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Review

Prevalence of alcohol use disorders in schizophrenia – a systematic review and meta-analysis

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Koskinen J, Löhönen J, Koponen H, Isohanni M, Miettunen J. Prevalence of alcohol use disorders in schizophrenia – a systematic review and meta-analysis.

Objective: Our aim was to present recent studies of alcohol use disorders (AUDs) in patients with schizophrenia, estimate overall prevalence and characteristics affecting the prevalence of AUDs.
Method: We conducted a search using three literature databases and a manual search on articles published in 1996–2008. Meta-regression was used to study how prevalence is affected by different study characteristics. Articles that reported diagnoses according to DSM or ICD diagnostic systems were included.
Results: Altogether 60 studies met our criteria. The median of current AUD prevalence was 9.4% (inter-quartile range, IQR 4.6–19.0, 18 studies) and median of lifetime AUD prevalence 20.6% (IQR 12.0–34.5, 47 studies). In studies using DSM-III-R median prevalence was higher than that in studies using DSM-IV, ICD-9 or ICD-10 (32/17/11/6%).
Conclusion: Approximately every fifth patient with schizophrenia had lifetime AUD diagnosis. When contrasted with the most recent review, there might be a descending trend in AUD prevalence in patients with schizophrenia.

Key words: schizophrenia; alcohol; substance use disorders

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Summations

- The systematic literature search found a wide range of prevalence estimates of alcohol use disorders (AUD) in patients with schizophrenia. However, AUDs are common in patients with schizophrenia.
- The prevalence estimates of AUDs in patients with schizophrenia were higher in studies using DSM-III-R or DSM-IV dignostic criteria.
- Patient type, location or gender distribution did not significantly affect the prevalence estimates.

Considerations

- Study characteristics and their effect on the prevalence of AUDs could be studied more efficiently by conducting a separate meta-analysis and using specific keywords in article search.
- The presented sample is from in- and out-patient settings, mainly from Western countries. Only articles written in English are included; without language limitations a more comprehensive view on global AUD prevalence estimates in patients with schizophrenia might have been achieved.

Introduction

Alcohol use disorders (AUDs) are common in patients with schizophrenia. Previous systematic reviews have found a wide range (12–55%) of AUD prevalence in patients with schizophrenia (1, 2). Previous studies published between the years 1960 and 1989 were reviewed by Mueser et al. (1) and those from the years 1990–2001 by Cantor-Graae et al. (2). Both reviews presented results

from several substance use disorders, and the included studies varied greatly in methodological, diagnostical and sample characteristics. However, it remains unclear how these factors affect prevalence and what is the overall estimate of AUD prevalence in patients with schizophrenia.

There are several reasons why it is important to study AUD in patients with schizophrenia. There is strong evidence that comorbid AUD worsens clinical outcomes in patients with schizophrenia: they have more psychotic symptoms and more severe depressive symptoms (3, 4); poorer treatment compliance; increased somatic morbidity; risk of violence, criminality and suicides; more negative psychosocial events, e.g. divorce and unemployment; more admissions and longer hospitalization periods; taken together, in addition to adding to individual's suffering, they also increase the costs of the treatment (5–7). Although there are two previous systematic reviews considering AUD in patients with schizophrenia, a meta-analysis on this topic has not yet been conducted.

Aims of the study

i) systematically collect and review studies published in 1996–2008 on AUD in patients with schizophrenia and contrast the prevalence of AUDs in previous reviews;
ii) estimate the overall prevalence of AUD in patients with schizophrenia;
iii) find out how study design and sample characteristics affect prevalence of AUD in patients with schizophrenia.

Material and methods

In order to find articles reporting the prevalence of AUD in patients with schizophrenia published in 1996–2008 as extensively as possible, we conducted a search using three electronic databases (PsycINFO, PubMed and Web of Science). Several searches were conducted; the latest was performed in January 2009. The keywords used were 'schizophreni*', 'psychosis', 'psychoses' and 'psychotic' to find studies on schizophrenic psychoses and 'alcoholism', 'alcohol abuse', 'alcohol dependence', 'alcohol use disorder', 'substance use disorder', 'substance abuse' and 'substance dependence' and 'dual diagnosis'. At the same time a similar search was performed for cannabis use disorders. Altogether 3323 articles were found, of which 611 articles were evaluated in detail after analysing the abstracts.

In addition, we performed a manual literature search for the same time period from the journals *Acta Psychiatria Scandinavica*, *American Journal of Psychiatry*, *Archives of General Psychiatry*, *British Journal of Psychiatry*, *Journal of Clinical Psychiatry*, *Psychiatry Research*, *Schizophrenia Bulletin*, *Schizophrenia Research* and *Social Psychiatry and Psychiatric Epidemiology*. These journals were selected because they had published a considerable proportion of the articles included (approximately 40%) on this topic based on our systematic database search. We contacted approximately 30 authors to receive unpublished data.

