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Association between alcohol and substance use disorders and psychiatric service use in patients with severe mental illness: a nationwide Danish register-based cohort study

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Abstract

Background. Substance use disorder is highly prevalent in people with psychiatric disorders, and known to impede the psychiatric treatment. Some studies show increased rates of service use, while others show a decrease. These conflicting results are further hampered by a lack of large-scale studies. The aim of this study was to investigate the association between substance use disorder and psychiatric service use in psychiatric patients.

Methods. The study was a prospective registry-based cohort study including patients with severe mental illness. The primary outcome was the number of hospitalisations, bed days and the number of psychiatric emergency department contacts. The association was calculated with incidence rate ratio with 95% confidence intervals.

Results. The study included all psychiatric patients born since 1955. In total, 21 558 patients with schizophrenia (47.54% with substance use disorder), 80 778 patients with depression (28.78% with substance use disorder), 10 560 patients with bipolar affective disorder (40.08% with substance use disorder) and 69 252 patients with a personality disorder (39.18% with substance use disorder) were included. Patients with comorbid substance use disorder had significantly increased rates of hospitalisations, bed days and psychiatric emergency department contacts ($p < 0.001$) for the majority of the included substances, compared with patients without such disorders.

Conclusion. Substance use disorder was associated with an increased number of hospitalisations, bed days and increased number of psychiatric emergency department contacts for the majority of the included substances.

Introduction

Alcohol and substance use disorder among patients with severe mental illness is a serious comorbidity with a prevalence of about 20–50% depending on the type of mental illness (Toftdahl *et al.* 2016). Patients with substance use disorder have a significantly higher risk of all-cause mortality than psychiatric patients without substance use disorder (Hjorthøj *et al.* 2015). Moreover, studies have found that substance use disorder worsens the patient's prognosis as the effect of pharmacological treatment is weakened, and the interventions of psychosocial and psychotherapeutic treatment will be more complicated (Wobrock *et al.* 2013; Large *et al.* 2014). Studies have also found that patients with substance use disorder have a higher rate of readmissions, a higher rate of violence, non-compliance, relapse, self-harm, injury and infectious diseases and are more likely to be homeless (Leon *et al.* 1998; Wobrock *et al.* 2013; Large *et al.* 2014; Sara *et al.* 2014).

While psychiatric hospital contacts have been suggested as a measure/indicator of illness severity, reports of the association of comorbid substance use disorder with hospital contacts, health care utilisation and readmission has been conflicting. Some studies have found a significant increase in hospitalisation (McCrone *et al.* 2000; Wright *et al.* 2000; Picci *et al.* 2013; Patel *et al.* 2016; Toftdahl *et al.* 2016), and some studies have found a decrease (Ries *et al.* 2000; Wu *et al.* 2015), which is indicating that further research is required.

The aim of this study was to conduct the first large-scale population-based study about association between patients with schizophrenia, bipolar affective disorder, depression and personality disorder with and without comorbid substance use disorder on a number of psychiatric hospitalisations, bed days and a number of psychiatric emergency department contacts in the Danish nationwide register-based study.

We tested the hypothesis that patients with both severe mental illness and substance use disorder would have a higher rate of service use, compared with patients with severe mental illness without substance use disorder.

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Methods

Population

We used the Danish Civil Registration System (Pedersen *et al.* 2006), which provides all citizens with permanent residency in Denmark with a unique identification number that allows us to link to the Psychiatric Central Research Register (Mors *et al.* 2011), which gives coded information about all psychiatric admissions including diagnoses (given by medical doctors) and dates of admission and discharge. The latter was established in 1969 and therefore we included all patients born in Denmark from 1 January 1955 to minimise the risk of the population having incident diagnoses prior to the inception of the register. Data were obtained up to August 2013.

The study included all patients registered with the diagnoses of schizophrenia (ICD-8 295, ICD-10 F.20.x), bipolar affective disorder (ICD-8 296.19, 296.39, ICD-10 F31), depression (ICD-8 296.09, 296.29, 298.09, 300.49, ICD-10 F32-F34) or personality disorders (ICD-8 301 and all subtypes, ICD-10 F60-F61). If a patient was registered with more than one such diagnosis, he or she was included in all relevant study populations. We included patients in the population regardless of whether they had substance use disorders diagnosed before or after the psychiatric disorder, or not at all. There were no exclusion criteria.

Only patients treated in hospital settings were included, and not those treated exclusively in primary treatment facilities.

