RESEARCH REPORT

Substance misuse and psychiatric illness: prospective observational study using the general practice research database

Martin Frisher, Ilana Crome, John Macleod, David Millson, Peter Croft

Objectives: To quantify the relation between substance misuse and psychiatric illness in the UK general practice population in terms of (a) the relative risk of developing one condition given prior exposure to the other and (b) the proportion of cases of one condition attributable to exposure to the other.

Design: Population based prospective observational study using the general practice research database (GPRD) between 1993 and 1998. The 230 GP practices represent 3.1% of the population.

Setting: England and Wales.

Participants: 1.4 million registered patients of whom 3969 had both substance misuse and psychiatric diagnoses between 1993 and 1998.

Main outcome measures: Relative risk (RR) for subsequent psychiatric illness among participants exposed to substance misuse and RR for subsequent substance misuse among participants exposed to psychiatric illness. Population attributable risk (PAR) of psychiatric illness attributable to substance misuse and of substance misuse attributable to psychiatric illness.

Results: The baseline prevalence of psychiatric illness over the study period was 15% and 0.3% for substance abuse. RR for psychiatric illness for substance misusers compared with non-substance misusers was 1.54 (95% CI 1.47 to 1.62). RR for substance misuse among psychiatric compared with non-psychiatric cases was 2.09 (95% CI 1.99 to 2.22). PAR for psychiatric illness attributable to substance misuse was 0.2%. PAR for substance misuse attributable to psychiatric illness was 14.2%.

Discussion: Only a comparatively small proportion of psychiatric illness seems possibly attributable to substance use whereas a more substantial proportion of substance use seems possibly attributable to psychiatric illness. This study does not support the hypotheses that comorbidity between substance misuse and psychiatric illness is primarily the result of substance misuse or that increasing comorbidity is largely attributable to increasing substance misuse.
estimated the proportion of cases of each condition attributable to exposure to the other assuming a causal relation between the two.

**METHODS**

The sampling frame for this study is the GPRD. The GPRD is the world’s largest computerised database of patient records and is owned by the Medicines and Healthcare Products Regulatory Agency. Contributing GPs record all prescriptions and all significant morbidity and these data are subjected to routine quality assessment. The Office of National Statistics (ONS) supplied the data for this study. The data supplied included medical histories for all cases with a diagnosis of substance misuse and all cases meeting the definition of comorbidity described below. For all other patients, ONS supplied denominator data in the form of tables of patient years of exposure. Over the six year study period there were 6,202,083 patient years of exposure; of these 936,123 involved patients consulting for a psychiatric condition (15.1%) and 22,904 (0.37%) involved patients consulting for substance misuse.

**Defining substance misuse disorders and psychiatric illness**

As well as routine validation, GPRD psychiatric data have been the subject of an in depth study, which concluded that the accuracy of the computer categories for schizophrenia, non-affective psychosis, and all non-organic psychoses was good (88%–91%) and compared favourably with psychiatric case registers. As part of this study, we addressed concerns that substance misuse and psychiatric illness might not be recorded in GP records. Examination of over 200 sets of case notes showed that over 90% of patients treated for substance misuse or psychiatric illness in secondary care settings are known to their GP.

In this study, 1,693 diagnostic codes for psychiatric illness were identified. These codes were classified into six diagnostic groups: (a) psychoses, (b) schizophrenia, (c) paranoia, (d) neurosis, (e) personality disorders, and (e) other disorders (which includes “insomnia not otherwise specified”, “behaviour problems”, “hallucinations”, “hallucinations auditory”, “behaviour antisocial”, and “disorder behaviour”).

Altogether 258 Oxmis and Read codes for substance misuse disorders were identified. The main codes used (in descending order) were “drug addiction”, “heroin addiction”, “drug dependence”, “drug abuse”, “habitual drug abuse”, “opiate abuse”, “misuse of drugs”, and “drug misuse”. As in our previous paper, all these diagnoses were defined as “substance misuse” for the purposes of this analysis. Because of low numbers, issues relating to specific substances are not addressed in this paper. This classification does not include alcohol or tobacco related disorders.

**Comorbidity case definition**

All patients were free from either substance misuse or psychiatric diagnosis for at least one year at study entry date. A case was defined as comorbid when a patient has received diagnoses for both psychiatric illness and substance misuse at some time between 1993 and 1998. Between 1993 and 1998 there were 3,969 remaining comorbid cases, divided into three groups. Group 1: baseline substance misuse (substance misuse is first diagnosis in the study period); n = 1,588. Group 2: baseline psychiatric illness (psychiatric illness is first diagnosis in the study period); n = 2,162. Group 3: baseline comorbidity (that is, where both psychiatric illness and substance misuse are diagnosed on same day in the study period); n = 219.

**Analysis**

The relative risk of psychiatric illness among substance misusers compared with non-substance misusers was calculated as was the relative risk of substance misuse among psychiatric cases compared with non-psychiatric cases. The 95% confidence intervals for the relative risks were calculated. Linear regression was performed to assess whether the proportion of comorbid cases with a baseline diagnosis of substance misuse changed significantly over the study period. The analysis was conducted using StatsDirect version 2.3.7 (http://www.statsdirect.com).

