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The temporal dynamics of relationships between cannabis, psychosis and depression among young adults with psychotic disorders: findings from a 10-month prospective study

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ABSTRACT

Background. The aim was to examine the temporal relationships over 10 months between cannabis use and symptoms of psychosis and depression in people with schizophrenia and related disorders. The design was a prospective study of 101 patients with schizophrenia and related disorders who were assessed monthly over 10 months on medication compliance, cannabis and other drug use, symptoms of depression and symptoms of psychosis.

Method. Linear regression methods to assess relationships between cannabis use and symptoms of psychosis and depression while adjusting for serial dependence, medication compliance and other demographic and clinical variables.

Results. Cannabis use predicted a small but statistically significant increase in symptoms of psychosis, but not depression, after controlling for other differences between cannabis users and non-users. Symptoms of depression and psychosis did not predict cannabis use.

Conclusion. Continued cannabis use by persons with schizophrenia predicts a small increase in psychotic symptom severity but not vice versa.

INTRODUCTION

Evidence has accumulated that cannabis use and psychotic symptoms and disorders are associated both in the general population (Tien & Anthony, 1990; Degenhardt & Hall, 2001) and among persons with schizophrenia and other psychoses (Cohen & Klein, 1970; Barbee *et al.* 1989; Wheatley, 1998). Much of the more recent epidemiological work has involved general population cohort studies (Arseneault *et al.* 2002; Van Os *et al.* 2002; Zammit *et al.* 2002; Fergusson *et al.* 2003; Macleod *et al.* 2004; Henquet *et al.* 2005), which have found that cannabis use in adolescence or young adulthood predicts psychotic symptoms or psychotic illnesses in early adult life.

In many of these studies, uncertainty remains about the temporal relationship between cannabis use and psychotic symptoms given the long time-intervals between assessment of cannabis use and psychotic symptoms. A recent study provided greater specificity on the temporal relationship by assessing cannabis use and psychotic symptoms over periods of hours. It found that cannabis use in one time-period

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predicted 'unusual perceptions' in the following period, most markedly among persons reporting some psychotic symptoms at baseline (Verdoux *et al*. 2002).

How significant is this relationship among persons who have developed schizophrenia and related disorders? This is an important clinical question given the high prevalence of cannabis use among persons with psychotic disorders, the severity of the consequences of recurrences of psychosis, and remaining ambiguities about the extent to which cannabis use is responsible for relapse to, or exacerbation of, psychotic symptoms in this group. Cannabis use has previously been found to be associated with relapse (Negrete *et al*. 1986; Jablensky *et al*. 1992; Linszen *et al*. 1994; Martinez-Arevalo *et al*. 1994; Degenhardt & Hall, 2002; Degenhardt *et al*. 2003*a*; Hall *et al*. 2004), but it is unclear to what extent it was a causal factor in such events.

Persons with psychotic disorders are highly likely to have co-morbid mental health problems, with the most pervasive being depressive symptoms or episodes (Bartels & Drake, 1989; Bartels *et al*. 1992; Kendler *et al*. 1996). Recent years have seen increasing interest in the association between cannabis use and depression (Degenhardt *et al*. 2003*b*), with some evidence suggesting that cannabis use predicts increased risk of depressive episodes later in life (Bovasso, 2001; Patton *et al*. 2002). There has been no examination to date, however, of the possibility that cannabis and depression may also be related among persons who have psychotic illnesses.

Both drug use and mental health states are dynamic, in that their symptoms may fluctuate considerably over time. This study considers the possibility that drug use and mental health changes may influence each other. In using a short time-frame in our measurements, we examined temporally related drug use and mental health states. Our study cannot shed light on whether any changes or associations observed reflect permanent changes or the impact of the acute effects of cannabis.

To the best of our knowledge, there has been no previous research examining the dynamics of the relationship between cannabis use, depression and psychotic symptoms among people with psychotic disorders. Given the high prevalence of both cannabis use and depression among this group, clarification of the mechanism behind these relationships is crucial in deciding how clinicians should respond to cannabis use among patients with schizophrenia and other psychoses.

Aims

In the current study, we present data on cannabis use and psychotic symptoms in a prospective study of 101 people with psychotic disorders and a history of cannabis use, who were assessed monthly over a 10-month period. We concurrently examined potential relationships over this time between cannabis use and psychotic and depressive symptoms, while controlling for any confounding effects of age, gender, other drug use, and medication compliance.