Exposure

The substance use disorders included in this study were alcohol (ICD-8 291, ICD-10 F10), opioids (ICD-8 304.0, 304.1, ICD-10 F11), cannabis (ICD-8 304.5, ICD-10 F12), sedatives and hypnotics (ICD-8 304.2, 304.3, ICD-10 F13), cocaine (ICD-8 304.4, ICD-10 F14), stimulants (ICD-8 304.6, ICD-10 F15), hallucinogens (ICD-8 304.7, ICD-10 F16) and volatile solvents and multiple drug use (ICD-8 304.8, 304.9, ICD-10 F18, F19). Because substance use disorder often occurs for a while before they are registered, people were categorized as exposed to the substance use disorder in question regardless of when it occurred. Somatic indicators of substance use disorder were found using ICD-10 codes for diseases occurring in relation to substance use in both the Psychiatric Central Research Register and the somatic National Patient Register, which was established in 1977 (Lynge *et al.* 2011). We used the following ICD-10 codes: E52 (niacin deficiency), E24.4 (alcohol-induced pseudo-Cushing's syndrome), G31.2 (alcohol-related degeneration of nervous system), G62.1 (alcoholic polyneuropathy), G72.1 (alcoholic myopathy), I42.6 (alcoholic cardiomyopathy), K29.2 (alcoholic gastritis), K70 (alcoholic liver disease), K86.0 (alcohol-induced chronic pancreatitis), O35.4 [maternal care for (suspected) damage to foetus from alcohol], Y57.3 (alcohol deterrents), Z50.2 (alcohol rehabilitation), Z71.4 (alcohol abuse counselling and surveillance), Z72·1 (alcohol use) and ICD-8 codes: 571.0 (alcoholic cirrhosis).

From the Danish National Prescription Registry, we included the following anatomical therapeutic classification codes (Kildemoes *et al.* 2011): disulfiram (ATC-code N07BB01), calcium carbimide (ATC-code N07BB02) or acamprosate (ATC-code N07BB03) for alcohol use disorder. For non-alcohol substance use disorder: buprenorphine (ATC-code N07BC01), methadone (ATC-code N07BC02) and levacetylmethadol (ATC-code N07BC03).

Substance use categories were mutually not exclusive.

Outcome

The study outcome is the rate of psychiatric hospitalisations, bed days in a psychiatric hospital and the number of psychiatric emergency department contacts, from the Psychiatric Central Research Register.

Statistical analysis

The association between substance use disorder and use of psychiatric services was analysed with Poisson regression with robust standard errors and the natural logarithm of observation time included as offset. The results are presented in two sets of analysis with incidence rate ratio (IRR) and 95% confidence intervals (95% CI).

All patients were followed from the date of diagnosis with a mental health disorder until death, migration or end of study, summarised in person years.

Incidence rate (IR) was estimated for every outcome for patients with and without substance use disorder.

We created two models. In model 1, each substance use disorder was entered independently and without covariate adjustment. In model 2, all substance use disorders were entered simultaneously and their effects thus mutually adjusted and further adjusted for age at the onset of mental illness, sex and other comorbidities such as self-harm and other psychiatric diagnoses.

A sensitivity analysis was conducted to see if the results changed if only the more recent data were included in the analysis. We included data from 1994 to use exclusively data within the ICD-10 system.

All analyses were conducted in STATA/MP 13.1.

Results

Demographic information for the study population is presented in Table 1. The study included 21558 patients with schizophrenia, followed for 263.153.8 person-years, of which 47.5% had a substance use disorder, 541 (2.5%) emigrated during follow-up and 2445 (11.3%) died during follow-up. Of the 80 778 patients with depression followed for 599 217.6 person-years, 28.8% had a substance use disorder, 1808 (2.2%) emigrated during follow-up and 2947 (3.6%) died during follow-up. Of the 10 560 patients with bipolar affective disorder followed for 80 959.6 person-years, 40.1% had a substance use disorder, 182 (1.7%) emigrated during follow-up and 574 (5.4%) died during follow-up. Of the 69 252 patients with a personality disorder followed for 844 391.9 person-years, 39.2% had a substance use disorder, 2982 (4.3%) emigrated during follow-up and 5171 (7.5%) died during follow-up.

Alcohol was the most used substance with a prevalence of 23.3–34.5%, followed by cannabis with a prevalence of 5.5–20.6% and volatile solvents and multiple drug use with a prevalence of 5.0–17.5%. The remaining substances had a prevalence of between 0.2% and 6.7%.

Rates of psychiatric hospitalisation

In patients with schizophrenia, both overall substance use disorder and all individual types of substance use disorder were significantly associated with an increased number of admissions, with the exception of hallucinogen use disorder (IRR 1.08, 95% CI 0.93–1.26) in the fully adjusted model (Table 2). Substance

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Table 1. Patients' characteristics – register-based data

