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Variations in COVID-19 vaccination uptake among people in receipt of psychotropic drugs: cross-sectional analysis of a national population-based prospective cohort

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Background

Coronavirus disease 2019 (COVID-19) has disproportionately affected people with mental health conditions.

Aims

We investigated the association between receiving psychotropic drugs, as an indicator of mental health conditions, and COVID-19 vaccine uptake.

Method

We conducted a cross-sectional analysis of a prospective cohort of the Northern Ireland adult population using national linked primary care registration, vaccination, secondary care and pharmacy dispensing data. Univariable and multivariable logistic regression analyses investigated the association between anxiolytic, antidepressant, antipsychotic, and hypnotic use and COVID-19 vaccination status, accounting for age, gender, deprivation and comorbidities. Receiving any COVID-19 vaccine was the primary outcome.

Results

There were 1 433 814 individuals, of whom 1 166 917 received a COVID-19 vaccination. Psychotropic medications were dispensed to 267 049 people. In univariable analysis, people who received any psychotropic medication had greater odds of receiving COVID-19 vaccination: odds ratio (OR) = 1.42 (95% CI 1.41–1.44). However, after adjustment, psychotropic medication use was associated with reduced odds of vaccination (OR_{adj} = 0.90, 95% CI 0.89–0.91). People who received anxiolytics (OR_{adj} = 0.63, 95% CI 0.61–0.65), antipsychotics (OR_{adj} = 0.75, 95% CI 0.73–0.78) and hypnotics (OR_{adj} = 0.90, 95% CI 0.87–0.93) had reduced odds of being vaccinated. Antidepressant use was not associated with vaccination (OR_{adj} = 1.02, 95% CI 1.00–1.03).

Conclusions

We found significantly lower odds of vaccination in people who were receiving treatment with anxiolytic and antipsychotic medications. There is an urgent need for evidence-based, tailored vaccine support for people with mental health conditions.

Keywords

Covid-19; vaccines; mental health; equity; psychotropic medicines.

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Background

The coronavirus disease 2019 (COVID-19) pandemic, caused by the novel coronavirus, SARS-CoV-2, is a global disaster that has highlighted and exacerbated health inequalities.[1] The pandemic caused depression and anxiety; non-pharmaceutical interventions led to isolation; societal disruption affected job security; and mental health services were disrupted globally.[2,3] A number of vaccines against COVID-19 have been rapidly developed and delivered. As of October 2021, four vaccines, the BNT162b2 mRNA (Pfizer-BioNTech), ChAdOx1 nCoV-19 adenoviral (Oxford-AstraZeneca), mRNA-1273 (Moderna) and Ad26.COV2-S (Janssen) vaccines have been approved by the UK Medicines and Healthcare products Regulatory Agency. The COVID-19 vaccination programme in the UK began on 8 December 2020, with priority given to older age groups, residents and staff in care homes, healthcare workers, people who are clinically extremely vulnerable, and people with informal caring responsibilities. Subsequent delivery among the general population was prioritised from older to younger age groups and towards those with specific clinical conditions. The effectiveness of the vaccination strategy in controlling transmission depends on high uptake levels in the population. High levels of vaccine hesitancy have been documented in certain groups such as young adults, females, people from ethnic minorities and those in low-income households.[4,5]

People who have mental illness, including schizophrenia, bipolar disorder, schizoaffective disorder and major depressive disorder, are at increased risk of COVID-19 infection and experience higher rates of COVID-19 hospital admission and death.[6,7] People who have mental illness have higher levels of non-communicable diseases such as cardiovascular and respiratory diseases, diabetes and cancer[8] resulting in a life expectancy 15–20 years shorter than their peers.[9] This situation arises from a complex interplay of biological, psychological and social factors, which may be partly mediated by a higher prevalence of hazardous health behaviours such as smoking, and not engaging in health protective behaviours, including health screening.[10,11] For these reasons, the UK's Joint Committee on Vaccinations and Immunisation identified people with mental illness as a priority for COVID-19 vaccination, as did, for example, the governments of Denmark, Germany and the Netherlands.[12] There have been mixed reports about uptake of COVID-19 vaccination in those with poor mental health.[4,13,14] One Danish study reported only

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slightly lower vaccine willingness among people with mental illness than among the wider population.[13]

Aims

To our knowledge, no previous study has examined COVID-19 vaccination uptake at a national level among people who have mental health conditions. It is important to understand the relationship between psychiatric morbidity and uptake of COVID-19 vaccination to understand the equity of service provision and to evaluate the effects of current approaches for reaching people who have mental health conditions. Northern Ireland has higher rates of mental health conditions compared with other UK nations, with rates 25% higher than England.[15] As of October 2021, Northern Ireland also has the lowest COVID-19 vaccination uptake of the four UK nations according to government reporting.[16] We aimed to investigate the association between mental health conditions (overall and individually) and vaccination uptake in the adult population. We used primary care dispensing of psychotropic drugs as an indicator of mental health conditions. We explored whether mental health conditions explained the lower uptake of COVID-19 vaccination among people who live in deprived areas.

