



Assessing the impact of cannabis use on trends in diagnosed schizophrenia in the United Kingdom from 1996 to 2005

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ABSTRACT

A recent systematic review concluded that cannabis use increases risk of psychotic outcomes independently of confounding and transient intoxication effects. Furthermore, a model of the association between cannabis use and schizophrenia indicated that the incidence and prevalence of schizophrenia would increase from 1990 onwards. The model is based on three factors: a) increased relative risk of psychotic outcomes for frequent cannabis users compared to those who have never used cannabis between 1.8 and 3.1, b) a substantial rise in UK cannabis use from the mid-1970s and c) elevated risk of 20 years from first use of cannabis. This paper investigates whether this has occurred in the UK by examining trends in the annual prevalence and incidence of schizophrenia and psychoses, as measured by diagnosed cases from 1996 to 2005. Retrospective analysis of the General Practice Research Database (GPRD) was conducted for 183 practices in England, Wales, Scotland and Northern Ireland. The study cohort comprised almost 600,000 patients each year, representing approximately 2.3% of the UK population aged 16 to 44. Between 1996 and 2005 the incidence and prevalence of schizophrenia and psychoses were either stable or declining. Explanations other than a genuine stability or decline were considered, but appeared less plausible. In conclusion, this study did not find any evidence of increasing schizophrenia or psychoses in the general population from 1996 to 2005.

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1. Introduction

The risk of developing psychoses as a result of cannabis use has been the topic of extensive research. A systematic review concluded that people who have ever used cannabis have a significantly higher risk of developing psychoses, with those using cannabis more frequently being at particularly high risk. The meta-analysis indicated an odds ratio of 1.41 (95% CI 1.20–1.65) for ever use and 2.09 (95% CI 1.54–2.84) for frequent use compared to never use (Moore et al., 2007).

More recently Zammit et al. (2008) conducted a systematic review to look specifically at whether cannabis use leads to

worse outcomes in people with psychotic disorders, measured by relapse or rehospitalisation, symptom severity, and response and adherence to treatment. They found that few studies adjusted for factors known to influence mental health outcomes, such as alcohol or other drug use (Jane-Lopis and Matytsina, 2006; Regier et al., 1990) and socio-demographic characteristics (Lauronen et al., 2007; Munk-Jorgensen and Mortensen, 1992). Furthermore, an important limitation of many studies is that they have failed to distinguish the direction of association between cannabis use and psychosis; although using cannabis is associated with a greater risk of developing psychosis, there is also an evidence of increased cannabis use following psychosis onset (Hides et al., 2006; Ferdinand et al., 2005). This is consistent with higher rates of substance use in general among psychotic patients (Gregg et al., 2007), and in psychiatric illness overall (Frisher et al., 2005). It is therefore difficult to establish a causal relationship

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between cannabis use and the development of psychotic disorders.

An alternative approach to investigating this link is to examine population rates in psychosis and schizophrenia and to compare these to known trends in cannabis use. It is analogous to investigating changes in the incidence and prevalence of lung cancer following changes in smoking trends (see [Doll and Peto, 1976](#)). A UK study reported that cannabis use increased fourfold between 1972 and 2002, increasing 18-fold among under-18s ([Hickman et al., 2007](#)). The study then considers a scenario whereby the risk of schizophrenia is elevated 1.8-fold among 'light or short-term' users and 3.1 among 'heavy or long-term' users. These risks affect only those starting cannabis use when aged under 20, but elevated risk lasts for 20 years. Under this scenario, increases in cannabis would lead to increases in schizophrenia incidence and prevalence of 29% and 19% respectively, between 1990 and 2010. The corresponding figures for women are 24% and 14%. More recent data from the British Crime Survey (BCS: [Roe and Man, 2006](#)) report that cannabis use has started to decrease during the last decade, particularly among young people aged 16–24; 21.4% of this age group reported having used cannabis in the last year during the 2005/06 survey, compared with 26.0% in 1996.