METHOD

Sample

English-speaking males and females aged 16–50 years, with a diagnosis of schizophrenia, schizophreniform disorder or schizo-affective disorder, who reported a history of cannabis use that included using cannabis in the 6 months prior to recruitment were eligible for inclusion in the study. All patients were currently being treated in community mental health centres in the Northern Sydney Area Health Service in Sydney, Australia. All participants in this study had been diagnosed with a schizophrenia spectrum disorder by a hospital or community psychiatrist. Patients with bipolar disorder and those who reported injecting amphetamines in the previous 4 months were excluded. Trained research assistants completed all interviews.

Ethics clearance

The study was approved by the Northern Sydney Area Health Services Ethics Committee and the University of Sydney Ethics Committee.

Measures

The primary outcome variables for this study were: symptoms of psychosis, measured with the Brief Psychiatric Rating Scale (BPRS; Ventura *et al*. 1993), symptoms of depression as measured by the Calgary Depression Scale for Schizophrenia (CDSS; Addington *et al*. 1990); and cannabis use, measured by the number of

days in the past month in which the participant had used cannabis. Cannabis and alcohol use was measured as the number of days used in the past month, a continuous variable in the range 0–28; amphetamine use – binary, any use in the past month; medication compliance was ascertained by self-report and patient file audits and coded categorically.

The BPRS is a widely used clinician rating scale that provides an assessment of common symptoms of psychopathology, particularly including psychotic symptoms. The primary purpose of the BPRS is to allow assessment of treatment change across a comprehensive set of common symptom characteristics. The BPRS was used to assess the presence of current symptoms and their severity. The BPRS is a semi-structured interview, consisting of 24 items that rate symptom presentation and severity on a seven-point scale, with higher scores reflecting more severe pathology.

The CDSS is a nine-item observer-rated measure specifically designed for measuring depression in schizophrenia (Addington *et al.* 1990). It compensates for the negative symptoms and extra-pyramidal side-effects of medication associated with schizophrenia.

Data analysis

The relationship between the continuous outcome variables (BPRS and cannabis use) was analysed using generalized estimating equation (GEE) models (Diggle *et al.* 1994). GEEs enable linear models to adjust for the effect of serial dependence, in which multiple observations taken over time on the same individual are assumed to be correlated with one another. Unlike repeated measures analysis of variance (ANOVA), GEE models use all available observations, making them particularly useful when some individuals have missing data over long follow-up periods. These GEEs model the mean response at each time-point as a function of observations at that time-point and the previous time-point, while assuming that the nine such observations for any one individual are correlated with one another (reducing the effective sample size of the overall model). GEEs enable non-normally distributed responses to be studied in a time-dependent series, but more importantly for this paper, they enable all available data to be used. For example, in a repeated measures ANOVA model, a single missing observation for an individual will cause that individual to be removed from the model whereas in these GEE models, all available observations for that individual are used. The number of observations is therefore the total number of observed data points on all individuals over time. Because some of these observations are on the same individual, they do not contribute much information, and statistical theory enables us to estimate an effective sample size, which determines the true power of the model. In these models, regression coefficients can be interpreted in a similar way to regression coefficients in a standard linear regression model. We have presented non-standardized regression coefficients (i.e. we do not use effect sizes).

The GEE models in this study regressed each outcome on observations of both outcomes in the previous month (referred to as lagged outcomes) and the observed values of the other outcome in the current month. The following three univariate models were tested:

(1) BPRS as outcome, with cannabis use, depression, BPRS scores, medication compliance and amphetamine use in the previous month as predictors.
(2) Cannabis use as outcome, with depression, BPRS, cannabis use, medication compliance and amphetamine use in the previous month as predictors.
(3) Depression as outcome, with depression, BPRS, cannabis use, medication compliance and amphetamine use in the previous month as predictors.

Significant relationships were then used to build multiple linear regression GEE models. In both univariate and multiple regression models, serial dependence in observations was modelled using an exchangeable correlation matrix. This choice was based on estimates of the correlation matrix for BPRS scores and cannabis use across the 10 time-points. The following covariates were included in these regression models: current value of the other outcome variable (cannabis or BPRS, as appropriate), age, gender, alcohol and amphetamine use, depression (measured by the CDSS), and month of measurement.

