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RESEARCH PAPER

Prevalence of common chronic respiratory diseases in drug misusers: a cohort study

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Abstract

Background: A randomised controlled trial of substance misuse indicated that many patients who use methadone have respiratory symptoms and/or are prescribed respiratory medications. There is little research in this area.

Aims: To determine the prevalence of respiratory disease and prescriptions among drug misusers.

Methods: This historical cohort study of drug misusers and matched controls analysed routinely collected primary care data. The prevalence of common chronic respiratory diseases, class and number of respiratory medications were examined.

Results: The cohort of 18,570 patients (9,285 per group) was mostly male (64%, n=11,890) and aged 31–59 years (76%, n=14,060). After adjusting for age, gender, deprivation and smoking status, the results showed that more drug misusers than controls had a diagnosis of asthma or chronic obstructive pulmonary disease (17.1% vs. 10.9%; adjusted odds ratio (OR) 1.61, 95% confidence interval (CI) 1.46 to 1.77, and 2.4% vs. 0.8%; OR 1.86, 95% CI 1.42 to 2.44, respectively) and were prescribed more chronic respiratory medications: short-acting β_2-agonists (16.4% vs. 7.9%; OR 2.00, 95% CI 1.80 to 2.22), long-acting β_2-agonists (1% vs. 0.4%; OR 1.93, 95% CI 1.29 to 2.89), and inhaled corticosteroids (10.6% vs. 7.6%; OR 1.49, 95% CI 1.33 to 1.67). All differences were statistically significant ($p<0.001$).

Conclusions: Drug misusers have a significantly higher prevalence of respiratory diseases and respiratory prescriptions than matched controls. Further work is needed to determine the reasons for this.

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Introduction

Background

In the UK around four million people use illicit drugs annually.[1] It is estimated that 36.2% of the adult population have used an illicit drug at some point in their life, with 8.6% of the population reporting illicit drug use in the last year.[2] Although a large percentage of this is cannabis use, heroin use has steadily increased since the 1980s.[1,3] Between 2009 and 2010 in Scotland, 10,325 people were newly recorded as drug misusers, 66% of whom were misusing heroin.[4]

The economic and social burden of problem drug use is substantial. It costs Scotland approximately £2.6 billion annually,[3] and the Scottish Health Boards' ring-fenced budget for drug misuse services for 2010/2011 is £28.6 million.[2] In England and Wales the cost of problem drug misuse in terms of healthcare (primary, secondary and tertiary care) is estimated to be £283–509 million a year.[1] Problem drug use is also associated with a substantial personal cost. Drug misusers often have complex co-morbidities and suffer from a range of medical and social conditions including hepatitis, HIV, heart disease, psychiatric disease, homelessness, and financial problems.[1,3]

A recent large randomised controlled trial of substance misuse[5] observed that many patients being treated with methadone maintenance therapy have respiratory symptoms. This observation has also been supported by anecdotal evidence from clinical

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colleagues, although there is little published research in this area.[6] Previous studies have reported an association between drug misuse and asthma exacerbations[7-10] and respiratory disease and lower quality of asthma care among drug misusers.[11] Other previous studies also suggest a possible association between asthma mortality and drug misuse.[12-14] However, conflicting results have been reported for the association between the development of chronic respiratory disease and drug misuse.[15-18] From the small amount of published information in this area, it could be hypothesised that patients who misuse drugs may be more susceptible to respiratory disease and may also be receiving suboptimal treatment. This could potentially lead to increased morbidity, exacerbations and, ultimately, increased mortality.

Objectives

The aim of this exploratory study was to determine if the prevalence and management of respiratory conditions in drug misusers are different from that observed in the general population. Specific objectives were to determine: (1) the prevalence of diagnosed respiratory diseases (including chronic obstructive pulmonary disease (COPD) and asthma); (2) the class and number of respiratory prescriptions among drug misusers; and (3) whether these prevalence rates differ from those observed in non-drug users (controls).