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**Table 1 Relative risk of psychiatric illness and substance misuse**

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<td>% Non-substance misusers who develop psychiatric illness 1993–1998</td>
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<td>% Substance misusers who develop psychiatric illness 1993–1998</td>
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<td>23.30</td>
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<td>Relative risk of psychiatric illness (substance v non-substance abusers)</td>
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<td>% Non-psychiatric cases who develop substance illness 1993–1998</td>
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<td>% Psychiatric cases who develop substance misuse 1993–1998</td>
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<td>Relative risk of substance misuse (psychiatric v non-psychiatric cases)</td>
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**Figure 1 Annual proportions of first diagnoses among comorbid cases diagnosed each year from 1993 to 1998.**
We examined the effect of the two types of relative risk on the whole population by calculating population attributable risk (PAR). This is the maximum proportion of the outcome in the total population (exposed and unexposed cases) that is attributable to the exposure. In this study, two PARS (with 95% confidence intervals) were calculated. Firstly, where the outcome is substance misuse and the exposed cases are those exposed to psychiatric illness and secondly where the outcome is psychiatric illness and the exposed cases are those exposed to substance misuse.

**RESULTS**

Table 1 shows that patients exposed to substance misuse were 1.54 times (95% CI 1.48 to 1.62) more likely to develop psychiatric illness than those not exposed to substance misuse. Patients exposed to psychiatric illness were 2.09 (95% CI 1.99 to 2.02) times more likely to develop substance misuse than those not exposed to psychiatric illness.

Figure 1 shows that the proportion of substance misuse diagnoses occurring before psychiatric diagnoses remained stable over the study period ($t = 0.47$, df = 4, $p = 0.65$).

Table 2 shows the proportion of illness in the population potentially explained by exposure to substance misuse or psychiatric illness.

**DISCUSSION**

**Study strengths and limitations**

These are the first longitudinal data from the UK relating substance misuse to psychiatric illness in the general population. Exposure and outcome assessment were by a clinician and therefore possibly less vulnerable to the bias that may influence uncorroborated self-report. The measures reflected clinically significant substance misuse and psychiatric illness.

The data reported here are comparatively recent and arguably have more relevance to current practice than previous historical studies. However, as the study is based on diagnoses recorded by GPs, there are limitations. They depend on people’s use of primary care services and the diagnostic behaviour of GPs and many factors are likely to influence these variables. In most instances, GPs did not record specific substance of misuse and therefore these data cannot be used to clarify causal hypotheses regarding specific drug exposures and specific psychiatric outcomes (or vice versa). In particular these data cannot directly inform the ongoing debate as to whether cannabis use causes psychosis.

Our substance exposure measure was substance misuse perceived to be clinically significant by a GP. In our study the rate of substance abuse over the study period was (0.37%). We are aware of only one study that provides comparable epidemiological data on problematic drug use. In that study, seven estimates were provided, ranging from 0.35% to 0.57%. Substance use not associated with the experience of overt problems is unlikely to have been captured in the current study. Finally, various factors (particularly aspects of early life adversity) may confound the association between substance misuse and psychiatric illness. We had no data on these factors and therefore no opportunity to consider their influence in our analyses. Caution is therefore required with regard to any causal inference drawn from these data.

**Interpretation of study findings**

We have already reported that comorbidity of substance misuse and psychiatric illness increased by 62% during the study period. In this study, a diagnosis of substance misuse was associated with an increased risk of a subsequent diagnosis of psychiatric illness ($RR = 1.54$). This risk was lower than that for psychiatric cases developing substance misuse compared with non-psychiatric cases ($RR = 2.09$). If the above association between problematic substance misuse and increased risk of psychiatric illness is causal (and we have discussed problems associated with this assumption above) then, on the basis of these data, elimination of all such substance misuse would reduce the incidence of all psychiatric illness by only 0.2% and schizophrenia/psychoses by 0.1%. These very low rates reflect the combination of the relative risk (1.54) and the low rates of problematic substance misuse in the population (0.37%).

These results, therefore, do not suggest that problematic substance misuse makes an important contribution to the population burden of psychiatric illness. Substance misuse that was unrecorded in GPRD data (for example, cannabis use not declared to a GP) may have had an influence that we were unable to detect. It seems unlikely, however, that this influence would have approached the magnitude of the population attributable risks suggested by some, given that visible problem drug users (for example, people receiving substitute opioid prescriptions) tend to have rates of cannabis use substantially higher than those seen in the general population.

Over the study period, the population rates of both psychiatric illness and substance misuse in the UK population have increased. During the same period our study found that most comorbid cases present with psychiatric illness before they present with substance misuse. Furthermore, there was no significant change in this trend over the study period. These data do not support the hypotheses that increasing comorbidity is largely attributable to increasing substance misuse. Comparisons between the 1993 and 2000 national psychiatric morbidity surveys also provide further ecological evidence against an important causal relation between drug use and psychiatric illness. Between these years, reported illicit drug dependence approximately doubled while the reported prevalence of both neurotic and psychotic disorders remained stable. Even if substance misuse causes increased risk of psychiatric illness our finding suggests that attempts to prevent comorbidity by focusing on detection of substance misuse in primary care may meet with limited success. This is because the diagnosis...
of psychiatric illness in primary care is much more common than and generally precedes that of substance misuse.

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CONTRIBUTORS

IC and MF had the original idea for this research, which was developed by IC, MF, DM, and PC; MF and PC designed the study; MF analysed the data, and drafted the manuscript; JM redrafted the manuscript and suggested new analyses; All authors contributed to the writing of the manuscript. MF is guarantor.

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Competing interests: none.

Scientific and ethical approval: the study was approved by the GPRD Scientific Ethical Advisory Group (SEAG).

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