Eur Arch Psychiatry Clin Neurosci (2012) 262:607–616
DOI 10.1007/s00406-012-0305-z

ORIGINAL PAPER

The lifetime and past-year prevalence of dual diagnosis in people with schizophrenia across Europe: findings from the European Schizophrenia Cohort (EuroSC)

Giuseppe Carrà · Sonia Johnson · Paul Bebbington · Matthias C. Angermeyer · Dirk Heider · Traolach Brugha · Jean-Michel Azorin · Mondher Toumi

Received: 23 December 2011 / Accepted: 29 February 2012 / Published online: 17 March 2012

Abstract Relatively little is known about rates of comorbid drug and alcohol problems in people with schizophrenia outside the USA. Most studies have recruited from single countries. Newly available data provided an unmatched opportunity to investigate the prevalence of comorbid dependence on alcohol and other psychoactive substances in people with schizophrenia in France, Germany and the UK at the same time. The European Schizophrenia Cohort study data set used semi-structured clinical interviews to establish DSM-IV diagnoses. 1,208 patients were interviewed in nine centres. The lifetime rate for comorbid dependence on any substance was highest in the UK (35 %), but considerably lower in Germany (21 %) and in France (19 %), and generally more than double the past-year rates. Dependence on alcohol and on other psychoactive substances showed similar variations (comorbid alcohol dependence: UK 26 %; Germany 18 %; France 14 %; comorbid drug dependence: UK 18 %; Germany 8 %; France 7 %). Differences within countries persisted after controlling for individual characteristics. The relative odds of dependence were higher than in the general population, but varied between countries and centres. Dependence disorders are a common problem in people with schizophrenia in Western Europe, although effective service configurations have yet to be developed. Overall, these European rates are less than those reported from the USA. Research comparing people with current comorbidity with those who are no longer dependent is needed.

Keywords Dual diagnosis · Schizophrenia · Cross-sectional study · Prevalence study · Europe

G. Carrà (✉) · S. Johnson · P. Bebbington
Department of Mental Health Sciences, University College London, Charles Bell House. 67-73 Riding House Street, London W1W 7EY, UK
e-mail: g.carra@ucl.ac.uk; carra_giuseppe@fastwebnet.it

M. C. Angermeyer · D. Heider
Department of Psychiatry, University of Leipzig, Leipzig, Germany

T. Brugha
Department of Health Sciences, University of Leicester, Leicester, UK

J.-M. Azorin
SHU Psychiatrie Adultes, Hôpital Sainte Marguerite, Marseille, France

M. Toumi
Health Economics Department, Lundbeck SA, Paris, France

Introduction

Comorbid drug and alcohol problems in people with schizophrenia ("dual diagnosis") are of growing concern, due to their association with poor clinical and social outcomes [1]. The Epidemiologic Catchment Area (ECA) study found that 47 % of people with schizophrenia had a comorbid substance use disorder, with odds of meeting criteria for such a disorder 4.6 times higher for individuals with schizophrenia than for the rest of the US population [2]. In the National Comorbidity Survey, half of those meeting criteria for a mental disorder also met those for lifetime substance use, with a rate of 45 % in people with non-affective psychosis [3].

The ECA data are often quoted as standard rates for comorbidity in psychosis, but, even within the US, there is evidence that rates of dual diagnosis vary considerably between settings and geographical locations [4]. In particular, it has been suggested that dual diagnosis may be less prevalent in rural than in urban areas [5]. Thus, it is

uncertain how much rates of dual diagnosis can be generalised from the major studies quoted above. However, there is a dearth of cross-national data from clinical populations on the prevalence of such comorbidity in Europe and there has been no large-scale comparison between European countries so far. Some local studies have been carried out in the UK since the early 1990s: they report comorbidity rates between 20 and 37 % in various mental health settings, the highest rates being in inpatients, crisis team clients and forensic settings, as well as in inner-city areas [6]. Evidence from Germany and France is less consistent, with reported lifetime rates around 40 % [7, 8].

This comorbidity is not merely the chance co-occurrence of the two disorders. Thus, recent research has focused on additional questions such as the temporal relationship between substance use disorders and schizophrenia (e.g., [9]), including contribution of potential mediating factors, as well as the influence of particular substances on the course of schizophrenia [10].

However, the epidemiological studies carried out so far have been hampered by methodological issues and cannot be considered conclusive. Samples have often been based on clinical convenience rather than on epidemiological principles [6], and the assessment of substance use has often been sub-optimal, with relatively few studies making full diagnostic assessments [11]. Frequency has been described in relation, variously, to point, period and lifetime prevalence [12], and dependence on alcohol and on other drugs is often not reported separately, though their consequences may differ in people with schizophrenia [13].

Understanding variations in prevalence of comorbid substance misuse is important for two major reasons. First, good prevalence data are crucial to planning services for clients with dual diagnosis. Secondly, in aetiological terms, geographical variation in substance misuse in psychosis is important in appreciating how far local social circumstances are responsible for the prevalence of particular substance comorbidities. Such variations are just as apparent in the prevalence of drug and alcohol use and misuse in the general population. For example, the prevalence of active drug dependence has been estimated at 1.4 % in the US and 0.5 % in the UK [14], though high-risk groups were similar (being male, unmarried, and of low socio-economic status —SES— and living in urban settings). Likewise, there are considerable differences in general population lifetime and current prevalence of alcohol and drug misuse within the European Union [15–17].