Methods

Study design and data sources

The study was a retrospective matched cohort study using data collected from general practices managed by the Primary Care Clinical Informatics Unit (PCCIU), Scottish Programme for Improvement in Clinical Effectiveness (SPICE).[19] These anonymous data, collected from UK GP Practice Administration Systems for Scotland (GPASS) bi-annually, include patient demographic data, consultation data, morbidity measures, and prescriptions issued. The 12-month observation period was from 1 January 2008 to 31 December 2008. Approval was given for the use of PCCIU data by the PCCIU Research Team following peer review of the study protocol. The study used secondary analysis of anonymised audit data so patient consent or ethical approval were not required. Read clinical classification code groups used are available from the authors on request.

Setting, patients and timescale

Two frequency matched populations of patients (the drug misuse group and the non-drug misuse/control group) were identified. Eligibility criteria for the drug misuse group were: (a) aged 16–59 years on 1 January 2008 and (b) had ever had a drug misuse Read clinical classification code (READ)[20] and/or a record of being prescribed a substitute opiate prescription (e.g. methadone), currently or in the past. The frequency matched control group (non-drug misuse group) were: (a) aged 16–59 years on 1 January 2008 and (b) had no drug misuse READ code[20] or history of having ever received a substitute opiate prescription.

Patients in the control group were excluded if they had ever been coded as a drug misuser or had ever been on substitute prescribing before 1 January 2008. The control group was frequency matched to the drug misuse group for distribution of age (<20, 20–24, 25–30, >30 years), gender, and deprivation (using the Carstairs Scoring System[21]). All drug misusers were identified and allocated a study number. Possible control matches were identified for all age groups, gender, and deprivation combinations. All possible control subjects were assigned an identifier and then, using a standard SQL programme to randomise the list, every third or fourth patient (depending on control group size) was selected until two populations with an equal number of patients matched for age group, sex, and deprivation was reached. For example, if there were 20 males aged 20–24 in deprivation category 1, then 20 randomly generated controls with these characteristics were identified and frequency matched to them. Inclusion criteria for both populations were that they were living patients, permanently registered with a GP practice on the PCCIU database during the observation period.

Main outcome measures

The main outcomes were (a) the prevalence of common respiratory diseases (respiratory system disease, asthma and COPD) ever appearing in patients' medical records from birth up to 31 December 2008 and (b) the number and class of respiratory medication prescriptions (short-acting β_2-agonists (SABA), long-acting β_2-agonists (LABA), combination LABA and inhaled corticosteroids (ICS) preparations).

Statistical analysis

Statistical analysis was conducted using SPSS V.19. Comparisons of the presence of a respiratory condition (diagnosis ever appearing in the patient's clinical record from birth up until 31 December 2008) was used as a proxy measure for point prevalence of respiratory disease (and, as such, is not a measure of lifetime risk for developing respiratory disease). The presence of each type of respiratory medication (in 2008) was also compared in the drugs misuse and control groups. Frequencies and percentages of gender, age group, deprivation category, and smoking status (ever smoked (current and ex-smokers) vs. never smoked) were calculated. The continuity corrected chi-squared test was used to test for associations between smoking status and drug misuse (vs. controls). Frequencies and percentages of drug misusers and controls with each outcome (e.g. diagnosis of disease, presence of a certain prescription group) were presented. Medians, percentiles and Mann-Whitney U tests were used for discrete numerical variables (i.e. prescription counts). Logistic regression was used to calculate the unadjusted odds ratio (OR) with 95% confidence intervals (95% CI) for drug misuser versus control for each outcome. Multivariable logistic regression analysis was used to adjust for gender, age group, deprivation category, and tobacco smoking status. For the respiratory disease outcomes, interactions between drug misuse (vs. controls) and each of the factors adjusted for in the models were investigated. The asthma group included Read codes defined by the Quality and Outcomes Framework (QOF)[22] as criteria for asthma, and the COPD group included codes defined by QOF for COPD.[22] The respiratory system disease group was developed separately using high level READ codes[20] plus all related sub-codes including asthma and COPD informed by QOF[22] for respiratory system diseases.[23] Smoking status was defined by the QOF[22] criteria for a smoker.