Backwards stepwise removal based on the likelihood-ratio statistic was used to select the

Table 1. *Characteristics of the sample at baseline and final follow-up*

	Baseline	10 months
Baseline demographics	($n=101$)	
Male (%)	89	
Mean age (S.E.)	25·3 (6·4)	
Employed (%)	21	
Receiving social security benefits (%)	61	
Married/*de facto* (%)	4	
Living in independent accommodation (%)	86	
Drug use characteristics	($n=101$)	($n=70$)
Cannabis use past month (%)	69	43
Daily cannabis use past month (%)	21	17
Used 3 g cannabis or more per week (%)	18	21
Tobacco use past month (%)	88	86
Alcohol use past month (%)	85	73
Amphetamine use past month (%)	11	3
Clinical characteristics	($n=101$)	($n=70$)
Mean BPRS (psychotic symptoms) score	43·4	38·3
Mean CDSS (depressive symptoms) score	5·0	3·3

BPRS, Brief Psychiatric Rating Scale; CDSS, Calgary Depressive Scale for Schizophrenia.

final model. Variables of interest were retained in the model if they were statistically significant at $p=0{\cdot}05$, with no consideration of the clinical significance of the effect. The models were fit in SAS version 8.2 (SAS Institute Inc., Cary, NC, USA). After fitting, a design effect was estimated for each outcome variable, thereby treating the individual as the cluster. An estimate of the effective sample size was based on this estimated design effect. Residuals from the chosen final models were investigated to check for violations of the assumptions underlying the model (statistical independence of residuals within strata of time, approximately normally distributed residuals). All models were found to be acceptable. For this study a minimum of 175 effective observations was expected to be required to show a moderate effect size for each of the outcomes, using standard methods for the calculation of power in regression models (Hsieh *et al.* 1998). Observed effective sample sizes were between 135 and 161 (depending on the outcome measured), indicating that the study was slightly underpowered for tests of small effects.

RESULTS

One hundred and one eligible patients completed the baseline interview and questionnaires. Table 1 presents the baseline demographics, drug use and mental health characteristics of the sample, as well as drug use and mental health characteristics at the final (10-month) follow-up. The mean age was 24 years and 61% were on sickness benefits (median duration of 6 months). The majority of patients were single and male; most lived with others and only 23% were in paid work.

Most participants started using cannabis in mid-adolescence (median age 15 years), with regular use beginning at 17 years. Sixty-nine per cent reported cannabis use in the past month. One in five of the sample (21%) had smoked cannabis daily in the past month and 18% reported using 3 g or more of cannabis per week in the past month. These rates were similar at the 10-month follow-up (Table 1). At baseline, 88% reported using tobacco, and 85% reported using alcohol in the past month. Eleven per cent had used amphetamines orally in the past month, 9% used ecstasy, 3% cocaine and 2% opioids (taken orally). These rates of other drug use were similar among the sample interviewed at the 10-month follow-up (Table 1). The mean BPRS score at baseline was 43·2, and at 10 months it was 38·3. The mean CDSS score was 5·0 at baseline, and 3·5 at the 10-month follow-up.

Of a possible 1010 observations of the two main outcomes, there were 818 observations for cannabis and 788 observations for psychotic symptoms. These rates might be considered acceptable given the group was being followed up over time.

Table 2 shows the results of the univariate regression models. The parameter estimates and p values in Table 2 represent values obtained from separate univariate models, where each predictor in turn was regressed against the outcome shown, adjusted only for time. To reduce the table size, all such relationships have been shown as a single line (with the variable for time excluded). Each parameter estimate and p value should be interpreted as representing the univariate relationship between the given variable and the outcome of interest.

Cannabis use during a given month had a small but statistically significant effect on psychotic symptoms (as measured by the BRPS) at the beginning of the following month: each additional day of cannabis use increased the

Table 2. *Univariate GEE models of the outcome variables and their prior observations*

	Estimate	Standard error	*t* statistic	*p* value
Psychotic symptoms[a] and prior …				
cannabis use	0·129	0·065	1·99	0·05
depressive symptoms[b]	0·382	0·103	3·70	0·0002
medication compliance	0·702	0·570	1·23	0·2
psychotic symptoms	0·466	0·038	12·15	<0·0001
Cannabis use and prior …				
psychotic symptoms	−0·021	0·050	−0·42	0·7
depressive symptoms	−0·144	0·077	−1·86	0·06
medication compliance	0·497	0·472	1·05	0·3
cannabis use	0·940	0·016	58·66	<0·0001
Depressive symptoms and prior …				
cannabis use	0·040	0·400	1·79	0·07
depressive symptoms	0·350	0·059	5·92	<0·0001
medication compliance	0·512	0·306	1·67	0·09
psychotic symptoms	0·065	0·019	3·50	0·0005

GEE, Generalized estimating equation.
[a] Psychotic symptoms measured by the Brief Psychiatric Rating Scale (BPRS).
[b] Depressive symptoms measured by the Calgary Depressive Scale for Schizophrenia (CDSS).

mean BPRS score by 0·13. This effect size means that changing from no cannabis use to daily cannabis use would increase psychosis symptoms by 3·9 points (on a scale of 24 to 168); in other words, it was estimated that daily cannabis use increased BPRS scores by 3% of the possible total score in the following month. BPRS score in the previous month, by comparison, was a much stronger predictor (Table 2).