Most previous studies on dual diagnosis in people with schizophrenia involved small sample sizes and recruited exclusively from single countries and specific settings. Our aim was to use a large and representative cohort of people with schizophrenia in community mental health care in the UK, France and Germany, to investigate the prevalence of comorbid disorders due to the use of alcohol and of psychoactive substances other than alcohol. We hypothesised that, after adjusting for all relevant clinical and social variables, people with schizophrenia in the UK would have significantly higher dual diagnosis rates than their counterparts in France and Germany, reflecting differences in general population substance misuse.

Methods

Sample

The European Schizophrenia Cohort (EuroSC) survey was a naturalistic follow-up of a cohort of people aged 18–64, suffering from schizophrenia, and in contact with secondary psychiatric services in nine community mental health catchment areas in France, Germany and the UK. The current analysis is based on cross-sectional data from the first-stage interview. The research project obtained local ethical approval in each country. The settings, sampling strategies and inclusion/exclusion criteria are fully described elsewhere [18]. In brief, in France, people were recruited from three centres located in a city or in medium-sized towns from northern (Lille), central (Lyon) and southern France (Marseille). In Germany, four catchment areas were identified for the study: two in the former East Germany (Leipzig and the nearby Altenburg area, subsequently pooled and referred to hereafter as Leipzig) and two in the former West (Hemer and the County of Heilbronn). The British study centres were Islington, an inner-city area of London and a reasonably affluent area of Leicestershire, comprising both villages and medium-sized towns. There were no specialised programs available to meet the complex needs of people with schizophrenia and comorbid drug and alcohol problems in any of the centres at the time the study was carried out.

In relation to different organisational contexts, random sampling from lists of service users was adopted in all the French centres and in London, while an exhaustive inclusion strategy was used for the German centres and Leicestershire. Eligible patients were aged 18–64 years at the time of enrolment in the study, had a diagnosis of schizophrenia according to DSM–IV criteria and had given signed informed consent. People who had been hospitalised for the past 12 months, or were planning to leave the area, making follow-up assessment impracticable, were excluded.

Procedure

Individuals from the final list of participants were contacted consecutively, seeking their informed consent. If they agreed, they were interviewed at home or in a clinical facility over approximately 3 h. The study was observational,

as no intervention was made either by, or at the behest of, the research team.

Instruments

An extensive battery of instruments was used to collect information during face-to-face interviews. Only those relevant to this paper are presented here.

- Past History and Sociodemographic Description Schedule [19], an adaptation based on the third draft of 1977 [20].
- Diagnostic interviews: SCAN–Schedules for Clinical Assessment in Neuropsychiatry—version 1.0 [21] was used to evaluate the 4-week period before interview and the most significant period of earlier psychopathology. However, in the UK and Germany, SCAN was used with its component algorithm to establish diagnoses of schizophrenia. In France, the SCID (the Structured Clinical Interview for DSM-IV [22]) was used to identify schizophrenia. Patients were excluded if the diagnosis of schizophrenia was not confirmed by SCAN or by SCID. In all three countries, SCAN 1.0 algorithms were used to derive diagnoses of comorbid mental and behavioural disorders due to use of alcohol and psychoactive substances other than alcohol.

Definitions of dual diagnosis

We chose to focus on dependence rather than the harmful use of substances, because the latter is a residual diagnosis that cannot be made in people who meet criteria for dependence. Moreover, while the diagnosis of dependence, as defined in DSM–IV and ICD–10, has consistently been shown to be reliable and valid, reliability is far weaker for harmful use (*abuse* in DSM-IV) [23].

Our threefold definition of dual diagnosis was based on ICD-10 diagnoses of lifetime and past-year comorbid dependence, due to the use of (1) any psychoactive substance, of (2) alcohol alone, or of (3) any psychoactive substance other than alcohol (F10-F16 and F18-F19). For brevity, in the text, tables and figures, we refer to (1) *overall substance dependence*, (2) *alcohol dependence and* (3) *drug dependence.* As polysubstance dependence is not uncommon among people with schizophrenia, any attempt to attribute the observed dependence syndrome to a single substance or a class of substances was often difficult if not impossible. Thus, we chose to use the broad categories described above.

Analysis

Analyses were carried out using STATA version 10 for Windows. All statistical tests used the 5 % level of significance, and all p values were two-tailed.

Clearly, differences between survey areas in rates of dual diagnosis might arise because of variations in the individual sociodemographic or clinical characteristics of the participants. We identified potentially relevant variables from the published literature (e.g., [1]) and then carried out univariate analyses to identify patient attributes characteristic of dual diagnosis, both sociodemographic (gender, age, family situation, living conditions, ethnic group, migration status, years of education, centre of residence and current employment) and clinical (schizophrenia subtype, course, negative symptoms, age at onset and length of illness). We then carried out logistic regression analyses of the effect of area of residence on the prevalence of dual diagnosis (rigorously defined, as above), controlling for those sociodemographic and clinical variables that we found to be significantly related to dual diagnosis beyond the 5 % significance level. The variables thereby eligible for control differed slightly in relation to our three different categories of dual diagnosis, although there was appreciable overlap. These analyses carry the assumption that any residual differences in dual diagnosis rates between areas will incorporate the effects of area level characteristics and may be largely due to them.

Results

In total, 1,204 people with schizophrenia participated in the study, 284 in France (Lille = 100, Lyon = 99, Marseille = 85), 302 in the UK (London = 150, Leicester = 152) and 618 in Germany (Leipzig = 398, Hemer = 120, Heilbronn = 100). The sample as a whole had suffered from schizophrenia for a considerable period (13.5–16.6 years), with no significant difference in duration between centres [18]. There were minor but significant differences in age at onset between some of the individual centres. The majority of cases were of the paranoid subtype of schizophrenia. This diagnosis applied to three quarters of all cases in Germany and the UK, although in France, it only accounted for around 60 %.