Table 1. Demographic of the cohort

Baseline characteristics	Number of patients, n (%) (N=18,570)
Sex	
Male	11,890 (64.0)
Female	6,680 (36.0)
Age group (years)	
16-19	146 (0.8)
20-24	954 (5.1)
25-30	3,410 (18.4)
31-59	14,060 (75.7)
Deprivation category*	
1 (most affluent)	188 (1.0)
2	664 (3.6)
3	1,770 (9.5)
4	5,582 (30.1)
5	3,832 (20.6)
6	3,428 (18.5)
7 (most deprived)	3,106 (16.7)

Note: Numbers (n) should be divided by 2 to obtain the number of patients in the drug misuser group and the control group.

*The Carstairs deprivation scoring system was used.

Table 2. Type of drug misuse

	Number of patients, n (%)
Drug misuse non-specified	5,646 (71.6%)
Opioid misuse	3,261 (41.3%)
Hypnotic or anxiolytic misuse	1,541 (19.5%)
Cannabis misuse	709 (9.0%)
Cocaine misuse	208 (2.6%)
Glue sniffing misuse	200 (2.5%)
Amphetamine or other psychostimulant misuse	166 (2.1%)
Ecstasy misuse	45 (0.6%)
Hallucinogen misuse	26 (0.3%)

*Some of the 7,883 patients had more than one drug misuse READ[20] code.

Results

Demographics of the cohort

The cohort consisted of 18,570 patients (9,285 per group). The majority (64%, n=11,890) were male and most (76%, n=14,060) were aged between 31 and 59 years (see Table 1). The median deprivation score in each population was 5 (IQR 4–6). The majority of the drug misuse group (85.9%, n=7,978) were either current or ex-smokers compared with half of the control group (46.6%, n=4,331). Of the 9,285 patients in the drug misuse group, 7,883 had a drug misuse READ code.[20] The other 1,403 only had a record of being prescribed a substitute opiate prescription. In the 7,883 patients with a drug misuse READ code,[20] the type of drug misuse is shown in Table 2.

The only variable that had missing information was smoking status (unknown or not recorded) which was missing in 979 (5.3%) patients. The proportion of patients with missing smoking status differed between drug misusers and controls (drug misusers n=337 (3.6%); controls n=642 (6.9%); p<0.001). The majority of patients with missing smoking data were male (Table 3). A significantly greater proportion of drug misusers than controls ever smoked (85.9% vs. 46.6%; p<0.001).

Table 3. Demographics by whether smoking status was recorded and drug misuse

Baseline characteristics	Smoking status recorded N=17,591 (94.7%)		Smoking status not recorded N=979 (5.3%)	
	Drug misusers, n (%)	Controls, n (%)	Drug misusers, n (%)	Controls, n (%)
Sex				
Male	5,663 (63.3)	5,365 (62.1)	282 (83.7)	580 (90.3)
Female	3,285 (36.7)	3,278 (37.9)	55 (16.3)	62 (9.7)
Age group (years)				
16-19	67 (0.7)	58 (0.7)	6 (1.8)	15 (2.3)
20-24	445 (5.0)	425 (4.9)	32 (9.5)	52 (8.1)
25-30	1,605 (17.9)	1,540 (17.8)	100 (29.7)	165 (25.7)
31-59	6,831 (76.3)	6,620 (76.6)	199 (59.1)	410 (63.9)
Deprivation category*				
1 (most affluent)	90 (1.0)	90 (1.0)	4 (1.2)	4 (0.6)
2	321 (3.6)	312 (3.6)	11 (3.3)	20 (3.1)
3	860 (9.6)	821 (9.5)	25 (7.4)	64 (10.0)
4	2,689 (30.1)	2,597 (30.0)	102 (30.3)	194 (30.2)
5	1,847 (20.6)	1,801 (20.8)	69 (20.5)	115 (17.9)
6	1,650 (18.4)	1,589 (18.4)	64 (19.0)	125 (19.5)
7 (most deprived)	1,491 (16.7)	1,433 (16.6)	62 (18.4)	120 (18.7)
Smoking status				
Ever	7,978 (89.2)	4,331 (50.1)	-	-
Never	970 (10.8)	4,312 (49.9)	-	-
Missing	-	-	337 (3.6)	642 (6.9)

*The Carstairs Deprivation scoring system was used.