Method

Data sources

We constructed a national cohort using a unique data-set consisting of national linked primary care registration, vaccination and pharmacy dispensing data. We used information on vaccination from the Vaccine Management System (VMS), linked to population data from the National Health Authority Information System (NHAIS, recording eligibility for healthcare in Northern Ireland), and data on medications dispensed by community pharmacists from the Enhanced Prescribing Database. We used emergency department attendance data and secondary care Patient Administration System data as part of the process to identify whether a person was resident in Northern Ireland. The Patient Administration System data included all acute hospital sites in Northern Ireland, but not all mental health and intellectual disability (also known as learning disability in UK heathcare) settings. Primary care consultation and diagnostic data were not available for the project. All data were linked by the unique identifier and then an anonymous data-set was made available to the research team through the Business Services Organisation's online Secure Research Platform (Supplementary Figure 1).

The cohort was defined as people aged 18 and over on 1 December 2020 and identified the vaccine status for those still alive in Northern Ireland on 9 September 2021, which was the final day of data provision. The project was approved by the Honest Broker Service Governance Board, project number 064. The study used fully anonymised data and therefore participant consent was not required.

Study population

Northern Ireland has a universal, free at the point-of-service healthcare system with eligibility based on registration in NHAIS. This register comprises the entire population registered with a GP and, for each patient, holds basic demographic information relating to age, gender and current address, as well as a unique identifier (the health and care number), which can be used for linkage across health-related data-sets. NHAIS also receives regular updates from the General Register Office on the date and cause of death, which adds to the reliability of the data. The study cohort was based on all registered individuals aged 18 years and over on 1 December 2020 and living in Northern Ireland. Residents in institutional dwellings such as care homes ($n = 14\,547$) were not included in the study as they were subject to specific targeted interventions and uptake is recognised to be uniformly high.[17] Identifying such residents is recognised to be difficult[18] but here we used any of:

(a) an indicator on NHAIS related to care home payment;
(b) residence at a property with ten or more residents with a mean age of >65 years;
(c) being aged over 70 and having more than ten reverse transcription polymerase chain reaction (RT-PCR) tests before 8 December 2020 (a proxy for participation in a care home mass testing programme); or
(d) aged over 70 and receiving the BNT162b2 vaccine before 1 February 2021, as during this period it was only available to health and social care workers and care home residents.

Other cohort attributes were derived from the household and address information in NHAIS. The unique property reference number (UPRN), which identifies individual residences such as houses and flats, was used as a proxy for households and thus to identify the number of people per household (categorised into single-person households, two-person, three or four and five or more person households). Socioeconomic status was also based on address; the UPRN was used to assign the property value used by central government to determine the level of local tax payable by each household. Property values were categorised as (<£100 000; £100 000–£124 999; £125 000–£199 999; £200 000–249 999; £250 000+). Individuals were also allocated, based on their area of residence, to quintiles of deprivation using the Northern Ireland Multiple Deprivation Measure 2017.[19]

Health status

Given the extant literature of the co-occurrence of mental and physical health problems[8] we included a measure of multimorbidity. This measure was based on a count of the number of different British National Formulary (BNF) chapters the patient had been receiving drugs from. To be included in the count, a medicine had to be prescribed in both of two 3-month periods in the 6 months before the vaccination programme was implemented. This method was adapted from one validated in other multimorbidity studies using administrative data.[20] Medications related to contraceptives (BNF chapter 7, section 3) were removed as these do not indicate an illness, and medicines related to psychiatric morbidity (BNF chapter 4 sections 1, 2 and 3) were removed from this overall measure so that they could be investigated separately.

Exposure definition

We used prescriptions to create four variables; hypnotics (BNF chapter 4.1.1) anxiolytics (BNF chapter 4.1.2), antipsychotics (BNF chapter 4.2) and antidepressants (BNF chapter 4.3). As with the general health status indicator, the medicine had to be prescribed in both 3-month periods before the start of the vaccination period to be counted. We selected the period of time before the start of the vaccination programme to avoid the possibility of any causal relationship in the opposite direction, such as one in which prescription of psychotropic medication was influenced by vaccine status.