The differences in the sociodemographic characteristics of participants were more salient: nearly all varied significantly according to centre of residence. In particular, people from Leipzig were significantly older ($F = 4.45$, $p < 0.0001$). However, intra-national patterns were not consistent, apart from the fact that more participants lived with relatives and fewer were homeless in France, while more participants were currently employed in Germany [18, 24].

The prevalence rates for the different forms of comorbid lifetime dependence in the various centres are displayed numerically in Table 1 and graphically in Fig. 1, with the equivalent odds ratios and 95 % confidence limits for dual diagnosis. We chose London as the reference category on

Table 1 Prevalence of lifetime dependence by centre%, ORs (95 % CIs) after controlling for sociodemographic and clinical variables

Centre[a]	Overall substance dependence[b]		Rank	Alcohol dependence[c]		Rank	Drug dependence[d]		Rank
London (N 150)	42.0 % (63/150)	1.00	1	34.0 % (51/150)	1.00	1	19.3 % (29/150)	1.00	1
Leicester (N 152)	28.3 % (43/152)	0.54 (0.32–0.91; $p = 0.022$)	2	18.4 % (28/152)	0.50 (0.28–0.89; $p = 0.019$)	3	16.4 % (25/152)	0.75 (0.39–1.45; $p = 0.40$)	2
Lille (N 100)	12.0 % (12/100)	0.15 (0.07–0.31; $p < 0.0001$)	8	7.9 % (8/101)	0.17 (0.07–0.40; $p < 0.0001$)	8	3.9 % (4/100)	0.15 (0.05–0.48; $p < 0.01$)	8
Lyon (N 99)	22.0 % (22/99)	0.34 (0.18–0.63; $p < 0.001$)	5	18.2 % (18/99)	0.48 (0.25–0.92; $p = 0.029$)	4	5.0 % (5/99)	0.18 (0.06–0.51; $p < 0.001$)	7
Marseille (N 85)	23.5 % (20/85)	0.34 (0.18–0.64; $p < 0.001$)	5	16.5 % (14/85)	0.36 (0.18–0.73; $p < 0.005$)	6	12.6 % (11/85)	0.61 (0.26–1.41; $p = 0.251$)	4
Leipzig (N 398)	17.3 % (69/398)	0.30 (0.18–0.48; $p < 0.001$)	7	13.8 % (55/398)	0.35 (0.21–0.60; $p < 0.0001$)	7	5.3 % (21/398)	0.27 (0.14–0.54; $p < 0.0001$)	6
Hemer (N 120)	25.8 % (31/120)	0.40 (0.22–0.71; $p = 0.002$)	4	19.2 % (23/120)	0.41 (0.22–0.76; $p < 0.005$)	5	10.8 % (13/120)	0.49 (0.22–1.06; $p = 0.071$)	5
Heilbronn (N 100)	31.0 % (31/100)	0.52 (0.29–0.94; $p < 0.033$)	3	22.0 % (22/100)	0.60 (0.31–1.12; $p = 0.109$)	2	18 % (18/100)	0.73 (0.34–1.54; $p = 0.414$)	3
Total (N 1,204)	24.2 % (291/1,204)			18.2 % (219/1,204)			10.5 % (126/1,204)		

[a] London was the reference category

[b] Controlled for gender, family situation, age, length of illness, overall illness course

[c] Controlled for gender, living conditions, overall illness course

[d] Controlled for gender, family situation, living conditions, age, years of education, age of illness onset, length of illness

the grounds that the general population rates of alcohol and substance abuse there are particularly high in the European context. The ORs were controlled for the sociodemographic and clinical variables significantly associated with dual diagnosis.

Nearly, a quarter (24 %) of all participants had suffered from comorbid dependence on any substance at some point in their life. Such comorbidity was seen in over a third of the British sample (35 %), whereas in Germany and France, it accounted for a fifth (21 and 19 %, respectively). Comorbid alcohol dependence rates were twice as high in the UK as in France, and comorbid drug dependence rates three times as high (26 vs. 14 %, and 18 vs. 7 %, respectively). German participants had comorbidity rates slightly higher than the French (18 % for alcohol and 8 % for drugs). The large differences between England and the other two countries were statistically significant ($\chi^2 = 27.3$, 18.2, and 24.4, for comorbid overall substance dependence, alcohol dependence and drug dependence, respectively; $p < 0.0001$ for all).

However, rates of comorbidity also varied considerably between centres within the same country. The lifetime prevalence rates of comorbid alcohol dependence ranged in the UK between 18.4 % (Leicester) and 34.0 % (London), in France between 7.9 % in Lille and 18.2 % in Lyon, and in Germany between 13.8 % in Leipzig and 22.0 % in Heilbronn. In the UK, lifetime rates of comorbid drug dependence were fairly similar in London (19.3 %) and in Leicester (16.4 %), but there was a greater than threefold difference in France between Lille (3.9 %) and Marseille (12.6 %) and in Germany between Leipzig (5.3 %) and Heilbronn (18.0 %). Comorbidity due to drug dependence was low in Leipzig, Lille and Lyon, while Marseille had relatively more drug dependence than the other French centres.

The rank order of odds ratios for lifetime comorbidity (Table 1) was very similar for substance dependence overall and for alcohol dependence (understandably, given that most of the overall comorbidity was due to the latter). The rank order of the drug dependence differed somewhat more from that of overall dependence, although the ordering remained generally similar.