Table 4: Unadjusted and adjusted odds ratios of drug misusers versus controls for different respiratory outcomes

	Respiratory disease outcome		
	Respiratory system disease	Asthma	COPD
Drug misuser vs. control			
n (%)	4,165 (44.9) vs. 2,925 (31.5)	1,590 (17.1) vs. 1,009 (10.9)	219 (2.4) vs. 74 (0.8)
Unadjusted OR (95% CI)	1.77 (1.67 to 1.88)‡	1.69 (1.56 to 1.84)‡	3.01 (2.31 to 3.92)‡
Multivariable logistic regression model, adjusted OR (95% CI)			
Drug misuser vs. control	1.73 (1.62 to 1.86)‡	1.61 (1.46 to 1.77)‡	1.86 (1.42 to 2.44)‡
Female vs. male	1.36 (1.28 to 1.45)‡	1.38 (1.27 to 1.50)‡	1.45 (1.145 to 1.83)†
Age group, years (vs. 31-59)			
16-19	1.61 (1.12 to 2.30)*	1.56 (1.01 to 2.42)*	
20-24	1.28 (1.12 to 1.48)‡	1.46 (1.22 to 1.74)‡	0.10 (0.02 to 0.39)†[1]
25-30	1.079 (1.00 to 1.17)	1.20 (1.08 to 1.34)‡	0.07 (0.03 to 0.18)‡
Deprivation category (vs. 7, most deprived)			
1, most affluent	1.26 (0.92 to 1.71)	1.52 (1.01 to 2.29)*	0.64 (0.16 to 2.68)
2	1.04 (0.87 to 1.24)	1.33 (1.04 to 1.69)*	0.48 (0.21 to 1.12)
3	1.14 (1.01 to 1.29)*	1.37 (1.15 to 1.63)‡	0.64 (0.39 to 1.05)
4	1.16 (1.05 to 1.27)†	1.26 (1.10 to 1.44)‡	0.72 (0.51 to 1.00)
5	0.79 (0.71 to 0.88)‡	1.16 (1.00 to 1.34)*	0.72 (0.50 to 1.04)
6	1.02 (0.92 to 1.13)	1.21 (1.04 to 1.40)*	0.96 (0.68 to 1.36)
Ever smoked vs. never smoked	1.01 (0.94 to 1.09)	1.08 (0.97 to 1.21)	10.13 (5.15 to 19.92)‡

[1]Due to small numbers in the 16-19 year old age group, this age group was combined with the 20-24 year age group.

*p<0.05; †p<0.01; ‡p<0.001.

Prevalence of respiratory disease

The prevalence and ORs of respiratory system disease, asthma, and COPD for drug misusers versus controls are given in Table 4. After adjusting for age group, gender, deprivation category and smoking status, drug misusers had a 61% increased odds of asthma (adjusted OR 1.61 (95% CI 1.46 to 1.77); p<0.001) and an 86% increased odds of COPD (adjusted OR 1.86 (95% CI 1.42 to 2.44); p<0.001) compared with controls. Females overall were more likely than males to have any respiratory disease. Smokers were no more likely to be diagnosed with any respiratory system disease or asthma than non-smokers; however, they were 10 times more likely to be diagnosed with COPD. For the outcomes of respiratory system disease and asthma, statistically significant interactions were found between drug misuse (vs. controls) and gender (p=0.001 for both), and between drug misuse (vs. controls) and age group (p=0.003 and p<0.001, respectively). A higher proportion of female and male drug misusers had respiratory disease or asthma than female and male controls; a greater proportion of female drug misusers had respiratory system disease or asthma than male drug misusers (Figure 1A and C). With increasing age, drug misusers were more likely to have a respiratory system disease or asthma than controls (Figure 1B and D). There were no significant interactions between drug misuse (vs. controls) and smoking status for any of the disease outcomes.