	Schizophrenia *n* (%)	Depression *n* (%)	Bipolar affective disorder *n* (%)	Personality disorder *n* (%)
N	21 558	80 778	10 560	69 252
Male	13 374 (62.04%)	30 134 (37.30%)	4371 (41.39%)	26 890 (38.83%)
Substance use disorder	10 248 (47.54%)	23 251 (28.78%)	4232 (40.08%)	27 130 (39.18%)
Age first diagnosis mean (S.D.)	27.64 (8.37)	31.94 (10.58)	34.73 (10.29)	27.58 (8.52)
Age first substance use disorder mean (S.D.)[a]	27.02 (8.46)	30.96 (10.27)	31.86 (10.03)	27.78 (8.93)
Alcohol	7437 (34.50%)	18 800 (23.27%)	3471 (32.87%)	21 301 (30.76%)
Opioid	1450 (6.73%)	2394 (2.96%)	379 (3.59%)	4199 (6.06%)
Cannabis	4450 (20.64%)	4423 (5.48%)	1001 (9.48%)	6878 (9.93%)
Sedatives and hypnotics	1164 (5.40%)	2121 (2.63%)	494 (4.68%)	3386 (4.89%)
Cocaine	604 (2.80%)	792 (0.98%)	202 (1.91%)	1170 (1.69%)
Stimulant	1194 (5.54%)	1173 (1.45%)	249 (2.36%)	1905 (2.75%)
Hallucinogens	217 (1.01%)	131 (0.16%)	35 (0.33%)	331 (0.48%)
Other	3781 (17.54%)	4005 (4.96%)	930 (8.81%)	7736 (11.71%)
Preceding anxiety[b]	1620 (7.51%)	4623 (5.72%)	1026 (9.72%)	4789 (6.92%)
Preceding self-harm[b]	6236 (28.93%)	13 268 (16.43%)	2973 (28.15%)	9405 (13.58%)
Preceding schizophrenia[b]	–	1284 (1.59%)	681 (6.45%)	1782 (2.57%)
Preceding depression[b]	3472 (16.11%)	–	4039 (38.25%)	826 (1.19%)
Preceding bipolar affective disorder[b]	526 (2.44%)	845 (1.05%)	–	10 644 (15.37%)
Preceding personality disorder[b]	6014 (27.90%)	8222 (10.18%)	2497 (23.65%)	–
Preceding schizotypal disorder[b]	1701 (7.89%)	634 (0.78%)	242 (2.29%)	703 (1.02%)
Preceding ADHD[b]	470 (2.18%)	868 (1.07%)	270 (2.56%)	1109 (1.60%)
Preceding autism[b]	329 (1.53%)	501 (0.62%)	78 (0.74%)	274 (0.40%)
Preceding eating disorder[b]	477 (2.21%)	1738 (2.15%)	246 (2.33%)	1972 (2.85%)

[a]Age at first substance use disorder refers to the first time the substance use disorder is registered.
[b]'Preceding' refers to mental disorders preceding the main mental disorder, e.g. schizophrenia.
ADHD, attention-deficit hypersensitivity disorder.

use disorder roughly doubled the number of hospitalisations per year, with IRRs ranging between 1.90 and 2.58, but were somewhat reduced in the fully adjusted model.

In patients with bipolar affective disorder, both overall and most individual types of substance use disorder were significantly associated with increased hospitalisations with around twice as many admissions per year, IRR ranging between 1.76 and 2.54. In the fully adjusted model, IRR ranged between 0.60 and 1.71. While associated with increased rates of hospitalisation in the basic models, hallucinogen use disorder showed a significant decrease in hospitalisation in the fully adjusted model with IRR 0.60 (95% CI 0.42–0.86).

In patients with depression, overall as well as individual types of substance use disorder were significantly associated with an increased number of hospitalisations with around twice to four times as many hospitalisations per year. In the fully adjusted model, only opioid and hallucinogen use disorders were no longer significantly associated with the rates of hospitalisations.

In patients with personality disorder, both overall and individual types of substance use disorder were significantly associated with increased hospitalisations in both models with around twice to almost four times as many admissions per year, except for opioids in the fully adjusted model which showed a significant decrease in hospitalisation with IRR 0.90 (95% CI 0.84–0.96).

Rates of bed days

In patients with schizophrenia, substance use disorder was significantly associated with increased bed days (Table 3). They had up to twice as many bed days per year if they had a substance use disorder, IRR ranged between 1.39 and 2.20. Use of opioids and sedatives were non-significant in the fully adjusted model.

In patients with bipolar affective disorder, substance use disorder was significantly associated with increased bed days, IRR ranged between 1.54 and 2.81, although these results were diminished in the fully adjusted model.

In patients with depression, substance use disorder was significantly associated with increased bed days with around twice to four times as many days admitted per year.

In patients with personality disorder, substance use disorder was significantly associated with increased bed days in both models with around twice to almost four times as many admissions per year. In the adjusted model, opioids showed a significant decrease in days admitted with IRR 0.85, 95% CI 0.78–0.93.

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Table 2. IRs and IRRs for psychiatric hospitalizations according to mental disorders and SUDs