London ranked first for overall substance dependence, alcohol dependence and drug dependence, followed by Leicester and by Heilbronn as regards alcohol. The lowest prevalences were consistently seen in Lille. Leipzig also had low rates, but the centres in the former West Germany had relatively high rates, though this might be partly explained by the fact that people with schizophrenia resident in Leipzig were on average older.

In relation to comorbid alcohol dependence, only the difference between London and Heilbronn failed to reach conventional levels of significance. The numbers of people

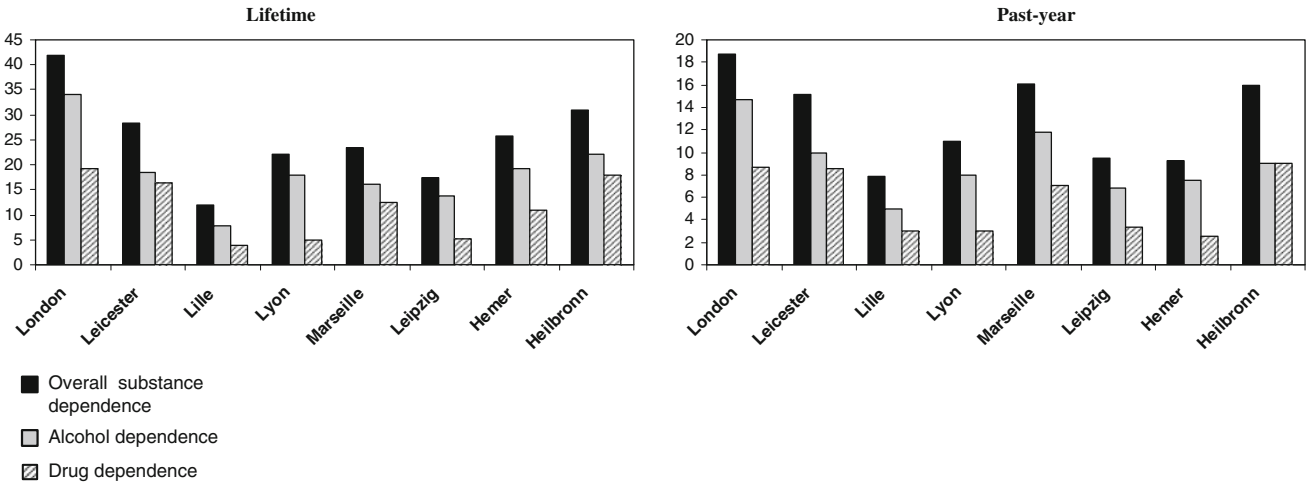

Fig. 1 Prevalence% of dependence by centre

with comorbid drug dependence were generally lower, and only Leipzig, Lyon and Lille had rates significantly lower than the London rate.

The past-year prevalences of comorbidity were appreciably lower than lifetime rates, being 12 % for overall dependence, 9 % for dependence on alcohol and 5 % for dependence on drugs. In England, comorbidity was 12.2 % for alcohol and 8.6 % for other drugs. The corresponding figures for France were 7.9 and 4.2 %, while those for Germany were 7.3 and 4.1 %. Once more the rates in Germany and France were very similar, while the rates in Britain were higher.

In Table 2 and in Fig. 1, we show the breakdown by individual centre for past-year comorbidity. The range of values is noticeably narrower than for lifetime dependence. For overall substance dependence, the range lies between 7.9 % (Lille) and 18.7 % (London), for alcohol dependence between 5.0 % (Lille) and 14.7 % (London), and for drug dependence between 2.5 % (Hemer) and 9.0 % (Heilbronn). London remains the centre with the highest rates for comorbidity due to overall substance dependence and alcohol dependence, but is overtaken by Heilbronn in relation to comorbid drug dependence. Lille again has low rates for all types of dependence. The corrected odds ratios shown are sometimes significant, sometimes not. Lille, Leipzig and Hemer have overall substance dependence rates and alcohol dependence rates that are significantly lower than those seen in London, while none of the differences in relation to drug dependence reach conventional levels of significance.

The differences between lifetime rates and past-year rates of comorbidity are interesting, in that they imply that an appreciable proportion of the participants in this survey had, one way or another, recovered from episodes of substance dependence. This is demonstrated graphically in Fig. 2, which shows the proportion of people with a lifetime history of dependence who reported that the problem had continued within the past year. This was really quite variable from centre to centre. Thus, participants in London and Hemer, whose lifetime rate was high, both had relatively low proportions of participants with continuing problems, while those from Marseille had rather higher proportions. Hemer was characterised by low lifetime rates and relatively speaking even lower past year rates, while Lille, with the lowest lifetime rates, showed the highest levels of persistence.

Discussion

We analysed a large international sample of people with schizophrenia, involving nine community mental health centres in different regions of three European countries. ICD-10 and DSM-IV equivalent research diagnoses for schizophrenia and for comorbid dependence were based on formal diagnostic interviews. We were thus able to study area of residence in relation to differences in rates of concurrent lifetime and past-year dependence due to the use of any substance, of alcohol, and of substances other than alcohol.