Prevalence of prescriptions for respiratory medication

The prevalence of having one or more prescriptions for respiratory medication (in 2008) was compared between drug misusers and controls and is shown in Table 5. These results are adjusted for age, gender, deprivation, and smoking status. Drug misusers were approximately twice as likely to be prescribed SABA, LABA, or a compound bronchodilator as controls. However, they were only 50% more likely to be prescribed ICS.

As a sensitivity analysis, we refitted the logistic regression models for all of the above outcomes assuming that those with missing smoking status were smokers. This had little effect on the magnitude of the OR for drug misuse (vs. control). The same was found when we assumed those with missing smoking status had never smoked. For example, for asthma outcome, the ORs for drug misuse versus control were 1.69 (95% CI 1.54 to 1.86) and 1.57 (95% CI 1.43 to 1.73) when we took missing data as ever smoked and never smoked, respectively.

Quantity of respiratory prescriptions

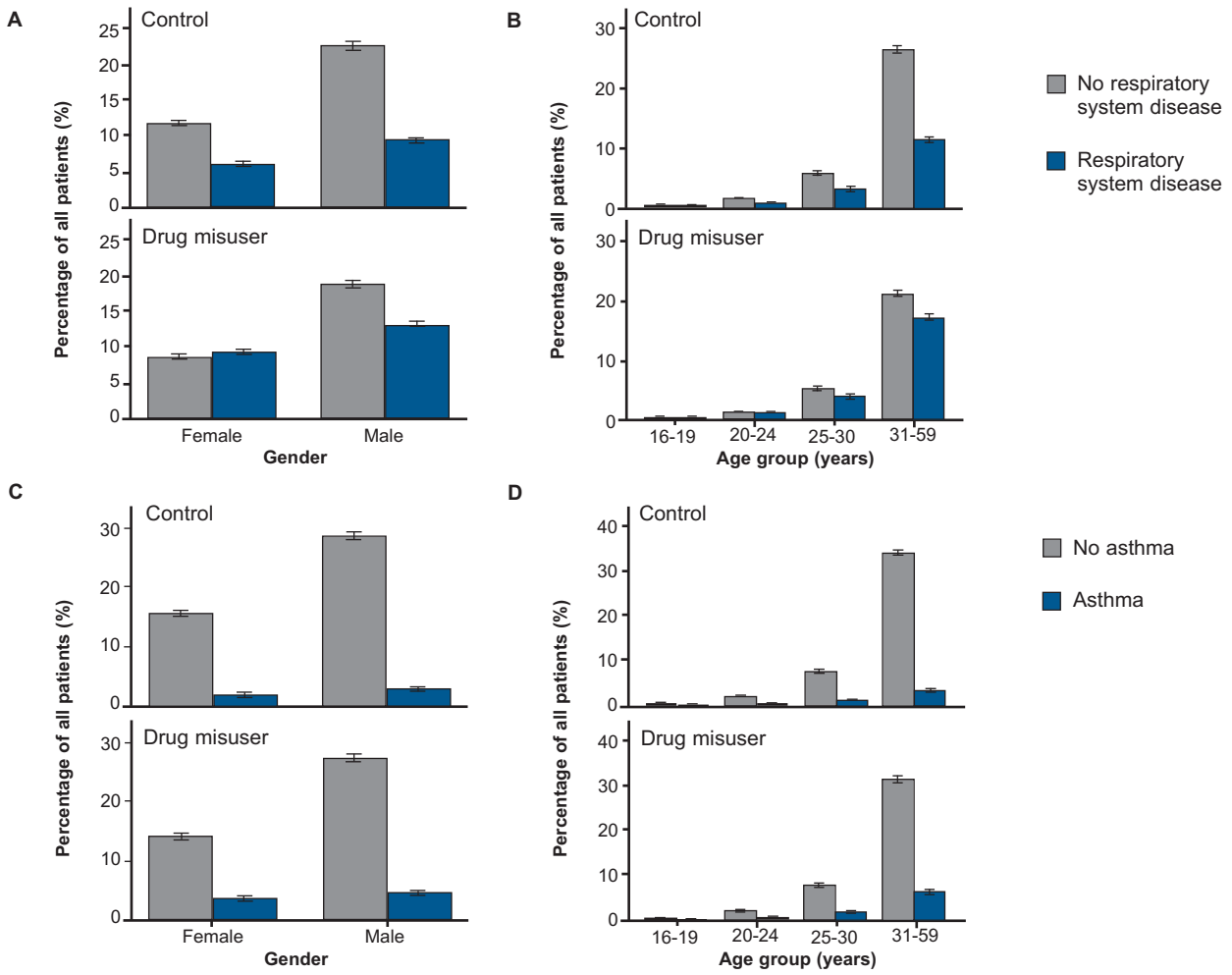
The median quantity of prescriptions for SABA and ICS during 2008 was also statistically significantly higher in drug misusers than in controls. The median (IQR) quantity of SABA prescribed in drug users and controls was 4 (2–8) and 3 (1–7), respectively (p<0.001) and the median (IQR) quantity of ICS prescribed for drug misusers and controls was 4 (2–8) and 2 (1–5), respectively (p<0.001).

