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Prevalence of substance use disorders in psychiatric patients: a nationwide Danish population-based study

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Abstract

Purpose The present study established the national prevalence of substance use disorders (SUDs) among Danish psychiatric patients. Furthermore, patients with SUDs and those without SUDs were compared on a range of socio-demographic, clinical, and treatment characteristics.

Methods Data were obtained from several Danish population-based registers. The study population was defined as all individuals with incidents of schizophrenia, schizotypal disorder, other psychoses, bipolar disorder, depression, anxiety, obsessive–compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and personality disorders since 1969. The prevalence of SUDs was examined for the following psychoactive substances: alcohol, opioids, cannabis, sedatives, cocaine, psycho-stimulants and hallucinogens.

Results A total of 463,003 patients were included in the analysis. The prevalence of any lifetime SUD was: 37 % for schizophrenia, 35 % for schizotypal disorder, 28 % for other psychoses, 32 % for bipolar disorder, 25 % for depression, 25 % for anxiety, 11 % for OCD, 17% for PTSD, and 46 % for personality disorders. Alcohol use disorder was the most dominating SUD in every psychiatric category (25 % of all included patients). Patients with SUDs were more often men, had fewer years of formal education, more often received disability pension and died due to unnatural causes.

Conclusions The study was the most comprehensive of its kind so far to estimate the prevalence of SUDs in an unselected population-based cohort, and it revealed remarkably high prevalence among the psychiatric patients. The results should encourage continuous focus on possible comorbidity of psychiatric patients, as well as specialised and integrated treatment along with increased support of patients with comorbid disorders.

Keywords Psychiatric disorder · Substance use disorder · Abuse · Comorbidity · Dual diagnosis

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Introduction

Substance use disorders (SUDs) and other psychiatric disorders such as schizophrenia, bipolar disorder, depression, and anxiety disorders are highly prevalent disorders worldwide [1–4], and lifetime and 12-month use, harmful use as well as dependence of substances are documented to be more prevalent in psychiatric patient populations when compared to the general population [5–12].

Today, SUDs and psychiatric disorders are internationally considered among the top ten most disabling disorders worldwide and comparable to cancer, cardiovascular diseases, and diabetes in terms of disability-adjusted life years [13]. Patients with severe psychiatric disorders, including people with SUDs, have a higher risk of morbidity and mortality than individuals in the general population [14–16]. Moreover, psychiatric patients with comorbid SUDs

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more often experience serious adverse complications, such as: higher frequency of relapse of psychiatric disorder and rehospitalisation, disruptive behaviour and violence, residential instability, decreased functional status, and medication noncompliance among others [17–19]. Comorbid disorders comprise a greater burden and exposure to health strains on the individual level, whereas increased health costs and a greater societal burden can also be anticipated from the economic perspective. Thus, it is important to clarify to what extent SUDs are present among psychiatric patients.

Already in 1990, an American landmark study revealed high rates of comorbidity among individuals with mental and addictive disorders and simultaneously addressed the need for improving prevention efforts [6]. A general enhanced focus on the common presence of SUDs in psychiatric patients has generated more awareness and as a result, attempts of more integrative treatment approaches have been implemented [20]. However, despite the fact that health authorities acknowledge that SUDs are very much overrepresented among psychiatric patients, specific explanations of their common association still remain unclear [21–23].

Most studies to estimate the overlap of SUDs and other psychiatric disorders have been designed as survey studies of nationally representative groups of the American population [2, 5–7]. None have yet been conducted for a whole nation's population and furthermore, almost no evidence has characterised whether use of specific substances is related to specific psychiatric disorders [24, 25].

To the best of our knowledge, this was the most comprehensive study to establish prevalence based on a whole population. Through the available data from the Danish nationwide registers, we aimed both to examine the general prevalence of SUDs among psychiatric patients, the prevalence of specific SUDs in subgroups of patients, and

whether patients with SUDs could be characterised differently than those without.

Materials and methods

Information on all people living in Denmark who have been diagnosed with and treated for a psychiatric disorder since 1969 was accessible using the unique personal identification number: the Danish Civil Registration System (CRS) number. Since this number is used in all Danish registers, it is possible to link all individual-level information across all Danish registers [26].

The study population consisted of all patients registered with a psychiatric disorder in the Psychiatric Central Register. The register was established in 1969 and contains information on all psychiatric inpatient and partial hospital admissions since 1969, as well as all outpatient psychiatric contacts and psychiatric emergency department visits from 1995 [27]. The Psychiatric Central Register has used the diagnostic codes of the International Classification of Diseases, 8th edition, (ICD-8) from 1969 to 1993, and since 1994, the codes follow the 10th edition, (ICD-10) [28].