The inclusion criteria for study collection were that the study reported information on the prevalence of alcohol abuse/dependence, the sample consisted (at least 80%) of individuals with schizophrenia spectrum diagnosis (schizophrenia, schizophreniform disorder, schizoaffective disorder and delusional disorder) or articles reported the prevalence rates by diagnostic group (in samples that were less than 80% schizophrenia spectrum), the subjects were older than 16 years of age and the study sample was larger than 15. Only articles reporting schizophrenia spectrum disorders and AUD diagnoses according to DSM (Diagnostic and Statistical Manual of Mental Disorders by American Psychiatry Association) or ICD (International Classification of Diseases by World Health Organisation) diagnostic system criteria were included. We excluded studies with samples that might have biased the presented prevalences of AUDs in the study, e.g. samples recruited from prisons, forensic psychiatry units or shelters for the homeless. Trials and intervention studies were also excluded. Only articles written in English were included.

We collected information on the diagnostic system used. In our article, the terminology of AUDs is adopted from the DSM diagnostic system (abuse and dependence). We compared whether the diagnostic system (ICD-9, ICD-10, DSM-III-R or DSM-IV) had an effect on the presented prevalences. For schizophrenia, the criteria differ mainly in terms of the duration of psychotic symptoms: in ICD the symptoms should last 1 month and in DSM 6 months before making the diagnosis.

We compared prevalences between first-episode and long-term patient samples. The average duration of illness was determined from the studies; the minimum reported average duration was 9 years. All these studies were categorized as long-term patient samples. In addition, we determined the study location and whether the sample consisted of in- or out-patients. Information on gender distribution, proportion of patients with schizophrenia, mean age and age range was collected where they were reported.

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We present the number of studies as well as the mean, standard deviation, median, inter-quartile range (IQR), and range of prevalence estimates of AUD in each of these variables of interest. We studied the heterogeneity using Cochran Q-statistic (8). Because of statistically significant heterogeneity (Q = 39 000, $P < 0.001$) we present random mean estimates, which is a conservative weighting method giving the same weight to all studies. When evidence is found of heterogeneity in the prevalence estimates between studies, metaregression with z-test can be used to analyse associations between prevalences and study characteristics (8). Metaregression was used to compare the effect of diagnostic systems (DSM vs. ICD), study setting (first episode vs. long-term sample, in-patients vs. out-patients) and location (North America vs. Europe) with prevalence estimates. Both gender distribution (proportion of male patients) and mean age were studied as continuous variables. For reasons of presentation these were categorized into three groups. The results of meta-regression are presented adjusted for the method of alcohol use diagnosis, so that variables for abuse (no/yes), dependence (no/yes) and time period (lifetime/current) are included in the metaregression models. In additional analyses we compared our findings in lifetime abuse prevalence with those by Mueser et al. (1) and Cantor-Graae et al. (2) using meta-regression (z-test). The data were analysed with STATA 9.0 (9).

Results

Altogether 60 studies met our criteria. The studies are summarized in Table 1. From each study the following details are presented where available: first author of the study, publication year, location of the study (country), diagnostic system, distribution of schizophrenia diagnoses (schizophrenia or schizophrenia spectrum), duration of illness/first-episode sample, study setting, mean age and age range, sample size, gender distribution, alcohol use diagnosis (current/lifetime, abuse/dependence) and prevalence (%) of patients with AUD. As seen from Table 1 studies vary greatly by study designs and sample characteristics.

Table 2 shows the prevalences in the studies grouped according to the type of current/lifetime alcohol use diagnosis. Total median prevalence of AUD in patients with schizophrenia was 17.8% (IQR 9.7–28.6, 60 studies). Median of lifetime AUD prevalence was 20.6% (IQR 12.0–34.5, 47 studies) and median of current AUD prevalence 9.4% (IQR 4.6–19.0, 18 studies).

Figure 1 presents the studies categorized by different study characteristics. For each study characteristic mean prevalence estimates (with 95% confidence interval), median and range are shown. The studies using DSM-III-R reported substantially higher median prevalence estimates than studies using DSM-IV, ICD-9 or ICD-10 (32.4/17.4/11.4/6.2%). In meta-regression, differences between mean prevalence diagnostic systems were also statistically significant (z = −4.03, $P < 0.001$). For mean age and duration of illness, we present current and lifetime diagnoses separately. The median prevalence estimates of current AUD is lower in older (mean age 30 years or more) than in younger patient samples (23.4 vs. 11.0%); however, in meta-regression this difference was not statistically significant (z = 1.19, P = 0.23). In lifetime AUD diagnoses, the prevalence was significantly higher (z = 2.46, P = 0.01) in 30- to 39-year age group compared with other age groups (median 24.0% vs. 14.5%). Other study characteristics did not affect the AUD prevalence.