Outcome definition

The vaccination status of patients was derived from the VMS and defined as having at least one dose of a COVID-19 vaccine up to and including 9 September 2021. The VMS collates information from any setting where vaccination is delivered – GP practice, clinic, care home, patient's home (housebound), ward (long-stay patients) and community pharmacy, the date, dose and type of all vaccines administered.

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Analytic approach

Administrative data can contain individuals who are no longer part of the study population because it is not possible to elicit the fact of their having left a region from the administrative data. Following the approach described in Vasileiou et al,[21] we assigned a weight of one to every individual who was identified as having on or after 1 January 2020 any hospital admission, emergency department attendance, any prescription dispensed, a COVID-19 test taken, or a COVID-19 vaccine administered. Individuals who had no contact with any of these healthcare services were weighted such that the sum of weights for their combined gender and 5-year age band was equal to the NISRA 2020 mid-year population estimate. This resulted in an individual weight for each record between zero and one.

We agreed a statistical analysis plan before commencing the analysis. The statistical analysis code is available on the DaCVaP GitHub repository (https://github.com/HDRUK/DaCVaP). We followed the Reporting of studies Conducted using Observational Routinely-collected Data checklist to guide transparent reporting of this cohort study.

We report results for the entire population over 18 years of age, and a subgroup analysis for the younger age groups (those aged 18–39 years), chosen *a priori* with the aim of understanding whether the same risk factors were associated with vaccination in younger age group, who had less time to get vaccinated. We described the cohort with weighted counts and percentages by strata.

We conducted logistic regression analyses with binary vaccination status that included all vaccinations up to and including 9 September 2021 as the dependent variable. The models were first adjusted for demographic, socioeconomic and health indicators with mental health prescriptions added to the fully adjusted models. Logistic regression for the vaccine status in a cross-sectional study design was used in preference to Cox proportional hazards in a longitudinal design because the date of eligibility for vaccination is difficult to define at an individual level for comorbidities, age groups, occupation, health and caregiver status in a longitudinal design. All adult age groups were eligible for vaccination in Northern Ireland at the time of our study.

Our primary outcome was any first vaccination; this included Pfizer-BioNTech, Oxford-AstraZeneca and Moderna vaccines as during the study period Janssen was not administered in Northern Ireland. Secondary outcomes were second-dose vaccination, compared with the single-dose-only population, and the unvaccinated population. As a supplementary analysis to investigate how sociodemographic factors and comorbidities influenced dispensing of psychotropic medications, we performed univariable and multivariable logistic regression with each of anxiolytic, hypnotic, antidepressant and antipsychotic use as binary dependent variables.

Weighting was necessary for the regression because the 'null' records for people who were no longer truly present in the region would otherwise introduce bias: they were by definition unvaccinated and had no contact with healthcare services, including receiving no medications. Failing to correct for this would increase the relative odds of medication use in the vaccinated group. Down-weighting them reduces this bias by reducing the overall unvaccinated subgroup who have no healthcare contacts to the size estimated in the age- and gender-specific population estimate. We used *R* version 4.1.0 and *glm* using the *weights* option for univariable and multivariable binary logistic regression with the weights described above, with Wald 95% confidence limits.

Role of the funding source

The sponsor of the study had no role in study design, data analysis, data interpretation, writing of the report, or the decision to submit the paper for publication.

Results

The cohort consisted of 1 433 814 individuals, of which 267 049 (19%) individuals had received psychotropic medication in both serial 3-month periods before the vaccination programme started. Antidepressants, used by 21% of women and 12% of men, were the most common medication, and antipsychotic medication used by 2% of the adult population was the least common; and around 3% had been prescribed hypnotics and anxiolytics.

Table 1 (and Supplementary Table 1 available at https://doi.org/10.1192/bjp.2022.36) shows the cohort characteristics on each of the four different types of medication. The use of psychotropic medication increased with age. Women were more likely to be prescribed anxiolytics, hypnotics and antidepressants than men; in the fully adjusted models, men were more likely to be prescribed antipsychotics than women (odds ratio (OR) = 1.51, 95% CI 1.47–1.55; Supplementary Table 2). Strong deprivation gradients were evident across all four mental health categories, which were attenuated upon adjusting for other characteristics.

There were substantial associations between the extent of physical ill health (as measured by the number of prescription categories dispensed in the previous 6 months) and psychotropic medication use, especially for antidepressants (OR = 19.01, 95% CI 18.54–19.49) for those on five different non-psychotropic medications compared with those on none). Comorbidity was common among mental health categories with the strongest association between antidepressants and antipsychotics, even after adjusting for other factors.

