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Substance misuse in first-episode psychosis: 15-month prospective follow-up study*

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Background Well-designed prospective studies of substance misuse in first-episode psychosis can improve our understanding of the risks associated with comorbid substance misuse and psychosis.

Aims To examine the potential effects of substance misuse on in-patient admission and remission and relapse of positive symptoms in first-episode psychosis.

Method The study was a prospective 15-month follow-up investigation of 103 patients with first-episode psychosis recruited from three mental health services.

Results Substance misuse was independently associated with increased risk of in-patient admission, relapse of positive symptoms and shorter time to relapse of positive symptoms after controlling for potential confounding factors. Substance misuse was not associated with remission or time to remission of positive symptoms. Heavy substance misuse was associated with increased risk of in-patient admission, relapse and shorter time to relapse.

Conclusions Substance misuse is an independent risk factor for a problematic recovery from first-episode psychosis.

Declaration of interest None.

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Research on substance misuse in psychotic disorders has been hampered by methodological limitations including selection bias, lack of diagnostic rigour, failure to control for potential confounding variables and a lack of prospective follow-up studies (Blanchard *et al*, 2000; Murray *et al*, 2003). Prospective studies of first-episode psychosis can address these issues and improve our understanding of the risks associated with comorbid substance misuse and psychosis. A small number of prospective studies have reported that substance misuse is associated with a problematic recovery from recent-onset psychosis (Linszen *et al*, 1994; Strakowski *et al*, 1998; Sorbara *et al*, 2003). Consistent with the findings of these studies, our hypotheses for the current study were that substance misuse in first-episode psychosis would be associated with increased risk of in-patient admission, a longer time to remission of positive symptoms, and earlier and increased risk of relapse of positive symptoms.

METHOD

Participants

Consecutive in-patient and out-patient admissions of individuals with first-episode psychosis were screened for the study between January and December 1997 at the Central East Area Mental Health Service (CEAMHS) and the Northern Area Mental Health Service (NAMHS), and between March and July 2001 at the Early Psychosis Prevention and Intervention Centre (EPPIC) in Melbourne, Australia. The CEAMHS and the NAMHS are generic mental health services for adults with serious mental illnesses and EPPIC is a specialist mental health service for youth with first-episode psychosis. The services provide comprehensive care within defined catchment areas and are funded by the state government. The inclusion criteria for the study were age 15–30 years, fluency in English, ability to give informed consent, and clear evidence of a functional psychotic disorder. The exclusion criteria were organic aetiology, learning disability, history of brain damage or epilepsy, and more than 6 months of prior treatment for a psychotic disorder. The aims of the study were fully explained to the participants, who provided written informed consent. The research and ethics committees of the North-Western Mental Health Program approved the study. In total 126 patients (EPPIC n=71; CEAMHS n=32; NAMHS n=23) were recruited to the study. Twenty-three patients had missing data regarding the presence of any substance misuse during follow-up owing to their not being contactable at the 9-month or 15-month time point and were excluded from further analyses, leaving a sample of 103 patients (EPPIC n=59, CEAMHS n=25, NAMHS n=19). For patients who were eligible for the study at EPPIC (n=95), no significant difference was found between patients included (n=59) and not included (n=36) in the current analyses on demographic variables, psychotic disorder diagnosis or duration of untreated psychosis.

Measures and procedure

A baseline assessment was completed at entry to treatment, and follow-up assessments were undertaken 3 months, 9 months and 15 months following the initial assessment. An updated version of the Royal Park Multidiagnostic Instrument for Psychoses (RPMIP; McGorry *et al*, 1990) was used to diagnose DSM–IV (American Psychiatric Association, 1994) psychotic disorders based on assessment at baseline and 3-month follow-up. Diagnoses were subsequently categorised as schizophrenia-spectrum psychosis (schizophrenia, schizophreniform, schizoaffective or delusional) or other psychosis (bipolar, major depression, not otherwise specified, substance-induced or brief). The RPMIP was also used to estimate the duration of untreated psychosis in days, defined as the time from onset of psychotic symptoms to treatment entry. The Chemical Use, Abuse and Dependence Scale (CUAD; McGovern & Morrison, 1992) was used to diagnose DSM–III–R (American Psychiatric Association, 1987) substance misuse (criteria met for abuse or dependence) during the 15-month follow-up period. Substance misuse was assessed at the 9-month time point (for the interval between baseline and 9

