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Original article

Association of Covid-19 vaccination uptake with recorded self-harm, neurodevelopmental disorders and mental health conditions during the Covid-19 pandemic: A nationwide e-cohort study in Wales, UK

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ABSTRACT

Background: Understanding COVID-19 vaccine uptake among individuals who self-harm or with mental health conditions is critical to addressing health inequalities and guiding public health strategies/pandemic preparedness. Evidence on temporal trends and sociodemographic factors shaping vaccine uptake within these populations remains limited.

Methods: We linked Wales Immunisation System data to demographic and healthcare records for 2.2 million individuals. Using modified Poisson regressions and growth models, we explored the association between self-harm, neurodevelopmental disorders, mental health conditions, and vaccine uptake from 8 December 2020–8 December 2023. Models were adjusted for age, sex, deprivation, ethnicity, and physical comorbidities.

Findings: Attention Deficit Hyperactivity Disorder (ADHD), conduct disorder, drug use, and, to a lesser extent, self-harm were associated with lower incidence of vaccination. Conversely, those with autism spectrum disorder, or learning difficulty had slightly higher incidence of vaccination. Individuals with severe mental illness (SMI: schizophrenia, bipolar disorder and other psychotic disorders) exhibited a steeper initial increase and earlier peak in uptake, but their final coverage was lower. Belonging to an ethnic minority group and, to a lesser extent, being male, younger, or leaving in highly deprived areas were also associated with reduced uptake.

Interpretation: Disparities in vaccine uptake exist among individuals with self-harm and mental health conditions, driven by intersecting health and social factors. Tailored interventions, effective communication, and trust-building strategies are critical to reducing these inequities. Underserved groups including those with SMI, ADHD, and self-harm, should be prioritised in future vaccination campaigns to improve equity.

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Research in context

Evidence before this study

We searched PubMed and Medline for the terms: *(COVID-19 vaccine) AND (mental health OR self-harm OR ASD OR ADHD OR depression OR anxiety OR schizophrenia OR bipolar disorder OR (alcohol AND misuse) OR (drugs AND misuse) OR (learning AND difficulties) OR (conduct AND disorder)) NOT (meta-analysis OR systematic review OR review) NOT (vaccine efficacy) NOT (adverse events) NOT(infection) NOT (side effects OR complication) NOT (vaccine-induced) NOT (psychopharmacology) NOT (transmission) NOT (serological) NOT (wastage) NOT (stroke OR myocarditis) NOT (hospitalization) NOT (children OR child OR childhood) NOT (safety OR sequelae) AND (electronic records OR population data)* on the 9th of July 2024. Seven articles were found in Medline and 32 articles were found in PubMed initially. We subsequently excluded six articles from low-quality/'predatory' journals, and another fifteen as not relevant after initial screening. The final selection included 18 original research papers. Overall, most evidence before this study showed a positive association between mental health disorders and COVID-19 vaccine hesitancy. The majority were cross-sectional and/or based on self-report, and therefore did not actually assess actual rates of COVID-19 vaccination uptake, nor it's trajectory over time. *Few studies have systematically examined COVID-19 vaccination uptake at the population level. The available evidence suggests an overall negative association between mental health conditions and vaccination uptake.* Notable exceptions are a potential positive association between people with severe mental illness (SMI) being more likely to be vaccinated against COVID-19 than people without SMI in the Greater Manchester area in the UK, and a higher vaccination uptake by the population with mental disorders noted in a nationwide South Korean study.

Added value of this study

This study offers a comprehensive, population-based analysis of COVID-19 vaccine uptake patterns among individuals with self-harm, neurodevelopmental disorders and mental health conditions. By linking individual-level data from the Wales Immunisation System with detailed demographic and healthcare records, it analyses a large, representative population, enabling robust and nuanced insights. The use of advanced growth models allows for an in-depth examination of temporal trends in vaccine uptake, capturing differences in progression, delays, and peak levels across various mental health conditions.

The study identifies distinct trajectories for specific groups, such as individuals with self-harm, Severe Mental Illness (SMI), and Attention Deficit Hyperactivity Disorder (ADHD), highlighting patterns of under-vaccination, slower growth in uptake, and lower final uptake. These findings move beyond static associations, presenting dynamic trends that reveal the unique challenges and disparities experienced by these populations. For instance, individuals with SMI exhibited accelerated growth of vaccine uptake during a short period of time, a trend likely driven by prioritisation policies.

Additionally, the study evaluates how sociodemographic factors—including sex, age, deprivation, and ethnicity—intersect with mental health conditions to shape vaccination outcomes. By integrating these dimensions, the research underscores the role of overlapping vulnerabilities in exacerbating health inequalities, providing actionable insights for targeted public health interventions and equitable vaccine strategies.

Implications of all the available evidence

The evidence highlights the critical need for targeted public health strategies in future pandemics to address inequalities in vaccine uptake among vulnerable populations, particularly individuals with self-harm, ADHD, and mental health conditions (e.g. SMI). These groups require sustained and tailored interventions to improve vaccine acceptance and coverage. Effective strategies should include prioritising high-risk groups, implementing condition-specific and culturally competent communication campaigns, and actively combating misinformation.

Our findings also demonstrate the significant influence of sociodemographic factors- such as being male, younger, living in deprived areas, and belonging to ethnic minority groups - on vaccination uptake trajectories. This underscores the necessity of integrated policies that address both health and social inequities. Policymakers must consider the interplay between mental health and sociodemographic factors to design inclusive vaccination campaigns that promote equitable healthcare access and outcomes. While prioritisation of individuals with SMI has shown some success, their lower final vaccine uptake indicates that additional and sustained efforts are required to mitigate barriers and ensure comprehensive coverage for all vulnerable groups.

Introduction

Prioritising COVID-19 vaccination for individuals with mental health conditions, particularly those with severe mental illness (SMI), is crucial for reducing disproportionate health risks and preparing for future pandemics. Evidence from past health crises has shown that individuals with SMI face increased infection rates, hospitalisation, and mortality [1–3]. Such vulnerabilities stem from not only pre-existing health disparities but also barriers in healthcare access, which can delay protective interventions like vaccination [4]. The elevated mortality and morbidity risks among this group underscore the importance of an inclusive and adaptive public health approach that integrates mental health in its response strategies.

The COVID-19 vaccination programme in Wales, initiated on 8 December 2020, included SMI and neurodevelopmental conditions among its priority groups. The Joint Committee on Vaccination and Immunisation (JCVI) categorised people with SMI, learning difficulties, and Autism Spectrum Disorder (ASD) in Priority Group 6, recognising them as highly vulnerable populations due to their compounded health risks [5]. The UK's decision to elevate individuals with mental health conditions within its priority framework was progressive, making it one of very few countries in Europe to prioritise this group early [6]. This decision sets a precedent for addressing health inequities in pandemic preparedness and response.