Discussion

Main findings

These results demonstrate a greater prevalence of chronic respiratory diseases and respiratory prescriptions in a sample of drug misusers (current or past) than in matched controls who have never used drugs when adjusted for smoking status. The median quantity of SABA and ICS prescriptions was significantly higher in drug misusers than in controls. The results for prevalence of respiratory diseases and respiratory medication use show similar patterns; drug misusers

Figure 1. Proportion (95% CI) of drug misusers and controls having (A) respiratory system disease by gender (p value for interaction = 0.001), (B) respiratory system disease by age group (p=0.003), (C) asthma by gender (p=0.001), (D) asthma by age group (p<0.001)



had a significantly higher prevalence of chronic respiratory disease (asthma and COPD) and were prescribed significantly more medications used for the treatment of COPD and asthma than controls.

Strengths and limitations of this study

This study has a number of strengths and limitations. The strengths lie in the large dataset and use of well matched controls. The fact that the data were drawn from a large number of UK practices also ensures that a variety of social and demographic locations are represented.[19] The likelihood of patient selection bias has been reduced by the inclusion of patients currently on substitute treatment, current and previous drug misusers. This ensures that the sample is highly representative of drug misusers throughout the UK, making the results generalisable. The use of a frequency matched sample design further reduces the possibility of bias and increases the validity of the results.

The study does, however, have limitations. The drug misuse population were younger with higher deprivation scores and a higher proportion of males compared with the general population; 76% of the cohort were aged 31–59 years, the median deprivation score was 5 and 64% were male. Although this is therefore less representative of the general population and may reduce the power of the study, it is important to acknowledge that the sample is representative of the drug misusing population. The data include respiratory prescription and diagnosis/consultation READ codes.[20] However, it is not possible to explore the accuracy of diagnosis and adequacy of management of respiratory disease, although these accurately reflect current clinical practice. The results also do not indicate the prevalence of undiagnosed chronic respiratory diseases (in both drug misusers and controls) nor do they differentiate between the purposes of the medication. The increased prescription rate for inhaled therapy in drug misusers may support an increased prevalence of asthma, COPD, or both. In addition, although the results were adjusted for overall smoking status, it was not possible using this dataset to give comparative results or to adjust for actual levels of tobacco consumption in the drug misuse group compared

Table 5: Unadjusted and adjusted odds ratios of drug misusers versus controls for different prescriptions for respiratory medication

