
4	240 (8.8)	–	–
5–10	231 (8.5)	–	–

\*Differences between means within each variable differed significantly  $p < 0.005$  (t-test for independent samples for sex, illicit drug use and psychological distress); ANOVA for age groups, occupational status, psychoactive medicinal drug use and alcohol use patterns).

†Differences between categories within each variable except for sex differed significantly  $p < 0.005$  (chi-squared ( $\chi^2$ ) test for  $2 \times n$  tables). ANOVA, one-way analysis of variance; AUDIT-4, Alcohol Use Disorder Identification Test 4; SCL-5, Symptom Checklist 5.

years (16.9%) and decreased substantially with increasing age (for those 50–64 years it was 10.7%; 65–79 years 1.3% and for those >80 years it was 0.8%).

The prevalence of multimorbidity in patients using psychoactive medicinal drugs was higher (68.7%, mean number of disorders: 2.56; SD: 1.61) than for those using illicit drugs (62.0%, mean number of disorders: 2.23; SD: 1.47) (table 1). 65.5% of those using one medication and 73.3% using ≥2 medications were multimorbid, respectively (table 1).

Overall, 85.5% of patients with multimorbidity used any of the three substance groups, either individually or in combination with each other. The prevalence of individual and combined substance use is shown in table 2. Of all patients, 2.9% used all three substance groups concomitantly, and of these 61.8% were multimorbid compared with those without multimorbidity (38.2%). The most frequent combination of substances was alcohol and psychoactive medicinal drugs (18.3%). Of a total of 787 patients using psychoactive medicinal drugs (table 1),

**Table 2** Prevalence of individual substance use and combined substance use (alcohol use includes any level of drinking, from low-risk drinking to risky drinking) among patients with and without multimorbidity (single diseased)

N (%)	Single-diseased patients n (%)*	Patients with multimorbidity n (%)*
All patients (n=2359, 100%)	1018 (43.2)	1341 (56.8)
Not taken any drug (n=308, 13.1%)	114 (37.0)	194 (63.0)
Combined substance use		
Combined illicit drugs and alcohol (n=43, 1.8%)	23 (53.5)	20 (46.5)
Combined psychoactive medicines and alcohol (n=432, 18.3%)	154 (35.6)	278 (64.4)
Combined psychoactive medicines and illicit drugs (n=24, 1.0%)	7 (29.2)	17 (70.8)
Combined all three substances (n=68, 2.9%)	26 (38.2)	42 (61.8)
Individual substance use		
Only psychoactive medicines (n=222, 9.4%)	45 (20.3)	177 (79.7)
Only alcohol (n=1253, 53.1%)	648 (51.7)	605 (48.3)
Only illicit drugs (n=9, 0.4%)	1 (11.1)	8 (88.9)

\*Differences between the prevalence of psychoactive substance use and combination of substances among single-diseased and those with multimorbidity differed significantly with a  $p < 0.001$  for all of the substances and combinations of substances (chi-squared ( $\chi^2$ ) test for 2×n tables).

only 28.2% used these alone and not in combination with illicit drugs or alcohol. Combinations of drugs in general were more prevalent in patients with multimorbidity compared with those without multimorbidity, except for the combination of illicit drugs and alcohol, which

was more frequent among those without multimorbidity (53.5% vs 46.5%) (table 2).

Table 3 depicts the ORs for the association between multimorbidity and the predictor variables including alcohol use patterns, illicit and psychoactive medicinal

**Table 3** ORs for multimorbidity by age, sex, occupational status, psychological distress and substance use (n=2136)

	Multimorbidity (unadjusted OR, 95% CI)	Multimorbidity (adjusted OR, 95% CI)*
Male (vs female)	0.87 (0.74 to 1.01)	0.95 (0.78 to 1.16)
Age years		
18–34	Reference	Reference
35–54	1.51 (1.17 to 1.95)	1.24 (0.92 to 1.66)
50–64	2.50 (1.98 to 3.17)	1.98 (1.48 to 2.64)
65–79	4.23 (3.35 to 5.34)	3.18 (2.06 to 4.93)
≥80	8.66 (6.22 to 12.07)	6.72 (3.79 to 11.90)
Occupational status		
Economically active	Reference	Reference
Retired	4.23 (3.52 to 5.07)	1.36 (0.91 to 2.03)
Economically non-active	2.85 (2.24 to 3.62)	1.50 (1.10 to 2.05)
Psychological distress (SCL-5)	1.43 (1.18 to 1.74)	1.28 (1.01 to 1.63)
Substance use		
Alcohol use patterns		
Low-risk drinking (scores 1–3)	Reference	Reference
Abstinence (score 0)	1.79 (1.44 to 2.22)	1.50 (1.15 to 1.95)
Alcohol use in excess of low-risk guidelines (scores 4–6)	0.71 (0.59 to 0.87)	0.96 (0.76 to 1.21)
Hazardous drinking (scores 7–8)	0.74 (0.54 to 1.02)	1.18 (0.81 to 1.71)
Risky alcohol use and possible alcohol dependence (scores ≥9)	1.41 (1.02 to 1.94)	1.53 (1.05 to 2.24)
Psychoactive medicinal drugs	2.09 (1.75 to 2.50)	1.34 (1.07 to 1.67)
Illicit drugs	1.26 (0.90 to 1.76)	1.22 (0.80 to 1.85)