This is because research demonstrates that individuals with mental health conditions, including self-harm, depression, bipolar disorder, and schizophrenia, are at significantly higher risk of severe outcomes from COVID-19, such as hospitalisation and mortality, compared to the general population [1–3,7]. Moreover, disparities linked to socioeconomic status, ethnic minority background, and healthcare accessibility further intensify these risks, making targeted vaccination strategies essential [8]. By ensuring timely vaccine access for these populations, future public health initiatives can better mitigate the impact of emerging health threats and enhance resilience among high-risk groups. Understanding how vaccination uptake changes over time is crucial for policy development. Identifying periods of stagnation or decline enables timely, targeted

interventions to improve coverage, particularly among vulnerable populations.

Despite growing evidence on COVID-19 vaccine uptake, research on population-level trends remains limited, particularly in the context of mental health conditions. Existing studies often focus on cross-sectional analyses or specific subgroups, lacking a systematic examination of temporal trends. This study addresses this gap by analysing comprehensive population data to assess how different mental health conditions influence vaccine uptake over time. In this study we examined the association between having a diagnostic record of self-harm, attention deficit hyperactivity disorder (ADHD), ASD, learning difficulty, conduct disorder, depression, anxiety, eating disorder, bipolar disorder, schizophrenia, other psychotic disorders, alcohol or drugs use, and COVID-19 vaccine uptake in the Welsh population aged 16 and above. We adjusted for sex, age, physical comorbidities, ethnicity, and socioeconomic deprivation. We also analysed the progress of COVID-19 vaccine uptake by studying the cumulative uptake over the first year of the roll-out. This analysis aims to inform and improve public health strategies for vulnerable populations in future pandemics.

Methods

Study design and participants

The index date was set on the 8th December 2020 [9] which corresponds to the start of the vaccination programme in the UK. In this nationwide, retrospective, electronic cohort study, we derived our cohort from 3,620,119 individuals in the Wales immunization system (WIS - A national, patient-level vaccination register) to include all individuals aged 16 years and over who were alive and living in Wales at the index date, and who had linked sex (male or female), age, deprivation, and were registered to a GP providing data to the Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com) for at least one year before the index date (Supplementary figure 1). Ethical approval was granted from the Secure Anonymized Information Linkage (SAIL) Information Governance Review Panel (an independent body consisting of a range of independent government, regulatory, and professional agencies, in line with ethical permissions already granted to the analysis of data in the SAIL Databank) – approval number 1537. The SAIL Databank is a secure, remotely accessible, privacy-protecting trusted research environment that curates linked de-identified data from multiple sources at individual, household and geographical levels for the population of Wales. All data within SAIL is treated in accordance with the Data Protection Act 2018 and is compliant with the General Data Protection Regulation. Under permissions granted to the SAIL Databank, individuals' informed consent was not necessary. Results were requested out of the SAIL gateway and reviewed independently to ensure they comply with its information governance policies [10,11].

Procedures

We linked data on an individual level using a unique anonymised linkage field that replaces any identifiable information, such as names and addresses within the SAIL databank. Datasets used were Covid Vaccination Dataset (CVVD), Welsh Demographic Service Dataset (WDSD), Annual District Death Extract (ADDE), ONS 2011 Census Wales (CENW), Welsh Longitudinal General Practice Dataset (WLGP), Patient Episode Dataset for Wales (PEDW), and Emergency Department Dataset (EDDS). Full details and references in supplementary table 1.

We queried primary care (WLGP), hospital admission (PEDW), and emergency services (EDDS) data within the SAIL Databank to identify records of self-harm, neurodevelopmental disorders (ASD, and ADHD), and mental health conditions (depression, anxiety, eating disorder, bipolar disorder, schizophrenia, alcohol use disorder, and drug use disorder) at any time point prior to 8 December 2020. Diagnoses were identified using validated clinical code lists and algorithms, based on clinical coding systems Read code (Version 2) for primary care, ICD-10 codes for hospital admissions, and both ICD-10 and NHS Wales Data Dictionary (www.datadictionary.wales.nhs.uk) for emergency services. The full definition, method of development, validation details are openly accessible in the Adolescent Mental Health Data Platform – Concept Library (https://conceptlibrary.saildatabank.com/ADP/phenotypes/), with further details are provided in Supplementary Table 2.

Outcomes were binary variables indicating whether a person had been vaccinated with one dose or more (1+ dose: 0/1), and vaccinated with at least three doses including potential booster doses (3+ doses: 0/1) on weekly basis from the index date (8th of December 2020) up to one-year follow-up (8th December 2021), and to the end of three-year follow-up (8th of December 2023).

Covariates included: sex (male or female); age on the 8th of December 2020 as a categorical variable that included young people (16–24 years), adults (25–64 years), and older adults (65 years and over). Given that vaccination uptake was not linearly associated with age but instead driven by policy-defined priority groups, a categorical approach for age was deemed most appropriate, and the selected age bands are in line with mental health research practices [7]. We used Welsh Index of Multiple Deprivation (an official measure of small area, approximately 1500 individuals, deprivation in Wales) quintiles, as a categorical variable from 1 (least deprived) to 5 (most deprived) [12], ethnicity (White, Black, Asian, Other, or Unknown), Charlson Comorbidity Index (CCI) as a categorical variable representing 0, 1, or 2 and more comorbidities from primary and secondary care data [13,14].

Analyses

Main analysis

We queried data within the SAIL Databank using IBM DB2 9·7 SQL. All statistical analyses were conducted in R (version 4·3·3) with R-Studio (version 2022·04·0) and Stata 18·0. Unless otherwise stated, the level of significance was set at $p = 0{\cdot}05$, with 95 % confidence intervals (CIs). We used descriptive statistics and binomial probabilities with Wilson continuity correction [15] to summarize the characteristics of the cohort. We used modified Poisson regression with robust standard error to calculate the incidence rate ratios of being vaccinated (1 + dose: 0/1) after one year of follow-up accounting for sex (M/F), deprivation quintile (from 1 – least deprived, to 5 – most deprived), age (16–24, 25–64, and 65 + years old), ethnic category (White, Black, Asian, Other, Unknown), Charlson Comorbidity Index (0, 1, or 2 and more physical comorbidities), and records of self-harm, ADHD, ASD, learning difficulty, conduct disorder, depression, anxiety, eating disorder, schizophrenia, bipolar disorder, other psychotic disorders, alcohol use, and drugs use.