months) and the 15-month time point (for the interval between 9 months and 15 months). Substances assessed for included alcohol, amphetamine, benzodiazepine, cannabis, cocaine, hallucinogen, inhalant, opioid and phencyclidine. Diagnoses of substance misuse were based on the 17 items rated 'true' or 'false' for each substance. Each item corresponds to a criterion of DSM–III–R substance abuse or dependence. Individual substance use severity scores are based on weighted scores from 1 to 4 for the 17 items rated 'true' for each substance. The sum of individual substance use severity scores provides a total substance use severity score. The higher total substance use severity score at the 9- or 15-month time point was used to calculate the total substance use severity score during the follow-up period. As in the study by Kavanagh *et al* (2004), any misuse of substances other than alcohol or cannabis was defined as 'other substance misuse' and the presence of at least two of alcohol, cannabis or other substance misuse was defined as 'poly-substance misuse'. Patients with substance misuse were grouped according to the pattern of substance misuse as follows: cannabis misuse; other but not cannabis misuse; or alcohol misuse only. Substance misuse was categorised as mild or heavy based on a median split of CUAD total substance use severity scores.

Remission and relapse of positive psychotic symptoms were the primary clinical outcomes. The Brief Psychiatric Rating Scale (BPRS; Lukoff *et al*, 1986) was used to rate remission and relapse of positive symptoms according to the following criteria: remission was defined as a score of 3 (mild) or less on all of the BPRS Psychotic sub-scale items (hallucinations, conceptual disorganisation, unusual thought content and suspiciousness) for at least 2 weeks; relapse was defined as a score of 4 (moderate) or more on any of the BPRS Psychotic sub-scale items for at least 1 week after achieving remission. Assessment for remission and relapse was undertaken at all three follow-up assessments and, if relevant, estimates of the date of onset and offset of remission or relapse were derived by asking patients to recall the date when criteria were first met, using prompts of significant calendar dates if necessary. Medication compliance was rated on a four-point scale: 1 for 0–24% compliance (no or irregular compliance); 2 for 25–49% compliance (rather irregular compliance); 3 for 50–74% compliance (rather regular compliance); 4 for 75–100% compliance (regular compliance). Ratings were subsequently recoded to denote compliance (a score of 4) or non-compliance (a score of 3 or less). Medication non-compliance during follow-up was subsequently defined as the presence of a score less than 4 at any time during follow-up. All diagnostic and clinical assessments were based on patient interviews supplemented by data derived from informants (family members and/or clinicians) and a review of medical records.

In-patient admission following the initial 3-month treatment period was the primary outcome related to in-patient service use. Most patients with first-episode psychosis are admitted to hospital during treatment for the initial acute phase (Power *et al*, 1998). Hence, we examined whether substance misuse was associated with an increased risk of admission to hospital following the initial 3-month treatment period, henceforth referred to as 'in-patient admission'. Information regarding the number and duration of in-patient admissions was obtained from clinical files and an electronic database.

Experienced raters completed clinical assessments after receiving training in the administration of the RPMIP and BPRS prior to commencement of the study. Inter-rater agreement on the 24 BPRS items and the 4 BPRS Psychotic sub-scale items was assessed by comparing ratings made by the first author (D.W.) and a second rater on five cases. Agreement was defined as the percentage of items that were rated within one point by both raters. A minimum of 95% agreement was achieved on the 24 BPRS items and the 4 BPRS Psychotic sub-scale items.