\*All adjusted for the other listed variables in model.  
SCL-5, Symptom Checklist 5.

drug use, and psychological distress. The likelihood for being multimorbid increased substantially with increasing age. Patients with risky alcohol use were more likely to be multimorbid compared with those with low risk drinking habits (OR 1.53; 95% CI 1.05 to 2.24), the same applied to abstainers (OR 1.50; 95% CI 1.15 to 1.95). Multimorbidity was not significantly associated with hazardous drinking (OR 1.18; 95% CI 0.81 to 1.71). There was a significant positive association between multimorbidity and psychoactive medicinal drug use (OR 1.34; 95% CI 1.07 to 1.67), and multimorbidity and psychological distress (OR 1.28 95% CI 1.01 to 1.63). No significant association between multimorbidity and illicit drugs was detected.

### Sensitivity analysis

The results from our sensitivity analyses were similar to those from the main regression model (online supplemental table 1) except for self-reported psychological distress which was not significantly associated with multimorbidity. The ORs for all variables included in the model were slightly attenuated and remained significantly associated with multimorbidity.

### DISCUSSION

In this study of acute medically ill patients, we found an association between multimorbidity and psychological distress, psychoactive medicinal drug and risky alcohol use. No association between multimorbidity and illicit drug use was found. Substance use was widespread and the majority of multimorbid patients used alcohol and psychoactive medicinal drugs and a combination of both.

Our findings are commensurate with prior reports on the high prevalence of multimorbidity among those non-economically active and older populations and the association between ageing and multimorbidity.<sup>1 34</sup> The increase in global ageing and long-term conditions indicate that the number of people with multimorbidity in the future is set to rise.<sup>1</sup> Older adults are often not screened for SUDs.<sup>9</sup> This underpins the importance of the identification of substance use among the elderly; which if not integrated in the disease management might compromise their treatment effectiveness. This applies particularly to alcohol which was widely used by the older patients in our study, which are prescribed medications for multiple conditions. Therefore, the probability for adverse events, non-adherence and drug interactions might be elevated due to the diminished metabolic efficiency for both alcohol and other substances and requires careful management among the older patients drinking in a risky manner.<sup>35 36</sup> Nevertheless, in our study, the prevalence of multimorbidity among the young patients (18–34) was high (35%). The reason for this might be that our hospital comprises patients from boroughs with low income and low life expectation rates in Norway.<sup>25</sup> This finding is in concordance with other studies reporting an earlier manifestation of multimorbidity among those socioeconomically deprived.<sup>34</sup> The majority of the young

patients in our study used substances, and one-third reported to have psychological distress. From a preventive perspective, the young patients should be timely targeted in view of their substance use, mental health and overall morbidity in order to avoid decrements in quality of life, health complications and possible frailty in later stages of life.

Patients with psychological distress were more likely to be multimorbid compared with single-diseased patients. However, our sensitivity analysis showed that this association did not remain after removal of mental- and behavioural disorders. This might indicate that self-reported psychological distress was mainly associated to mental and behavioural disorders, as previously reported.<sup>6</sup>

The observed augmented risk for multimorbidity among abstainers in our main analysis may reflect the fact that some former drinkers became abstainers due to health problems.<sup>37</sup> These results indicate that risky alcohol use should be considered in a multifaceted management regimen for multimorbid patients.

The prevalence of psychoactive medicinal drug use was higher among multimorbid patients compared with single-diseased patients. Nonetheless, 73.3% of patients using two or more psychoactive medical drugs were multimorbid, which might reflect a plausible unhealthy drug use. Clinical guidelines rarely account for multimorbidity.<sup>38</sup> As a result, patients with multimorbidity might be prescribed several drugs, although each of these is recommended by a disorder-specific guideline, leading to a possibly higher number of drugs used. However, we examined only psychoactive medicinal drugs, and some of the patients might have used them non-medically. Regardless of the manner of use, when several psychoactive medications are used by multimorbid patients the risk of drug–drug interactions increases with the number of co-existing disorders and the number of drugs taken.<sup>39</sup>

More than half of the patients combining all three substances were multimorbid. The adverse effects of multimorbidity and substance use on the functioning and quality of life might be greater than the individual effects expected from multimorbidity or substance use alone. A high proportion of multimorbid patients combined psychoactive medicinal drugs and alcohol. Patients used mainly benzodiazepines, opioids and z-hypnotics; which when combined with alcohol might generate an additive effect with increased CNS suppression and an increased risk of adverse events and fatal outcomes, even when the individual substances are used as prescribed.<sup>40</sup> Regarding this, assessing alcohol use among multimorbid patients using prescription psychoactive medications should be a priority, in order to target patients that need to reduce their alcohol use. Furthermore, interventions that target reductions in alcohol consumption do not necessarily incorporate other substances, except for tobacco use.<sup>41</sup> Given the high prevalence of substance use among hospitalised populations, including ours, other substances should be incorporated alongside alcohol interventions.<sup>11</sup>