	Respiratory prescriptions			
	SABA	LABA	Compound bronchodilator or (LABA+ICS)	ICS
Drug misuser vs. control				
n (%)	1520 (16.4) vs. 736 (7.9)	92 (1.0) vs. 39 (0.4)	479 (5.2) vs. 248 (2.7)	987 (10.6) vs. 702 (7.6)
Unadjusted OR (95% CI)	2.27 (2.07 to 2.50)‡	2.37 (1.63 to 3.45)‡	1.98 (1.70 to 2.32)‡	1.45 (1.31 to 1.61)‡
Multivariable logistic regression model, adjusted OR (95% CI)				
Drug misuser vs. control	2.00 (1.81 to 2.22)‡	1.93 (1.29 to 2.89)†	1.81 (1.52 to 2.14)‡	1.49 (1.33 to 1.67)‡
Female vs. male	1.89 (1.73 to 2.07)‡	1.59 (1.12 to 2.24)†	2.00 (1.73 to 2.33)‡	1.77 (1.60 to 1.96)‡
Age group, years (vs. 31-59)				
16-19	0.94 (0.56 to 1.59)		0.60 (0.22 to 1.63)	0.77 (0.41 to 1.44)
20-24	0.69 (0.55 to 0.87)†		0.41 (0.25 to 0.65)‡	0.63 (0.48 to 0.82)‡
25-30	0.77 (0.68 to 0.87)‡	0.24 (0.12 to 0.47)‡[1]	0.49 (0.39 to 0.63)‡	0.72 (0.62 to 0.83)‡
Deprivation category (vs. 7, most deprived)				
1, most affluent	1.14 (0.72 to 1.81)		2.77 (1.53 to 5.01)‡	1.35 (0.84 to 2.18)
2	0.97 (0.74 to 1.28)	0.42 (0.13 to 1.41)[2]	1.26 (0.80 to 2.01)	1.23 (0.93 to 1.64)
3	1.13 (0.94 to 1.36)	0.91 (0.47 to 1.77)	1.39 (1.01 to 1.93)*	1.07 (0.86 to 1.32)
4	1.12 (0.97 to 1.29)	0.70 (0.42 to 1.18)	1.52 (1.18 to 1.95)†	1.13 (0.96 to 1.33)
5	1.03 (0.89 to 1.20)	0.98 (0.58 to 1.64)	1.48 (1.14 to 1.94)†	1.12 (0.94 to 1.33)
6	1.25 (1.08 to 1.46)†	0.89 (0.51 to 1.53)	1.48 (1.13 to 1.94)†	1.33 (1.12 to 1.58)†
Ever smoked vs. never smoked	1.35 (1.19 to 1.52)‡	1.74 (1.04 to 2.91)*	1.22 (1.00 to 1.48)*	0.87 (0.77 to 0.99)*

[1]Due to small numbers in the 16-19 and 20-24 year old age groups, these age groups were combined with the 25-30 year age group.

[2]Due to small numbers in deprivation category 1, this category was combined with deprivation category 2.

*p<0.05; †p<0.01; ‡p<0.001.

ICS=inhaled corticosteroid, LABA=long-acting beta-agonist, SABA=short-acting beta-agonist.

with that in the control group.

There is also variation in coding between the two outcomes of interest. The prescription results refer to the year 2008 whereas disease coding refers to ever having the disease (asthma/COPD) recorded in the medical records from birth up until 31 December 2008. If the code has not been removed (a rare event), it can be taken as a proxy for point prevalence. Some bias between the drug misuse and control groups may have occurred as drug misuse patients may have had more occasion to visit their GP practice, alert them to any respiratory symptoms and/or request respiratory prescriptions.

A further consideration is how the data on smoking were used. Smoking status was used as an adjustment at the analysis stage in this study rather than in the frequency matching stage. This approach was taken to enable the effect of smoking to be considered independent of the matched groups. However, as a smaller proportion of the controls were smokers (current and ex-smokers) compared with the drug misuse group (46.6% (n=4,331) vs. 85.9% (n=7,978)), if the control group had also been matched for smoking status the effect size may have been even larger. It is an important observation that fewer smoking data were available for controls than for drug misusers. This may reflect the fact that drug misusers were more likely to be in contact with their GPs and suffer from other co-morbid conditions, and this may mean that their records were updated more often.