Main findings

Comorbidity due to overall lifetime substance dependence was particularly prevalent in the UK sample (35 %), while it was considerably lower in Germany (21 %) and in France (19 %). These national differences were similar for alcohol dependence (Britain 26 %, Germany 16 % and France 14 %) and drug dependence (Britain 18 %, Germany 8 % and France 7 %). Lifetime rates were more than

Table 2 Prevalence of past-year dependence by centre%, ORs (95 % CIs) after controlling for sociodemographic and clinical variables

Centre[a]	Overall substance dependence[b]		Rank	Alcohol dependence[c]		Rank	Drug dependence[d]		Rank
London (N 150)	18.7 % (28/150)	1.00	1	14.7 % (22/150)	1.00	1	8.7 % (13/150)	1.00	2
Leicester (N 152)	15.1 % (23/152)	0.88 (0.37–2.07; $p = 0.770$)	2	9.9 % (15/152)	0.67 (0.32–1.39; $p = 0.284$)	2	8.6 % (13/152)	1.01 (0.19–0.92; $p = 0.964$)	1
Lille (N 100)	7.9 % (8/100)	0.18 (0.04–0.87; $p = 0.034$)	8	5.0 % (5/100)	0.26 (0.09–0.74; $p = 0.012$)	8	3.0 % (3/100)	0.33 (0.08–1.30; $p = 0.116$)	7
Lyon (N 99)	11.0 % (11/99)	0.30 (0.08–1.11; $p = 0.072$)	6	8.1 % (8/99)	0.49 (0.20–1.19; $p = 0.117$)	6	3.0 % (3/99)	0.34 (0.08–1.30; $p = 0.116$)	6
Marseille (N 85)	16.1 % (14/85)	0.79 (0.27–2.29; $p = 0.673$)	4	11.8 % (10/85)	0.66 (0.29–1.52; $p = 0.338$)	3	7.1 % (6/85)	0.80 (0.27–2.37; $p = 0.699$)	4
Leipzig (N 398)	9.5 % (38/398)	0.41 (0.17–0.94; $p = 0.037$)	5	6.8 % (27/398)	0.51 (0.26–0.99; $p = 0.050$)	5	3.3 % (13/398)	0.49 (0.20–1.17; $p = 0.111$)	5
Hemer (N 120)	9.2 % (11/120)	0.24 (0.06–0.91; $p = 0.036$)	7	7.5 % (9/120)	0.38 (0.15–0.93; $p = 0.034$)	7	2.5 % (3/120)	0.27 (0.07–1.01; $p = 0.053$)	8
Heilbronn (N 100)	16.0 % (16/100)	0.82 (0.32–2.08; $p = 0.687$)	3	9.0 % (9/100)	0.56 (0.23–1.34; $p = 0.196$)	4	9.0 % (9/100)	0.93 (0.35–2.50; $p = 0.897$)	3
Total (N 1,204)	12.4 % (149/1,204)			8.7 % (105/1,204)			5.2 % (63/1,204)		

[a] London was the reference category

[b] Controlled for gender, family situation, currently employed, age, length of illness

[c] Controlled for gender, overall illness course

[d] Controlled for gender, living conditions, age, age of illness onset, length of illness

double the past-year rates. It should be noted that the rates found in our tri-national European sample are appreciably lower than those that have been reported from the United States [2–4]. It is clear that research from the USA on substance dependence in schizophrenia cannot unreservedly be applied in the European context.

There were also differences within countries, and these persisted after controlling for individual characteristics. Among covariates with a significant impact on comorbid rates, some were typical sociodemographic features, such as gender, age, education, employment, family situation and living conditions. However, some clinical characteristics needed to be controlled for in estimating prevalence rates and ORs: thus age of onset and illness course also had an influence on comorbidity. Nevertheless, the social characteristics of the areas from which the samples were drawn might have an important bearing on the chances of suffering from comorbid dependence. London (Islington), Marseille and the formerly West German Heilbronn are all urban areas of considerable social deprivation. People recruited from the more affluent and suburban area of Leicestershire (UK) had comparatively lower comorbid rates. This seems consistent with earlier studies suggesting that dual diagnosis may be less prevalent in rural than in urban areas [5], though a definitive trend towards higher rates in urban areas did not emerge in our study. Further analyses may be needed to explore the role of urbanicity as one of the factors that may moderate or mediate the association between specific substance use and schizophrenia.

It is likely that people with schizophrenia are vulnerable to developing dependence, and this may be especially so in cultures where heavy drinking and binge drinking are common and where drug containment policies are ineffective [25]. This is more true of England than France or Germany. If the relative frequency of dual diagnosis reflects differences in cultural attitudes towards the use of alcohol and other substances, there are inevitable public health implications. Thus, public health strategies to change alcohol- and drug-related behaviour in the general population should also have a beneficial effect in reducing comorbid dependence. In the context of the recent global strategy to reduce the harmful use of alcohol [26], it is clear that Britain lags in the implementation of strategies readily capable of adoption, particularly in pricing and the application of other constraints, and there have been constant criticisms of the way drug dependence is handled through the criminal justice system.

Limitations

Patients were selected on the basis of their consent to participation in the study, and information on non-responders

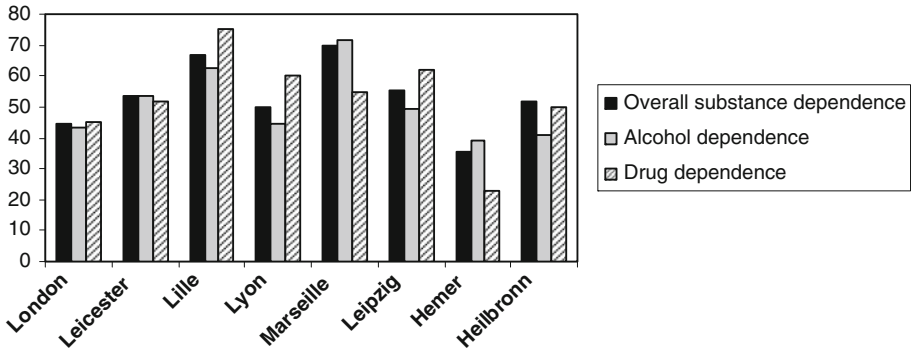

Fig. 2 Proportion of past-year dependence among lifetime dependent people with schizophrenia by centre