Only a minority of patients did use illicit drugs alone, these were mostly combined with alcohol and psychoactive medicinal drugs. Since patients are more prone to using psychoactive medicinal drugs non-medically, the combination of illicit and psychoactive medicinal drugs might indicate a non-medical use of these prescription drugs.<sup>42</sup> A combination of psychoactive medicinal and illicit drugs can have serious medical consequences, reflected in increased ED visits.<sup>11 43</sup> Furthermore, use of illicit drugs may impair adherence to prescribed controlled regimens in some patients and cause detrimental drug-drug interactions.<sup>44</sup> Given the under-reporting in both psychoactive medicinal and illicit drugs,<sup>31 45</sup> blood sample screening might be an appropriate tool to assess drug use and deliver adequate care to these patients.

More than half of our patient population was multimorbid. Patients with multimorbidity have more frequent and complex interactions with the healthcare services and account for substantial healthcare costs.<sup>46</sup> Integrating substance use in the disease management of patients with multimorbidity is important for the burden reduction on the healthcare system. Several brief instruments measuring substance use in addition to blood sample screening may be used and should be a priority among patients with multimorbidity.<sup>47 48</sup> Furthermore, monitoring multimorbidity in relation to substance use might mitigate this significant public health challenge. In view of its magnitude, an improvement will require a coherent and focused action across multiple sectors and among policy-makers.

### Limitations

Due to the cross-sectional design of the study, the ability to make casual inference was limited. However, this was beyond the scope of this study.

The use of blood samples for assessment of psychoactive medicinal and illicit drugs does not compare directly to self-reported alcohol use which measures alcohol consumption during a year period. Nonetheless, an under-reporting of drug use is evident in studies comparing self-reported drug use with biological samples.<sup>31 45 49</sup> Therefore, a recent and objective blood sample might reflect to an extent the drug use among patients. Given the dose-response association between AUDIT-4 and the biological marker phosphatidylethanol,<sup>24</sup> the results from all three substance groups are to a great extent comparable to each other.

We were not able to distinguish between medical and non-medical use of psychoactive prescription drugs. Regardless of manner of use, examining their distribution, concomitant use and combination patterns with other substances in patients with multimorbidity is of importance.

Finally, the inclusion of acute diseases and other signs and symptoms might have inflated the prevalence of multimorbidity.<sup>50</sup> However, this might reflect a more realistic daily clinical practice, as previously suggested.<sup>51</sup>

### CONCLUSIONS

The observed association between multimorbidity and risky alcohol use, and psychoactive medicinal drug use among patients adds further value to the evidence on substances' harms to health.

Our findings call for more research on multiple psychoactive substance use and multimorbidity. Research on the relationship between multimorbidity and substance use patterns and/or drug-drug interactions among medical patients at all ages is warranted. Consequently, this may have great implications for the clinical practice and public health.

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**Supplemental Table.****Odds ratios (OR) for multimorbidity by age, sex, occupational status, psychological distress, and substance use (n=2099)**

	<b>Multimorbidity (unadjusted OR, 95% CI)*</b>	<b>Multimorbidity (adjusted OR, 95% CI)*</b>
<b>Male (vs. female)</b>	0.86 (0.74 - 1.0)	0.92 (0.76 - 1.11)
<b>Age years</b>		
18-35	1	1
36-50	1.42 (1.09 - 1.85)	1.21 (0.89 - 1.63)
51-65	2.43 (1.91 - 3.09)	1.92 (1.43 - 2.58)
66-79	4.47 (3.53 - 5.67)	3.33 (2.15 - 5.15)
≥80	9.24 (6.61 - 12.91)	7.07 (4.0 - 12.48)
<b>Occupational status</b>		
Economically active	1	1
Retired	4.26 (3.56 - 5.11)	1.32 (0.89 - 1.97)
Economically non-active	2.38 (1.87 - 3.03)	1.42 (1.03 - 1.95)
<b>Psychological distress (SCL-5)</b>	1.22 (1.0 - 1.48)	1.12 (0.88 - 1.42)
<b>Substance use</b>		
<b>Alcohol patterns</b>		
Low-risk drinking (scores 1-3)	1	1
Abstinence (score 0)	1.79 (1.44 - 2.22)	1.53 (1.18 - 1.99)
Alcohol use in excess of low-risk guidelines (scores 4-6)	0.74 (0.61 - 0.91)	0.99 (0.79 - 1.26)
Hazardous drinking (scores 7-8)	0.70 (0.51 - 0.97)	1.13 (0.78 - 1.66)
Risky alcohol use and possible alcohol dependence (scores ≥ 9)	1.26 (0.91 - 1.75)	1.54 (1.05 - 2.28)
<b>Psychoactive medicinal drugs</b>	1.95 (1.63 - 2.33)	1.27 (1.01 - 1.58)
<b>Illicit drugs</b>	1.07 (0.76 - 1.51)	1.10 (0.71 - 1.69)

\*All adjusted for the other listed variables in model