Neither BPRS nor CDSS scores predicted increased cannabis use in the following month, and cannabis use did not predict increased depression scores in the following month.

Table 3 shows the results of multivariable analyses. In Table 3, intercept terms attract the standard interpretation of a regression model. After adjusting for confounders, cannabis use was estimated to have an even smaller effect on BPRS: 28 days' use (i.e. daily use) of cannabis increased BPRS at the beginning of the following month by 2·4 points on average (Table 3) compared to no use.

Cannabis use in a given month had no significant relationship with depression score at the beginning of the following month. Amphetamine use in a given month, by contrast, was associated with lower scores in that month. The association between psychotic symptomatology and depression scores also remained significant when only questions from the BPRS assessing positive psychotic symptoms were included (i.e. when the association of depression with positive symptoms of psychosis only was examined; results not shown).

Multivariable analyses suggested that the most significant predictor of current cannabis use was current use of oral amphetamines and prior use of cannabis. Neither prior psychotic symptoms (BPRS) nor depressive symptoms (CDSS) predicted cannabis use in the following month (Table 3).

DISCUSSION

Among a sample of adults with schizophrenia and related disorders, there were significant prospective associations over 10 months between symptoms of psychosis, depression and cannabis use. Increased psychotic or depressive symptoms did not robustly predict increased cannabis use in the following month; neither did cannabis use robustly predict increased depression scores in the following month. However, there was a statistically significant, but very small, increase in psychotic symptomatology in the month following increased cannabis use. Adjustment for medication compliance, amphetamine use and the co-morbidity between depression and psychotic symptoms did reduce the estimated predictive effect of cannabis use upon psychotic symptomatology, but the effect nonetheless remained statistically robust.

Table 3. *Multiple regression models of significant predictors of psychosis, depression and cannabis use*

Variable	Estimate	Standard error	*t* statistic	*p* value
Psychotic symptoms[a] and …				
intercept	20·275	1·449	13·99	<0·001
prior cannabis use	0·084	0·033	2·33	0·01
prior psychotic symptoms[a]	0·374	0·044	8·57	<0·0001
current depressive symptoms	1·002	0·098	10·20	<0·0001
sex	3·585	0·956	3·75	0·0002
Cannabis use and …				
intercept	2·969	1·444	2·06	0·04
prior cannabis use	0·842	0·032	26·75	<0·0001
any current amphetamine use	4·222	1·238	3·41	0·0006
age	0·087	0·037	2·34	0·02
Depressive symptoms[b] and …				
intercept	−2·489	1·110	−2·24	0·03
prior psychotic symptoms	0·025	0·017	1·48	0·1
prior depressive symptoms	0·353	0·070	5·02	<0·0001
any current amphetamine use	−1·202	0·301	4·00	<0·0001
age	0·101	0·039	2·57	0·01

Where predictors do not appear in this table, it indicates that the variables did not remain significant predictors in the model. Intercept terms attract the standard interpretation of a regression model.

[a] Psychotic symptoms measured by the Brief Psychiatric Rating Scale (BPRS).

[b] Depressive symptoms measured by the Calgary Depressive Scale for Schizophrenia (CDSS).

These findings are consistent with previous work in suggesting that controlling for psychotic symptoms at some prior point substantially reduces the size of the relationship between cannabis use and psychotic symptoms at a follow-up time-point (Arseneault *et al*. 2002). It extends earlier findings by using the multiple monthly assessment points to show that the strongest predictors of depressive and psychotic symptoms among persons with psychosis are the previous monthly prior levels of these symptoms. By comparison, cannabis use had a statistically non-significant effect on depression, and a statistically significant but clinically small effect on psychotic symptomatology (BPRS scores).