Confounders were selected a priori based on existing literature and expert consensus. The final models adjusted for age, sex, socioeconomic deprivation (measured using the Welsh Index of Multiple Deprivation), ethnicity, and comorbid physical health conditions. Mental health-related exposures (self-harm, neurodevelopmental disorders, and mental health conditions) were included separately in the models. We initially explored stepwise regression to refine model selection [16], but since results were consistent with the pre-specified approach, we proceeded with the original confounder selection and removed the stepwise regression step. We also conducted sensitivity analyses to assess the incidence of being vaccinated (3 + doses: 0/1) after three years of follow-up yielding similar results.

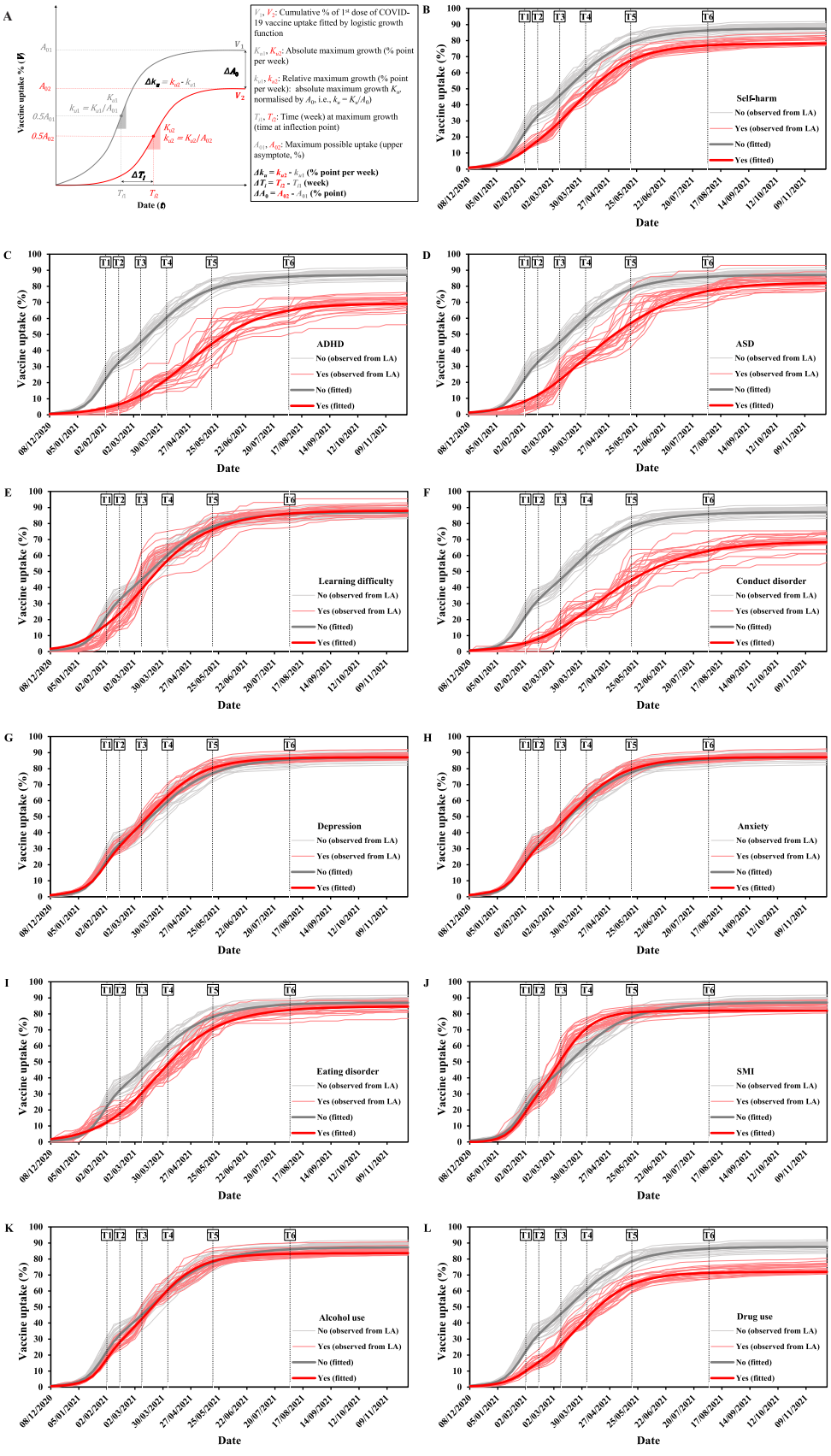

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Fig. 1. **(A)** Schematic illustration of the three-parameter nonlinear least squares (NLS) using unified-logistic function to fit the uptake (%) of the first dose of COVID-19 vaccine over time (t) for individuals with each of the 11 conditions/behaviours in this study (V_2) and the respective remaining population who were eligible to vaccination (V_1). The model estimates the relative maximum growth of uptake (k_u), time at maximum growth (T_i), maximum possible uptake (A_0), as well as the difference of these estimates between the two populations (Δk_u, ΔT_i, ΔA_0). **(B-L)** Weekly cumulative uptake (%) of the first dose of COVID-19 vaccine within 52 weeks from the vaccine roll-out date in Wales (8 December 2020) for all studied conditions/behaviours (red, see legend title) and the remaining general population (grey). ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorders; SMI: severe mental illness. Thin lines: uptake for the 22 Welsh local authorities (LAs); bold lines: model fitted ('fitted') uptake by NLS. T1: priority group (PG) 1 vaccinated; T2: PG1-4 vaccinated, PG5-6 eligible; T3: PG5 vaccinated, PG7-9 eligible; T4: PG1-9 vaccinated, PG10 eligible; T5: 18–29 years eligible; T6: 16–17 years eligible.

Cumulative vaccine uptake over the first year

To examine the uptake of the first dose of the COVID-19 vaccine over the first year, we calculated and modelled weekly cumulative vaccine uptake (%) using logistic growth functions (LGFs) with nonlinear least-squares (NLS) [17,18] (Fig. 1). We assumed a static population and used the total population at the start of the vaccine roll-out as the denominator. We estimated three parameters: k_u (growth rate in % points per week), T_i (time of maximum growth, in weeks), and A_0 (maximum uptake, in %). These parameters respectively represent the relative maximum uptake growth, the timing of peak growth, and the maximum possible uptake over time (Fig. 1A). Separate models were run for each exposure variable, including combining schizophrenia, bipolar disorder, and other psychotic disorders as severe mental illness (SMI) to increase statistical power, resulting in 11 models. Each model included three specifications (unadjusted, main-effects-only adjusted, and fully adjusted). Adjustments were made by adding linear terms to k_u, T_i, and A_0 to account for covariates and interactions (detailed in Supplementary Methods). Unadjusted and main-effects-only adjusted models estimated changes (Δk_u, ΔT_i, ΔA_0) between reference and non-reference groups (Fig. 1A). Covariates in the main-effects-only adjusted models included sex, age group, deprivation (WIMD), ethnicity, CCI, and the number of comorbidities from the 11 studied exposures, excluding the main exposure. Variables like WIMD, ethnicity, and CCI were recoded for model convergence (see Supplementary Methods for details).