As of 9 September 2021, 1 166 917 adults had received at least one first dose vaccination in Northern Ireland (81% of the adult population). Coverage was over 90% for people aged more than 60 years and 64% for those aged 18–29. The odds of having at least one vaccination was lower in males (OR_{adj} = 0.92, 95% CI 0.92–0.93).

People who lived in the greatest value houses or least deprived areas had greater odds of vaccination (OR_{adj} = 2.12, 95% CI 2.06–2.17, and OR_{adj} = 1.54, 95% CI 1.51–1.57) in fully adjusted models. Approximately 90% of people receiving medications for two or more physical conditions had been vaccinated with at least one dose, whereas 75% of those on no such medications were vaccinated. In a univariable analysis, people on any psychotropic medication were more likely to be vaccinated than those who were not on such medications (OR = 1.42, 95% CI 1.41–1.44), however, when adjusted for demographic, socioeconomic factors and multimorbidity, having psychotropic medications was associated with a significantly reduced odds of vaccination (OR_{adj} = 0.90 95% CI 0.89–0.91).

Table 2 shows the odds of being vaccinated (with at least one dose) according to the type of psychotropic medication prescribed. In the unadjusted models, both antidepressants and hypnotics were associated with increased odds of being vaccinated; however, these were markedly reduced with adjustment for sociodemographic, socioeconomic and physical health factors. In the fully adjusted models, individuals in receipt of anxiolytics (OR_{adj} = 0.63, 95% CI 0.61–0.65), on antipsychotics (OR_{adj} = 0.75, 95% CI 0.73–0.78) and hypnotics (OR_{adj} = 0.90, 95% CI 0.87–0.93) had reduced odds of COVID-19 vaccination. Antidepressant use was not associated with vaccination (OR_{adj} = 1.02, 95% CI 1.00–1.03).

We completed analyses on second-dose vaccinations compared with unvaccinated and second dose compared with first dose only as secondary outcomes (Supplementary Table 3). The results revealed similar trends with those in receipt of anxiolytics, antipsychotics and hypnotics having a lower likelihood of vaccine uptake and there were negligible differences for those in receipt of antidepressants.

The difference between the adjusted and the fully adjusted models in Table 2 shows that controlling for mental health had

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Table 1 Variation in use of psychotropic medication according to type of medication[a] [Typesetter: In both tables please align data by adding thin spaces to numbers over 1000 as per house style for tables and ensure all alignment is then correct.]