Psychiatric disorders included in this study were: schizophrenia, schizotypal disorder, other psychoses, bipolar disorder, depression, anxiety, obsessive–compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and personality disorders. See Table 1 for definition criteria, subtypes, and ICD-8 and ICD-10 codes of the psychiatric disorders. These specific disorders were included primarily because of their general high prevalence in the population and their occurrence in adulthood.

To avoid possible multiple representations of the same individuals in the analyses (if patients had more than one of the included psychiatric diagnoses) and to ensure

Table 1 Definition criteria of the study population

Psychiatric disorder	ICD-10 code(s)	ICD-8 code(s)
Schizophrenia	F20	295 (all subtypes)
Schizotypal disorder	F21	None
Other psychoses (including: delusional disorder, acute and transient psychotic disorder, schizo-affective disorder, and other non-organic psychosis)	F22–F25, F28–F29	297 (all subtypes), 298.29, 298.39, 298.89, 298.99, 299.09, 301.09, 301.29
Bipolar disorder	F31	296.19, 296.39
Depression	F32–F34	296.09, 296.29, 298.09, 300.49
Anxiety	F40–F41	300.09, 300.29
OCD	F42	300.39
PTSD	F43.1	None
Personality disorders (including: paranoid, schizoid, dissocial, emotionally unstable, histrionic, anankastic, anxious, dependent, unspecified, mixed and other personality disorder)	F60–F61	301 (all subtypes, except 301.09, 301.29)

diagnostic accuracy, the patient's most severe diagnosis was included. We followed the sequence of the ICD-10 diagnosis hierarchy that is listed above and in Table 1.

Only patients born before 1997 were included. The rationale was that we primarily focused on psychiatric disorders of adulthood, and that we assumed that an age of at least 16 years would constitute a reasonably risk of developing a SUD.

Substance use disorders (SUDs)

The study included SUDs of the following substances: alcohol, opioids, cannabis, sedatives, cocaine, psycho-stimulants, hallucinogens, volatile solvents, and multiple drug use.

Using the CRS number, several data sources were combined to obtain information on possible SUDs. First, the Psychiatric Central Register and the National Patient Register contained information on registered SUDs in ICD-8 (303–304 with subtypes) and ICD-10 codes (the F1 chapter). The National Patient Register was established in 1977 and contains information on all inpatient treatment in somatic hospitals. Since 1995, it also included information on outpatient treatment and emergency department contacts. [29]. See Table 2 for definition criteria and ICD-8 and ICD-10 codes.

Second, information on individuals referred by public health services for treatment of SUDs has been retrieved from the Registry of Drug Abusers Undergoing Treatment since 1996 [30]. The main substance for referral was considered as indicative of an SUD of that specific substance.

Third, relevant alternative somatic diagnoses from the Psychiatric Central Register and the National Patient Register were used as indicative of alcohol use disorder (e.g. alcohol-related somatic diseases). See Table 2 for alternative definition criteria and ICD-8 and ICD-10 codes.

Finally, information obtained from the Danish Medicinal Products Register [31], which contains records on all redeemed prescriptions since 1995, was used as indicative of SUD of alcohol and opioids. Prescribed and redeemed medications from pharmacies that indicated alcohol use disorder were: disulfiram (Antabuse), calcium carbimide, and acamprosate. Medications that indicated opioid use disorder were: buprenorphine, methadone, and levacetyl-methadol. See Table 2 for specific anatomical therapeutic chemical (ATC) codes.

Unlike the described hierarchical ordering of the psychiatric disorders, all registered diagnoses of SUDs were included in the analyses if patients presented with SUDs of several different substances.

Other information

Socio-demographic information, represented as educational status and whether the patients received disability

Table 2 Definition criteria of substance use disorders (SUDs)

SUD	ICD-10 code(s)	ICD-8 code(s)	Medications [anatomical therapeutic chemical (ATC) code]
Alcohol	F10, E52 (niacin deficiency), 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), and Z72.1 (alcohol use)	291, 303, and 571.0 (alcoholic cirrhosis)	Disulfiram (N07BB01), calcium carbimide (N07BB02), and acamprosate (N07BB03)
Opioids	F11	304.0, 304.1	Buprenorphine (N07BC01, N07BC51), methadone (N07BC02), and levacetylmethadol (N07BC03)
Cannabis	F12	304.5	None
Sedatives	F13	304.2, 304.3	None
Cocaine	F14	304.4	None
Psycho-stimulants	F15	304.6	None
Hallucinogens	F16	304.7	None
Volatile solvents	F18	None	None
Multiple drug use and use of other psychoactive drugs	F19	None	None

pension, was obtained from Statistics Denmark [32]. Information on causes of death was obtained from the Cause of Death Register [33], which contains information on the primary cause of death of all deceased individuals in Denmark. Information from the register was last updated December 2011.