In studies published between 1960 and 1989 (1), the median lifetime abuse prevalence was 19% (range 12–30%, n = 6), whereas in the studies published in 1990–1995 (2) the median of prevalences in lifetime abuse or dependence diagnosis was 36% (range 21–54%, n = 10). In our meta-analysis, the median of lifetime abuse was 14% (range 2–47%, 19 studies) and the median of any lifetime AUD diagnosis was 21% (range 1–57%, 47 studies). The change in AUD prevalences from studies published in 1990–1995 to the current study was statistically significant (z = 2.59, P = 0.01).

Discussion

Main results

Our results show a descending trend in AUD prevalence compared with the most recent review. However, AUDs are still common in patients with schizophrenia: approximately 10% had current and 20% had lifetime AUD diagnosis. As seen in previous studies as well as in our systematic review, there is great variation in the prevalence of AUDs in patients with schizophrenia. The variation may be explained by many factors, such as different study designs and sample characteristics. In our results the diagnostic system affected the prevalence of AUD in patients with schizophrenia, so that the prevalence of AUDs was higher especially in studies using DSM-III-R.

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Table 1. Studies presenting results on alcohol use disorders in patients with schizophrenia

Reference	Country	Diagnostic system (schizophrenia and alcohol use disorders)	Mean duration of illness (schizophrenia) (years)	Distribution of schizophrenia diagnosis*	Setting	Mean age [range]	Sample size (male/female)	AUD diagnosis	Patients with AUD diagnosis (%)
Addington & Addington (10)	Canada	DSM-IV	First-episode	Spectrum (79% schizophrenia)	In-patients	25.0 [–]	300 (~210/90)	Lifetime abuse/dependence	11.0
Akvardar et al. (11)	Turkey	DSM-IV	16.0	Schizophrenia	In-and out-patients	39.3 [–]	49 (26/23)	Lifetime abuse and dependence	4.1 and 4.1
Altamura et al. (12)	Italy	DSM-III-R	18.8	Spectrum (92% schizophrenia)	Out-patients	38.0 [–]	81 (55/26)	Lifetime abuse/dependence	35.9
Archie et al. (13)†	Canada	DSM-IV	First-episode	–	In-patients	24.3 [–]	200 (156/44)	Lifetime abuse and dependence	9.3 and 3.8
Barnett et al. (14)†	UK	DSM-IV	–	Schizophrenia	Out-patients	–	82	Lifetime abuse and dependence	7.4 and 5.7
Bühler et al. (15)	Germany	ICD-9	First-episode	Spectrum	In-patients	30.0 [12–59]	232	Lifetime abuse	23.7
Cantor-Graae et al. (2)	Sweden	DSM-IV	21.0	Schizophrenia	In- and out-patients	48.0 [–]	87 (54/33)	Current and lifetime abuse	14.9 and 47.1
Clark et al. (16)	USA	ICD-9	–	Schizophrenia	Out-patients	37.4 [–]	1705 (1238/467)	Current abuse	4.6
Compton et al. (17)	USA	DSM-IV	First-episode	Spectrum (67% schizophrenia)	In-patients	20.0 [18–29]	18 (16/2)	Lifetime dependence	16.7
Compton et al. (18)	USA	DSM-IV	–	Spectrum (64% schizophrenia)	In- and out-patients	42.9 [–]	248 (153/95)	Lifetime abuse/dependence	18.1
Compton et al. (19)	USA	DSM-IV	First-episode	Spectrum (40% schizophrenia)	In-patients	22.8 [18–40]	25 (19/6)	Lifetime abuse and dependence	8.0 and 12.0
Dawe et al. (20)	Australia	DSM-IV	11.1	Schizophrenia	In- and out-patients	38.0 [16–48]	71 (53/18)	Current abuse and dependence	1.4 and 23.4
De Lisi et al. (21)	Costa Rica, USA	DSM-III-R	19.6	Spectrum (73% schizophrenia)	In- and out-patients	41.7 [–]	393 (242/151)	Lifetime abuse	23.8
Depp et al. (22)	USA	DSM-IV	27.9	Schizophrenia	Out-patients	58.5 [–]	55 (27/28)	Current abuse/dependence	10.9
Dervaux et al. (23)	France	DSM-III-R	–	Spectrum (91% schizophrenia)	In- and out-patients	34.7 [–]	100 (68/32)	Lifetime abuse/dependence	27.0
Dervaux et al. (24)	France	DSM-III-R	11.8	–	In-and out-patients	34.1 [–]	114	Lifetime abuse and dependence and both	3.5, 26.3 and 29.8
Deshmukh et al. (25)	USA	DSM-III-R or –IV	–	Schizophrenia	In- and out-patients	31.6 [–]	34 (34/-)	Lifetime abuse and dependence and both	8.8, 32.4 and 41.2
Di Michele & Bolino (26)	Italy	ICD-10 and DSM-IV	12.6	Schizophrenia	Out-patients	40.3 [25–58]	40	Lifetime abuse/dependence	17.5
Dubertret et al. (27)	France	DSM-IV	11.3	Schizophrenia	In-patients	–	205 (139/65)	Lifetime abuse/dependence	19.5
Farrelly et al. (28)†	Australia	DSM-III-R	First-episode	Spectrum (46% schizophrenia)	In-patients	21.7 [16–29]	91	Current abuse/dependence	1.1
Fischer et al. (29)	USA	DSM-III-R	–	Schizophrenia	In-patients	38.1 [22–55]	139 (124/15)	Lifetime abuse	34.5
Fowler et al. (30)	Australia	DSM-III-R	12.7 (with AUD)	Schizophrenia	Out-patients	36.3 [18–60]	194 (141/53)	Lifetime and current abuse, lifetime and current dependence	1.5 and 2.1, 46.9 and 16.0
Gråwe et al. (31)	Norway	ICD-9 Clinical diagnosis	–	–	In-patients	36.0 [–]	1046 (659/387)	Lifetime abuse	10.3