Variable	Anxiolytics, *n* (%)	Hypnotics, *n* (%)	Antidepressants, *n* (%)	Antipsychotics, *n* (%)
Gender				
Female	26 072 (3.6)	26 816 (3.7)	153 004 (20.9)	15 266 (2.1)
Male	13 893 (2.0)	15 872 (2.3)	83 425 (11.9)	14 791 (2.1)
Age bands, years				
18–29	2901 (4.2)	6251 (9.0)	11 464 (16.4)	1030 (1.5)
30–39	5450 (3.9)	8484 (6.1)	26 222 (18.7)	2504 (1.8)
40–49	7537 (3.8)	9112 (4.6)	45 715 (23.0)	5285 (2.7)
50–59	9347 (3.6)	8959 (3.5)	59 044 (23.0)	7586 (2.9)
60–69	7362 (3.0)	5204 (2.2)	43 693 (18.1)	6058 (2.5)
70–79	5167 (2.1)	2888 (1.2)	31 136 (12.4)	4605 (1.8)
≥80	2201 (0.8)	1790 (0.6)	19 155 (6.9)	2989 (1.1)
Household				
1	9634 (5.6)	11 532 (6.7)	42 277 (24.7)	8041 (4.7)
2	10 674 (3.4)	12 785 (4.1)	60 243 (19.2)	7096 (2.3)
3–4	12 908 (2.2)	12 300 (2.1)	89 348 (15.2)	9299 (1.6)
≥5	2880 (1.9)	2466 (1.6)	18 076 (11.8)	2452 (1.6)
Missing	3869 (1.9)	3605 (1.7)	26 485 (12.8)	3169 (1.5)
Deprivation				
Most deprived	11 878 (4.3)	10 891 (3.9)	60 174 (21.7)	9768 (3.5)
2	9127 (3.1)	10 210 (3.5)	51 788 (17.7)	7012 (2.4)
3	7393 (2.5)	8529 (2.9)	46 123 (15.7)	5616 (1.9)
4	6807 (2.3)	7235 (2.4)	42 763 (14.4)	4547 (1.5)
Least deprived	4760 (1.7)	5823 (2.1)	35 581 (13.0)	3114 (1.1)
House value				
<74 999	13 451 (5.1)	13 381 (5.1)	65 084 (24.8)	10 756 (4.1)
75 000–99 999	10 618 (3.6)	10 389 (3.5)	57 954 (19.7)	7451 (2.5)
100 000–124 999	5691 (2.4)	5966 (2.6)	36 877 (15.9)	3911 (1.7)
125 000–199 999	6443 (1.7)	8105 (2.1)	49 832 (13.0)	4438 (1.2)
200 000–249 999	1227 (1.2)	1637 (1.6)	10 448 (10.1)	838 (0.8)
>250 000	927 (0.9)	1482 (1.5)	8237 (8.4)	674 (0.7)
Missing	1608 (2.8)	1728 (3.0)	7997 (13.7)	1989 (3.4)
Settlement band				
Urban	10 426 (3.6)	9062 (3.1)	54 972 (19.1)	8058 (2.8)
Intermediate	19 508 (2.9)	21 068 (3.2)	116 372 (17.4)	14 682 (2.2)
Rural	10 031 (2.1)	12 558 (2.6)	65 085 (13.6)	7317 (1.5)
Physical multimorbidity				
0	3975 (0.5)	3698 (0.5)	49 036 (6.1)	5174 (0.6)
1	6711 (2.7)	6510 (2.6)	48 285 (19.4)	5747 (2.3)
2	7403 (4.7)	7857 (5.0)	43 370 (27.5)	5567 (3.5)
3	7526 (7.4)	8220 (8.0)	37 866 (37.0)	5021 (4.9)
4	6189 (9.9)	7090 (11.3)	27 825 (44.5)	3957 (6.3)
5	8161 (14.9)	9313 (17.0)	30 047 (54.7)	4591 (8.4)
Anxiolytics				
No	–	30 576 (2.2)	208 112 (14.9)	21 646 (1.6)
Yes	39 965 (100.0)	12 112 (30.3)	28 317 (70.9)	8411 (21.0)
Hypnotics				
No	27 853 (2.0)		209 609 (15.1)	22 514 (1.6)
Yes	12 112 (28.4)	42 688(100.0)	26 820 (62.8)	7543 (17.7)
Antidepressants				
No	11 648 (1.0)	15 868 (1.3)	–	7789 (0.7)
Yes	28 317 (12.0)	26 820 (11.3)	23 6429 (100.0)	22 268 (9.4)
Antipsychotics				
No	31 554 (2.2)	35 145 (2.5)	21 4161 (15.3)	–
Yes	8411 (28.0)	7543 (25.1)	22 268 (74.1)	30 057 (100.0)

a. Data represent the counts and percentages of people who were prescribed the medication according to classification category. The percentage is the number of people prescribed the column medicine, out of the weighted row population (shown in Table 2).

only marginal effects on the vaccination uptake among people who were deprived (by area or house value). Before adjustment for psychotropic medication use there was a twofold difference in odds of vaccination between those living in the more expensive compared with less expensive housing (OR_{adj} = 2.14, 95% CI 2.08–2.20) and a marked difference between the least and most deprivation quintiles (OR_{adj} = 1.55, 95% CI 1.52–1.58); adjustment for psychotropic medications had virtually no effect on these socioeconomic gradients.

Supplementary Table 4 presents the unadjusted and adjusted ORs for vaccine uptake in those under 40 years of age. There was a similar trend in the under 40 population with variations across different types of mental health issues. Antidepressants were associated with increased odds of vaccination in the unadjusted and fully adjusted models, and all other types of psychotropic medications were associated with decreased odds of vaccination. In the fully adjusted analyses, the use of anxiolytics was associated with reduced odds of vaccination (OR_{adj} = 0.57, 95% CI 0.53–0.60). Individuals who were prescribed antipsychotics (OR_{adj} = 0.75, 95% CI 0.71–0.80) and hypnotics (OR_{adj} = 0.78, 95% CI 0.72–0.84) had lower odds of vaccination compared with those who did not receive those medicines.