Data analysis

Univariate binary logistic regression was used to assess the effects of substance misuse on in-patient admission (yes/no), remission (yes/no) and relapse (yes/no). Kaplan–Meier survival analysis was used to compare the time to remission and time to relapse following remission between patient groups using the log-rank test. To adjust for potential confounding variables, multivariate binary logistic and Cox proportional hazards regression models were constructed. These models involved simultaneous entry of substance misuse and the following variables: gender, age, psychotic disorder diagnosis (schizophrenia-spectrum or other psychosis), duration of untreated psychosis (log-transformed owing to positive skewness) and medication compliance. All statistical tests were two-tailed and outcomes treated as significant at or below the 0.05 probability level. Statistical analyses were undertaken using the Statistical Package for the Social Sciences, version 12.0.1 for Windows.

RESULTS

Participants

The mean age of the 103 patients was 21.6 (s.d.=3.5) years. The patients were predominantly male (71%) and single (90%), and approximately a third (34%) of the patients had completed secondary school. The majority of patients were diagnosed with schizophrenia-spectrum psychosis (75%) and hospitalised during the first 3 months of treatment (76%). No significant difference was found between these 103 patients and the 23 patients excluded from analyses because of missing substance misuse data on demographic or clinical variables, including the rates of any or individual lifetime substance misuse at baseline.

Rates of substance misuse

Overall, 53% of patients (55 out of 103) were given a diagnosis of substance misuse during follow-up; these included cannabis 42% (43 out of 103), alcohol 30% (30 out of 100) and other substance misuse 17% (17 out of 98). Thirteen of the 17 patients diagnosed with other substance misuse met criteria for amphetamine and/or hallucinogen misuse. The rate of poly-substance misuse was 30% (31 out of 102). Of the patients with a diagnosis of substance misuse, 57% (31 out of 54, missing data for 1 patient) met criteria for poly-substance misuse. The varying denominator for these analyses is owing to missing data on misuse of some individual substances.

In-patient admission

The rates of in-patient admission for patients with and without a diagnosis of substance misuse were 45% (25 out of 55) and 15% (7 out of 48) respectively (Table 1). Logistic regression analyses showed that substance misuse was significantly associated with in-patient admission during follow-up and remained so after controlling for the effects of gender, age,

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Table 1 Associations between substance misuse and in-patient admission following the initial 3-month period, remission and relapse during the 15-month follow-up

Substance misuse	Clinical outcome								
	In-patient admission (n=103)			Remission (n=103)			Relapse (n=98)		
	% (n)	OR (95% CI)	Adjusted OR (95% CI)[1,2]	% (n)	OR (95% CI)	Adjusted OR (95% CI)[1,2]	% (n)	OR (95% CI)	Adjusted OR (95% CI)[1,3]
Yes	45 (25)	4.9 (1.9–12.8)***	3.8 (1.2–11.8)*	93 (51)	0.3 (0.03–2.5)	NA[4]	51 (26)	5.1 (2.0–13.0)***	4.7 (1.3–16.7)*
No	15 (7)			98 (47)			17 (8)		

NA, not applicable; OR, odds ratio.
1. Adjusted for gender, age, psychotic disorder diagnosis (schizophrenia-spectrum or other psychosis), duration of untreated psychosis (log-transformed) and medication non-compliance.
2. Missing compliance data for 1 patient; n=102.
3. Missing compliance data for 1 patient; n=97.
4. Multivariate analyses were not performed owing to the small number of patients who did not achieve remission (n=5).
*$P<0.05$, **$P<0.01$, ***$P<0.001$.

psychotic disorder diagnosis, duration of untreated psychosis and medication compliance. The mean number of in-patient admission days was 12.0 (s.d.=19.9, median=0) for patients diagnosed with substance misuse compared with 1.4 (s.d.=4.2, median=0) for patients without substance misuse (Mann–Whitney U-test, $Z=-3.6$, $P<0.001$). When patients were grouped according to the pattern of substance misuse, 21 out of 43 patients with cannabis misuse, 3 out of 5 patients with other substance misuse but not cannabis misuse, and 1 out of 7 patients with alcohol misuse only were hospitalised following the first 3 months of treatment.