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Table 1. Continued

Reference	Country	Diagnostic system (schizophrenia and alcohol use disorders)	Mean duration of illness (schizophrenia) (years)	Distribution of schizophrenia diagnosis*	Setting	Mean age [range]	Sample size (male/female)	AUD diagnosis	Patients with AUD diagnosis (%)
Gut-Fayand et al. (32)	France	DSM-III-R	33.2	Spectrum (96% schizophrenia)	In- and out-patients	33.2 [–]	50 (32/18)	Lifetime abuse and dependence	2.4 and 1.8
Harkavy-Friedman et al. (33)	USA	DSM-III-R	16.0	Spectrum (72% schizophrenia)	In- and out-patients	37.6 [–]	156 (94/62)	Lifetime abuse/dependence	24.4
Harkavy-Friedman et al. (34)	USA	DSM-IV	10.0	Spectrum (80% schizophrenia)	In-patients	31.6 [–]	100 (61/39)	Lifetime abuse/dependence	12.1
Haro et al. (35)	Italy, Portugal, Spain, Ireland, UK	DSM-IV and ICD-10	–	Schizophrenia	Out-patients	40.2 [–]	6516 (3753/2763)	Lifetime abuse	2.5
Holthausen et al. (36)	Netherlands	DSM-IV	First admission	–	In-patients	24.8 [–]	118 (87/31)	Current abuse	2.2
Kamali et al. (37)	Ireland	DSM-IV	15.1	–	In-patients	38.4 [–]	102 (68/34)	Lifetime and current abuse/dependence	46.1 and 24.5
Kamali et al. (38)	Ireland	DSM-III-R	First-episode	–	In- and out-patients	27.0 [–]	100 (62/38)	Current abuse	8.0
Karam et al. (39)	Lebanon, Israel	DSM-III-R	–	Schizophrenia	In-patients	34.5 [–]	18 (12/6)	Lifetime abuse	44.4
Kavanagh et al. (40)	Australia	DSM-III-R	–	Schizophrenia	In-patients	–	430	Lifetime abuse/dependence	27.4
Kendler et al. (41)	USA	DSM-III-R	–	–	In- and out-patients	30.2 [15–54]	40 (16/24)	Lifetime dependence and abuse/dependence	43.2 and 57.0
Kirkpatrick et al. (42)	USA	DSM-IV	11.3	Schizophrenia	In- and out-patients	33.8 (current) 34.4 (lifetime) [–]	154 (103/51) (current) 122 (84/38) (lifetime)	Current and lifetime abuse/dependence,	3.9 and 15.5
Krausz et al. (43)	Germany	ICD-9	–	Schizophrenia	In-patients	39.1 [18–60]	99 (45/54)	Lifetime abuse and dependence	8.1 and 18.2
Kuo et al. (44)	Taiwan	DSM-III-R, -III, -IV	–	Schizophrenia	In- and out-patients	32.9 [–]	78 (38/40)	Lifetime abuse/dependence	1.3
Leslie & Rosenheck (45)	USA	ICD-9	–	Schizophrenia	Out-patients	52.0 [–]	34 925 (33 031/2894)	Lifetime abuse	16.0
Lin et al. (46)	Taiwan	DSM-IV	12.4	–	In-patients	37.7 [–]	336 (194/142)	Lifetime abuse/dependence	11.9
Margolese et al. (47)	Canada	DSM-IV	First-episode	Spectrum (62% schizophrenia)	Out-patients	38.8 [–]	207 (120/87)	Current abuse/dependence	10.1
McCreadie et al. (48)	UK	ICD-10	18.0	Schizophrenia	In- and out-patients	45.0 [–]	250 (154/96)	Current dependence	6.8
McGirr et al. (49)	Canada	DSM-IV	–	Spectrum (84% schizophrenia)	In-and out-patients	–	36 (26/10)	Current and lifetime abuse/dependence	8.6 and 20.6
Messias & Bienvenu (50)	USA	DSM-III	–	Schizophrenia	In- and out-patients	35.7 [–]	212 (97/115)	Lifetime abuse/dependence	38.0
Modestin et al. (51)	Switzerland	ICD-10	13.2	Schizophrenia	In- and out-patients	40.6 [–]	525 (~278/247)	Lifetime harmful use/dependence	3.4
Moilanen et al. (52)	Finland	DSM-III-R	–	Schizophrenia	In- and out-patients	31.0 [31–31]	96 (63/33)	Lifetime abuse/dependence	16.7