Data from all registers were extracted in July 2013.

Data analysis

Prevalence numbers were estimated using cross-tabulations. Characteristics were expressed in either means or percentage numbers. Chi-square tests or independent sample t tests were carried out, and significance was expressed in P values. Confidence intervals of mean use of psychiatric services, and P values comparing use of psychiatric services between individuals with SUDs and without, were estimated using bootstrapping with 2500 replications because of severe deviations from the assumption of normal distribution of these variables. The variables disability pension and number of unnatural deaths were adjusted for age and year of diagnosis, using multiple logistic regression. In some analyses, the observed number of patients was decreased due to limitations of the data source. This included: age of psychiatric diagnosis, disability pension and contacts in outpatient clinics and emergency departments.

All analyses were conducted in SPSS version 20 and Stata/MP version 13.1.

Results

The study population

A total of 463,003 patients met the criteria for the included psychiatric disorders, hierarchically ordered as previously described:

53,035 patients with schizophrenia, 5640 with schizotypal disorder, 56,065 with other psychoses, 24,567 with bipolar disorder, 197,057 with depression, 40,552 with anxiety, 5953 with OCD, 7343 with PTSD and 72,791 with personality disorders.

Prevalence of SUDs

Of the 463,003 patients, a total of 140,811 (30.4 %) patients were also registered in the different Danish registers with a diagnosis of an SUD of:

Alcohol: 114,359 patients (24.7 %), opioids: 17,563 (3.8 %), cannabis: 20,964 (4.5 %), sedatives: 21,520 (4.7 %), cocaine: 3368 (0.7 %), psycho-stimulants: 6182 (1.3 %), and/or hallucinogens: 1514 (0.3 %). Additional

SUDs were: volatile solvents: 426 patients (0.09 %) and/or multiple drug use and use of other psychoactive substances: 15,994 (3.5 %). The latter two SUDs were included in estimates of the prevalence of any SUD among the patients; however, they will not be commented on or presented individually in the forthcoming results.

Table 3 presents the distribution of the 463,003 patients with or without SUDs in each psychiatric category and their characteristics regarding: age when first registered with a psychiatric diagnosis, gender, educational status, if disability pension was received, hospitalised days per year, the number of outpatient contacts per year, the number of emergency department contacts per year, and the proportion of deaths from unnatural causes. Analyses adjusted for age and year of diagnosis are presented for the outcomes disability pension and deaths from unnatural causes.

General prevalence of SUDs

SUDs were most prevalent in patients with personality disorders (46 %). In patients with schizophrenia, schizotypal disorder and bipolar disorder the prevalence was 32–37 %, in patients with other psychoses, depression, and anxiety it was 25–28 %, and a relatively lower prevalence was seen in patients with PTSD (17 %) and OCD (11 %).

Age of first diagnosis, gender, education, and disability pension

Patients with schizotypal disorder, bipolar disorder, depression, anxiety, OCD, and personality disorders and SUDs were significantly older (2–4 years) when they received their first diagnosis of a psychiatric disorder.

Patients with SUDs were significantly more often men, with the highest proportion among those with schizophrenia (70 % men).

In all psychiatric categories, patients with SUDs most likely only completed mandatory education (average 50 % of patients across all psychiatric categories).

Moreover, all patients with SUDs were significantly more likely to receive disability pension when compared to patients without SUDs. Adjustment for age and year of diagnosis did not change any of the P values, which all remained statistically significant.

Treatment characteristics

Patients with schizophrenia and schizotypal disorder and SUDs had significantly more/longer admissions per year than the same patients without SUDs. Patients with other psychoses, bipolar disorder, and depression without SUDs had in contrast significantly more/longer admissions than the same patients with SUDs.

Table 3 Characteristics of patients in specific psychiatric categories with or without SUDs from 1969 to 2013