	Schizophrenia			Bipolar affective disorder			Depression			Personality disorder		
Type of SUD	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)
Any SUD	0.39 (0.37–0.40)/ 0.85 (0.82–0.87)	2.19 (2.09–2.30) $p < 0.001$	2.02 (1.92–2.12) $p < 0.001$	0.33 (0.32–0.35)/ 0.73 (0.69–0.77)	2.19 (2.03–2.36) $p < 0.001$	1.97 (1.81–2.14) $p < 0.001$	0.14 (0.14–0.15)/ 0.40 (0.39–0.42)	2.80 (2.68–2.93) $p < 0.001$	2.52 (2.41–2.63) $p < 0.001$	0.13 (0.13–0.14)/ 0.39 (0.38–0.40)	2.94 (2.81–3.06) $p < 0.001$	2.83 (2.71–2.96) $p < 0.001$
Alcohol	0.89 (0.86–0.92)	2.02 (1.93–2.12) $p < 0.001$	1.55 (1.48–1.63) $p < 0.001$	0.75 (0.71–0.80)	2.10 (1.94–2.27) $p < 0.001$	1.71 (1.56–1.87) $p < 0.001$	0.42 (0.41–0.43)	2.66 (2.54–2.78) $p < 0.001$	2.06 (1.96–2.17) $p < 0.001$	0.40 (0.39–0.42)	2.67 (2.57–2.79) $p < 0.001$	1.98 (1.89–2.08) $p < 0.001$
Opioids	1.28 (1.19–1.36)	2.29 (2.13–2.44) $p < 0.001$	1.08 (1.00–1.17) $p = 0.049$	0.97 (0.81–1.14)	2.05 (1.71–2.44) $p < 0.001$	0.87 (0.70–1.08) $p = 0.193$	0.52 (0.48–0.56)	2.41 (2.22–2.63) $p < 0.001$	0.91 (0.83–1.00) $p = 0.055$	0.52 (0.49–0.55)	2.36 (2.21–2.51) $p < 0.001$	0.90 (0.84–0.96) $p = 0.003$
Cannabis	0.99 (0.95–1.03)	1.90 (1.81–1.99) $p < 0.001$	1.25 (1.18–1.32) $p < 0.001$	0.88 (0.79–0.96)	1.92 (1.73–2.14) $p < 0.001$	1.13 (1.00–1.28) $p = 0.044$	0.55 (0.52–0.58)	2.66 (2.49–2.84) $p < 0.001$	1.35 (1.26–1.45) $p < 0.001$	0.57 (0.55–0.60)	2.71 (2.65–2.94) $p < 0.001$	1.42 (1.34–1.50) $p < 0.001$
Sedatives and hypnotics	1.30 (1.22–1.39)	2.28 (2.14–2.48) $p < 0.001$	1.10 (1.01–1.19) $p = 0.033$	1.12 (1.00–1.24)	2.44 (2.17–2.74) $p < 0.001$	1.28 (1.12–1.48) $p < 0.001$	0.73 (0.69–0.78)	3.53 (3.29–3.78) $p < 0.001$	1.49 (1.37–1.61) $p < 0.001$	0.67 (0.63–0.70)	3.19 (2.96–3.32) $p < 0.001$	1.56 (1.47–1.67) $p < 0.001$
Cocaine	1.52 (1.38–1.65)	2.58 (2.35–2.83) $p < 0.001$	1.13 (1.02–1.26) $p = 0.023$	1.22 (0.97–1.42)	2.53 (2.05–3.12) $p < 0.001$	1.27 (0.99–1.61) $p = 0.054$	0.73 (0.64–0.83)	3.32 (2.89–3.80) $p < 0.001$	1.13 (0.98–1.29) $p = 0.083$	0.85 (0.77–0.93)	3.70 (3.31–4.00) $p < 0.001$	1.18 (1.06–1.32) $p = 0.002$
Stimulants	1.41 (1.31–1.51)	2.47 (2.31–2.68) $p < 0.001$	1.28 (1.17–1.40) $p < 0.001$	1.20 (0.97–1.42)	2.50 (2.07–3.03) $p < 0.001$	1.10 (0.88–1.38) $p = 0.399$	0.76 (0.68–0.85)	3.50 (3.12–3.93) $p < 0.001$	1.23 (1.08–1.41) $p = 0.002$	0.81 (0.75–0.87)	3.52 (3.30–3.88) $p < 0.001$	1.34 (1.23–1.47) $p < 0.001$
Hallucinogens	1.27 (1.07–1.47)	2.12 (1.80–2.48) $p < 0.001$	1.08 (0.93–1.26) $p = 0.323$	0.87 (0.54–1.19)	1.76 (1.21–2.55) $p < 0.001$	0.60 (0.42–0.86) $p = 0.005$	0.91 (0.62–1.20)	4.04 (2.93–5.58) $p < 0.001$	1.09 (0.74–1.60) $p = 0.669$	0.74 (0.61–0.87)	3.08 (2.59–3.69) $p < 0.001$	1.19 (1.02–1.39) $p = 0.029$
Volatile solvents and multiple drug use	1.19 (1.14–1.23)	2.43 (2.28–2.52) $p < 0.001$	1.44 (1.34–1.54) $p < 0.001$	1.09 (0.99–1.19)	2.49 (2.26–2.76) $p < 0.001$	1.42 (1.25–1.60) $p < 0.001$	0.67 (0.64–0.71)	3.37 (3.17–3.59) $p < 0.001$	1.54 (1.42–1.68) $p < 0.001$	0.62 (0.60–0.65)	3.26 (3.16–3.47) $p < 0.001$	1.72 (1.62–1.84) $p < 0.001$

The adjusted models are adjusted for: other substances, other psychiatric diagnoses, preceding diagnoses, and number of preceding hospitalizations, bed days and emergency room contacts.
[a]For any SUD, numbers are IRs and 95% CIs per year for individuals without and with SUD, respectively. For specific types of SUDs, numbers are IRs and 95% CIs per year for individuals with that particular type of SUD.
[b]Numbers are IRRs comparing individuals with a given type of SUD to individuals without that given type of SUD.
SUD, substance use disorder; IR, incidence rate; IRR, incidence rate ratio; CI, confidence interval.