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Table 1. Continued

Reference	Country	Diagnostic system (schizophrenia and alcohol use disorders)	Mean duration of illness (schizophrenia) (years)	Distribution of schizophrenia diagnosis*	Setting	Mean age [range]	Sample size (male/female)	AUD diagnosis	Patients with AUD diagnosis (%)
Mueser et al. (53)	USA	DSM-III-R	–	Spectrum (51% schizophrenia)	In-patients	38.8 [–]	173 (154/19)	Lifetime abuse/dependence	51.4
Nesvåg et al. (54)	Sweden	DSM-III and –IV	16.1	Spectrum (81% schizophrenia)	Out-patients	41.0 [–]	69 (50/19)	Lifetime abuse/dependence	14.5
Olfson et al. (55)	USA	DSM-III-R	–	–	In-patients	36.5 [18–64]	262 (160/102)	Current abuse/dependence	24.0
Pristach & Smith (56)	USA	DSM-III-R	10.9	Schizophrenia	In-patients	35.4 [–]	42 (28/14)	Lifetime abuse/dependence	54.8
Rabinowitz et al. (57)	Israel	ICD-9, clinical diagnosis	–	Schizophrenia	In-patients	–	7872 (4766/3106)	Current abuse	2.6
Rabinowitz et al. (58)	USA	DSM-III-R	First-episode	–	In-patients	–	224 (146/78)	Lifetime abuse/dependence	37.3
Ringen et al. (59)	Norway	DSM-IV	7.1	Spectrum (74% schizophrenia)	In- and out-patients	33.0 [18–65]	252 (147/105)	Lifetime abuse	13.5
Rossi Menezes & Ratto (60)	Brazil	ICD-10	–	Spectrum (95% schizophrenia)	Out-patients	41.5 [18–65]	119 (∼63/56)	Current dependence	5.9
Sim et al. (61)	Singapore	DSM-IV	First-episode	Spectrum (89% schizophrenia)	In-patients	27.3 [18–40]	53 (53/-)	Lifetime dependence	1.9
Soliman & Reza (62)	UK	ICD-10	9.1	Schizophrenia	In-patients	39.6 [–]	131	Lifetime harmful use/dependence	9.0
Verdoux et al. (63)†	France	DSM-IV	First-episode	Spectrum (44% schizophrenia)	In-patient	31.0 [16–59]	27 (15/12)	Lifetime abuse/dependence	22.2
Wade et al. (64)†	Australia	DSM-III-R	First-episode	–	In-patients	21.3	93 (68/25)	Lifetime abuse/dependence	32.3
Wilk et al. (65)	USA	DSM-IV	–	Schizophrenia	In-patients	– [15–54]	273	Lifetime abuse/dependence	17.2
Wobrock et al. (66)	Germany	ICD-10	First-episode	–	In-patients	25.7 [–]	68 (∼45/23)	Lifetime harmful use	5.9
Xafenias et al. (67)	Greece	DSM-IV	–	–	In-patients	–	105	Current abuse/dependence	19.0
Ziedonis & Trudeau (68)	USA	DSM-III-R	–	Spectrum (64%schizophrenia)	Out-patients	44.0 [–]	497 (253/244)	Current abuse	38.8

*Distribution of diagnoses: samples from patients with schizophrenia only are mentioned here as schizophrenia and samples from schizophrenia spectrum patients mentioned as spectrum, proportion of patients with schizophrenia presented in parentheses.

†Also unpublished data from the authors.