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Table 2 Unadjusted and adjusted odds ratios for examining variation (weighted) in full cohort[a]

	Cohort, *n* (column %)	Vaccinated, *n* (row %)	Unadjusted OR (95% CI)	Adjusted (95% CI)	Fully adjusted (95% CI)
Gender					
Female	732 504 (51.1)	603 293 (82.4)			
Male	701 310 (48.9)	563 624 (80.4)	0.88 (0.87–0.88)	0.93 (0.92–0.94)	0.92 (0.92–0.93)
Age bands, years					
≥80	69 745 (4.9)	63 263 (90.7)			
70–79	139 927 (9.8)	131 327 (93.9)	1.56 (1.51–1.62)	1.56 (1.51–1.62)	1.58 (1.52–1.64)
60–69	198 712 (13.9)	184 363 (92.8)	1.32 (1.28–1.36)	1.43 (1.38–1.48)	1.47 (1.42–1.51)
50–59	257 166 (17.9)	228 744 (88.9)	0.82 (0.80–0.85)	0.97 (0.94–1.00)	1.01 (0.98–1.04)
40–49	242 023 (16.9)	201 523 (83.3)	0.51 (0.50–0.52)	0.66 (0.64–0.68)	0.69 (0.67–0.71)
30–39	250 532 (17.5)	181 014 (72.3)	0.27 (0.26–0.27)	0.39 (0.37–0.40)	0.40 (0.39–0.41)
18–29	275 708 (19.2)	176 683 (64.1)	0.18 (0.18–0.19)	0.26 (0.26–0.27)	0.27 (0.26–0.28)
Household					
1	171 428 (12.0)	144 490 (84.3)			
2	314 104 (21.9)	270 818 (86.2)	1.17 (1.15–1.19)	1.12 (1.10–1.14)	1.11 (1.09–1.13)
3–4	587 909 (41.0)	481 910 (82.0)	0.85 (0.84–0.86)	1.17 (1.15–1.19)	1.15 (1.13–1.17)
5+	153 372 (10.7)	107 976 (70.4)	0.44 (0.44–0.45)	0.73 (0.72–0.75)	0.72 (0.70–0.73)
Missing	207 001 (14.4)	161 723 (78.1)			
Deprivation					
Most deprived	276 734 (19.3)	205 196 (74.1)			
2	293 043 (20.4)	232 596 (79.4)	1.34 (1.33–1.36)	1.12 (1.10–1.13)	1.11 (1.10–1.13)
3	293 343 (20.5)	240 691 (82.1)	1.59 (1.57–1.61)	1.22 (1.20–1.24)	1.21 (1.19–1.23)
4	297 232 (20.7)	249 682 (84.0)	1.83 (1.81–1.85)	1.30 (1.28–1.32)	1.29 (1.27–1.32)
Least deprived	273 462 (19.1)	238 752 (87.3)	2.40 (2.36–2.43)	1.55 (1.52–1.58)	1.54 (1.51–1.57)
House value					
<74 999	262 813 (18.3)	198 538 (75.5)			
75 000–99 999	294 879 (20.6)	229 647 (77.9)	1.14 (1.13–1.15)	1.22 (1.20–1.24)	1.21 (1.20–1.23)
100–124 999	232 607 (16.2)	189 820 (81.6)	1.44 (1.42–1.46)	1.46 (1.44–1.48)	1.45 (1.42–1.47)
125–199 999	384 088 (26.8)	328 731 (85.6)	1.92 (1.90–1.95)	1.82 (1.79–1.84)	1.80 (1.77–1.83)
200–249 999	103 176 (7.2)	90 218 (87.4)	2.25 (2.21–2.30)	2.11 (2.05–2.16)	2.08 (2.03–2.14)
>250 000	97 852 (6.8)	86 164 (88.1)	2.39 (2.34–2.44)	2.14 (2.08–2.20)	2.12 (2.06–2.17)
Missing	58 399 (4.1)	43 799 (75.0)			
Settlement band					
Urban	288 136 (20.1)	223 796 (77.7)			
Intermediate	668 530 (46.6)	544 803 (81.5)	1.27 (1.25–1.28)	1.04 (1.03–1.06)	1.04 (1.03–1.06)
Rural	477 147 (33.3)	398 318 (83.5)	1.45 (1.44–1.47)	1.12 (1.11–1.14)	1.12 (1.10–1.14)
Prescriptions					
0	807 784 (56.3)	608 279 (75.3)			
1	248 418 (17.3)	215 180 (86.6)	2.12 (2.1–2.15)	1.4 (1.38–1.42)	1.44 (1.41–1.46)
2	157 820 (11.0)	141 761 (89.8)	2.90 (2.85–2.95)	1.56 (1.52–1.59)	1.63 (1.60–1.67)
3	102 251 (7.1)	93 043 (91.0)	3.31 (3.24–3.39)	1.70 (1.65–1.74)	1.83 (1.78–1.88)
4	62 598 (4.4)	57 589 (92.0)	3.77 (3.66–3.88)	1.87 (1.81–1.93)	2.07 (2.0–2.14)
5	54 943 (3.8)	51 065 (92.9)	4.32 (4.18–4.46)	2.12 (2.04–2.2)	2.44 (2.35–2.54)
Anxiolytics					
No	1 393 849 (97.2)	1 134 650 (81.4)			
Yes	39 965 (2.8)	32 267 (80.7)	0.96 (0.93–0.98)	–	0.63 (0.61–0.65)
Hypnotics					
No	1 391 126 (97.0)	1 130 053 (81.2)			
Yes	42 688 (3.0)	36 864 (86.4)	1.46 (1.42–1.5)	–	0.90 (0.87–0.93)
Antidepressants					
No	1 197 385 (83.5)	964 663 (80.6)			
Yes	236 429 (16.5)	202 254 (85.5)	1.43 (1.41–1.45)	–	1.02 (1.00–1.03)
Antipsychotics					
No	1 403 757 (97.9)	1 143 196 (81.4)			
Yes	30 057 (2.1)	23 721 (78.9)	0.85 (0.83–0.88)	–	0.75 (0.73–0.78)