Table 3. IRs and IRRs for psychiatric bed days according to mental disorders and SUDs

	Schizophrenia			Bipolar affective disorder			Depression			Personality disorder		
Type of SUD	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)
Any SUD	24.37 (23.53–25.21)/ 38.69 (37.57–39.80)	1.59 (1.52–1.66) $p < 0.001$	1.52 (1.45–1.59) $p < 0.001$	13.11 (12.34–13.88)/ 21.48 (20.21–22.74)	1.64 (1.51–1.78) $p < 0.001$	1.58 (1.45–1.72) $p < 0.001$	4.68 (4.54–4.83)/ 10.02 (9.68–10.37)	2.14 (2.04–2.24) $p < 0.001$	2.00 (1.91–2.10) $p < 0.001$	5.65 (5.44–5.86)/ 12.35 (11.96–12.73)	2.19 (2.08–2.29) $p < 0.001$	2.09 (1.99–2.19) $p < 0.001$
Alcohol	37.84 (36.61–39.07)	1.39 (1.32–1.45) $p < 0.001$	1.15 (1.09–1.20) $p < 0.001$	21.44 (20.06–22.82)	1.54 (1.42–1.68) $p < 0.001$	1.33 (1.22–1.45) $p < 0.001$	10.06 (9.67–10.44)	1.99 (1.89–2.09) $p < 0.001$	1.60 (1.52–1.69) $p < 0.001$	12.42 (12.00–12.85)	1.94 (1.85–2.04) $p < 0.001$	1.46 (1.38–1.54) $p < 0.001$
Opioids	53.35 (49.76–56.94)	1.80 (1.68–1.93) $p < 0.001$	1.04 (0.96–1.13) $p = 0.320$	28.14 (21.61–34.67)	1.76 (1.39–2.22) $p < 0.001$	0.86 (0.69–1.06) $p = 0.155$	13.38 (12.09–14.67)	2.19 (1.98–2.42) $p < 0.001$	0.95 (0.85–1.06) $p = 0.338$	16.11 (14.91–17.32)	2.03 (1.87–2.20) $p < 0.001$	0.85 (0.78–0.92) $p < 0.001$
Cannabis	46.73 (44.76–48.71)	1.69 (1.61–1.78) $p < 0.001$	1.24 (1.17–1.31) $p < 0.001$	29.57 (26.01–33.14)	1.95 (1.71–2.22) $p < 0.001$	1.21 (1.07–1.37) $p = 0.001$	14.96 (13.91 –16.02)	2.55 (2.37–2.75) $p < 0.001$	1.40 (1.29–1.52) $p < 0.001$	20.03 (18.94–21.11)	2.74 (2.58–2.91) $p < 0.001$	1.47 (1.37–1.57) $p < 0.001$
Sedatives and hypnotics	48.31 (44.71–51.91)	1.60 (1.48–1.73) $p < 0.001$	1.02 (0.94–1.11) $p = 0.584$	30.98 (25.96–36.01)	1.98 (1.67–2.34) $p < 0.001$	1.24 (1.05–1.46) $p = 0.011$	17.84 (16.48–19.21)	2.99 (2.76–3.25) $p < 0.001$	1.51 (1.37–1.66) $p < 0.001$	19.02 (17.78–20.26)	2.42 (2.26–2.60) $p < 0.001$	1.39 (1.28–1.50) $p < 0.001$
Cocaine	67.10 (60.72–73.48)	2.20 (1.99–2.43) $p < 0.001$	1.23 (1.11–1.36) $p < 0.001$	45.10 (30.90–59.31)	2.81 (2.05–3.87) $p < 0.001$	1.55 (0.17–2.05) $p = 0.002$	19.08 (16.17–21.99)	3.06 (2.62–3.57) $p < 0.001$	1.09 (0.92–1.30) $p = 0.304$	29.60 (26.12–33.08)	3.60 (3.29–4.05) $p < 0.001$	1.34 (1.18–1.51) $p < 0.001$
Stimulants	62.50 (57.95–67.04)	2.11 (1.95–2.27) $p < 0.001$	1.27 (1.17–1.39) $p < 0.001$	39.93 (29.76–50.11)	2.50 (1.93–3.24) $p < 0.001$	1.10 (0.86–1.40) $p = 0.452$	19.87 (17.49–22.25)	3.23 (2.86–3.65) $p < 0.001$	1.27 (1.11–1.46) $p = 0.001$	28.17 (25.49–30.85)	3.52 (3.20–3.88) $p < 0.001$	1.43 (1.28–1.59) $p < 0.001$
Hallucinogens	60.48 (50.56–70.40)	1.95 (1.65–2.30) $p < 0.001$	1.15 (0.98–1.34) $p = 0.079$	42.31 (18.29–66.34)	2.58 (1.46–4.56) $p < 0.001$	0.85 (0.50–1.45) $p = 0.557$	27.60 (17.53–37.68)	4.36 (3.02–6.28) $p < 0.001$	1.07 (0.71–1.60) $p = 0.757$	29.39 (22.62–36.17)	3.48 (2.76–4.39) $p < 0.001$	1.33 (1.06–1.66) $p = 0.014$
Volatile solvents and multiple drug use	52.12 (49.84–54.39)	1.92 (1.82–2.02) $p < 0.001$	1.36 (1.27–1.46) $p < 0.001$	32.82 (28.85–36.79)	2.20 (1.93–2.50) $p < 0.001$	1.40 (1.22–1.62) $p < 0.001$	17.02 (15.89–18.15)	2.97 (2.77–3.19) $p < 0.001$	1.50 (1.37–1.65) $p < 0.001$	20.08 (19.08–21.08)	2.89 (2.73–3.05) $p < 0.001$	1.66 (1.54–1.78) $p < 0.001$