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Table 2. Prevalence of alcohol use disorders in patients with schizophrenia by type of alcohol use diagnosis

Alcohol use diagnosis	Number of studies	Mean (%)	Median (%)	Inter-quartile range	Range
Lifetime					
Abuse	19	17.0	13.5	5.9–24.0	1.5–47.1
Dependence	10	22.3	18.7	12.0–32.4	3.8–46.9
Abuse or dependence	29	24.5	20.6	13.5–35.9	1.3–57.0
Total*	47	23.4	20.6	12.0–35.9	1.3–57.0
Current					
Abuse	9	10.6	4.6	2.1–14.9	1.1–38.8
Dependence	4	13.0	11.4	6.4–19.7	5.9–23.4
Abuse or dependence	8	12.8	10.5	6.3–21.5	1.1–24.5
Total*	18	12.4	9.4	4.6–19.0	1.1–38.8
Total†	60	20.9	17.8	9.7–28.6	1.1–57.0

*In total higher prevalence estimates are used from abuse and dependence diagnoses (altogether 11 studies reported both abuse and dependence on lifetime diagnoses and three from current diagnoses).
†Five studies reported both lifetime and current AUD diagnosis.

Prevalence and time trends of AUDs in patients with schizophrenia

Studies in our sample present mainly results from patient samples that are under treatment. Subjects in clinical studies of shizophrenia are unlikely to be representative of all patients with schizophrenia; therefore, the prevalence estimate presented in this meta-analysis concern mainly patients under treatment. In our results, the prevalence of median current alcohol abuse was 5% and that of dependence 11%. The lifetime prevalences were somewhat higher: 14% for lifetime abuse and 19% for dependence. Some original studies reported markably higher lifetime dependence than abuse prevalences (24, 25, 30). In two (24, 25) of these three studies, the prevalence estimates of abuse and dependence are not overlapping. This could explain the higher prevalence of dependence, which after all is more severe diagnosis. Other original studies reporting both lifetime abuse and dependence prevalences do not show substantial differences in prevalences either way.

To compare our results with that of previous studies, we pooled the prevalences of AUDs reported in reviews published by Mueser et al. (1) and Cantor-Graae et al. (2). The inclusion criteria in these reviews were comparable with ours: however, there are probably differences in methods as, e.g. diagnostic systems have changed during the years. The studies included were published in 1960–1989 (1) and 1990–1995 (2). These reviews mainly report the prevalence of lifetime alcohol abuse or dependence in patients with schizophrenia, and only these prevalences are therefore compared.

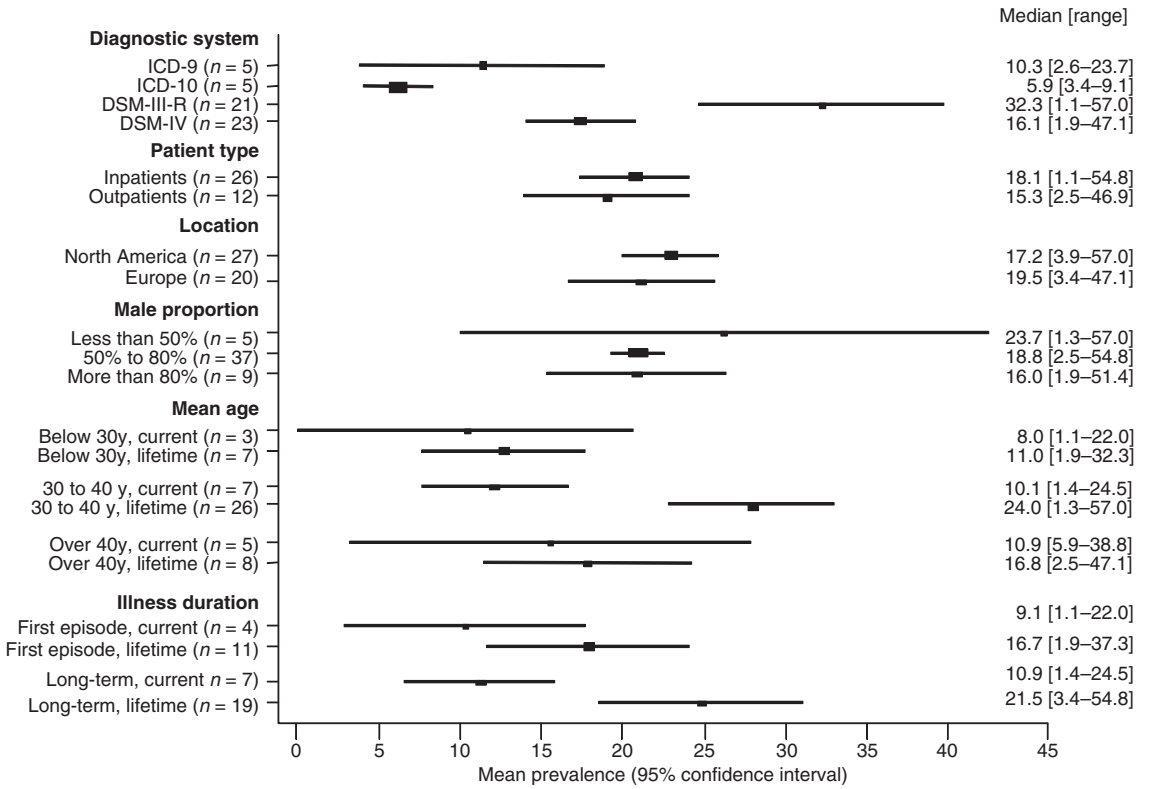

Fig. 1. Prevalence of alcohol use disorders by study characteristics.