a. Adjusted models excluded mental health.

Discussion

Main findings

Overall, approximately one in five adults in Northern Ireland were in receipt of a psychotropic medication, and this was a significant risk factor for lower uptake of the COVID-19 vaccines after adjustment for sociodemographic and health characteristics. There was evidence that the degree of disparity varied according to the type of medication, with the most extreme effects in those prescribed anxiolytics and antipsychotics. This trend persisted when we restricted the analyses to the under 40 years of age population, with more extreme odds ratios for those who were under 40 and in receipt of anxiolytics and hypnotics. We demonstrated that the higher prevalence of mental health conditions among people who live in more deprived areas did not explain the marked social gradients in vaccination uptake.

To our knowledge, this is the first nationwide study investigating variation in COVID-19 vaccination uptake among individuals with severe and common mental health disorders. Our whole-population study was conducted at a time when all adults were eligible, in contrast to two early reports.[4,14]

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Limitations

The findings should be interpreted in the context of some methodological limitations that relate mainly to the use of psychotropic medications as proxy for mental health conditions, which was a methodological choice made as a result of the absence of individual-level primary and secondary care diagnostic data. We could have chosen to use admission to psychiatric in-patient services, which would have the benefit of high specificity but would have excluded the much larger proportion of psychiatric ill health that is managed in the community. Primary care data are not yet available for population-wide record-linkage research studies in Northern Ireland, although they too may lack precision.[22] There is an established body of literature that uses psychotropic medications as an indicator of mental ill health in countries where access to primary care data are limited. For example, this approach was recently used in Manitoba, Canada, to indicate changes in mental health in children and adolescents during the COVID-19 pandemic.[23] The benefits of using psychotropic medication as a proxy for mental ill health include population-wide coverage and reasonable face validity. The limitations include the potential for confounding by variation in access to health services and in the availability of non-pharmacological treatments. The use of psychotropic medications for relatively common non-psychiatric conditions is also a significant consideration. However, most of these caveats will lead to an underestimation of the size of the association between poor mental health and vaccine uptake rather than producing a spurious association. For example, a misclassification of patients with true mental ill health, either because they are being treated non-pharmacologically or because we do not have access to clozapine prescriptions which, in Northern Ireland, is only dispensed in secondary care, will tend to reduce the difference between psychiatric patients and the rest of the population. The misclassification bias arising from the inclusion of people who have been prescribed psychotropic medications for physical, rather than for mental, health problems is also more likely to lead to an underestimation of the association between poor mental health and vaccinations rather than being an explanation of it, because, as we have shown, people with physical health problems are more likely to receive vaccination and that this increases with the number of conditions.

Uncertainty about the true population size from administrative data is a potential source of bias, as people who have left the region but whose records cannot detect this will become part of the unvaccinated group who do not receive medicines. Weighting them to compensate for these extra records relies on the population estimate; if the population estimate was very inaccurate this could result in over- or underweighting people in the cohort who genuinely were in the region but had no contact with healthcare services.