Remission of psychotic symptoms

For patients who achieved remission of positive symptoms during follow-up (98 out of 103), the mean duration of remission (that is, the period from the time that remission criteria were first met to psychotic relapse or the end of follow-up) was 343.7 days (s.d.=133.6, median=386.0). The rates of remission during follow-up for patients with and without a diagnosis of substance misuse were 93% (51 out of 55) and 98% (47 out of 48) respectively. Univariate logistic regression analyses showed that the association between substance misuse and remission was not statistically significant (Table 1). Multivariate analyses were not undertaken owing to the small number of patients who did not achieve remission (n=5).

Time to remission of psychotic symptoms

A Kaplan–Meier survival analysis showed no significant difference between patients with substance misuse (n=55, 4 censored cases; median time to remission 39 days, 95% CI 22–56) and patients without substance misuse (n=48, 1 censored case; median time to remission 41 days, 95% CI 31–51) on days to remission (log-rank test, χ^2=1.1, d.f.=1, P=0.300). A Cox regression analysis showed that substance misuse was not significantly associated with time to remission (hazard ratio 0.8, 95% CI 0.5–1.2, P=0.277) after controlling for the effects of gender, age, psychotic disorder diagnosis, duration of untreated psychosis and medication compliance.

Relapse of psychotic symptoms

For patients who achieved remission during follow-up (n=98), the rates of relapse of positive symptoms during follow-up for patients with and without a substance misuse diagnosis were 51% (26 out of 51) and 17% (8 out of 47) respectively. Logistic regression analyses showed that substance misuse was significantly associated with relapse and remained so after controlling for the effects of gender, age, psychotic disorder diagnosis, duration of untreated psychosis and medication compliance (Table 1). When patients were grouped according to the pattern of substance misuse, 23 out of 40 patients with cannabis misuse and 2 out of 4 patients with other substance misuse but not cannabis misuse relapsed, compared with 1 out of 7 patients with alcohol misuse only.

Time to relapse of psychotic symptoms

For patients who achieved remission (n=98), a Kaplan–Meier survival analysis showed that substance misuse was a significant risk factor for time to relapse (Fig. 1). Patients with a diagnosis of substance misuse (n=51, 25 censored cases) had a significantly shorter time to relapse of psychotic symptoms compared with patients without substance misuse (n=47, 39 censored cases; log-rank test, χ^2=12.7 d.f.=1, $P<0.001$). The median time to relapse for patients with substance misuse was 378 days (95% CI 271–485, mean=359). The median time to relapse for patients without substance misuse could not be calculated because fewer than half the patients relapsed (mean 477 days). A Cox regression analysis showed that substance misuse remained significantly associated with shorter time to relapse after controlling for the effects of gender, age, psychotic disorder diagnosis, duration of untreated psychosis and medication compliance (hazard ratio 2.8, 95% CI 1.2–6.7, P=0.021).

Relationship between severity of substance misuse and in-patient admission, relapse and time to relapse

Patients whose substance misuse was categorised as heavy (n=27), mild (n=28) and none (n=48) were compared on rates of in-patient admission and relapse and time to relapse. The heavy substance misuse group had a higher rate of in-patient admission (52%; 14 out of 27) than the mild substance misuse group (39%; 11 out of 28), who in turn had a higher rate of in-patient admission than the no substance misuse group (15%, 7 out of 48). A univariate logistic regression analysis showed that patients with heavy or mild substance misuse were significantly more likely to be admitted for in-patient care than patients who did not misuse substances (Table 2). Heavy but not mild substance misuse