Characteristics	Psychiatric disorder								
	Schizophrenia	Schizotypal disorder	Other psychoses	Bipolar disorder	Depression	Anxiety	OCD	PTSD	Personality disorders
Total *n*									
SUD	19,420 (37 %)	1970 (35 %)	15,863 (28 %)	7835 (32 %)	49,984 (25 %)	10,060 (25 %)	680 (11 %)	1247 (17 %)	33,752 (46 %)
No SUD	33,615 (63 %)	3670 (65 %)	40,202 (72 %)	16,732 (68 %)	147,073 (75 %)	30,492 (75 %)	5273 (89 %)	6096 (83 %)	39,039 (53 %)
Age when registered with psychiatric disorder [mean (±SD)]									
SUD	27.9 (±8.2)	29.7 (±9.0)	42.1 (±15.4)	36.3 (±9.8)	33.9 (±10.3)	31.6 (±9.7)	25.6 (±10.2)	36.4 (±13.0)	26.4 (±8.2)
No SUD	27.8 (±8.7)	26.8 (±9.0)	52.1 (±21.1)	33.4 (±10.2)	31.2 (±10.5)	29.1 (±9.9)	21.3 (±9.7)	37.6 (12.9)	25.8 (±8.4)
P value*	0.06	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.002	<0.001
Men (%)									
SUD	70	64	58	53	50	49	56	67	60
No SUD	50	53	34	36	31	28	42	49	35
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Highest educational degree (%) SUD/no SUD									
Mandatory education	59/44	53/46	51/37	36/31	42/35	51/41	55/48	49/36	54/44
High school	7/8	10/13	3/3	5/4	3/4	3/6	5/11	6/9	2/5
Vocational training	19/17	22/20	24/17	30/22	31/23	29/27	23/20	26/25	25/25
University	8/11	13/17	11/11	22/19	15/16	12/20	13/17	12/18	9/17
Not registered[a]	7/22	3/3	11/32	7/24	9/22	5/6	4/3	7/13	9/10
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Disability pension (%)									
SUD	80	50	61	55	43	44	27	40	55
No SUD	67	37	41	38	27	23	12	36	34
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
P value adjusted for age and year of diagnosis	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.02	<0.001
Hospitalised days per year [mean (95 % CI)][b]									
SUD	44.5 (43.6–45.4)	21.2 (19.0–23.4)	22.8 (22.0–23.6)	22.9 (21.9–24.0)	13.3 (12.9–13.6)	8.0 (7.3–8.7)	11.7 (8.2–15.3)	10.9 (7.4–14.4)	10.2 (9.9–10.6)
No SUD	41.0 (40.1–41.8)	17.5 (15.7–19.3)	31.9 (31.1–32.6)	28.1 (27.1–29.0)	21.2 (20.7–21.5)	7.4 (6.7–8.1)	14.2 (11.5–16.9)	9.6 (7.3–11.9)	10.3 (9.7–10.8)
P value	<0.001	0.01	<0.001	<0.001	<0.001	0.20	0.28	0.56	0.90
Number of contacts in outpatient clinics per year [mean (95 % CI)]									
SUD	12.8 (12.5–13.1)	9.5 (8.9–10.2)	5.1 (4.9–5.3)	6.9 (6.6–7.2)	4.0 (3.9–4.1)	3.5 (3.3–3.7)	4.3 (3.7–4.9)	3.8 (3.3–4.3)	3.0 (2.9–3.2)
No SUD	12.1 (11.9–12.3)	9.2 (8.8–9.6)	5.3 (5.2–5.4)	7.4 (7.2–7.7)	5.2 (5.2–5.3)	4.4 (4.3–4.6)	4.9 (4.6–5.1)	5.1 (4.8–5.3)	4.4 (4.2–4.5)
P value	<0.001	0.39	0.10	0.01	<0.001	<0.001	0.10	<0.001	<0.001
Number of emergency department contacts per year [mean (95 % CI)]									
SUD	1.3 (1.3–1.4)	0.94 (0.79–1.1)	1.4 (1.3–1.5)	1.2 (1.1–1.4)	0.94 (0.89–0.99)	0.83 (0.73–0.92)	0.61 (0.42–0.81)	1.1 (0.56–1.6)	0.53 (0.45–0.60)
No SUD	0.82 (0.77–0.87)	0.53 (0.45–0.61)	1.2 (1.1–1.3)	1.0 (0.9–1.1)	0.93 (0.88–0.98)	0.85 (0.76–0.95)	0.62 (0.29–0.94)	0.49 (0.38–0.60)	0.41 (0.34–0.47)
P value	<0.001	<0.001	0.03	0.002	0.81	0.68	0.98	0.03	0.02

Table 3 continued

Characteristics	Psychiatric disorder								
	Schizophrenia	Schizotypal disorder	Other psychoses	Bipolar disorder	Depression	Anxiety	OCD	PTSD	Personality disorders
Number of unnatural deaths[c]									
SUD	1676 (8.6 %)	72 (3.7 %)	1420 (9.0 %)	515 (6.6 %)	3319 (6.6 %)	409 (4.1 %)	20 (2.9 %)	32 (2.6 %)	4336 (12.8 %)
No SUD	2140 (6.4 %)	47 (1.3 %)	2301 (5.7 %)	950 (5.7 %)	6308 (4.3 %)	308 (1.0 %)	29 (0.5 %)	18 (0.3 %)	1722 (4.4 %)
P value	<0.001	0.80	<0.001	<0.001	<0.001	<0.001	0.18	0.002	<0.001
P value adjusted for age and year of diagnosis	0.01	0.07	0.63	0.03	<0.001	0.003	0.63	0.13	0.50