One surprising finding of the current study was some suggestive evidence that drug use (cannabis and amphetamines) was more likely given better mental health in the previous month (as evidence by lower levels of psychotic symptomatology and depression in the previous month). If these findings are replicated in other work, they would suggest that it may be those individuals with higher functioning in the area of mental health who are more likely to use drugs. This possibility has in fact been given some support in cross-sectional research conducted some years ago, whereby patients with better pre-morbid adjustment were more likely to use cannabis (Arndt *et al*. 1992).

Given that the consequence of this drug use appeared to be either ambiguous (amphetamines) or negative (cannabis) upon psychotic symptomatology, it would seem that any increased likelihood of drug use among those with better mental health functioning may not be maintained.

Limitations

Although probably slightly underpowered for identifying these effects, the study had close to the required number of observations for all reasonable assumptions about effect size and serial dependence. Given the very small effect sizes that could be detected in this study, which are clinically small, we consider that any smaller effects that we may have missed would be of doubtful clinical significance.

Future controlled intervention research might examine the impact that reducing cannabis use has upon psychotic symptomatology. It is possible that some unmeasured variable that may have covaried with cannabis use and psychotic symptomatology could account for the remaining association. Future work needs to control for a wider range of covariates.

These findings add to the existing literature in two ways. First, they show the specificity of the effects of cannabis use on symptoms of psychosis (rather than depression) in a sample of persons with schizophrenia. Second, we did not find any evidence that increased psychotic or depressive symptoms in a given month predicted increased cannabis use in the following month. This finding was consistent with that of other studies in failing to provide support for the 'self-medication hypothesis' of the association between cannabis use and psychotic (Van Os *et al.* 2002; Verdoux *et al.* 2003; Henquet *et al.* 2005) or depressive (Bovasso, 2001; Degenhardt *et al.* 2003*b*) symptoms; specifically, the study failed to find a robust prospective relationship between either depressive or psychotic symptoms at one time-point and cannabis use at the next time-point.

What is the clinical significance of a very small but statistically significant effect of cannabis use upon psychotic symptoms? Although there is a relationship between more frequent use of cannabis and increased psychotic symptoms, preceding psychotic (and depressive) symptoms were much stronger, clinically important predictors of future psychotic (and depressive) symptoms. Nonetheless, cannabis use is a potentially more 'modifiable' behaviour. In the interim, clinicians should provide balanced information to people with psychosis about the risks of cannabis use. It would appear that among persons who have developed psychosis, cannabis use may cause a small increase in psychotic symptoms. This effect, which was small even when cannabis use was daily, should not be over-exaggerated.

CONCLUSIONS

There was no evidence in this prospective study of young adults with schizophrenia and related disorders that cannabis was used in response to increased psychotic or depressive symptoms, nor that cannabis use predicted increased depressive symptomatology. There was a clinically very small but statistically significant effect of cannabis use upon psychotic symptoms. The most important predictors of both depressive and psychotic symptomatology among this group were prior mental health states. Clinicians need to be aware of the relative importance of these factors, and provide patients with realistic messages about the possible risks that cannabis use poses to their mental health.

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DECLARATION OF INTEREST

None.

REFERENCES

Addington, D., Addington, J. & Schissel, B. (1990). A depression rating scale for schizophrenics. *Schizophrenia Research* **3**, 247–251.

Arndt, S., Tyrrell, G., Flaum, M. & Andreasen, N. C. (1992). Comorbidity of substance abuse and schizophrenia: the role of premorbid adjustment. *Psychological Medicine* **22**, 379–388.

Arseneault, L., Cannon, M., Poulton, R., Murray, R., Caspi, A. & Moffitt, T. E. (2002). Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *British Medical Journal* **325**, 1212–1213.

Barbee, J. G., Clark, P. D., Crapanzo, M. S., Heintz, G. C. & Kehoe, C. E. (1989). Alcohol and substance abuse among schizophrenic patients presenting to an emergency psychiatry service. *Journal of Nervous and Mental Disease* **177**, 400–417.

Bartels, S. J. & Drake, R. E. (1989). Depression in schizophrenia: current guidelines to treatment. *Psychiatric Quarterly* **60**, 337–357.

Bartels, S. J., Drake, R. & McHugo, G. (1992). Alcohol abuse, depression, and suicidal behaviour in schizophrenia. *American Journal of Psychiatry* **149**, 394–395.

Bovasso, G. (2001). Cannabis abuse as risk factor for depressive symptoms. *American Journal of Psychiatry* **158**, 2033–2037.

Cohen, M. & Klein, D. F. (1970). Drug abuse in a young psychiatric population. *American Journal of Orthopsychiatry* **40**, 448–455.