A recent study in Zurich drew comparisons between trends in cannabis use and the incidence of psychotic disorders in young people between 1977 and 2005 ([Ajdacic-Gross et al., 2007](#)). First admission rates for psychotic disorders remained constant for men and showed a downward trend for women; in the second half of the 1990s however there was a strong increase in the youngest age groups, particularly among males. This coincided with a distinct increase in cannabis availability (i.e. hemp shops) and consumption in the 1990s ([Delgrande Jordan et al., 2004](#); [Kuntsche, 2004](#)). This is contrary to reports that increases in population cannabis exposure have not been followed by upward trends in the incidence of psychotic disorders ([Macleod et al., 2006](#); [Arsenault et al., 2004](#); [Rey and Tennant, 2002](#)). However, it is important to take into account socio-cultural differences in cannabis availability and consumption; for this reason, it is more appropriate to focus on trends in cannabis use in the UK when comparing these to schizophrenia/psychosis trends in UK general practice.

The present study uses the General Practice Research Database (GPRD) to determine the annual rate of new and existing diagnosed cases of schizophrenia/psychosis occurring in a population over the 10-year period from 1996 to 2005. Approximately 95% of the UK population is registered with a general practitioner, and age and sex distributions of patients within the GPRD are similar to those reported by the National Population Census ([Garcia Rodriguez and Pérez Gutthann, 1998](#)). Socio-economic status is indicated at practice level by Index of Multiple Deprivation (IMD: [Office of the Deputy Prime Minister, 2004](#)) score, which is used to assign the practice to one of five quintiles based on the spread of scores within each country; the distribution of GPRD practices across these quintiles reflects that of the general population. Furthermore, the quality of GPRD data has been found to be satisfactory for clinical research, with validation studies reporting high levels of concordance between clinical and computer records ([Jick et al., 1991, 1992](#)).

Based on literature suggesting a) an elevated risk of developing schizophrenia/psychosis among cannabis users, b) a substantial rise in cannabis use in the UK from the mid-1970s onwards and c) an assumed elevated risk of 20 years, this model would predict a corresponding increase in schizophrenia/psychosis during our study period. The paper focuses on the age specific rates for patients aged 16–44 for three reasons. First, rates for all ages could be influenced by an ageing population. Second, a 20 year old commencing cannabis use in 1980 would be 45 in 2005. Third, 16–44 is a conventional category used in other studies.

2. Method

2.1. Sample

The data for this study comes from the GPRD, which is managed by the Medicines and Healthcare Products Regulatory Agency (MHRA). The data have been obtained under a license from the Medical Research Council (MRC). The study cohort comprises all patients aged 16–44 in 183 GPRD practices, with almost 600,000 patients within each study year. These practices were selected because they continuously submitted data from 1996 to 2005. The practices are drawn from the nine National Health Service (NHS) Regional Office areas for England, plus Scotland, Wales and Northern Ireland. The data represent approximately 2.3% of the UK population aged 16–44.

2.2. Recording of diagnosis on the GPRD

Diagnoses on the GPRD are recorded using Oxford Medical Information Systems (OXMIS) codes and Read codes. OXMIS codes were devised for use by GPs and are based on the International Classification of Diseases (ICD) and Office of Population and Census Statistics (OPCS) operation codes. Read codes are a coded thesaurus of clinical terms, which enable clinicians to make effective use of computer systems. Lists of codes for schizophrenia and psychoses were available from a previous study for the Department of Health ([Frisher et al., 2005](#)). For the present study there are 75 codes for schizophrenia and 304 for psychoses. However three codes account for three quarters of schizophrenia diagnoses (schizophrenic disorders, paranoid schizophrenia and schizo-affective disorders) and ten codes account for three quarters of psychoses diagnoses (Psychosis NOS, Nonorganic psychosis NOS, Paranoid states, Hallucinations, Paranoid psychosis, Paranoia, Psychotic episode, Hypomania, Mood-affective disorders, and Organic psychotic conditions).