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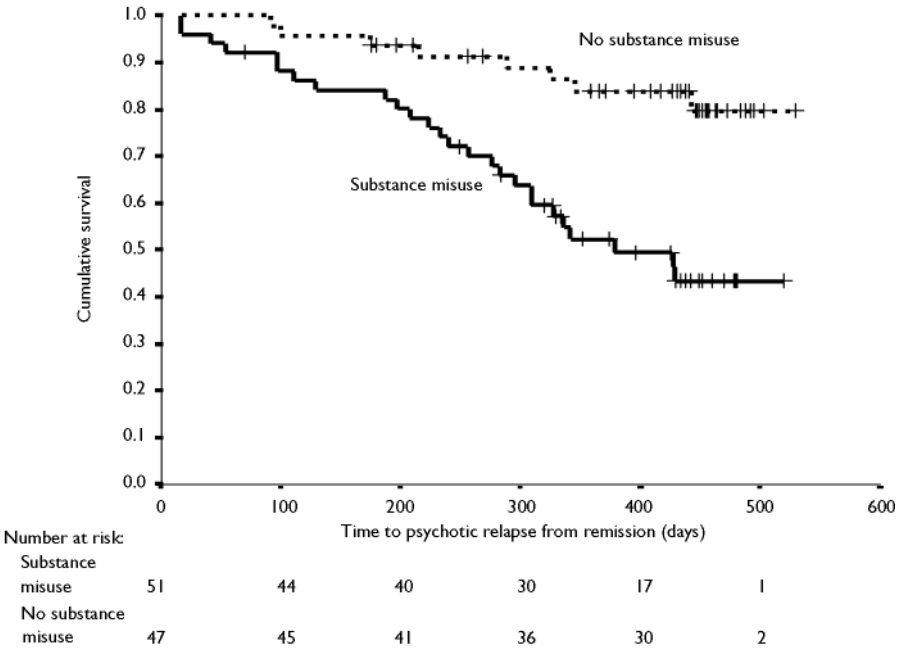

Fig. 1 Survival curves for time to psychotic relapse for patients in remission with substance misuse (n=51) and without substance misuse (n=47) during the 5-month follow-up.

remained significantly associated with in-patient admission after controlling for the effects of gender, age, psychotic disorder diagnosis, duration of untreated psychosis, and medication compliance (Table 2). Among patients whose disorder was in remission (n=98), those with heavy substance misuse had a higher rate of relapse (64%; 16 out of 25) than those with mild substance misuse (38%; 10 out of 26), who in turn had a higher rate of relapse than patients with no substance misuse (17%; 8 out of 47). A univariate logistic regression analysis showed that patients with heavy or mild substance misuse were significantly more likely to experience relapse compared with patients with no substance misuse. After adjusting for the effects of the covariates, heavy but not mild substance misuse was significantly associated with relapse (Table 2).

A Kaplan–Meier survival analysis showed that substance use severity was a significant risk factor for time to relapse (Fig. 2). Patients with heavy substance misuse (n=25, 9 censored cases; median 327 days, 95% CI 238–416) had a shorter time to relapse of psychotic symptoms than patients with mild substance misuse, a difference that just failed to reach statistical significance (n=26, 16 censored cases; log-rank test, χ^2=3.8, d.f.=1, P=0.052), and a significantly shorter time to relapse than patients with no substance misuse (n=47, 39 censored cases; log-rank test, χ^2=19.2, d.f.=1, $P<0.001$). Patients with mild substance misuse had a significantly shorter time to relapse than patients with no substance misuse (log-rank test, χ^2=4.3, d.f.=1, P=0.038). The median time to relapse for patients with mild and no substance misuse could not be calculated because fewer than half of these patients relapsed. A multivariate analysis showed that heavy substance misuse (hazard ratio 4.6, 95% CI 1.7–12.5, P=0.003) but not mild substance misuse (hazard ratio 2.0, 95% CI 0.8–5.4, P=0.160) was significantly associated with a shorter time to relapse compared with no substance misuse.

DISCUSSION

The aim of the study was to examine the potential impact of substance misuse on clinical outcome in individuals treated for first-episode psychosis. The findings supported the hypotheses that substance misuse is associated with increased risk of in-patient admission and earlier and increased risk of psychotic relapse. The hypothesis that substance misuse is associated with longer time to remission of positive symptoms was not supported.

