the different treatments. SSRIs mainly have direct beneficial effects on the two affective symptoms, which is in line with an individual patient meta-analysis comparing SSRIs to a placebo control condition[9]. The most important indirect effects of SSRIs are found for all cognitive symptoms, including highly clinically relevant symptoms such as suicidal thoughts and loss of interest, and specific arousal/somatic symptoms. SSRIs have detrimental effects on two specific arousal symptoms (i.e., somatic anxiety and agitation), which are common side effects of SSRIs that can be captured by the HDRS.

We also found that information from these networks could help in improving the identification of patients who were the most likely to benefit from one treatment relative to the other. That is, patients who suffered more from depressed mood and psychic anxiety and less from somatic anxiety and agitation were the most likely to benefit from SSRIs, whereas the opposite was true for CBT. It is, however, important to note that effect sizes were small (Cohen's d ranging from .10 in Q1 to –.16 in Q4), somewhat limiting the relevance of findings for clinical practice.

A symptom-specific approach is valuable, but also challenging, as more research is needed on the reliability and validity of assessing individual symptoms with individual (HDRS) items. In addition, the current categorization of symptoms – just like any categorization – may be overly simplistic, as, for example, affective symptoms may also comprise a cognitive component and cognitive symptoms an affective component. However, we do want to emphasize that a symptom-specific approach is highly promising in capturing the complex clinical response to depression treatments and in guiding the personalization of treatments.

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COVID-19 vaccination uptake in people with severe mental illness: a UK-based cohort study

The COVID-19 pandemic has exacerbated pre-existing health inequalities between people with severe mental illness (SMI) and the general population. These inequalities are rightly regarded as a human rights issue[1]. Rapidly accumulating evidence indicates that people with SMI are disproportionately affected by COVID-19 infection, showing increased risks of hospitalization and mortality[2].

Attention has recently turned to equitable COVID-19 vaccine allocation. Drawing on ethical frameworks, there have been calls – the first one appearing in this journal[3] – to prioritize people with SMI for vaccination. Having been severely affected by the pandemic, the UK has been among the fastest countries worldwide to deploy its vaccination plan and one of the few countries to explicitly prioritize persons with SMI[4]. Evidence on vaccine uptake among population subgroups in the UK is emerging[5]. However, more fine-grained evidence of uptake among people with different psychiatric diagnoses is necessary to evaluate delivery of vaccination plans and inform mental health practitioners.

We are investigating COVID-19 outcomes using de-identified electronic health record data from the Greater Manchester Care Record (GMCR), a shared care record for 2.8 million people, comprising real-time information from primary care, hospital admissions and mental health records. Using the GMCR, we compared vaccination rates in a sample of 1,152,831 adults with and without SMI. Individuals were followed up until June 30, 2021, ahead of the UK's relaxation of COVID-19 restrictions on July 19, 2021. Approval was granted by GMCR's secondary uses and research governance process.

All patients who were registered with a general practitioner in Greater Manchester on January 31, 2020, aged 18 years or over, and with a lifetime diagnosis of SMI recorded in their primary care record, were eligible for inclusion in the SMI sample. This sample was divided into three hierarchically defined, mutually exclusive groups of individuals with schizophrenia or related psychotic disorders (N=46,859), bipolar disorder (N=3,461), and recurrent major depressive disorder (N=134,661). Alongside this, we also obtained a 10% sample of individuals with diagnoses of other depressive disorders, excluding all previously mentioned diagnoses (N=45,586). For comparison purposes, we obtained records for 922,264 age and gender-matched controls with no evidence of SMI or depressive disorders, sampled at a 4:1 ratio

against cases.

Our outcome measure was the proportion of individuals who received at least one dose of COVID-19 vaccine by June 30, 2021, as recorded in their primary care records. We also sought to examine the proportions of individuals recorded as having declined vaccination. Conditional logistic regression models were used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CIs). Analyses controlled for sociodemographic covariates, including age, gender, ethnicity and Index of Multiple Deprivation (IMD) decile. Imputation was used for missing ethnicity (N=105,407; 9.1%), IMD (N=1,734; 0.2%) and gender (N=121; <0.1%) data. All statistical analyses were performed in R version 4.0.0.

Compared to matched controls, vaccination rates were highest among people with recurrent major depression (77.1%; aOR=1.22, 95% CI: 1.21-1.23), followed by bipolar disorder (75.7%; aOR=1.19, 95% CI: 1.14-1.23), other depressive disorders (75.1%; aOR=1.19, 95% CI: 1.18-1.20), and psychotic disorders (69.6%; aOR=1.03, 95% CI: 1.01-1.04). The prevalence of vaccination among all controls was 68.4%.

The proportion of individuals recorded as having declined vaccination by June 30, 2021 among all controls was 2.0%. Rates of having been recorded as declining vaccination were significantly higher across all mental disorders examined, with psychotic disorder diagnoses highest (5.0%; aOR=2.32, 95% CI: 2.22-2.42), followed by bipolar disorder (3.8%; aOR=1.91, 95% CI: 1.60-2.27), recurrent major depression (2.9%; aOR=1.43, 95% CI: 1.38-1.48) and other depressive disorders (2.8%; aOR=1.40, 95% CI: 1.32-1.48).

This is one of the few research studies internationally to report on COVID-19 vaccination uptake among people with mental disorders[5,6]. Our results show that people with SMI, particularly those with mood disorders, were significantly more likely to be vaccinated against COVID-19 than people without SMI. Despite this, however, individuals with psychiatric diagnoses, and particularly those with schizophrenia or related psychotic disorders, were significantly more likely to have a record of having declined vaccination for COVID-19.

A prior UK study reported that vaccination rates among people with SMI were significantly lower than people without SMI[5], but this analysis was restricted up until March 2021 among people aged 80 years and over. A study from Israel[6] – a country which also acted proactively regarding COVID-19 vaccination – also reported lower odds of vaccination among people with schizophrenia. Whilst it is encouraging that we did not see this gap in the UK, it seems that a significant proportion of people with SMI, and people with psychotic disorders in particular, remained unvaccinated as of June 30, 2021. This is concerning, given the higher rates of comorbid physical diseases observed in these groups, which may increase their risk of COVID-19 hospitalization and mortality[2], particularly as new variants arise and social distancing restrictions subside.

The higher odds of having declined a vaccine among people with SMI, and psychotic disorders in particular, warrant further attention. Taken at face value, this could indicate heightened vaccine hesitancy among people with SMI. Alternatively, this could merely be an artefact of vaccine deployment processes, reflecting that health care professionals may have more actively offered, discussed and/or recorded attempts to promote vaccination with people with SMI, thus resulting in the higher rates of recording declined vaccination offers.

While our results are limited to Greater Manchester, this constitutes a sizeable and important population in Northern England, a region known to have been disproportionately impacted by COVID-19[7]. Subtly different choices in data sources, regional boundaries and population denominators may have resulted in differences between our prevalence estimates and those recorded by central government. Furthermore, controls were matched using age and gender, but not comorbidities; thus, controls were likely to be physically healthier.

The notably higher odds of declining vaccination recorded among people with SMI, and particularly those with psychotic disorders, indicates that more targeted efforts may be required to support informed decision-making and encourage vaccine uptake among these vulnerable populations, while respecting personal autonomy.

Addressing the range of individual and systemic level barriers to vaccination that may apply among people with SMI warrants urgent investigation[8]. Alongside this, future research should explore the extent to which clinical and psychological predictors explain vaccination uptake and refusal among people with SMI.

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