was unavailable. Thus, people with schizophrenia and comorbid dependence may have been less likely to participate in the study. The ultimate effect of this in terms of selection bias is unknown, and it may well have varied between settings. While attempts were made to guarantee comparable recruitment procedures across the centres of the study, the organisation of mental health services was different and recruitment bias cannot be excluded. A full description about differences and similarities in the community mental health services involved in the study is presented elsewhere [18], indicating relevant variations in service patterns at a country and site level. However, in the UK, France and Germany, a high proportion of cases are actually cared for by community mental health teams, thus minimising selection bias. Thus, variations in rates could be hardly related to local treatment access and delivery issues, though policies embedded in the different mental health care systems in France, Germany and the UK might vary at least in terms of inpatients services available for addiction. Nevertheless, differences in clinical resources available should be included as additional confounding factors in future research. Unfortunately, we lacked information about duration of contacts with community mental health services and this might have influenced our figures. A longer and perhaps more impaired course might increase the chance of comorbid dependence in people with schizophrenia, although some patients give up psychoactive drug use when they become psychotic. Finally, the cross-sectional approach of our study based on sampling from standard community services does not allow estimates of the frequency of such comorbidity in terms of consecutive cases.

The procedure for identifying schizophrenia was based on the use of standardised instruments: in France, the SCID was used, while in the UK and Germany, diagnosis was based on SCAN. While different instruments may identify different cases, the cases identified by one instrument but not by the other are still likely to be similar in their correlates (e.g., comorbidity) because they are likely to be around the threshold of recognition anyway. The identification of substance dependence was uniform across the three countries. The reliability of ratings was not formally established during the survey, although there have been reliability studies for a number of specific SCAN 1.0 sections (e.g., [27, 28]).

For social and cultural reasons, people may not want to admit substance misuse, which in any case might be more stigmatised in some countries than others. It should also be noted that comorbidity based on lifetime estimates of dependence would cover cases where the dependence preceded the emergence of schizophrenia and indeed those where dependence had actually ceased before onset. The role of possible confounders has been addressed at the stage both of design (random sampling and exhaustive inclusion procedures) and of analysis (adjusting for a selected set of variables). The settings, the manner of delivery of interventions and the exclusion criteria are relatively similar to those found elsewhere, allowing reasonable generalisability within the involved countries, in terms of admitted and treated people with schizophrenia. Nevertheless, as comorbidity was assessed in treated populations, findings might not be the same in people out of contact with services.

Comparison with general population rates

National rates of dependence are a measure of population vulnerability, arising from linked factors like societal attitudes and relative availability and cost of the relevant substances. If people with schizophrenia have rates of comorbid dependence higher than the general population rate, this would provide a rough measure of additional vulnerability. We obtained the best available sources for the national lifetime alcohol and drug dependence rates in the general population of the countries in which the centres lie [15, 16, 29]. These are equivalent, in terms of year of data collection, though not in terms of assessment methods, to the prevalence rates of alcohol and drug dependence in our sample. The results are shown in Fig. 3. Furthermore, compared with members of the general population, the relative odds for alcohol dependence in people with schizophrenia were 2.6 in the UK, 1.7 in France and 2.1 in

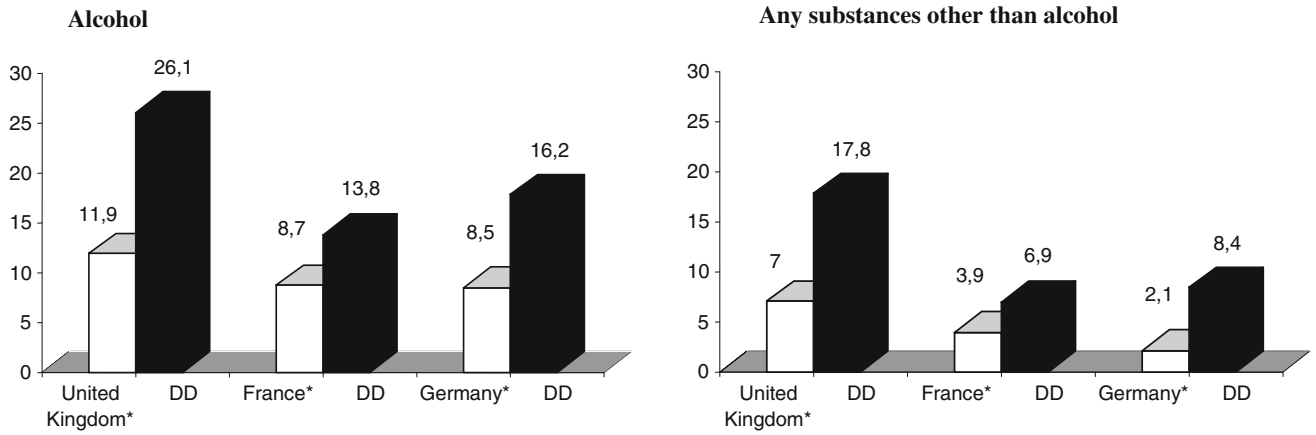

Fig. 3 National prevalence rates of lifetime dependence in general population* and in people with schizophrenia

Germany. Similar results were found for drug dependence with the relative odds ranging from 2.9 in the UK, to 1.8 in France and 4.3 in Germany. It appears therefore that people with schizophrenia are indeed particularly vulnerable to comorbid substance dependence, and that the level of abuse is associated with general population rates. The variation in odds ratios between jurisdictions is not readily interpretable, as they probably relate both to the minor variations in the sample characteristics and to general differences in the social context of people with schizophrenia.