Strengths and limitations

A range of methodological problems have affected the study of comorbid substance misuse and psychosis. Briefly, these problems include use of criteria to diagnose

Table 2 Associations between substance use severity and in-patient admission following the initial 3-month treatment period and relapse during the 15-month follow-up

Substance use severity	Clinical outcome					
	In-patient admission (n=103)			Relapse (n=98)		
	% (n)	OR (95% CI)	Adjusted OR (95% CI)[1,2]	% (n)	OR (95% CI)	Adjusted OR (95% CI)[1,3]
Heavy misuse	52 (14)	6.3 (2.1–19.0)***	5.7 (1.5–21.9)**	64 (16)	8.7 (2.8–26.5)***	10.9 (2.3–51.1)**
Mild misuse	39 (11)	3.8 (1.3–11.4)*	2.8 (0.8–9.8)	38 (10)	3.0 (1.0–9.1)*	2.3 (0.6–9.7)
No misuse[4]	15 (7)			17 (8)		

OR, odds ratio.
1. Adjusted for gender, age, psychotic disorder diagnosis (schizophrenia-spectrum or other psychosis), duration of untreated psychosis (log-transformed) and medication non-compliance.
2. Missing compliance data for 1 patient; n=102.
3. Missing compliance data for 1 patient; n=97.
4. Reference category.
*$P<0.05$, **$P<0.01$, ***$P<0.001$.

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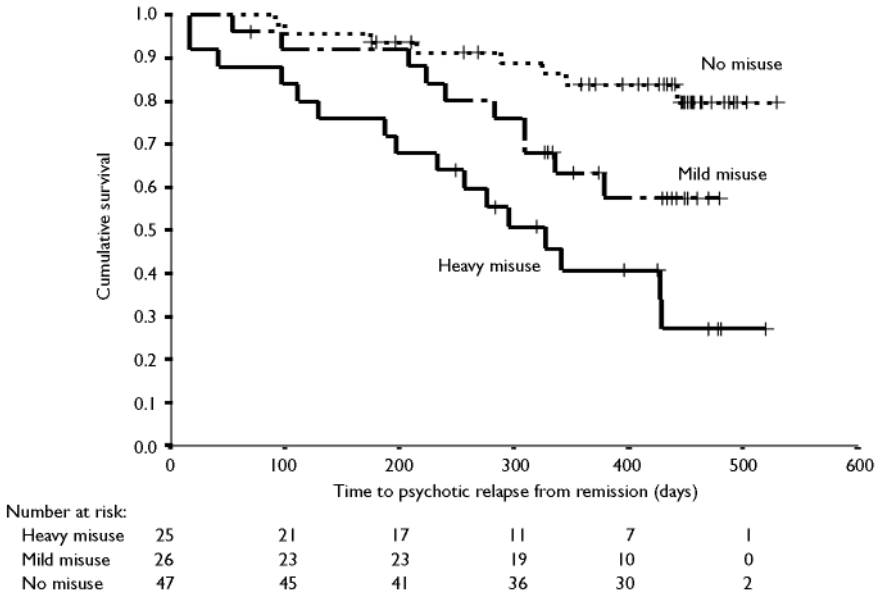

Fig. 2 Survival curves for time to psychotic relapse for patients in remission with no substance misuse (n=47), mild substance misuse (n=26) and heavy substance misuse (n=25) during the 15-month follow-up.

substance misuse other than abuse or dependence; limited assessment of a single substance or class of substances rather than a broader assessment that encompasses multiple substance use; analysis of the effects of past or lifetime substance misuse rather than current substance misuse; diagnosis of substance misuse based on unreliable methods such as chart review rather than the use of structured interviews combined with data collection from multiple sources; failure to control for medication non-compliance and other potential confounders; recruitment from hospital rather than in-patient and community-based settings; and a lack of prospective studies (Blanchard *et al*, 2000; Murray *et al*, 2003). Our study sought to address these problems in a sample of young patients treated at three psychiatric services for a broad range of first-episode psychotic disorders.