Degenhardt, L. & Hall, W. (2001). The association between psychosis and problematical drug use among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Psychological Medicine* **31**, 659–668.

Degenhardt, L. & Hall, W. (2002). Cannabis and psychosis. *Current Psychiatry Reports* **4**, 191–196.

Degenhardt, L., Hall, W. & Lynskey, M. (2003*a*). Testing hypotheses about the relationship between cannabis use and psychosis. *Drug and Alcohol Dependence* **71**, 37–48.

Degenhardt, L., Hall, W. & Lynskey, M. (2003*b*). Exploring the association between cannabis use and depression. *Addiction* **98**, 1493–1504.

Diggle, P., Liang, K.-Y. & Zeger, S. (1994). *Analysis of Longitudinal Data. Oxford Statistical Science Series 13*. Clarendon Press: Oxford.

Fergusson, D. M., Horwood, L. J. & Swain-Campbell, N. R. (2003). Cannabis dependence and psychotic symptoms in young people. *Psychological Medicine* **33**, 15–21.

Hall, W., Degenhardt, L. & Teesson, M. (2004). Cannabis use and psychotic disorders: an update. *Drug and Alcohol Review* **23**, 433–443.

Henquet, C., Krabbendam, L., Spauwen, J., Kaplan, C., Lieb, R., Wittchen, H. U. & van Os, J. (2005). Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *British Medical Journal* **330**, 11–14.

Hsieh, F., Bloch, D. & Larsen, M. (1998). A simple method of sample size calculation for linear and logistic regression. *Statistics in Medicine* **17**, 1623–1634.

Jablensky, A., Sartorius, N., Ernberg, G., Anker, M., Korten, A., Cooper, J. E., Day, R. & Bertelsen, A. (1992). Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study. *Psychological Medicine. Monograph Supplement* **20**, 1–97.

Kendler, K., Gallagher, T., Abelson, J. & Kessler, R. (1996). Lifetime prevalence, demographic risk factors, and diagnostic validity of nonaffective psychosis as assessed in a US community sample: the National Comorbidity Survey. *Archives of General Psychiatry* **53**, 1022–1031.

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.

Macleod, J., Oakes, R., Copello, A., Crome, I., Egger, M., Hickman, M., Oppenkowski, T., Stokes-Lampard, H. & Davey Smith, G. (2004). Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *Lancet* **363**, 1579–1588.

Martinez-Arevalo, M. J., Calcedo-Ordonez, A. & Varo-Prieto, J. R. (1994). Cannabis consumption as a prognostic factor in schizophrenia. *British Journal of Psychiatry* **164**, 679–681.

Negrete, J. C., Knapp, W. P., Douglas, D. & Smith, W. B. (1986). Cannabis affects the severity of schizophrenic symptoms: results of a clinical survey. *Psychological Medicine* **16**, 515–520.

Patton, G., Coffey, C., Carlin, J., Degenhardt, L., Lynskey, M. & Hall, W. (2002). Cannabis use and mental health in young people: cohort study. *British Medical Journal* **325**, 1195–1198.

Tien, A. Y. & Anthony, J. C. (1990). Epidemiological analysis of alcohol and drug use as risk factors for psychotic experiences. *Journal of Nervous and Mental Disease* **178**, 473–480.

Van Os, J., Bak, M., Hanssen, M., Bijl, R. V., de Graaf, R. & Verdoux, H. (2002). Cannabis use and psychosis: a longitudinal population-based study. *American Journal of Epidemiology* **156**, 319–327.

Ventura, J., Lukoff, D., Nuechterlein, K., Liberman, R., Green, M. & Shaner, A. (1993). Appendix 1: Brief Psychiatric Rating Scale (BPRS) expanded version (4.0) scales, anchor points and administration manual. *International Journal of Methods in Psychiatric Research* **3**, 227–243.

Verdoux, H., Gindre, C., Sorbara, F., Tournier, M. & Swendsen, J. (2002). Cannabis use and the expression of psychosis vulnerability in daily life. *European Psychiatry* **17**, 180S.

Verdoux, H., Gindre, C., Sorbara, F., Tournier, M. & Swendsen, J. (2003). Cannabis use and the expression of psychosis vulnerability in daily life: an experience sampling test study. *Psychological Medicine* **33**, 23–32.

Wheatley, M. (1998). The prevalence and relevance of substance use in detained schizophrenic patients. *Journal of Forensic Psychiatry* **9**, 114–129.

Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I. & Lewis, G. (2002). Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *British Medical Journal* **325**, 1199.