We defined under-vaccination in the non-reference group as having a negative Δk_u (slower growth rate in percent per week), a positive ΔT_i (delayed peak uptake in weeks), and a negative ΔA_0 (lower final uptake in cumulative percentage).

Weekly cumulative percentages, exposures, and other covariates were input into NLS models using the 'nlsur' function in Stata 18·0. Initial values ensured model convergence, and aggregated data were weighted by their denominators. Model fit was assessed using Akaike and Bayesian information criteria, unadjusted r^2, and residual analysis. Coefficients with confidence intervals (CIs) and robust standard errors (clustered within LAs) were reported.

We plotted marginal uptake predictions over time for exposed and non-exposed groups, alongside observed trends (Fig. 1B-1L). P-values and CIs corresponded to an uncorrected significance level ($p = 0{\cdot}05$, 95 % CIs), but Šidák-adjusted p-values ($p = 0{\cdot}0016$) were also reported for 33 comparisons (11 exposures across three model specifications).

Results

We identified a population of 3,620,119 individuals from WIS. Of these 2,216,859 were older than 16 years at the start of the vaccination programme in Wales on the 8th December 2020 (index date – see Table 1), with a valid Welsh address, deprivation data, registered with a GP providing data to SAIL at the index date, with at least 1 year of GP follow-up before the index date, and with a recorded sex: male or female (Supplementary figure 1). The final cohort included 1,097,462 (49·5 % of 2,216,859) females, with 557,241 (25·1 %) aged 65 years or more, 1400,233 (63·2 %) aged 25–64 years old, and 259,935 (11·7 %) aged 16–24 years (Table 1). 1,954,951 (88·2 %) individuals had received at least one dose of COVID-19 vaccine by the end of the three-year follow-up period, and 1,660,473 (74·9 %) had at least three doses of COVID-19 vaccine at the end of follow-up (see Table 1 for further details).

Vaccinated (1+ dose) at one year of follow-up

Adjusted results (Table 2) showed that individuals with a record of ADHD, conduct disorder, and drugs use had lower incidence of vaccination after one year of follow-up. Those with recorded self-harm or schizophrenia showed a similar but weaker signal, Conversely, individuals with a record of ASD or learning difficulty had slightly higher incidence of vaccination. No relevant differences were found in the incidence of being vaccinated for the remaining conditions (95 % CIs including or very close to 1). Other factors associated with lower incidence of being vaccinated included belonging to an ethnic minority group, and, to a lesser extent, being male (versus female), from more deprived areas, and younger. Having at least one physical comorbidity was associated with slightly higher incidence of being vaccinated. Full details in Table 2, with unadjusted results available in supplementary table 3. The sensitivity analysis accounting for a minimum of three doses of vaccination at three-year follow-up yielded similar results (supplementary table 4).

Vaccinated (1+ dose) at one year of follow-up stratified by age

The results of the modified Poisson regression accounting for vaccination (1 + dose) at one year follow-up stratified by age (65 + years, 25–64 years, and 16–24 years) showed some age differences but with no consistent pattern (Table 3). Factors associated with lower incidence of being vaccinated included belonging to an ethnic minority group and, to a lesser extent, being male (versus female), younger, and living in more deprived areas. Having at least one physical comorbidity (CCI) was associated with higher incidence of being vaccinated (Table 3).

Cumulative uptake of the initial dose of COVID-19 vaccine

In the general population, vaccine uptake increased rapidly, peaking at approximately 6·0 % per week around mid-March 2021 (14 weeks after rollout) and stabilising at approximately 85·0 % by week 52. After adjusting for covariates (Fig. 2), distinct patterns of under-vaccination were observed for specific groups compared to their 'non-exposed' counterparts. Individuals with a history of self-harm demonstrated slower uptake growth (-0·9 % per week), a delayed peak uptake (+0·8 weeks), and lower final uptake (-4·6 %). Those with ADHD showed reduced growth (-0·7 % per week), a delayed peak uptake (+2·3 weeks), and substantially lower final uptake (-10·1 %). Drug use was associated with slower growth (-1·0 % per week), delayed peak uptake (+0·9 weeks), and the lowest final uptake (-12·4 %). For individuals with conduct disorder, the peak uptake was delayed by 3·0 weeks, and the final uptake was lower (-11·9 %), although growth rates were not significantly affected. People with severe mental illness (SMI) exhibited higher growth (+2·3 % per week) and an earlier peak uptake (-0·6 weeks) compared to their counterparts, but their final uptake remained lower (-4·2 %). In contrast, individuals with depression and anxiety experienced only slight reductions in growth (~0.2 % per week), minor delays in peak uptake (~0·1 weeks), and slightly elevated final uptake (+0·5 to

Table 1
Demographic information: counts and percentages with 95 % confidence intervals.