The adjusted models are adjusted for: other substances, other psychiatric diagnoses, preceding diagnoses, and number of preceding hospitalizations, bed days and emergency room contacts.

[a]For any SUD, numbers are IRs and 95% CIs per year for individuals without and with SUD, respectively. For specific types of SUDs, numbers are IRs and 95% CIs per year for individuals with that particular type of SUD.

[b]Numbers are IRRs comparing individuals with a given type of SUD to individuals without that given type of SUD.

SUD, substance use disorder; IR, incidence rate; IRR, incidence rate ratio; CI, confidence interval.

Rates of psychiatric emergency department contacts

In patients with schizophrenia, substance use disorder was significantly associated with an increased number of emergency department contacts with around twice to almost four times as many contacts per year (Table 4).

In patients with bipolar affective disorder, substance use disorder was significantly associated with an increased number of emergency contacts with around twice to three times more contacts per year. In the fully adjusted model, hallucinogens showed a significant decrease in psychiatric emergency department contacts (IRR 0.53, 95% CI 0.33–0.85).

In patients with depression, substance use disorder was significantly associated with an increased number of emergency contacts, with around twice to four times as many contacts per year.

In patients with personality disorder, substance use disorder was significantly associated with an increased number of emergency contacts with around twice to five times as many contacts per year. In the fully adjusted model, opioids showed a significant decrease in emergency contacts with IRR 0.82, 95% CI 0.73–0.93.

Sensitivity analysis

We conducted a sensitivity analysis in order to investigate if our findings changed if only the more recent data were included in the analysis. We included data from 1994 to see if the increased focus on patients with both mental health disorders and substance use disorder and, at the same time, whether focusing on patients treated as outpatients in their immediate environment could affect the hospitalisation length. The results varied by <10% and showed no decrease in hospital length (data not shown).

Discussion

We examined the association between substance use disorder and hospitalisations, bed days and the number of psychiatric emergency department contacts in patients with severe mental illness. Substance use disorder among people with severe mental illness was associated with an increased number of hospitalisations, bed days and an increased number of psychiatric emergency department contacts for the majority of the included drugs. This indicates that psychiatric patients with substance use disorders need a longer and more targeted treatment including both their substance use and psychiatric disorder.

In patients, with mental illness, substance use disorder was associated with two to five more hospitalisations, more bed days and more psychiatric emergency department contacts. We found the strongest association for bipolar affective disorder and personality disorder. This is probably because patients with schizophrenia also have several admissions if they do not have a substance use disorder, which is shown by the relatively high IR for hospitalisation in schizophrenia.

The high rate of psychiatric emergency department contacts for all diagnoses showed a similarity to the rate we found in hospitalisations. This could reflect that patients with substance use disorder who make contact to the psychiatric emergency department afterword actually are admitted to the hospital for further inpatients treatment.

All associations were decreased in the fully adjusted model, which probably indicates that not one substance predominates; rather, it shows a comorbid substance use where the patient often uses more than one substance. Some substances was associated with lower service use, which is probably not true, it can be the result of the mutual adjustment or it can reflect that people use different substances for different durations or amounts, and therefor are less affected by the substance use.

In patients with personality disorder and opioid use disorder hospitalisation, bed days and psychiatric emergency department contacts significantly decreased, which was an unexpected finding. The reason for this could be a type 1 error. Another possible reason could be that patients who have a personality disorder and are abusing opioids have multiple problems and a very complex life situation that keeps them away from the healthcare system. Thirdly, it could be over adjustment, perhaps due to these patients having a very high prevalence of multiple substance use disorders. Finally, it could be related to the different duration and effects of different substances, or that patients with opioid use disorders may be more likely to suffer incarceration, hence being artificially protected against service use. These findings require further research.

The only study, to our knowledge, which used the same method as our study, is one that examined the association between hospitalisation and cannabis in England. They found an increased hospitalisation rate for patients who used cannabis with an IRR 1.50 after 5 years (Patel *et al.* 2016). In our study, cannabis and schizophrenia showed an IRR 1.90 and 1.25 in the fully adjusted model.