Italic P values are the statistically significant P values, defined as values less than the significance level of 0.05

SUD substance use disorder ever diagnosed, *OCD* obsessive–compulsive disorder, *PTSD* post-traumatic stress disorder

* Comparing SUD to no SUD within each psychiatric category

[a] Not registered could either be immigrants or unknown type of education

[b] Yearly contacts at treatment institutions only include patients that ever received treatment (at time of diagnosis or later)

[c] Unnatural deaths were defined as: accidents, homicides or suicides

Patients with schizophrenia were the only patient group, in which those with SUDs had significantly more outpatient contacts per year, compared to patients without SUDs. In contrast, patients with bipolar disorder, depression, anxiety, PTSD, and personality disorders and SUDs had significantly fewer outpatient contacts per year when compared to patients without SUDs.

Regarding emergency department contacts per year, patients with schizophrenia, schizotypal disorder, other psychoses, bipolar disorder, PTSD, and personality disorders and SUDs had significantly more contacts per year than the same patients without SUDs.

Deaths

The occurrence of deaths by unnatural causes, which included accidents, homicides and suicides, was overrepresented among patients with SUDs in every psychiatric category. Death by unnatural causes occurred to as many as 13 % of the included patients with personality disorders and SUDs. When adjusting for age and year of diagnosis, the differences between patients with SUDs and without were only statistically significant in schizophrenia, bipolar disorder, depression, and anxiety.

Temporality

We conducted an analysis of the temporal relationship between the psychiatric diagnosis and a possible diagnosis of SUD. The proportion of patients with an SUD, where the two diagnoses were given within 1 year, was 76 % for schizophrenia, 68 % for schizotypal disorder, 67 % for other psychoses, 73 % for bipolar disorder, 68 % for depression, 61 % for anxiety, 53 % for OCD, 58 % for PTSD, and 75 % for personality disorders. An additional analysis of whether the SUD was diagnosed before or after the psychiatric disorder, in the cases were they were not diagnosed simultaneously, revealed that in all psychiatric categories there was a higher proportion of patients diagnosed with SUDs first.

Specific types of SUDs in the psychiatric categories

Table 4 and Fig. 1 both show the prevalence of individual types of SUDs (excluding volatile solvents and multiple drug use) among all patients in the different psychiatric categories. Alcohol use disorder was dominating in all psychiatric categories with a prevalence of 20–39 % across the whole spectrum of psychiatric disorders (excluding PTSD and OCD with 13 and 9 %, respectively). Cannabis use disorder was the second most common type of SUD in patients with schizophrenia, schizotypal disorder, other psychoses, PTSD, and OCD. Patients with the remaining

Table 4 Prevalence of specific SUDs in patients in specific psychiatric categories

Psychiatric disorder (total *n*)	Substance use disorder							
	Alcohol (%)	Opioids (%)	Cannabis (%)	Sedatives (%)	Cocaine (%)	Psycho-stimulants (%)	Hallucinogens (%)	Any SUD (%)
Schizophrenia (53,035)	27.6	5.3	13.2	4.7	1.8	3.6	1.2	36.6
Schizotypal disorder (5640)	25.0	3.5	11.6	4.3	1.7	2.3	0.4	34.9
Other psychoses (56,065)	22.7	3.5	4.9	4.5	0.8	1.4	0.4	28.3
Bipolar disorder (24,567)	27.6	2.6	3.3	4.9	0.7	0.9	0.1	31.9
Depression (197,057)	20.9	2.8	2.1	3.9	0.4	0.7	0.1	25.4
Anxiety (40,552)	20.0	2.4	2.9	4.1	0.6	0.9	0.1	24.8
OCD (5953)	8.8	1.2	2.3	1.0	0.2	0.6	0.02	11.4
PTSD (7343)	12.5	2.9	3.0	1.4	0.7	0.8	0.1	17.0
Personality disorders (72,791)	38.6	7.2	5.6	7.6	0.8	1.8	0.6	46.4

