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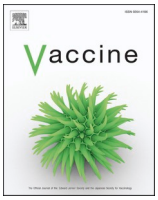

The association of maternal mental health with vaccination coverage and timeliness in early childhood – A historical cohort study in England using electronic health records

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ABSTRACT

Background: Maternal mental illness (MMI) affects almost a quarter of mothers and may impact a child's development and physical health. It remains unclear whether MMI is associated with altered utilization of vaccination services. Understanding this association could help to identify families in need of additional support.
Methods: Using primary care data from England, we conducted a historical cohort study of 397,519 children born in England between 2006 and 2014 with linked maternal records. Associations between different types of MMI (common mental disorders, severe mental illness and alcohol and substance use disorder) with childhood immunisation were explored using logistic regression for differences in coverage and accelerated failure time models for differences in timeliness before the child's fifth birthday.
Results: While there were no differences in vaccination coverage at the age of one, children of mothers with common mental disorders had lower odds of being vaccinated at the ages of two (OR 0.95, 95 %CI: 0.93–0.98) and five (OR 0.86, 95 % CI 0.84–0.89) in comparison to children of mothers with no record of MMI. Vaccination coverage was even lower for children of mothers with comorbid substance disorder and common mental disorder (OR 0.70, 95 % CI: 0.62–0.78 at the age of five). There were no significant differences in timeliness of vaccine receipt by MMI.
Conclusions: Inequalities in vaccination coverage associated with MMI grow with increasing age of the child. Extending support services for women with MMI beyond the child's first year of life could offer potential to improve vaccination uptake and reduce childhood infections.

1. Introduction

In 2022, more than 20 million children worldwide missed out on one or more vaccines delivered through routine vaccination programmes despite vaccines playing an essential role in preventing disease outbreaks [1,2]. Both vaccination coverage and timeliness, i.e., compliance with recommended age of vaccination, are essential for reducing infections in children [3–5]. The decision of whether and when to vaccinate a child usually lies with their caregivers, most commonly their mother [6]. Barriers to timely uptake of vaccines include personal beliefs [7,8], education [9], institutional trust [8], regional factors [10,11], socioeconomic status [12] or simply missing reminders [13].

Around 23 % of children are exposed to some form of maternal mental illness (MMI) in the United Kingdom with a higher prevalence in young children [14]. MMI is associated with a wide range of adverse physical and psychological outcomes in children [15,16]. Mental health disorders may alter the utilization of health services [17,18], although the effect on childhood vaccination services remains unclear. A study by Osam et al.(2020) using electronic health records found differences in coverage for children at the age of two and five years with a pronounced

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inequality towards children of mothers with substance use disorder [19], although it did not investigate vaccine timeliness or timing of MMI in relation to eligibility for childhood vaccinations.

We therefore aimed to investigate the association between MMI and vaccination coverage and timing using a large, representative cohort of mothers and children attending primary care in England.

2. Methods

2.1. Study design

We conducted a retrospective cohort study.

2.2. Data sources

We used data from the Clinical Practice Research Datalink (CRPD) Aurum version 2022.05.001, a primary care dataset from GP practices using EMIS software that contains anonymised patient-level information on symptoms, diagnoses, clinical tests, immunisations, prescriptions and referrals to other services coded using SNOMED CT (UK edition), Read version 2 and local EMIS Web® codes [20].

In May 2022, CPRD Aurum contained data from 41 million patients and was representative of the English population by geographical spread, age, sex and ethnicity [20]. For identifying mother-baby pairs, we used the Mother Baby Link (MBL) which uses an algorithm matching the date of delivery-related records of the mother with a baby's birthday if they occur within 60 days and a practice identifier [21]. To obtain more precise information on pregnancy dates, we used the linked CPRD pregnancy register [22]. The Hospital Episode Statistics Admitted Patient Care dataset (HES APC) was used to add information on the mother's ethnicity if missing in CPRD Aurum [23].

Additionally, we used the small area level dataset for the index of multiple deprivation (IMD)(24)and the death registration data from the Office for National Statistics (ONS) [23].

Data governance approval was obtained from CPRD (protocol number 22_001706) and ethical approval from the London School of Hygiene and Tropical Medicine's research ethics committee (reference number 27651).

2.3. Study population

We included all live births in CPRD Aurum between 1 January 2006 and 31 December 2014 that could be linked to a mother using the MBL. This period was chosen as the vaccination schedule did not change for the vaccines of interest and to avoid follow up in the COVID-19 pandemic.