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When we compared our results with that of studies published between 1960–1989 (1) and 1990–1995 (2), our median prevalence in lifetime abuse was statistically significantly lower. This change may mainly be due to variation in diagnostics, sampling and other methodological differences, but it may also indicate a descending trend in AUDs in patients with schizophrenia. Nowadays special treatment strategies including combination treatment and comprehensive care have been developed for patients with schizophrenia with comorbid AUD. Although clinicians are trained to recognize dual diagnosis patients, underdiagnosing of AUD still undoubtedly exists (5, 69, 70). In the majority of studies included in our sample, the AUD diagnoses were ascertained from several sources such as structured or semi-structured interviews, hospital charts, case notes and registers. Only in two studies (31, 57) the alcohol use diagnosis was based only on clinical diagnosis.

To avoid bias, we excluded studies presenting results from samples recruited from prisons, forensic psychiatry units or shelters for the homeless. In these samples, substance use disorders tend to be significantly more common than that in the general population (5, 71, 72). Our prevalence estimates may therefore underestimate the actual prevalence, as these patient samples are not present in our sample.

Diagnostics

In DSM-III-R alcohol dependence diagnosis includes both physiological symptoms, and behavioural symptoms, whereas alcohol abuse diagnosis is a residual category for diagnosing those who do not meet the criteria for dependence, but who drink despite alcohol-related physical, social, psychological or occupational problems, or who drink in dangerous situations. In the DSM-IV alcohol abuse criteria also included drinking despite recurrent social, interpersonal and legal problems as a result of alcohol use and the criteria for dependence became stricter. DSM-III and ICD-9 differ greatly, whereas DSM-IV and ICD-10 have been developed into more compatible systems, although differences still exist. ICD-10 does not differ much in terms of dependence diagnosis from DSM-IV diagnostics. Alcohol use that causes either physical or mental damage in the absence of dependence is categorized in ICD-10 as harmful. This category highlights the somatic problems related to alcohol use more than DSM-IV's abuse diagnosis. These medical conditions usually appear in older age, which may lead to underdiagnosing in younger populations in the case of ICD-10 (73, 74).

In our data, the studies using DSM-III-R diagnostic system reported higher estimates than those studies using DSM-IV, ICD-9 or ICD-10. These differences remained after taking into account other study characteristics (e.g. mean age and gender distribution). Similar results have been reported before: in previous studies comparing AUD diagnostics in DSM-III-R, DSM-IV and ICD-10 it has been presented that dependence diagnosis is most common in studies using DSM-III-R (75–77). Previous study has shown that the diagnosis of ICD-10's harmful use is not as common as abuse diagnoses in DSM systems (78), which are seen in our results as well.

In our results, the prevalence of alcohol abuse and alcohol dependence was rather similar. Therefore, we combined these diagnoses when studying covariates. Many original studies have also reported their results combined (see Table 1).

In our data set, there are 26 studies reporting results from schizophrenia samples with narrow diagnostic criteria and 21 studies were from schizophrenia spectrum samples with broader criteria. These differences in diagnostic criteria are not likely to affect our findings greatly. Only one study compared the prevalence of AUDs in patients with schizophrenia and schizoaffective disorder. Mueser et al. (53) studied the prevalence of lifetime alcohol abuse or dependence in an in-patient setting. They reported that patients with schizoaffective disorder had 1.4 times more often dual diagnosis.

Location of the study

The substance use profile is greatly affected by cultural factors. Unfortunately, there were only a few non-Western studies in our data set and therefore we were only able to compare North American and (western) European studies. There were no differences in AUD prevalence between North American and European samples.

In our sample, there was only one case–control study reporting the results of AUDs in in- and out-patients with schizophrenia compared with those on the general population written by the Scottish comorbidity study group (48). They found out that AUDs were somewhat more common in patients with schizophrenia (current abuse 16/9%, current dependence 7/3%, lifetime abuse 39/34% and lifetime dependence 19/8%).

We compared AUD prevalence in patients with schizophrenia with alcohol consumption in the countries in question reported by WHO (79). In general, in studies presenting results from countries with high consumption of alcohol, the

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prevalence of AUD in patients with schizophrenia was also higher than in studies from countries with lower alcohol consumption. However, there were some exceptions: e.g. in the UK alcohol consumption was high but the prevalence of AUD in patients with schizophrenia was low, whereas in Sweden alcohol consumption was low in general but AUD prevalence in patients with schizophrenia was high. However, alcohol consumption is not directly proportional to AUD diagnoses and consumption patterns are strongly associated with culture, which makes this kind of comparison challenging.