Characteristic	Subgroup	Full study sample		Vaccinated at 1-year follow-up		Not vaccinated at 1-year follow-up		Percentage of vaccine uptake at 1-year follow-up
		Count	Percentage (95 % CI)	Count	Percentage (95 % CI)	Count	Percentage (95 % CI)	
Total		**2216859**	**100·0 %**	**1939909**	**100·0 %**	**276950**	**100·0 %**	
Sex	Female	1119397	50·5 % (50·4, 50·6)	1006365	51·9 % (51·8, 51·9)	113032	40·8 % (40·6, 41·0)	89.9 % (89.8–90.0)
	Male	1097462	49·5 % (49·4, 49·6)	933544	48·1 % (48·1, 48·2)	163918	59·2 % (59·5, 59·4)	85.1 % (85.0–85.1)
Age category	65 + yr·	557241	25·1 % (25·1, 25·2)	531797	27·4 % (27·4, 27·5)	52233	18·9 % (18·7, 19·0)	95.4 % (95.4–95.5)
	25, 64 yr·	1400233	63·2 % (63·1, 63·2)	1200950	61·9 % (61·8, 62·0)	199273	72·0 % (71·8, 72·1)	85.8 % (85.7–85.8)
	16, 24 yr·	259395	11·7 % (11·7, 11·7)	207162	10·7 % (10·6, 10·7)	25444	9·2 % (9·1, 9·3)	79.9 % (79.7–80.0)
Ethnicity	White	1971056	88·9 % (88·9, 88·9)	1796771	92·6 % (92·6, 92·7)	174285	62·9 % (62·7, 63·1)	91.2 % (91.1–91.2)
	Black	11415	0·5 % (0·5, 0·5)	8773	0·5 % (0·4, 0·5)	2642	1·0 % (0·9, 1·0)	76.9 % (76.1–77.6)
	Asian	41792	1·9 % (1·9, 1·9)	36746	1·9 % (1·9, 1·9)	5046	1·8 % (1·8, 1·9)	87.9 % (87.6–88.2)
	Other	30929	1·4 % (1·4, 1·4)	24962	1·3 % (1·3, 1·3)	5967	2·2 % (2·1, 2·2)	80.7 % (80.3–81.1)
	Unknown	161667	7·3 % (7·3, 7·3)	72657	3·7 % (3·7, 3·8)	89010	32·1 % (32·0, 32·3)	44.9 % (44.7–45.2)
Deprivation[a]	1, Least deprived	449716	20·3 % (20·2, 20·3)	410333	21·2 % (21·1, 21·2)	39383	14·2 % (14·1, 14·4)	91.2 % (91.2–91.3)
	2	409810	18·5 % (18·4, 18·5)	364972	18·8 % (18·8, 18·9)	44838	16·2 % (16·1, 16·3)	89.1 % (89.0–89.2)
	3	453639	20·5 % (20·4, 20·5)	398556	20·5 % (20·5, 20·6)	55083	19·9 % (19·7, 20·0)	87.9 % (87.8–88.0)
	4	453983	20·5 % (20·4, 20·5)	393666	20·3 % (20·2, 20·3)	60317	21·8 % (21·6, 21·9)	86.7 % (86.6–86.8)
	5, Most deprived	449711	20·3 % (20·2, 20·3)	372382	19·2 % (19·1, 19·3)	77329	27·9 % (27·8, 28·1)	82.8 % (82.7–82.9)
CCI	0	1314268	59·3 % (59·2, 59·3)	1110279	57·2 % (57·2, 57·3)	203989	73·7 % (73·5, 73·8)	84.5 % (84.4–84.5)
	1	584908	26·4 % (26·3, 26·4)	527676	27·2 % (27·1, 27·3)	57232	20·7 % (20·5, 20·8)	90.2 % (90.1–90.3)
	2	317683	14·3 % (14·3, 14·4)	301954	15·6 % (15·5, 15·6)	15729	5·7 % (5·6, 5·8)	95.0 % (95.0–95.1)
Record	Self, harm	109263	4·9 % (4·9, 5·0)	86702	4·5 % (4·4, 4·5)	22561	8·1 % (8·0, 8·2)	79.4 % (79.1–79.6)
	ADHD	15773	0·7 % (0·7, 0·7)	11120	0·6 % (0·6, 0·6)	4653	1·7 % (1·6, 1·7)	70.5 % (69.8–71.2)
	ASD	12127	0·5 % (0·5, 0·6)	10007	0·5 % (0·5, 0·5)	2120	0·8 % (0·7, 0·8)	82.5 % (81.8–83.2)
	Learning difficulty	15661	0·7 % (0·7, 0·7)	13819	0·7 % (0·7, 0·7)	1842	0·7 % (0·6, 0·7)	88.2 % (87.7–88.7)
	Conduct disorder	8927	0·4 % (0·4, 0·4)	6296	0·3 % (0·3, 0·3)	2631	0·9 % (0·9, 1·0)	70.5 % (69.6–71.5)
	Depression	615596	27·8 % (27·7, 27·8)	540011	27·8 % (27·8, 27·9)	75585	27·3 % (27·1, 27·5)	87.7 % (87.6–87.8)
	Anxiety	453869	20·5 % (20·4, 20·5)	398157	20·5 % (20·5, 20·6)	55712	20·1 % (20·0, 20·3)	87.7 % (87.6–87.8)
	Eating disorder	11412	0·5 % (0·5, 0·5)	9635	0·5 % (0·5, 0·5)	1777	0·6 % (0·6, 0·7)	84.4 % (83.8–85.1)
	Bipolar disorder	12589	0·6 % (0·6, 0·6)	10660	0·5 % (0·5, 0·6)	1929	0·7 % (0·7, 0·7)	84.7 % (84.0–85.3)
	Schizophrenia	18033	0·8 % (0·8, 0·8)	14636	0·8 % (0·7, 0·8)	3397	1·2 % (1·2, 1·3)	81.2 % (80.6–81.7)
	Other psychotic disorders	20106	0·9 % (0·9, 0·9)	17168	0·9 % (0·9, 0·9)	2938	1·1 % (1·0, 1·1)	85.4 % (84.9–85.9)
	Alcohol use	142636	6·4 % (6·4, 6·5)	120435	6·2 % (6·2, 6·2)	22201	8·0 % (7·9, 8·1)	84.4 % (84.2–84.6)
	Drugs use	86547	3·9 % (3·9, 3·9)	63567	3·3 % (3·3, 3·3)	22980	8·3 % (8·2, 8·4)	73.4 % (73.2–73.7)
COVID, 19 vaccine	1 + dose	1954951	88·2 % (88·1, 88·2)					
	3 + doses	1660473	74·9 % (74·8, 75·0)					
Mental health comorbidities	0	1309094	59·0 % (59·0, 59·1)	1145437	59·0 % (59·0, 59·1)	163657	59·1 % (58·9, 59·3)	87.5 % (87.4–87.6)
	1	517967	23·4 % (23·3, 23·4)	462850	23·9 % (23·8, 23·9)	55117	19·9 % (19·8, 20·1)	89.4 % (89.3–89.4)
	2	389798	17·6 % (17·5, 17·6)	331622	17·1 % (17·0, 17·1)	58176	21·0 % (20·9, 21·2)	85.1 % (85.0–85.2)

ADHD – Attention Deficit Hyperactivity Disorder
ASD – Autism Spectrum Disorder
CCI – Charlson Comorbidity Index
* Different background colours used for the total, covariate and exposure variables
[a] Deprivation Quintile based on Wales Index of Multiplle Deprivation (WIMD)

Table 2
Modified Poisson regression accounting for COVID-19 vaccination (1 + dose) at 1-year follow-up.