2.3. Definition of incident and prevalent cases

A prevalent case is one that is recorded in a calendar year, irrespective of whether it has been recorded previously or not. An incident case is one that occurs for the first time in the study period. Only cases with a minimum 1-year lookback period (i.e. those registered on the database for at least a year prior to their first schizophrenia diagnosis) were included in the analysis of incidence. The lookback period was applied to all incident cases from 1996 onwards. This will ensure that a measure of genuinely new cases is obtained and not simply

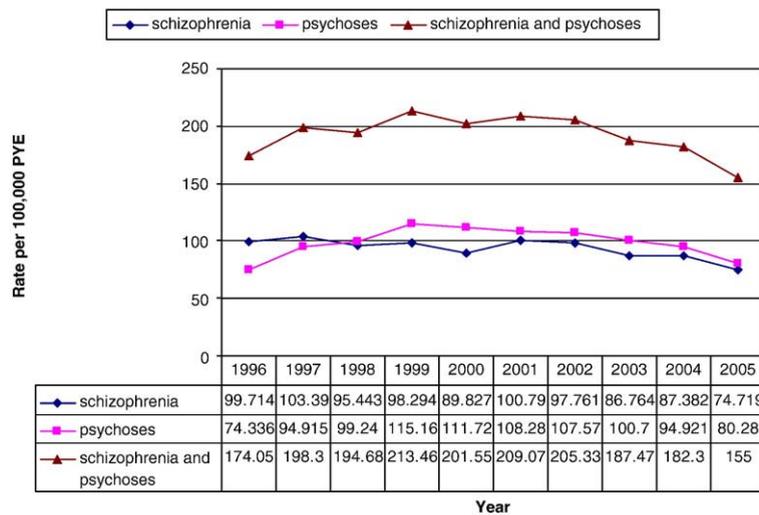


Fig. 1. Annual prevalence of schizophrenia and psychoses, 1996–2005.

existing cases registering onto the database for a short period of time. The average period of registration for incident cases is over 11 years.

2.4. Analysis

Annual incidence and prevalence rates were defined as the total number of cases of the disease in the population in a calendar year divided by patient years of exposure (PYE) in that year. PYE rather than persons are used as a case may not have been exposed for a complete year. For example, a patient who registered on 1st January 1996 and left the database on 1st January 1997 would have a value of one person year, whereas a patient who registered on 1st January 1996 and left on 1st July 1996 would have a value of 0.5 person years (i.e. six months of exposure). Time intervals from 1996 to 2005 were examined using linear trend test (Stats Direct).

3. Results

Fig. 1 shows the annual prevalence rates for schizophrenia and psychoses diagnoses. There was a significant decrease in the prevalence of schizophrenia diagnoses from 1996 to 2005 (Chi^2 for linear trend = 25.7 (1 DF), $P < 0.0001$). There was no significant change in the prevalence of psychoses diagnoses from 1996 to 2005 (Chi^2 for linear trend = 0.345456 (1 DF), $P = 0.7298$) but there was a significant decrease in the prevalence of psychoses diagnoses from 1999 to 2005 (Chi^2 for linear trend = 42.76, (1 DF) $P < 0.0001$).

Fig. 2 shows the annual incidence rates for schizophrenia and psychoses diagnoses. There was no significant change in the incidence of schizophrenia or psychoses diagnoses from 1996 to 2005 (Chi^2 for linear trend = 0.16 (1 DF) $P = 0.68$ and 0.23 (1 DF) $P = 0.6261$ respectively). From 1999 to 2005 there was a significant decrease in psychoses diagnoses (Chi^2 for linear trend = 21.25 (1 DF) $P < 0.0001$) but no significant