Study setting and patient characteristics

In our data, the differences between in- and out-patients were not statistically significant. Only in one original study, the prevalences between in- and out-patients were compared. In an Australian study by Dawe et al. (20), 57% of in-patients and 46% of out-patients had AUD.

There were seven studies reporting current AUD prevalence in long-term patient samples. The duration of illness varied between 7 and 33 years. Current AUD prevalence was presented in four studies from first-episode samples. We found no differences in current AUD prevalences between first-episode and long-term patient samples. As expected in long-term patients, the lifetime AUD prevalence was somewhat higher. In our sample, there were only a few studies comparing mean age between the AUD and non-AUD group. Therefore, we compared the reported mean age between the studies, which is not a very efficient method to study the possible effect of age. A better way to study the effects of age on the prevalence of AUDs in patients with schizophrenia would be to compare results presented in each study per individual age group (80). However, in lifetime AUD diagnoses, the prevalence was higher in older patient samples as expected.

In long-term samples of patients with schizophrenia, discrepant findings have been reported. Deshmukh et al. (25) found the AUD group to be somewhat younger (mean age 42.4/46.9 years), whereas Modestin and his study group (51) found that comorbid AUD in-patients were older than patients without any substance use disorder. Dawe et al. (20) reported that the first-episode patients with AUD were younger (mean age 23.4/27.5 years).

Among patients with schizophrenia, AUDs are reported to be more common in male patients (5). In our data set, the gender proportion did not show a significant difference, although our method was not very efficient for studying gender differences. There were some studies presenting results on prevalences in male and female patients. Rabinowitz et al. reported gender differences in Israeli (57) and American (58) samples. In these studies, AUDs were two to four times more common in male patients with schizophrenia. De Lisi et al. (21) reported that AUD was seven times more common in male patients with schizophrenia in Costa Rican and US samples.

Strengths of the study

This is a comprehensive systematic review of recent studies presenting results on AUDs in patients with schizophrenia. This is also the first meta-analysis on this topic. Our data are collected from a long time period (1996–2008) and thus it was possible to include a large number of studies ($n = 60$) that met the inclusion criteria. There was a wide variety of methods and results, and this heterogeneity made it challenging to pool the results. There are certain challenges such as inherent biases and differences in study designs when conducting meta-analyses on observational studies. We used the recommendations of Meta-analysis of Observational Studies in Epidemiology (MOOSE) (81) as guidelines when conducting this study. Specific inclusion criteria can be used to exclude studies with methodological problems. For instance, in the current study we included only articles using DSM or ICD diagnostic systems. Only articles reporting results on diagnoses based on the criteria of ICD-9, ICD-10, DSM-III-R or DSM-IV diagnostic systems (both in schizophrenia and in AUDs) were included. In the majority of the studies the diagnoses of schizophrenia and AUDs were ascertained from several sources.

Weaknesses of the study

We conducted a systematic database search and extensive manual search from several scientific journals. In addition, we contacted several authors to receive unpublished data. However, it is possible that some studies presenting results on the prevalences of AUDs in patients with schizophrenia are missing. We may have missed, e.g. studies where AUD is not the main interest of the article.

We used metaregression to examine the effect of study characteristics on the prevalence of AUDs. Because of possible differences in other study characteristics metaregression is not a very efficient method. We focused to estimate prevalence on AUDs in patients with schizophrenia and not in

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examining specific study characteristics separately. There are only a few studies among the original studies looking specifically at study characteristics. These studies are now discussed separately. Study characteristics could be more efficiently examined in a separate meta-analysis with specially developed inclusion and exclusion criteria. Another limitation is that prevalence estimates presented here are mainly from samples from Western countries. Because of limited resources we were able to include only articles published in English. Without language limitations perhaps a more comprehensive view on global AUD prevalence estimates in patients with schizophrenia could be achieved.

In conclusion, our results suggest that AUDs in patients with schizophrenia are common; however, there might be a descending trend. The decrease seen in prevalence estimates may be explained by stricter AUD criteria in diagnostic systems. Other sample characteristics did not affect the prevalence estimates.

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Declaration of interest

Professor Hannu Koponen reports having received lecturer fees from AstraZeneca, Eli Lilly Finland, H. Lundbeck, Janssen-Cilag, and Wyeth. He also disclosed consulting fees from AstraZeneca, GlaxoSmith Kline, and Janssen-Cilag. Dr. Matti Isohanni has received advisory panel payments from AstraZeneca. Dr. Johanna Koskinen, M.A. Johanna Löhönen and Dr. Jouko Miettunen have no conflict of interest.

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