			VACCINATED (on 08/12/2021)		
Variable	*Reference*	*Levels*	*Incidence Rate Ratios*	*CI*	*p*
(Intercept)			0.99	0.99 – 0.99	< 0.001
Sex	Female	Male	0.97	0.97 – 0.97	< 0.001
Deprivation: WIMD	1: Less deprived	2	0.98	0.98 – 0.99	< 0.001
		3	0.98	0.98 – 0.98	< 0.001
		4	0.97	0.97 – 0.97	< 0.001
		5: Most deprived	0.94	0.94 – 0.94	< 0.001
Age group	65 + yr.	25–64 yr.	0.95	0.95 – 0.96	< 0.001
		16–24 yr.	0.9	0.90 – 0.90	< 0.001
Ethnicity	White	Black	0.89	0.88 – 0.90	< 0.001
		Asian	0.99	0.98 – 0.99	< 0.001
		Other	0.92	0.92 – 0.92	< 0.001
		Unknown	0.51	0.51 – 0.51	< 0.001
CCI	0	1	1.03	1.03 – 1.03	< 0.001
		2 +	1.04	1.04 – 1.04	< 0.001
Self-harm	No	Yes	0.96	0.96 – 0.96	< 0.001
ADHD	No	Yes	0.89	0.88 – 0.90	< 0.001
ASD	No	Yes	1.02	1.01 – 1.02	< 0.001
Learning difficulties	No	Yes	1.04	1.03 – 1.05	< 0.001
Conduct disorder	No	Yes	0.89	0.88 – 0.90	< 0.001
Depression	No	Yes	1	1.00 – 1.00	< 0.001
Anxiety	No	Yes	0.99	0.99 – 1.00	< 0.001
Eating disorder	No	Yes	0.99	0.98 – 1.00	0.009
Schizophrenia	No	Yes	0.97	0.97 – 0.98	< 0.001
Bipolar disorder	No	Yes	1	1.00 – 1.01	0.477
Other psychotic disorder	No	Yes	1.01	1.00 – 1.02	0.002
Alcohol use	No	Yes	1	1.00 – 1.00	0.087
Drugs use	No	Yes	0.89	0.88 – 0.89	< 0.001
Observations			2,216,859		

ADHD: Attention Deficit Hyperactivity Disorder
ASD: Autism Spectrum Disorder
* Different background colours used for the intercept, covariate and exposure variables

+1·0 %). Individuals with learning difficulty exhibited slightly faster and earlier vaccine uptake, while those with alcohol use showed growth and timing similar to the general population, with slightly higher final uptake (+1·0 %).

From the analysis of all 11 NLS models (Supplementary Table 5), males showed higher but slower peak vaccine uptake growth and lower final uptake compared to females. Younger individuals were clearly under-vaccinated, with slower uptake growth (about 19 percentage points less per week for those aged 16–24 compared to the 65 + age group), a delay of about 15·6 weeks, and lower final uptake (12 percentage points lower). Living in deprived areas and belonging to an ethnic minority ('non-White') were also significant factors for under-vaccination. Individuals with physical comorbidities (measured by CCI) experienced faster, though not higher, uptake growth and higher final vaccine uptake. Further analysis showing the main effect only adjusted models, fully adjusted models, and models fit are available in supplementary tables 6-8, and yielded similar results.

Discussion

Our analysis of over 2.2 million individuals in Wales revealed significant disparities in COVID-19 vaccine uptake among people with mental health conditions. Lower incidence of vaccination were observed among individuals with recorded ADHD, conduct disorder, and drug use, and, to a lesser extent, self-harm. Conversely, those with autism spectrum disorder and learning difficulties showed a higher uptake. Notably, individuals with SMI experienced a faster and earlier uptake trajectory, likely due to prioritisation policies, but still had lower final vaccination rates. Under-vaccination patterns—characterised by slower growth, delayed peak uptake, and lower final coverage—were especially marked in those with self-harm, ADHD, and drug use. Sociodemographic disparities persisted, with lower uptake consistently associated with being male, younger, from more deprived areas, and belonging to ethnic minority groups. These findings underscore the compounded impact of mental health and social vulnerabilities on vaccine uptake.

There was a clear pattern of under-vaccination (characterised by delayed uptake (in weeks), reduced uptake growth (in % per week), and lower final uptake (in cumulative %)) among individuals with records of self-harm, ADHD, conduct disorder and drug use. The lower vaccine uptake and presence of hesitancy with COVID-19 vaccines have been reported in ADHD [19] and drug use [20] but our findings on self-harm are novel and concerning. The pattern of under-vaccination was not observed among other conditions/behaviours.

People with a recorded severe mental illness (SMI) exhibited higher growth (+2.3 % per week) and an earlier peak uptake (-0.6 weeks) compared to their counterparts, but their final uptake remained lower (-4.2 %). This increased higher growth and earlier peak uptake could be attributed to the strategy by the JVCI and the Welsh government to include individuals with SMI as priority group 6 for COVID-19 vaccines at the beginning of the vaccination programme [21]. Our findings are nevertheless consistent with the results from the UK [22] and Canada [20], suggesting that individuals with SMI did not show a decrease in uptake but still showed higher likelihood of declining vaccination [22, 23]. We did not find under-vaccination for those with learning difficulty, likely due to the inclusion of learning disability as a priority group in the vaccination programme [24].

We cannot fully disentangle the underlying reasons for the varied vaccine trends observed among different mental disorders. However, differences may be partly explained by how integrated these populations are into healthcare systems (due, in part, to prioritization schemes). In addition, the inherent nature of certain conditions may shape individuals' attitudes toward healthcare. For example, individuals with a history of self-harm might display impulsivity that contributes to higher vaccine hesitancy or inconsistent follow-up, while those with more severe symptoms may face challenges that hinder accessibility and adherence.

For sociodemographic factors, we found that being male, from more deprived areas, younger, and ethnic minority groups were associated with lower incidence of being vaccinated. Older adults (aged 65 and over) had a higher baseline probability of being vaccinated against COVID-19 compared to younger age groups. Across all age groups, self-harm, conduct disorder, and drug use were consistently associated with lower incidence of being vaccinated. These findings were in tight agreement with previous research using the same data source, showing poorer vaccine uptake for male, young age, residence in deprived areas, ethnic minorities, and lower number of physical comorbidities, a strong indication of inequality [25, 26]. Our data not only provide evidence on vaccine inequality, but also demonstrate additional role of sociodemographic factors in COVID-19 vaccine uptake for individuals who had previous history of self-harm, neurodevelopmental conditions, conduct disorder, learning difficulty, mental health problems, and substance use.

Strengths and limitations

The novelty of the analysis of the temporal trends of COVID-19 vaccine uptake lies in multiple areas. The ability to compare trends

Table 3
COVID-19 vaccination (1 + dose) at 1-year follow-up stratified by age groups (65 +, 25–64, 16–24 years old).