Ethnicity is not recorded in NHAIS, and therefore we could not adjust for it. We excluded care home residents from our study, because this group received very specific interventions and prioritisation for the administration of COVID-19 vaccinations. The results of our study may not be generalisable to other countries, given the high prevalence of medication use for mental health in Northern Ireland; however, they are keeping in line with the few studies reporting lower uptake of COVID-19 vaccinations in people with severe mental illness.[4,14]

Interpretation of our findings

The causes of the reduced odds of COVID-19 vaccination associated with mental health conditions are probably complex and multifactorial and may differ according to the condition. The reduced odds of vaccination for people who were prescribed antipsychotics is consistent with an Israeli study that found those with schizophrenia had lower and later uptake of vaccination compared with the general population,[14] and pre-publication findings from OpenSAFELY that reported lower uptake of COVID-19 vaccinations in those with severe mental illness early in the implementation of the vaccination programme.[4] It is reported that individuals with severe mental illness are less likely to engage with health-promoting activities, which may be related to difficulties accessing services, fears about immunisation, as well as difficulties in following and applying government guidance.[24] Regardless of the mechanism, the finding that people with mental health conditions, who are at high risk of symptomatic COVID-19 disease and experience higher rates of hospital admission and death,[6,7] have reduced odds of being vaccinated, should prompt investigation to understand and remedy this situation.

Although we do not have evidence to allow us to infer the reason for it, the lower uptake in individuals who were prescribed anxiolytics might be related to fears about the safety of COVID-19 vaccines[25] and perhaps avoidance behaviours that are common in anxiety disorders.[26] Hypnotic medication was associated with reduced odds of vaccination, particularly pronounced in younger people. Reports suggest that sleep problems and hypnotic prescriptions have increased during the pandemic, particularly, in younger age groups.[27,28] Sleep disturbances may interfere with executive cognitive functioning,[29] although the side-effects of hypnotics, such as drowsiness, memory impairment and psychomotor limitations might contribute to lower uptake. On the other hand, there was no association between use of antidepressants and vaccine uptake for the population as a whole and a weak positive association in younger people. This is an unexpected finding in the context of the association between vaccination and the other psychotropic medications. It may be because of the complex interaction between depression and physical comorbidities that has been noted for influenza vaccination uptake.[30] Investigation of this relationship in an independent cohort may yield further insights.

Implications

Vaccination is an important mechanism for reducing harm and disruption from the COVID-19 pandemic. Modelling suggests that vaccination improve the mental health of those most at risk of deaths or hospital admission by reducing levels of anxiety, although perhaps not for younger people who were at lower risk of harm from COVID-19.[31] We urgently need innovative, evidence-based approaches to support people who have mental health conditions to be vaccinated. It is likely that this should include endorsement of vaccination from trusted sources and offering opportunistic or scheduled vaccination associated with routine mental healthcare contacts, such as through community psychiatric services and pharmacies.[32] Monitoring and evaluation of such interventions will be crucial.

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Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1192/bjp.2022.36.

Data availability

The data used in this study are available in the Honest Broker Service (HBS) within the Business Services Organisation Northern Ireland (BSO), but as restrictions apply, they are not publicly available. All proposals to use data are subject to review by an independent HBS Governance Board (HBSGB). Before any data can be accessed, approval must be given by the HBSGB. When access has been granted, it is gained through a privacy protecting safe haven and remote access system. HBS has established an application process to be followed by anyone who would like to access data, which can be found at https://hscbusiness.hscni.net/services/2454.htm

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Author contributions

D.O.R., S.M. and D.T.B. conceived this study. S.M. drafted the protocol, which was contributed to by D.O.R. and D.T.B. Both S.M. and D.T.B. conducted all analyses and verified the data. S.M. drafted the manuscript. All authors contributed to the study design and revised the manuscript for important intellectual content. All authors gave final approval of the version to be published.

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Declaration of interest

D.T.B. is jointly employed by Queen's University Belfast, the Public Health Agency and the Department of Health (Northern Ireland) and is currently, or has been, a member of COVID-19 advisory groups in Northern Ireland and the UK including the UK Scientific Advisory Group for Emergencies and several of its subgroups. A.S. is a member of the Scottish Government Chief Medical Officer's COVID-19 Advisory Group and the New and Emerging Respiratory Virus Threats (NERVTAG) Risk Stratification Subgroup. C.R. is a member of the Scientific Pandemic Influenza Group on Modelling (SPI-M). All other authors report no conflicts of interest. S.V.K. acknowledges funding from a NRS Senior Clinical Fellowship (SCAF/15/02), the Medical Research Council (MC_UU_00022/2) and the Scottish Government Chief Scientist Office (SPHSU17). R.K.O. is a member of the National Institute for Health and Care Excellence Technology Appraisal Committee.

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