Interpretation of findings in relation to previously published work

This study is the first to suggest an association between drug misuse and receiving a diagnosis of asthma or COPD and respiratory prescriptions. Previous studies have been unable to provide such evidence,[12-18] although an association between drug misuse and acute asthma episodes has been reported. These include an association between cocaine misuse and intensive care unit admissions and between cocaine or heroin misuse and increased intubation rates in asthma exacerbations.[8] One study also reported that, while the use of cannabis alone (when compared with non-smokers) had no effect on forced expiratory volume in 1 second (FEV_1), patients using tobacco and cannabis had decreased FEV_1.[16] A very recent study has confirmed the lack of effect on pulmonary function of mild cannabis use.[23] One review paper identified conflicting results for the association between cannabis misuse and the development of chronic respiratory disease.[17]

Implications for future research, policy and practice

These results indicate that drug misusers have worse respiratory health than controls after adjusting for smoking, indicating that the association between drug misuse and chronic respiratory disease cannot be fully explained by the high prevalence of tobacco smoking seen in drug misusers.[24] This suggests that there may be more complex factors related to drug misuse which warrant further study. The associations may be due to the pharmacodynamic effect of illicit

drugs on the airways and/or the route of drug misuse, or social factors. These results therefore have implications for harm-reduction approaches to the treatment of substance misuse which encourages patients to move away from injecting heroin and to smoke it instead.[25] This study suggests that this may not be the most appropriate advice to give drug misusers who have respiratory disease, which may be adversely affected by smoking. The results also have implications with regard to management and diagnosis of chronic respiratory disease. Healthcare professionals coming into contact with drug misusers should have a high awareness of diagnosing/excluding chronic respiratory disease.

Further work focusing on the adequacy of diagnosis and management of respiratory disease in drug misusers is also necessary. This may lead to identification of the frequency of drug misusers with undiagnosed respiratory disease and thus be used to address the adequacy of current management leading to implementation of policy change.

Conclusions

Drug misusers have a significantly higher prevalence of respiratory diseases (asthma and COPD) and respiratory medication prescriptions than matched non-drug misusing controls after adjusting for tobacco smoking. This association between drug misuse and chronic respiratory disease has important implications for clinical practice. The results of this study could have implications for current harm-reduction practices and also in encouraging health practitioners to have a high threshold for diagnosing respiratory disease in drug misusers. Future research should aim to determine possible reasons for this association and to assess the extent of undiagnosed and inadequately managed respiratory disease in drug misusers.

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Contributorship This research was carried out by FP as a BMedSci project, supervised by MJ and MAM. Statistical analysis was conducted by DJM. Guidance was also provided by CM and JH, and SPICE data were provided by AC from PCCIU. MJ is the guarantor for the paper and had full access to all the data and took the final responsibility for the decision to submit the paper.

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Appendix 1.

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract- **p1**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **p1,2**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **p2**
Objectives	3	State specific objectives, including any prespecified hypotheses **p2**
Methods		
Study design	4	Present key elements of study design early in the paper **p2**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **p2**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls **p2**
		(*b*) For matched studies, give matching criteria and the number of controls per case **p2**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **p2**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **p2**
Bias	9	Describe any efforts to address potential sources of bias NA
Study size	10	Explain how the study size was arrived at NA – used full sample available
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **p2,3**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **p2**
		(*b*) Describe any methods used to examine subgroups and interactions **p2**
		(*c*) Explain how missing data were addressed – **NA no missing data**
		(*d*) If applicable, explain how matching of cases and controls was addressed **p2**
		(*e*) Describe any sensitivity analyses **p2**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **p3**
		(b) Give reasons for non-participation at each stage **NA**
		(c) Consider use of a flow diagram **NA**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **p3**
		(b) Indicate number of participants with missing data for each variable of interest **NA**
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure **p3,4**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

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		adjusted for and why they were included **p4**
		(*b*) Report category boundaries when continuous variables were categorized **p2**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **p4**
Discussion		
Key results	18	Summarise key results with reference to study objectives **p4**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **p5,6**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **p5**
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **NA**

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.