Fig. 1 Comparison of the subgroups of SUDs in the different psychiatric categories
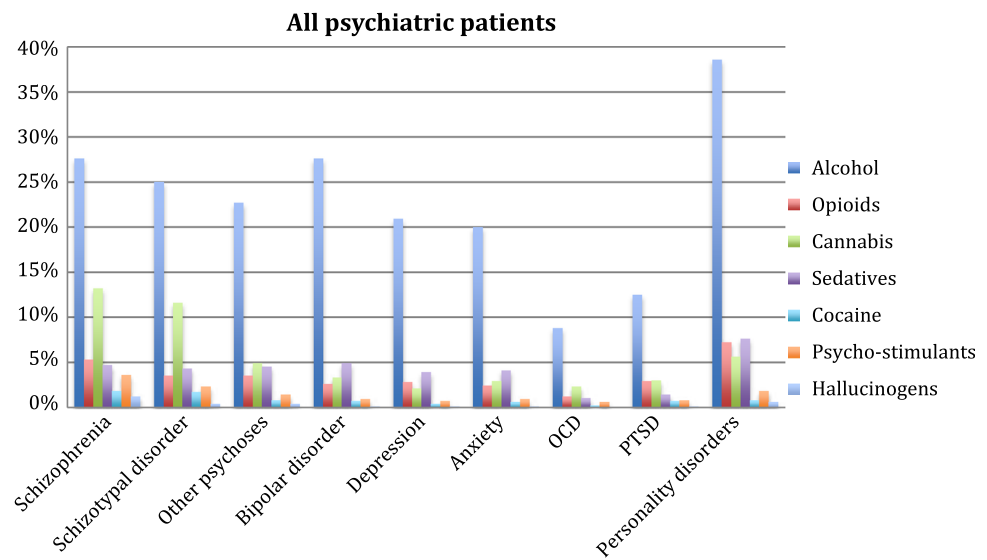
psychiatric disorders were more frequently registered with an SUD of sedatives. An SUD of opioids was relatively prevalent in patients with schizophrenia, schizotypal disorder, other psychoses, bipolar disorder, depression, PTSD, and personality disorders. SUDs of cocaine, psycho-stimulants and hallucinogens were the least frequent SUDs observed among patients, but were most prevalent in the schizophrenia spectrum disorders (schizophrenia, schizotypal disorder, and other psychoses).

A secondary analysis, only observing the prevalence of specific types of SUDs in incident cases of psychiatric disorders in the last 10 years (2003–2013), was performed to illuminate any possible time-specific changes when comparing with the entire examining period (1969–2013). It revealed that in incident cases within the last 10 years, there was an increase in prevalence of SUDs of especially cannabis, cocaine, and psycho-stimulants. In addition, in

these particular past 10 years, we observed a higher frequency of any SUD among patients with schizophrenia, other psychoses, and bipolar disorder.

Discussion

Main findings

Using the unique Danish nationwide, population-based registers, we revealed several central findings:

1. SUDs were seen in nearly half of the patients with a personality disorder, more than every third patient with a diagnosis of schizophrenia, schizotypal disorder, and bipolar disorder, and in every fourth patient with other psychoses, depression, and anxiety;

2. alcohol use disorder was unexceptionally the most frequent SUD, and the second most frequent SUDs were of cannabis, sedatives, and/or opioids;

3. noteworthy characteristics of patients with SUDs were an overrepresentation of male gender, only mandatory education, disability pension and deaths due to unnatural causes;

4. a more inconsistent pattern was observed regarding differences in utilisation of psychiatric treatment facilities between patients with SUDs and without, which will be discussed below.

Comparison with other prevalence studies

The present study surpassed previous studies in sample size and length of study period, and was based on numerous population-based registers that comprised comprehensive and detailed information covering the whole Danish population. The findings of the present study are strongly supported by previous studies, which have consistently reported that alcohol use disorder is the most prevalent SUD among individuals with psychiatric disorders, that more severe psychiatric disorders as well as personality disorders are very much associated to a high prevalence of SUDs, and that male gender and fewer years of education are overrepresented among patients with comorbid SUDs [6, 7, 11, 12, 24, 25, 34, 35].

The majority of studies have been made as survey studies of comorbidity in a selected group of individuals, designed to be nationally representative [6, 7]. One prior American study revealed surprisingly high lifetime prevalence of SUDs among examined individuals. Any SUD of alcohol and/or other drugs was observed in 47 % of individuals with schizophrenia, 84 % with antisocial personality disorder, 56 % with bipolar disorder, 27 % with depression, and 24 % with anxiety [6]. Yet, it is worth noting that surveys in general will possibly detect a higher rate of substance users in comparison with registers, through which only cases receiving intensive treatment are detected. Survey studies have the advantage of possibly providing more detailed and subjective investigations, but they rely on the participants' will and motivation to participate and could, therefore, preselect a better functioning group of patients. Opposed to this, the criteria of being included in a register-based study is the reception of treatment in any of the health care settings, which means that cases selected may be more severe [12]. One Danish study compared the prevalence of comorbid SUDs found in a thorough examination of case records and/or by interviewing hospitalised psychiatric patients to the prevalence found in the registers. A substantially lower prevalence was found in the registers (26 %) compared to the research data (50 %) [36].