This study has several limitations. First, the relatively small sample size might have limited the power to detect important associations of clinical significance. Second, substance misuse might have been underreported, given that the diagnosis of substance misuse relied upon patient interviews supplemented by collateral information and did not include biomedical screening tests. However, the relatively high rate of substance misuse found in the study tends to discount this possibility and is consistent with anecdotal reports from research interviewers that most patients were willing to discuss substance-related problems. Further, urine drug screens can only detect substance use within a limited period and cannot provide information about the functional impact of substance misuse necessary to make a diagnosis. Third, analysis of the independent effects of different types of substance misuse on outcome was not possible, given that more than half of the patients with a diagnosis of substance misuse met criteria for poly-substance misuse. The finding that 87% of patients with substance misuse met criteria for cannabis and/or other substance misuse tends to implicate these substances in the observed adverse effects of substance misuse. Descriptive analyses suggested that patients with alcohol misuse only were less likely to experience in-patient admission or relapse compared with patients reporting cannabis or other substance misuse. These findings are consistent with evidence for a stronger association between psychotic exacerbations and cannabis or stimulant misuse compared with alcohol misuse (Dixon, 1999). Fourth, the operational definition of remission (minimal positive symptoms for at least 2 weeks) may be criticised for the relatively low threshold for remission criteria to be met (Andreasen *et al*, 2005). However, 94 of the 98 patients in remission maintained their initial remission of positive symptoms for at least 8 consecutive weeks, which is similar to criteria used in other studies of first-episode psychosis (e.g. Lieberman *et al*, 1993; Amminger *et al*, 1997).

Comparison of current findings with other research

Several (but not all) prospective studies have reported associations between substance misuse and worse outcome in first-episode or recent-onset psychosis. Sorbara *et al* (2003) found that drug misuse but not alcohol misuse in first-episode psychosis was associated with an increased risk of in-patient admission. It is worth noting, however, that 5 of the 13 alcohol misusers were also diagnosed with drug misuse in this study. Linszen *et al* (1994) found that cannabis misuse in recent-onset psychosis was associated with earlier relapse and an increased risk of relapse of positive symptoms. Despite differences in the definitions of substance misuse and relapse, our study and Linszen *et al* (1994) found similar rates of relapse in misusing (51% and 42% respectively) and non-misusing patients (17% in both studies). Sevy *et al* (2001) did not find a link between substance misuse in first-episode psychosis and earlier relapse or an increased risk of relapse; this negative finding might have been owing to the analysis of effects of substance misuse diagnosed at initial presentation rather than during the follow-up treatment period.

In contrast to our findings, Strakowski *et al* (1998) reported that substance misuse in first-episode affective psychosis was associated with a longer time to symptomatic remission. Differences in sample characteristics and methodology between the two studies may help to explain the discrepant findings. For example, Strakowski *et al* (1998) recruited patients with bipolar or major depressive disorder with psychosis rather than a broad range of psychotic disorders, and operationally defined remission in terms of positive, negative and affective symptoms rather than positive symptoms alone. It is also feasible that the lack of association between substance misuse and remission of positive symptoms in our study might have resulted from variation in the severity of substance use following entry to treatment. That is, patients might have reduced or stopped their substance use immediately following entry to treatment in response to the onset of acute psychosis and/or subsequent treatment

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including in-patient admission. If this is correct, a short-term reduction in severity of substance use might have enabled substance misusers to achieve rapid remission while still meeting criteria for substance misuse during the follow-up period. Unfortunately, the collection of interval-based substance use data did not enable us to test this proposition.

The association between more severe substance use and in-patient admission as well as relapse of positive symptoms is consistent with a previous report of a dose–response relationship between frequency of cannabis misuse and relapse (Linszen *et al*, 1994). A dose–response relationship is consistent with a causal link between substance misuse and worse clinical outcome. The high rate of relapse following initiation of treatment for first-episode psychosis (Robinson *et al*, 1999), and the increased risk of chronicity (Wiersma *et al*, 1998) and higher costs (Almond *et al*, 2004) associated with relapse, suggest that relapse prevention should be a high priority in the treatment of early psychosis. A key challenge for effective relapse prevention programmes will be to develop and implement proven interventions for comorbid psychosis and severe substance misuse (Ley & Jeffery, 2003).

REFERENCES

Almond, S., Knapp, M., Francois, C., *et al* (2004) Relapse in schizophrenia: costs, clinical outcomes and quality of life. *British Journal of Psychiatry*, **184**, 346–351.

American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM–III–R). Washington, DC: APA.

American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM–IV). Washington, DC: APA.