Several previous studies have found that hospitalisation rates are increased by substance use disorders (Menezes *et al.* 1996; McCrone *et al.* 2000; Wright *et al.* 2000; Picci *et al.* 2013; Sara *et al.* 2014). An American study found that length of stay was 13–15% shorter in substance use disorder in one state, but in another, it was 35% longer (Bradley & Zarkin, 1996). Another American study found a 30% shorter admission for substance use disorder, and they excluded the patients who left the hospital against advice from the doctor (Ries *et al.* 2000). An Italian study found that, with schizophrenia, bed days were significantly higher with substance use disorder (Picci *et al.* 2013). They did not distinguish between different substances and they only looked at one admission.

The studies which found a decrease in hospitalisation for substance use disorder (Herr *et al.* 1991; Ries *et al.* 2000; Wu *et al.* 2015) have low sample sizes. The studies, however, do not refer to the treatment that patients with substance use disorder receive, which is likely to have an impact on hospitalisation. One study examined hospitalisation when patients were offered *managed care* and find a significant decrease in hospitalisation. However, they are readmitted more often during the first 6 months after discharge (Leon *et al.* 1998). These mixed results may indicate that it could be differences in the treatment, which are important in relation to hospitalisation.

To our knowledge, no prior studies examined the use of psychiatric emergency department contacts by the same method. A study from England found that the mean number of psychiatric emergency department contacts in patients with substance use disorder was 3.18, and in patients without substance use disorder, the mean number was 2.50. The study included <200 participants and used a cross-sectional design, which makes a comparison difficult and therefore further research is required (Menezes *et al.* 1996).

Strengths and limitations

The strength of the study is that the registers make it possible to include the entire Danish population and give us a large sample

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Table 4. IRs and IRRs for psychiatric emergency department contacts according to mental disorders and SUDs

	Schizophrenia			Bipolar affective disorder			Depression			Personality disorder		
Type of SUD	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)	IR[a]	IRR[b] (95% CI)	Adjusted IRR[b] (95% CI)
Any SUD	0.25 (0.24–0.27)/ 0.67 (0.63–0.71)	2.66 (2.45–2.89) $p < 0.001$	2.44 (2.24–2.65) $p < 0.001$	0.23 (0.21–0.25)/ 0.64 (0.60–0.69)	2.78 (2.49–3.11) $p < 0.001$	2.41 (2.15–2.70) $p < 0.001$	0.14 (0.13–0.14)/ 0.41 (0.39–0.42)	2.97 (2.84–3.11) $p < 0.001$	2.62 (2.50–2.74) $p < 0.001$	0.09 (0.09–0.10)/ 0.29 (0.28–0.30)	3.18 (2.98–3.39) $p < 0.001$	3.05 (2.86–3.25) $p < 0.001$
Alcohol	0.72 (0.67–0.76)	2.40 (2.22–2.63) $p < 0.001$	1.75 (1.59–1.92) $p < 0.000$	0.66 (0.61–0.71)	2.49 (2.23–2.79) $p < 0.001$	1.84 (1.61–2.09) $p < 0.001$	0.42 (0.41–0.44)	2.80 (2.67–2.93) $p < 0.001$	2.05 (1.94–2.16) $p < 0.001$	0.31 (0.29–0.32)	2.82 (2.67–3.03) $p < 0.001$	2.01 (1.87–2.16) $p < 0.001$
Opioids	1.09 (0.94–1.24)	2.66 (2.31–3.10) $p < 0.001$	1.11 (0.91–1.37) $p = 0.298$	0.82 (0.65–1.00)	2.16 (1.74–2.69) $p < 0.001$	0.80 (0.63–1.02) $p = 0.076$	0.54 (0.49–0.60)	2.57 (2.32–2.86) $p < 0.001$	0.92 (0.83–1.03) $p = 0.167$	0.38 (0.35–0.42)	2.38 (2.14 : 2.61) $p < 0.001$	0.82 (0.73–0.93) $p = 0.001$
Cannabis	0.80 (0.73–0.86)	2.16 (1.94–2.36) $p < 0.001$	1.30 (1.18–1.44) $p < 0.001$	0.80 (0.69–0.91)	2.23 (1.93–2.60) $p < 0.001$	1.26 (1.07–1.50) $p = 0.006$	0.59 (0.55–0.64)	2.95 (2.72–3.20) $p < 0.001$	1.42 (1.30–1.54) $p < 0.001$	0.46 (0.43–0.49)	3.07 (2.86–3.36) $p < 0.001$	1.60 (1.47–1.75 $p < 0.001$)
Sedatives and hypnotic	1.29 (1.14–1.43)	3.23 (2.81–3.61) $p < 0.001$	1.35 (1.14–1.61) $p = 0.001$	1.20 (1.01–1.39)	3.41 (2.88–4.04) $p < 0.001$	1.77 (1.46–2.13) $p < 0.001$	0.86 (0.79–0.93)	4.30 (3.95–4.69) $p < 0.001$	1.87 (1.70–2.05) $p < 0.001$	0.59 (0.54–0.64)	3.93 (3.56–4.26) $p < 0.001$	1.92 (1.72–2.14) $p < 0.001$
Cocaine	1.52 (1.30–1.74)	3.53 (3.05–4.13) $p < 0.001$	1.42 (1.18–1.71) $p < 0.001$	1.14 (0.85–1.43)	2.95 (2.28–3.81) $p < 0.001$	1.30 (1.01–1.68) $p = 0.039$	0.90 (0.76–1.04)	4.17 (3.55–4.89) $p < 0.001$	1.33 (1.15–1.54) $p < 0.001$	0.85 (0.75–0.95)	5.00 (4.45–5.71) $p < 0.001$	1.55 (1.32–1.83) $p < 0.001$
Stimulants	1.19 (1.05–1.34)	2.90 (2.52–3.27) $p < 0.001$	1.34 (1.13–1.58) $p = 0.001$	1.03 (0.79–1.26)	2.67 (2.19–3.39) $p < 0.001$	0.93 (0.72–1.19) $p = 0.555$	0.83 (0.71–0.96)	3.92 (3.37–4.55) $p < 0.001$	1.26 (0.08–1.47) $p = 0.003$	0.65 (0.57–0.72)	3.82 (3.47–4.42) $p < 0.001$	1.34 (1.16–1.55) $p < 0.001$
Hallucinogens	0.93 (0.59–1.27)	2.07 (1.43–2.98) $p < 0.000$	1.01 (0.69–1.46) $p = 0.970$	0.54 (0.28–0.81)	1.37 (0.84–2.23) $p = 0.214$	0.53 (0.33–0.85) $p = 0.008$	0.88 (0.48–1.28)	3.95 (2.50–6.24) $p < 0.001$	1.05 (0.71–1.55) $p = 0.807$	0.45 (0.33–0.56)	2.50 (1.95–3.29) $p < 0.001$	0.97 (0.77–1.23) $p = 0.820$
Volatile solvents and multiple drug use	0.93 (0.85–1.01)	2.58 (2.34–2.85) $p < 0.001$	1.34 (1.18–1.52) $p < 0.001$	0.96 (0.84–1.08)	2.77 (2.42–3.18) $p < 0.001$	1.44 (1.22–1.71) $p < 0.001$	0.69 (0.64–0.74)	3.55 (3.30–3.83) $p < 0.001$	1.46 (1.34–1.61) $p < 0.001$	0.46 (0.43–0.49)	3.29 (3.08–3.57) $p < 0.001$	1.54 (1.39–1.71) $p > 0.001$