			VACCINATED 65 + yr.			VACCINATED 25–64 yr.			VACCINATED 16–54 yr.		
Variable	*Reference*	*Levels*	*Incidence Rate Ratios*	*CI*	*p*	*Incidence Rate Ratios*	*CI*	*p*	*Incidence Rate Ratios*	*CI*	*p*
(Intercept)			33.82	32.57 – 35.11	**< 0.001**	15.59	15.35 – 15.84	**< 0.001**	11.08	10.73 – 11.44	**< 0.001**
Sex	Female	Male	0.89	0.86 – 0.91	**< 0.001**	0.72	0.71 – 0.72	**< 0.001**	0.75	0.73 – 0.76	**< 0.001**
Deprivation: WIMD	1: Less deprived	2	0.91	0.87 – 0.95	**< 0.001**	0.8	0.79 – 0.82	**< 0.001**	0.82	0.79 – 0.85	**< 0.001**
		3	0.83	0.79 – 0.86	**< 0.001**	0.74	0.73 – 0.75	**< 0.001**	0.67	0.65 – 0.69	**< 0.001**
		4	0.73	0.70 – 0.76	**< 0.001**	0.7	0.68 – 0.71	**< 0.001**	0.56	0.54 – 0.58	**< 0.001**
		5: Most deprived	0.61	0.59 – 0.64	**< 0.001**	0.57	0.56 – 0.58	**< 0.001**	0.42	0.40 – 0.43	**< 0.001**
Ethnicity	White	Black	0.28	0.23 – 0.34	**< 0.001**	0.45	0.42 – 0.47	**< 0.001**	0.44	0.40 – 0.49	**< 0.001**
		Asian	0.49	0.43 – 0.56	**< 0.001**	0.84	0.81 – 0.87	**< 0.001**	1.1	1.02 – 1.18	**0.009**
		Other	0.41	0.35 – 0.48	**< 0.001**	0.54	0.52 – 0.56	**< 0.001**	0.52	0.49 – 0.55	**< 0.001**
		Unknown	0.05	0.05 – 0.05	**< 0.001**	0.08	0.08 – 0.08	**< 0.001**	0.11	0.11 – 0.12	**< 0.001**
CCI	0	1	1.59	1.54 – 1.65	**< 0.001**	1.34	1.32 – 1.36	**< 0.001**	1.21	1.18 – 1.24	**< 0.001**
		2 +	1.24	1.20 – 1.28	**< 0.001**	2.5	2.43 – 2.57	**< 0.001**	1.78	1.55 – 2.04	**< 0.001**
Self-harm	No	Yes	0.78	0.70 – 0.87	**< 0.001**	0.76	0.74 – 0.78	**< 0.001**	0.71	0.68 – 0.74	**< 0.001**
ADHD	No	Yes	1.46	0.79 – 2.70	0.227	0.51	0.48 – 0.54	**< 0.001**	0.69	0.65 – 0.74	**< 0.001**
ASD	No	Yes	0.74	0.41 – 1.35	0.327	0.98	0.90 – 1.07	0.608	1.23	1.14 – 1.32	**< 0.001**
Learning difficulties	No	Yes	0.94	0.74 – 1.20	0.644	1.43	1.33 – 1.55	**< 0.001**	1.42	1.30 – 1.56	**< 0.001**
Conduct disorder	No	Yes	0.47	0.30 – 0.75	**0.002**	0.54	0.50 – 0.58	**< 0.001**	0.62	0.58 – 0.67	**< 0.001**
Depression	No	Yes	1.04	1.00 – 1.08	**0.03**	1.03	1.02 – 1.04	**< 0.001**	0.88	0.86 – 0.91	**< 0.001**
Anxiety	No	Yes	1.01	0.97 – 1.05	0.626	0.93	0.91 – 0.94	**< 0.001**	0.93	0.90 – 0.96	**< 0.001**
Eating disorder	No	Yes	1.17	0.61 – 2.23	0.637	0.8	0.75 – 0.86	**< 0.001**	1.14	1.02 – 1.28	**0.02**
Schizophrenia	No	Yes	0.49	0.42 – 0.58	**< 0.001**	0.88	0.83 – 0.93	**< 0.001**	0.93	0.75 – 1.14	0.485
Bipolar disorder	No	Yes	0.91	0.75 – 1.12	0.376	0.95	0.89 – 1.02	0.159	1.34	1.03 – 1.75	**0.028**
Other psychotic disorder	No	Yes	0.81	0.69 – 0.95	**0.008**	1.08	1.02 – 1.15	**0.015**	1.23	0.99 – 1.52	0.063
Alcohol use	No	Yes	0.96	0.90 – 1.02	0.166	1.01	0.99 – 1.03	0.48	0.8	0.75 – 0.85	**< 0.001**
Drugs use	No	Yes	0.65	0.59 – 0.73	**< 0.001**	0.47	0.46 – 0.48	**< 0.001**	0.5	0.47 – 0.53	**< 0.001**
Observations			557241			1400223			259395		

ADHD: Attention Deficit Hyperactivity Disorder
ASD: Autism Spectrum Disorder
* Different background colours used for the intercept, covariate and exposure variables

of uptake for a wide range of conditions/behaviours related to self-harm, mental health, neurodiversity and substance use is important. Using three sets of parameters, we were able to examine longitudinal uptake, from the rapid growth in uptake to the stages where uptake leveled off, using well-known growth function [17]. We compared these parameters for those with and without the considered mental health-related conditions while controlling for sociodemographic and clinical factors that are known determinants of (COVID-19) vaccine uptake [27].

Concerning limitations on interpreting the findings of uptake trajectories, the use of LGF to fit vaccine uptake was a purely data-driven approach. Further research using theoretically based methodologies, e.g., based on disease transmission and behaviour change dynamics [28] could help explore plausible mechanisms of change in vaccine uptake and how these mechanisms relate to growth/uptake. Due to limitations of structured routinely collected data, we could not explore the reasons behind individuals' vaccine hesitancy (e.g., stigma, worries about effectiveness and side effects of vaccines) [19]. Nonetheless, our models adequately fit to the observed data and thus the assumption of logistic growth of COVID-19 vaccine uptake appears to be valid. Some key relevant information was unavailable, such as accurate information on priority groups assigned to each individual. Our mental health measurements were limited to those recorded in structured form in primary and secondary care routinely collected data. Several categorical variables were processed to reduce number of categories and make the analysis tenable. Due to model convergence issues, we could not investigate effect modifications by age and ethnicity in the associations between vaccine uptake and ASD, learning difficulty, conduct disorder, and eating disorder.

Implications for policy and practice

Our findings highlight significant disparities in COVID-19 vaccine uptake among people with mental health conditions—especially those with ADHD, conduct disorders, drug use, and, to a lesser extent, self-harm—calling for targeted interventions to improve access and acceptance. These underscore the value of monitoring uptake trends to guide timely public health interventions. Identifying declines allows for targeted outreach and communication strategies to improve vaccination rates.