Clinical implications

It is known that the presence of substance misuse in people with schizophrenia is associated with considerably increased clinical burden and costs to mental health services [30]. We lack specific and effective interventions for patients whose needs are compounded by substance misuse [31–34]. The additional costs of treating people with dual diagnosis are therefore primarily responsive, rather than therapeutic. Where there are increased rates of dual diagnosis, it would therefore be reasonable to anticipate increased costs. However, this is not apparent in the unit cost data derived from the EuroSC study [35]. The annual unit costs per patient during the survey follow-up were estimated at €5,518 in Germany, €6,704 in the UK and €7,776 in France. These costs seem unrelated to the relative prevalences of dual diagnosis in the different countries. Certainly, considerable work is required before treatment and service provision will reflect a rational response to the needs of patients with dual diagnosis.

Improved clinical management of dual diagnosis has been a major concern of several European National Health Services. Options for service development have been widely discussed, as models from the USA are likely to be less effective in the European context of established community mental health services [6]. Such programmes require additional resources and perhaps radical redesign of service delivery systems. The needs of patients with dual diagnosis cannot be the only driver of service development. However, the sheer frequency of dual diagnosis and its associated burden of need mean that it is an important one. Thus, *local* prevalence rates and the impact on clinical and psychosocial outcomes should inform evidence-based allocation of resources in terms of the services and training needed.

The fact that, as previously reported (e.g., [36]), lifetime prevalence rates are generally more than twice the past-year rates suggest that, even in this vulnerable group, dependence is not necessarily permanent. Differences between centres do not detract from the fact that some people with schizophrenia in our sample, whatever their disadvantages, had managed to recover from dependence disorders. Comparison of people with current dual diagnosis with those who are no longer dependent as well as with other severe mental illnesses [37] and special populations [38] may provide clues to more effective therapeutic strategies.

Acknowledgments This study was funded by grants from Lundbeck A/S and from the German Federal Ministry of Education and Research. Our thanks to all the patients and staff that helped with the study and to the Camden and Islington Mental Health and NHS Foundation Trust and the Leicestershire Partnership NHS Trust R&D Programme and to those who collected the data and otherwise contributed to the main study.

Conflict of interest Giuseppe Carrà, Sonia Johnson, Dirk Heider and Traolach Brugha have not received any financial support by pharmaceutical companies in recent years. Paul Bebbington and Matthias C. Angermeyer are in retirement and have not received any financial support by pharmaceutical companies in recent years. Jean-Michel Azorin has received unrestricted research grants from H. Lundbeck A/S. Mondher Toumi was an employee of H. Lundbeck A/S.