Numerous investigations have tried to explain possible underpinning causal mechanisms of the high prevalence of comorbid SUDs. These include several explanatory psychosocial aspects [37] and efforts to re-evaluate and oppose the self-medication theory [38]. The self-medication theory was originally articulated as an aetiological explanation of substance abuse among psychiatric patients, suggesting that the choice of drugs is correlated to specific psychiatric symptoms and the abuse is an attempt to relieve such symptoms [39]. However, evidence also suggests that psychiatric patients start using substances for the same reasons as others in society, and similar, that the drugs of choice are regulated by market forces [23, 40, 41]. Overall, approaches to determine aetiology and explanatory models of the high prevalence still reveal an unclear picture.

The true prevalence of SUDs in Denmark is unknown, but official figures from 2005 estimate that 2.6 % of the Danish men and 1.0 % of the Danish women have an addiction to alcohol [42]. The prevalence of alcohol use disorder in the study was 25 %. Records on drug abuse in the Danish population estimate that approximately 0.6 % of the population in Denmark abuse drugs other than alcohol. Of these, one-third has an SUD of cannabis (0.2 % of the population) [43]. Comparably, 4.6 % of the patients in the study had a cannabis use disorder and summed 10 % of the patients had an SUD other than alcohol and/or cannabis. However, the estimates of substance abuse in the general Danish population were point prevalence and the age composition in the sample could have differed from that of the present study, and therefore, we cannot directly compare the prevalence to that found in the study.

Age at first treatment

The registers allowed us to collect data of when patients were referred to or sought treatment for a psychiatric disorder (not to misinterpret as the age of onset of the disorder). Patients with SUDs were in the majority of cases diagnosed and treated for their psychiatric disorder at a later age than people without SUDs. An explanation for our finding could be that the SUD in itself as well as other social factors related to substance abuse, such as unstable housing, unstable inter-personal relations, and low socioeconomic status, acts as barriers for accessing psychiatric treatment facilities and, consequently, delay help-seeking behaviour and treatment.

Education and disability pension

The main proportion of patients both with SUDs (average 50 %) and without SUDs (average 40 %) only had mandatory education (primary and first half of secondary school). This is a finding consistent with several other

studies [23]. Since the information pertained to the patients' highest achieved education, some patients (especially the younger and most recently diagnosed) could still be undergoing education. This could account for the bigger proportion of patients with only mandatory education, both among individuals with and without SUDs. Despite this, it was consistent that patients with SUDs both were less educated and also more often received disability pension. Disability pension is a governmental income substitute that is only given to disabled people, which after long clarification are expected to have no future in the labour market. Through our data material, we were not able to assess the underlying mechanisms; whether particular social circumstances, such as unemployment, were contributing aggravating factors that made these individuals more prone to substance abuse, or whether it was the substance abuse that preceded and consisted some of the causal background of these more debilitating life circumstances.

Psychiatric treatment facility utilisation

The associations between presence of SUDs and use of psychiatric treatment facilities were inconsistent and varied across the different psychiatric categories. Previous studies have shown that patients with comorbid SUDs have increased hospitalisation rates and use of treatment facilities [44, 45]. However, the findings in the present study did not quite seem to support this. Patients with schizophrenia and SUDs were the only patients that had significantly more hospitalised days and outpatient contacts per year than the same patients without SUDs. Approximately, half of the remaining psychiatric categories with SUDs had in contrast significantly fewer hospitalised days and outpatient contacts per year than patients without SUDs. One interpretation of this could be that providers of mental health care unintentionally exclude some psychiatric patients with SUD comorbidity. In patients with schizophrenia, where the prevalence of substance use has consistently been shown to be high (47 % reported in one study [6]), substance use can be expected as being part of the disorder [46] and, therefore, explain the better inclusion of these particular patients. The traditional organisation of treatment services has been a separation of psychiatric treatment and substance abuse treatment both in Denmark and internationally [47, 48]. As a consequence of this separation, patients were expected to have completed treatment in one sector before entering the other, which unfortunately, could have resulted in a rejection and under-treatment of patients with comorbidity in either sector. The present study also revealed that patients with SUDs had a marginally greater number of contacts with emergency departments, which is a finding supported by other studies [49, 50]. Treatment of these individuals was at risk of being emergency treatment, characterised by less consistent and continuous support and care than that obtainable in psychiatric hospitals and outpatient care units. In other words, the present observations suggest that patients with comorbid SUDs were marginalised and less likely to be included in psychiatric treatment facilities. This implies a criticism of the traditional services of mental health, as previously addressed in the literature [47, 48]. However, it is worth mentioning that establishing a treatment alliance with patients with comorbid SUDs could be associated with several complications and thereby contribute to the inconsistent care. Patients with SUDs could be less reliable in their contact, and generally have less compliant behaviour [17]. External circumstances, such as homelessness, could also contribute to the patients' marginalisation and inconsistent care [51]. However, despite these additional difficulties associated with co-occurring SUDs, we must assume that patients with comorbidity need additional support; at least to avoid possible under-treatment and rejection of vulnerable individuals.