The adjusted models are adjusted for: other substances, other psychiatric diagnoses, preceding diagnoses, and number of preceding hospitalizations, bed days and emergency room contacts.

[a]For any SUD, numbers are IRs and 95% CIs per year for individuals without and with SUD, respectively. For specific types of SUDs, numbers are IRs and 95% CIs per year for individuals with that particular type of SUD.

[b]Numbers are IRRs comparing individuals with a given type of SUD to individuals without that given type of SUD.

SUD, substance use disorder; IR, incidence rate; IRR, incidence rate ratio; CI, confidence interval.

size. At the same time, the method gives the opportunity for a prospective design and long follow-up.

Substance use disorders are underdiagnosed (Hansen *et al.* 2000). For this reason, we used several registers to obtain information on substance use disorders, and estimated lifetime substance use, which is likely to bring us closer to the correct proportion of substance use individuals.

This choice does not take into account that substance use disorder can change over time, and patients with substance use disorder are registered in accordance with their use throughout the follow-up period. If we had chosen time-varying substance use disorder, patients would be included later than the actual substance use started what is likely to have led to underestimates of the associations. If the substance amount varies or the patients cease the substance use, it can have an effect on hospitalisation. In addition, we do not know the extent of consumption of alcohol and drugs which do not involve the diagnosis of substance use disorder, but may still influence the mental health disorder and therefore the hospitalisation.

Patients with substance use disorders without other types of mental illness are usually not treated in the psychiatric system in Denmark. As such, it is less likely that underdiagnosis of mental illness in those with substance use disorder takes place, although substance use disorders may perhaps make accurate diagnosis more difficult.

In Denmark, patients with psychiatric disorders and comorbid substance use receive, to a certain degree, treatment for their substance use disorders as part of the psychiatric treatment facilities. Consequently, parts of the increased service use may be due to for instance detoxification. The data do not easily allow us to determine the extent to which this is the case.

Implications

This study provides us with highly valid documentation about service use among patients with both mental health and substance use disorders. This gives the opportunity to address this problem for patients who require better or different treatment than that currently available in the healthcare system, but we need more knowledge about the reasons for substance use disorder. Moreover, it is important to look at these results from an economic perspective for future cost-benefit studies, because a different treatment offered for this group of patients may save both money and give the patients an increased quality of life.

This study did not provide us with knowledge about why patients with both psychiatric and substance use disorders are more often admitted and have longer admissions. Is it because they suffer from more severe illnesses and are therefore abusing substances, or is it the substance use disorder that makes them require more treatment or for a longer duration? This requires further investigation in future studies.

This study did not show the distribution between patients admitted involuntarily and voluntarily, which could be important to see if an association is found because patients with substance use disorder are more frequently admitted involuntarily. Furthermore, we do not know how many patients have been deemed suitable for psychiatric treatment and if they will be admitted more often because of that judgement. These areas also require further research.

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Declaration of Interest. None

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