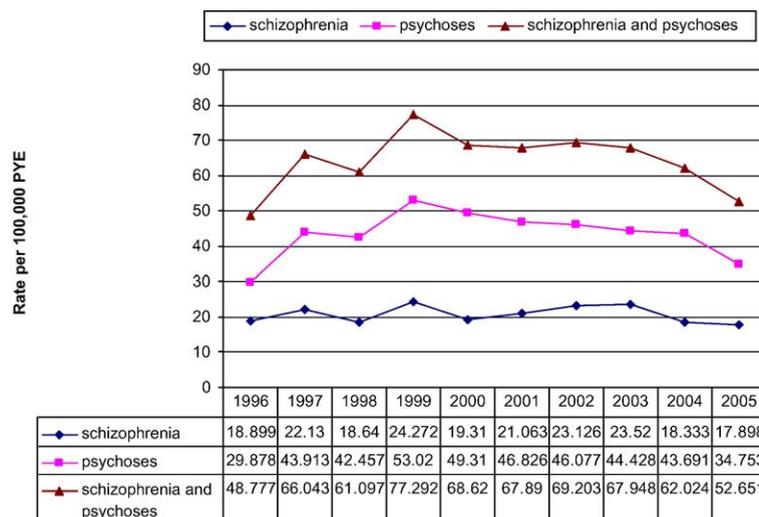


Fig. 2. Annual incidence of schizophrenia and psychoses, 1996–2005.

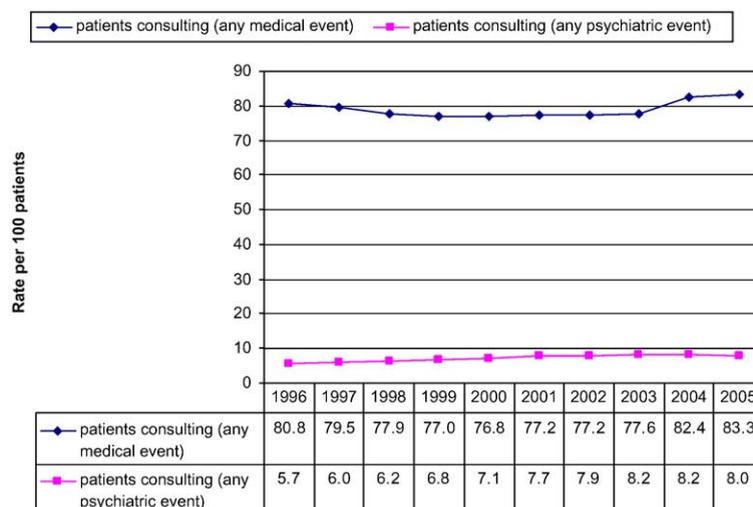


Fig. 3. Annual consultation rates for psychiatric and all medical events, 1996–2005.

change in the incidence of schizophrenia diagnoses (χ^2 for linear trend = 3.41 (1 DF) $P=0.0646$).

The mean age of onset for the observed schizophrenic cases was 29.7 years in 1996 ($SD=6.8$) and 31.3 in 2005 ($SD=8.1$). For psychosis onset the mean age was 30.8 in 1996 ($SD=7.7$) and 29.7 in 2005 ($SD=7.9$).

In order to check that the observed trends were not artefactual, annual consultation rates for any medical condition and for any psychiatric condition were calculated (see Fig. 3). The aim was to see whether general consultation rates also decreased over the study period. A sample of 35,000 patients aged 16–44 were examined. For any medical condition, the proportion of patients consulting increased from 80.8% in 1996 to 83.3% in 2005 (χ^2 for linear trend = 66.8 (1 DF) $P<0.0001$). For psychiatric conditions, the proportion of cases consulting increased from 5.7% in 1996 to 8.0% in 2006. This increase was significant (χ^2 for linear trend = 251.7 (1 DF) $P<0.0001$).

4. Discussion

4.1. Main findings

The results of this study indicate that the incidence and prevalence of diagnoses of schizophrenia and psychoses in general practice did not increase between 1996 and 2005. As well as the GPRD indicating declining prevalence of schizophrenia/psychoses, Hospital Episode Statistics (HES) data for admissions relating to schizophrenia and psychoses also show a decline from 1998/99 to 2005/06 (HES online, 2008). While the latter data could be due to policy, e.g. less care for such patients in hospital settings, this seems less likely for the general practice data. Though changes in diagnostic practice could account for the decline in schizophrenia in general practice, this might be because such patients might alternatively be diagnosed as psychotic. However this does not appear to have been occurring since psychoses incidence has remained stable. Along with diagnoses in hospital and general practice, there are also data on psychotic disorders in the general population. Between 1993

and 2000 National Psychiatric Morbidity Surveys the reported prevalence of psychotic disorders remained stable (Singleton et al., 2000).