Deaths

We observed a disproportionate number of deaths due to unnatural causes among the psychiatric patients with SUDs, which was statistically significant in patients with schizophrenia, bipolar disorder, depression, and anxiety (when adjusting for age and year of diagnosis). The literature supports that SUDs and psychiatric disorders both independently, and when co-occurring, increase the risk of dying due to unnatural causes [14, 15, 17, 52]. However, these studies have not thoroughly examined if psychiatric patients with SUD comorbidity have a consistent additional increased risk.

Strengths and limitations

The population-based registers representing different Danish services all contained detailed and unique information on the entire Danish population and thus provided several methodological advantages, including: a prospective design, a large and unselected study population, as well as a long follow-up. Despite these methodological advantages, the data source could have been associated with several limitations. First of all, the Psychiatric Central Register was the only register that contained information since 1969. All the additional registers that were used as data sources were established later than 1969; hence, all data regarding all included individuals were not obtainable from this year.

Another minor concern is related to the included patients with PTSD, where we could assume that a high proportion of the patients was immigrants or refugees. Due to this,

there is a risk that the registers lack diagnostically accurate information of incidents of psychiatric disorders and SUDs prior to immigration date.

Furthermore, the registers only contained registered diagnoses that were obtained in public health care settings. Given these settings, it could be expected that an unknown number of cases of SUDs was not diagnosed. The under-diagnosing of SUDs among psychiatric inpatients is already documented [36], and therefore, we most likely expect the prevalence numbers to be underestimates of reality.

The study population was defined by the use of a hier-archically ordering of the included psychiatric disorders. Consequently, if a patient had more than one registered diagnosis, this same person would only be represented with their most dominating disorder. 34 % of the patients had multiple psychiatric diagnoses (two or more). This finding could indicate that a number of patients actually suffer from more than one psychiatric disorder and findings are true comorbidity, or indicate that the psychopathology in some individuals develops over time. Nonetheless, our study method implies a risk of misclassification of the patients' diagnoses, and therefore, some of the shown associations could have been inaccurate. Since the registers only provide objective classifications, we were restricted to these measures.

Another important methodological concern of the study is that we presented the crude prevalence of ever being diagnosed with a psychiatric disorder and having a possible SUD independently of time, meaning that the disorders not necessarily were comorbid or co-occurring. We addressed this concern by conducting an additional analysis of the temporal association of the psychiatric disorders and SUDs, and it revealed that the disorders were mostly co-occurring (on average, 67 % were diagnosed within a year).

Finally, a limitation of the study was that not all inclu-ded individuals were followed their whole lifetime. Therefore, not all individuals contributed with a lifelong risk to develop a psychiatric disorder or an SUD, attain higher educational degree, receive disability pension, and die from unnatural causes, which all depend on age. Con-sequently, the observed estimates could be underestimates.

Implications

The present study provides a unique and valid documen-tation of a high prevalence of SUDs among patients with psychiatric disorders, which, due to register data, could even be underestimates. It emphasises how providers of mental health care services should address possible alcohol and drug abuse in all consulted patients, and vice versa for psychiatric comorbidity when treating individuals with SUDs. By thoroughly doing so, we could aim for earlier

treatment of any underlying pathology, and aim for pre-vention of social complications, other medical conditions, lower functioning, unstable housing, relapses of psychiatric disorders, noncompliance to medical treatment, among others. Complications that are all associated with both great individual and societal costs [4, 53]. The large extent of individuals with SUD comorbidity and the inconsistent pattern in their treatment also emphasise that patients with comorbid disorders need additional support and treatment.

The present study had its limitations and was further-more not capable of resolving any of the possible under-lying causal mechanisms. Thus, we encourage future research to examine this association on large scales with greater effort to clarify the temporal association of comorbid disorders and influencing risk factors.

Conclusion

To the best of our knowledge, this study was the largest prospective study so far to estimate prevalence rates of SUDs in individuals with psychiatric disorders. Generally, all types of SUDs were remarkably highly prevalent among patients diagnosed with all the included psychiatric disor-ders. More severe psychiatric disorders, such as the schizophrenia spectrum disorders and bipolar disorder, as well as personality disorders were more often associated with substance abuse. Alcohol use disorder was the most prevalent SUD in every psychiatric category, followed by use disorders of cannabis and sedatives. Characteristics associated with SUDs were male gender, fewer years of formal education, governmental supported income, less continuous health care utilisation for some subgroups of patients, and more deaths due to unnatural causes.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethics Register-based analyses in Denmark do not require consent from participants or ethical approval. The protocol was approved by the Danish Data Protection Agency.

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