Amminger, G. P., Resch, F., Mutschlechner, R., *et al* (1997) Premorbid adjustment and remission of positive symptoms in first-episode psychosis. *European Child and Adolescent Psychiatry*, **6**, 212–218.

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Andreasen, N. C., Carpenter, W. T., Kane, J. M., *et al* (2005) Remission in schizophrenia: proposed criteria and rationale for consensus. *American Journal of Psychiatry*, **162**, 441–449.

Blanchard, J. J., Brown, S. A., Horan, W. P., *et al* (2000) Substance use disorders in schizophrenia: review, integration, and a proposed model. *Clinical Psychology Review*, **20**, 207–243.

Dixon, L. (1999) Dual diagnosis of substance abuse in schizophrenia: prevalence and impact on outcomes. *Schizophrenia Research*, **35** (suppl.), S93–S100.

Kavanagh, D. J., Waghorn, G., Jenner, L., *et al* (2004) Demographic and clinical correlates of comorbid substance use disorders in psychosis: multivariate analyses from an epidemiological sample. *Schizophrenia Research*, **66**, 115–124.

Ley, A. & Jeffery, D. (2003) Cochrane review of treatment outcome studies and its implications for future developments. In *Substance Misuse in Psychosis: Approaches in Treatment and Service Delivery* (eds H. Graham, K. T. Mueser, M. Birchwood, *et al*), pp. 349–365. Chichester: John Wiley.

Lieberman, J., Jody, D., Geisler, S., *et al* (1993) Time course and biologic correlates of treatment response in first-episode schizophrenia. *Archives of General Psychiatry*, **50**, 369–376.

Linszen, D. H., Dingemans, P. M. & Lenior, M. E. (1994) Cannabis abuse and the course of recent-onset schizophrenic disorders. *Archives of General Psychiatry*, **51**, 273–279.

Lukoff, D., Liberman, R. P. & Nuechterlein, K. H. (1986) Symptom monitoring in the rehabilitation of schizophrenic patients. *Schizophrenia Bulletin*, **12**, 578–602.

McGorry, P. D., Singh, B. S., Copolov, D. L., *et al* (1990) Royal Park Multidiagnostic Instrument for Psychosis: Part II. Development, reliability, and validity. *Schizophrenia Bulletin*, **16**, 517–536.

McGovern, M. P. & Morrison, D. H. (1992) The Chemical Use, Abuse, and Dependence Scale (CUAD): rationale, reliability, and validity. *Journal of Substance Abuse and Treatment*, **9**, 27–38.

Murray, R. M., Grech, A., Phillips, P., *et al* (2003) What is the relationship between substance abuse and schizophrenia? In *The Epidemiology of Schizophrenia* (eds R. M. Murray, P. B. Jones, E. Susser, *et al*), pp. 317–342. Cambridge: Cambridge University Press.

Power, P., Elkins, K., Adlard, S., *et al* (1998) Analysis of the initial treatment phase in first-episode psychosis. *British Journal of Psychiatry*, **172** (suppl. 33), 71–76.

Robinson, D., Woerner, M. G., Alvir, J. J., *et al* (1999) Predictors of relapse following response from a first-episode of schizophrenia or schizoaffective disorder. *Archives of General Psychiatry*, **56**, 241–247.

Sevy, S., Robinson, D. G., Solloway, S., *et al* (2001) Correlates of substance misuse in patients with first-episode schizophrenia and schizoaffective disorder. *Acta Psychiatrica Scandinavica*, **104**, 367–374.

Sorbara, F., Liraud, F. & Assens, F. (2003) Substance use and the course of early psychosis: a 2-year follow-up of first-admitted subjects. *European Psychiatry*, **18**, 133–136.

Strakowski, S. M., Keck, P. E., McElroy, S. L., *et al* (1998) Twelve-month outcome after a first hospitalization for affective psychosis. *Archives of General Psychiatry*, **55**, 49–55.

Wiersma, D., Nienhuis, F. J., Slooff, C. J., *et al* (1998) Natural course of schizophrenic disorders: a 15-year follow-up of a Dutch incidence cohort. *Schizophrenia Bulletin*, **24**, 75–85.

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