Several policies tried to close the observed gap. Individuals with SMI, ASD, and learning difficulties were included in Priority Group 6 [5]. The Welsh Government also adopted an inclusive identification strategy that extended beyond electronic health records, encouraging collaboration between Health Boards, general practitioners, local authorities, and third-sector organizations. Clinical discretion was promoted to facilitate the inclusion of individuals in Priority Group 6 where appropriate. In addition, dedicated vaccination clinics were established to accommodate the specific needs of individuals with mental health issues, offering quieter environments and support from experienced mental health nurse vaccinators [29]. While these policies were a positive initial step that accelerated early uptake, they did not fully overcome persistent access difficulties and vaccine hesitancy.

We recommend that future vaccination programmes explicitly include other high-risk groups like those with ADHD, conduct disorder, drug use, and self-harm. Additionally, public health campaigns should partner with mental health services and community organisations to deliver culturally sensitive, condition-specific messaging that addresses stigma and misinformation [30]. Equity-driven approaches—such as mobile clinics, outreach to ethnic minority

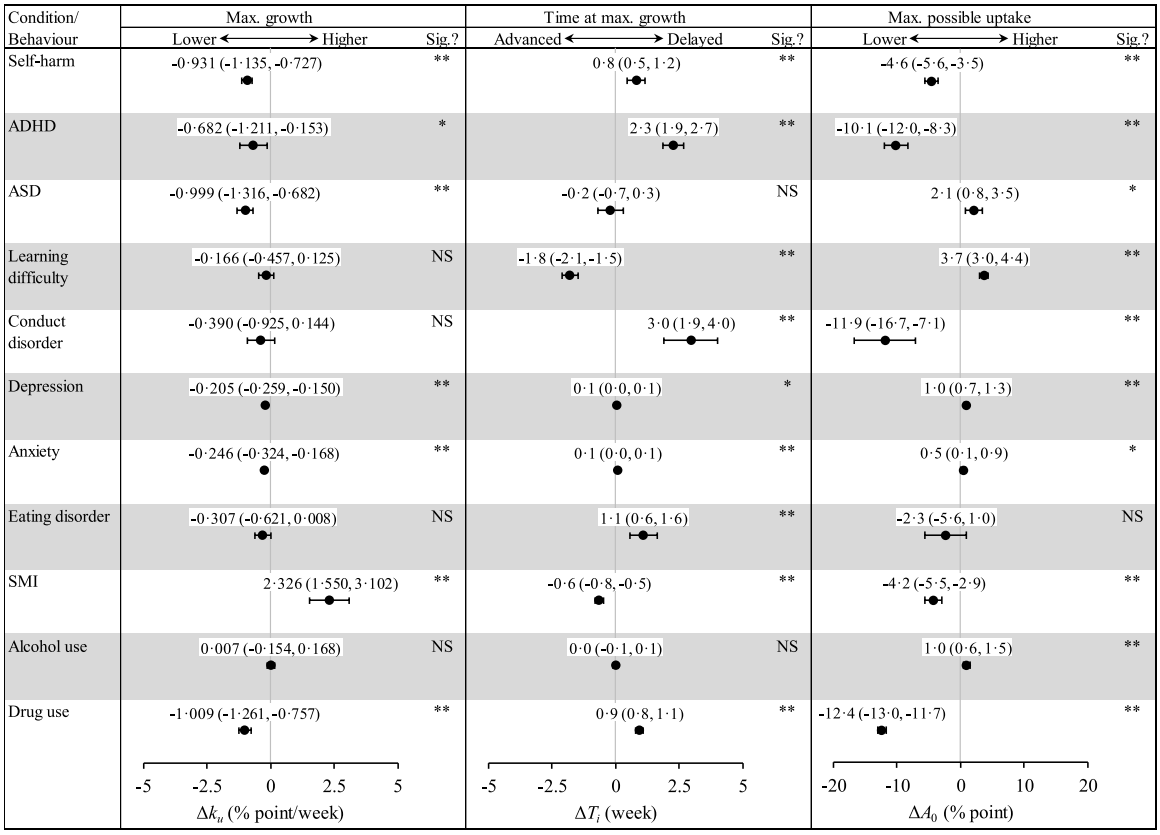

Fig. 2. Coefficients from main-effects-only adjusted NLS models comparing the first dose of COVID-19 vaccine uptake between individuals in each of the 11 'exposed' groups and the respective remaining populations (Δk_u, T_i, A_0). Models adjusted for the respective condition (as shown in figure), sex, age group, WIMD, ethnicity, CCI and the number of conditions/comorbidities less the condition already in the model. ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorders; SMI: severe mental illness. Value labels: point estimates and 95 % CIs without correction of multiple comparisons; Error bars: 95 % CIs without correction of multiple comparisons; * Significant at $p < 0.05$ without correction of multiple comparisons; ** Significant at $p < 0.05$ with Šidák correction of multiple (33) comparisons; NS: not significant.

groups, and targeted strategies for young people—are critical to address the observed, broader systemic inequalities that often disproportionately affect those with mental health issues [31].

Integrating mental health services into vaccination efforts can also embed mental health screening and support within public health responses, ensuring individuals with complex needs are not overlooked. The novel finding of under-vaccination in those who self-harm reinforces the value of condition-specific data in shaping policy. Ongoing monitoring and analysis of health and vaccination data should inform timely, adaptive responses to address the unique barriers faced by high-risk groups. By adopting these measures, policymakers can reduce health inequities, boost vaccine uptake, and strengthen public health resilience in future emergencies.

Contributors

O.Y.R. performed the data linkage, the statistical analysis and drafted the manuscript. S.C.L participated in the data analysis and drafted the manuscript. D.O. and R.S. drafted the manuscript. M.D.P.B reviewed the manuscript and the statistical analysis. A.J. conceived the study, supervised the design and coordination of the study, supervised analysis and drafted the manuscript. All authors read and approved the final manuscript.

Ethical approval

The research was approved by SAIL Information Governance Review Panel (approval number 1537).

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Declaration of Competing Interest

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Data sharing

The data used in this study are available in the SAIL Databank at Swansea University (Swansea, UK), but, as restrictions apply, they are not publicly available. All proposals to use SAIL data are subject to review by an independent Information Governance Review Panel. Before any data can be accessed, approval must be given by the Information Governance Review Panel. The Information Governance Review Panel carefully considers each project to ensure proper and appropriate use of SAIL data. When access has been granted, it is gained through a privacy-protecting safe haven and remote access system referred to as the SAIL Gateway. SAIL have established an application process to be followed by anyone who would like to access data via SAIL, details of which can be found at https://www.saildatabank.com/application-process. Derived data supporting the findings of this study are available from the corresponding author (AJ) on request at a.john@swansea.ac.uk.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2025.103014.

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