4.2. Links with trends in cannabis use

In terms of the model set out in the Introduction, the expected rise in diagnoses of schizophrenia and psychoses did not occur over a 10 year period. This study does not therefore support the specific causal link between cannabis use and the incidence of psychotic disorders based on the 3 assumptions described in the Introduction. This concurs with other reports indicating that increases in population cannabis use have not been followed by increases in psychotic incidence (Macleod et al., 2006; Arsenaault et al., 2004; Rey and Tennant, 2002). However, it is not in line with findings of a rise in first admission rates for psychotic disorders among young people in Zurich following increases in cannabis availability and consumption (Ajdacic-Gross et al., 2007). One factor involved in this discrepancy may be the potency of the cannabis consumed, which varies considerably within Europe (EMCDDA, 2008). In addition, a Netherlands study found that high-potency cannabis obtained from 'coffee shops' led to higher levels of tetrahydrocannabinol (THC) in the blood, with young males aged 18–45 at particular risk for excessive consumption (Mensinga et al., 2006).

4.3. Strengths of the GPRD for analyzing trends

While the UK does not have a national register of schizophrenia/psychoses, the General Practice Database provides a method of analyzing trends as reported in general practice. Previous research has shown that the classification of psychosis, schizophrenia, affective psychosis and non-affective psychosis on the GPRD is accurate, that the rate of misclassification is low and that there are few cases not entered onto computer (Nazareth et al., 1993). In addition, the GP is the most likely health professional to be in contact with such patients (Burns et al., 1998). Furthermore approximately 95% of the UK population is registered with a general

practitioner, with age and sex distributions of patients within the GPRD similar to those reported by the National Population Census (García Rodríguez and Pérez Gutthann, 1998). In addition, the average registration period observed for incident cases of schizophrenia/psychoses indicates that we have approximately 11 years of previous consultation history for these patients, suggesting that estimates of incidence are reliable. Thus data from general practice can provide a robust estimate of population trends.

4.4. Limitations of the study

The GPRD can only provide a measure of what is brought to the attention of the GP, therefore the possibility that declining trends are artefactual must be considered. However, the observed increase in rates of both general and psychiatric consultations over the study period, which coincides with the introduction of the Quality Outcomes Framework (QoF) in 2004 (Department of Health, 2008), suggests that this is not the case. Based on the study data it is not possible to comment on whether the observed trends are linked to cannabis use within the population studied. Although it is possible to identify diagnoses of substance misuse, GPs tend not to code the specific drugs involved, so the proportion linked to cannabis cannot be clearly established. Moreover, prior history of cannabis use that has not been severe enough to necessitate GP consultation will not be recorded. The results can only provide a measure of trends of GP recorded schizophrenia and psychoses, and we can only state whether these fit the expected trends based on models of a cannabis–schizophrenia association.

4.5. Conclusions

The most parsimonious explanation of the results reported here are that the schizophrenia/psychoses data presented here are valid and the causal models linking cannabis with schizophrenia/psychoses are not supported by this study. A number of alternative explanations have been considered and while they cannot be wholly discounted, they do not appear to be plausible. There are also other possibilities, for example causes of schizophrenia/psychoses may have declined thereby masking any causal effect of cannabis use on the prevalence of schizophrenia/psychoses. However, it is beyond the scope of this study to examine this hypothesis and we are therefore left with the most parsimonious explanation, namely that the underlying causes of schizophrenia/psychoses remained stable/declined over the study period.

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Contributors

Martin Frisher participated in conceptualising and developing the original research idea, designing the study, and analysing the data; Ilana Crome participated in conceptualising and developing the original idea for this research and in designing the study; Orsolina Martino participated in developing the study idea and analysing the data; Peter Croft participated in

the developing the study idea and in designing the study. All authors contributed to the writing of the manuscript and have approved the final version.

Conflict of interest

None.

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