References

1. Crawford V, Crome IB, Clancy C (2003) Co-existing problems of mental health and substance misuse (Dual Diagnosis): a literature review. Drugs 10:1–74
2. Regier DA, Farmer ME, Rae DS (1990) Co-morbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiological Catchment Area (ECA) study. JAMA 264:2511–2518
3. Kessler RC, Nelson CB, McGonagle KA, Edlund MJ, Frank RG, Leaf PJ (1996) The epidemiology of co-occurring addictive and mental disorders: implications for prevention and service utilization. Am J Orthopsychiatr 66:17–31
4. Swartz MS, Wagner HR, Swanson JW, Stroup TS, McEvoy JP, Canive JM, Miller DD, Reimherr F, McGee M, Khan A, Van Dorn R, Rosenheck RA, Lieberman JA (2006) Substance use in persons with schizophrenia: baseline prevalence and correlates from the NIMH CATIE study. J Nerv Ment Dis 194:164–172
5. Mueser KT, Essock SM, Drake RE, Wolfe R, Frisman L (2001) Rural and urban differences in patients with a dual diagnosis. Schizophr Res 48:93–107
6. Carrà G, Johnson S (2009) Variations in rates of comorbid substance use in psychosis between geographical areas and mental health settings in the UK. Soc Psychiatr Psychiatr Epidemiol 44:429–447
7. Soyka M, Albus M, Kathmann N, Finelli A, Hofstetter S, Holzbach R, Immler B, Sand P (2003) Prevalence of alcohol and drug abuse in schizophrenic inpatients. Eur Arch Psychiatr Clin Neurosci 242:362–372
8. Dervaux A, Laqueille X, Bourdel MC (2003) Cannabis and schizophrenia: demographic and clinical correlates. Encephale 29:11–17
9. Corcoran CM, Kimhy D, Stanford A, Khan S, Walsh J, Thompson J, Schobel S, Harkavy-Friedman J, Goetz R, Colibazzi T, Cressman V, Malaspina D (2008) Temporal association of cannabis use with symptoms in individuals at clinical high risk for psychosis. Schizophr Res 106:286–293
10. Foti DJ, Kotov R, Guey LT, Bromet EJ (2010) Cannabis use and the course of schizophrenia: 10-year follow-up after first hospitalization. Am J Psychiatr 167:987–993
11. Drake RE, Alterman AI, Rosenberg SR (1993) Detection of substance use disorders in severely mentally ill patients. Community Ment Health J 29:175–192
12. Goldfinger SM, Schutt RK, Seidman LJ, Turner WM, Penk WE, Tolomiczenko GS (1996) Self-report and observer measures of substance abuse among homeless mentally ill persons in the cross-section and over time. J Nerv Ment Dis 184:667–672
13. Potvin S, Sepehry AA, Stip E (2006) A meta-analysis of negative symptoms in dual diagnosis schizophrenia. Psychol Med 36: 431–440
14. Furr-Holden CD, Anthony JC (2003) Epidemiologic differences in drug dependence: a US-UK cross-national comparison. Soc Psychiatr Psychiatr Epidemiol 38:165–172
15. Rehm J, Room R, van den Brink W, Jacobi F (2005) Alcohol use disorders in EU countries and Norway: an overview of the epidemiology. Eur Neuropsychopharmacol 15:377–388
16. Rehm J, Room R, van den Brink W, Jacobi F (2005) Problematic drug use and drug use disorders in EU countries and Norway: an overview of the epidemiology. Eur Neuropsychopharmacol 15:389–397
17. European Monitoring Centre for Drugs and Drug Addiction-EMCDDA (2010) The state of the drugs problem in the European Union and Norway. Office for Official Publications of the European Communities, Luxembourg
18. Bebbington PE, Angermeyer M, Azorin JM, Brugha T, Kilian R, Johnson S, Toumi M, Kornfeld A (2005) The European Schizophrenia Cohort (EuroSC): a naturalistic prognostic and economic study. Soc Psychiatr Psychiatr Epidemiol 40:707–717
19. World Health Organization (1973) The international pilot study of schizophrenia. WHO Press, Geneva
20. Jablensky A, Schwarz R, Tomov T (1980) WHO Collaborative Study on impairments and disabilities associated with schizophrenic disorders. Acta Psychiatr Scand 285(suppl 62):152–159
21. World Health Organization (1992) SCAN: schedules for clinical assessment in neuropsychiatry. WHO Press, Geneva
22. Spitzer RL, Williams JB, Gibbon M, First MB (1992) The structured clinical interview for DSM-III-R (SCID). I: rationale, and description. Arch Gen Psychiatr 49:624–629
23. Hasin D, Hatzenbuehler ML, Keyes K, Ogburn E (2006) Substance use disorders: diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) and international classification of diseases, tenth edition (ICD-10). Addiction 101:59–75
24. Marwaha S, Johnson S, Bebbington P, Stafford M, Angermeyer MC, Brugha T, Azorin JM, Kilian R, Hansen K, Toumi M (2007) Rates and correlates of employment in people with schizophrenia in the UK, France and Germany. Br J Psychiatr 191:30–37
25. Norström T (2001) Per capita alcohol consumption and all-cause mortality in 14 European countries. Addiction 96(suppl 1): 113–128
26. World Health Organisation (2010) Global strategy to reduce the harmful use of alcohol. WHO Press, Geneva
27. Wing JK, Babor T, Brugha T, Burke J, Cooper JE, Giel R, Jablenski A, Regier D, Sartorius N (1990) Schedules for clinical assessment in neuropsychiatry. Arch Gen Psychiatr 47:589–593
28. Tomov T, Nikolov V (1990) Reliability of SCAN categories and scores: results of the field trials. In: Stefanis CN, Rabavilas AD, Soldatos CR (eds) Psychiatry: a world perspective. Excerpta Medica, Amsterdam, vol 1, pp 107–112
29. European Monitoring Centre for Drugs and Drug Addiction-EMCDDA (2003) The state of the drugs problem in the European Union and Norway. Office for Official Publications of the European Communities, Luxembourg
30. McCrone P, Menezes PR, Johnson S, Scott H, Thornicroft G, Marshall J, Bebbington P, Kuipers E (2000) Service use and costs of people with dual diagnosis in South London. Acta Psychiatr Scand 101:464–472
31. Johnson S, Thornicroft G, Afuwape S, Leese M, White IR, Hughes E, Wanigaratne S, Miles H, Craig T (2007) Effects of training community staff in interventions for substance misuse in dual diagnosis patients with psychosis (COMO study)—cluster randomised trial. Br J Psychiatr 191:451–452
32. Craig TKJ, Johnson S, McCrone P, Afuwape S, Hughes E, Gournay K, White I, Wanigaratne S, Leese M, Thornicroft G (2008) Integrated care for co-occurring disorders: psychiatric symptoms, social functioning, and service costs at 18 months. Psychiatr Serv 59:276–282
33. Hughes E, Wanigaratne S, Gournay K, Johnson S, Thornicroft G, Finch E, Marshall J, Smith N (2008) Training in dual diagnosis interventions (the COMO Study): randomised controlled trial. BMC Psychiatr. doi:10.1186/1471-244X-8-12
34. Altamura AC, Serati M, Albano A, Paoli RA, Glick ID, Dell'Osso B (2011) An epidemiologic and clinical overview of medical and psychopathological comorbidities in major psychoses. Eur Arch Psychiatr Clin Neurosci 261:489–508
35. Heider D, Bernert S, König HH, Matschinger H, Hogh T, Brugha TS, Bebbington PE, Azorin M, Angermeyer MC, Toumi M (2009) Medical mental health care costs of schizophrenia in France, Germany and the United Kingdom—Findings from the European Schizophrenia Cohort (EuroSC). Eur Psychiatr 24:216–224
36. Fowler IL, Carr VJ, Carter NT, Lewin TJ (1998) Patterns of current and lifetime substance use in schizophrenia. Schizophr Bull 24:443–455

37. Lagerberg TV, Sundet K, Aminoff SR, Berg AO, Ringen PA, Andreassen OA, Melle I (2011) Excessive cannabis use is associated with earlier age at onset in bipolar disorder. Eur Arch Psychiatr Clin Neurosci 261:397–405
38. Pompili M, Serafini G, Innamorati M, Biondi M, Siracusano A, Di Giannantonio M, Giupponi G, Amore M, Lester D, Girardi P, Möller-Leimkühler AM (2012) Substance abuse and suicide risk among adolescents. Eur Arch Psychiatr Clin Neurosci. doi: 10.1007/s00406-012-0292-0