Each mother had to be registered with a GP at least 15 months before delivery date from the MBL to ensure enough recording to assess mental health prior to birth and pregnancy [25].

All live-born children per woman were included as long as born within the study period. Maternal mental health was defined separately for each child.

Follow-up of the child started from their GP practice registration date, if a child was registered before the age of 40 days, allowing some time delay between being born and registering with a GP. Children registered older than 40 days were excluded. The follow up of the children ended with the earliest of the fifth birthday, end of registration with the GP practice, date of last data collection from the practice or death. We used the delivery date from the MBL as a substitute for the child's date of birth. Fig. S.1. shows the creation of the study population.

2.3.1. Childhood immunisations

We selected one vaccine from each of three key milestones in the National Health Service (NHS) routine childhood vaccine schedule [26]: first, the diphtheria, tetanus and pertussis (DTP) vaccine recommended at 8 weeks; second, the pneumococcal (PCV) vaccine recommended at one year; third, the measles mumps and rubella (MMR) vaccine routinely recommended at three years four months, or 18 months in some areas if there was a high-risk of measles outbreak [26]. Vaccination events were identified in primary care data [27] based on antigen and using vaccine-related codes and prescriptions [28]. We used a validated algorithm requiring a minimum age and a minimum gap between vaccine doses to ensure the quality of coding [29].

Timeliness was assessed by analysing the age in days at vaccine receipt. For vaccination coverage, we assessed the odds of children having been vaccinated by the ages 1, 2, and 5 years out of all children followed up until the age of interest. These metrics are summarised in Table 1.

We chose this approach over an up-to-date definition as only these vaccines had been consistently recommended at the same age during the study period and the recoding of these vaccines in primary care was validated in our previous study [30].

2.4. Maternal mental health

Mothers were defined as having a mental health issue if they had a record of either symptom, referral code, questionnaire with result or diagnosis in relation to a mental health issue of interest any time prior to the due date of respective vaccine of interest (see Table 2 and supplementary methods). Complete code lists are available online [31]. As mental health conditions may change over time and are often of episodic nature, we also performed a sensitivity analysis using different approaches to define mental health exposure with respect to time of diagnosis recorded (see sensitivity analysis).

MMI exposure at baseline was assessed at the first recommended date for the child's vaccination, e.g., for the DTP vaccine, the mental health exposure was assessed before the child's age of 8 weeks. If a woman had records of more than one category of mental health issue, she was classified as "any SMI" if there was at least one record for SMI, or she was classified into a co-morbid category "CMD & SUD" if there was a record of SUD.

Secondary analysis exploring the impact of more recent MMI recording was limited to women with a record of CMD, due to small numbers of women with other MMI and sufficient maternal follow up. A more recent diagnosis took precedence over an earlier record.

2.5. Covariates

Region of residency, maternal age at birth, child's sex, child's birth

Table 1
Definition of outcomes of interest for vaccination timeliness and coverage.

Vaccine of interest[1]	Age when recommended in NHS immunisation schedule	Vaccine timeliness	Vaccine coverage
First dose of diphtheria, tetanus, pertussis vaccine (DTP)	8 weeks	Attained age at vaccination	% of children vaccinated by their 1st anniversary
Third dose of pneumococcal vaccine (PCV)	1 year	Attained age at vaccination	% of children vaccinated by their 2nd anniversary
Second dose of the measles, mumps, rubella vaccine	3 years and 4 months (in accelerated schedules[2] sometimes from age 18 months)	Attained age at vaccination	% of children vaccinated by their 5th anniversary

[1] These vaccines were chosen to represent children at different ages when they become eligible for the vaccination.

[2] In areas at high-risk of measles outbreaks, the second dose can be given earlier from the age of 18 months which then fully replaces the appointment at age of 3 years and 4 months.

Table 2
Definitions of maternal mental illness in the study.

Category of maternal mental illness		
Mental health issue	*Definition*[1]	*ICD-10*
Common mental disorder (CMD)	Any term related to depression, anxiety, and general maternal mental health issue. Terms related to dementia or drug-induced health issue were excluded as well as depression as consequence of schizophrenia.	F32–39 F40–48 F53
Severe mental illness (SMI)	Any term related to schizophrenia, bipolar disorder, or psychosis. Drug-induced or dementia-related psychosis was excluded as well as depression with a psychotic component and a history of childhood psychosis.	F30–31 F20–29
Substance use disorder (SUD)	Any term related to alcohol or opioid use disorder, general terms for drug abuse and conditions which are consequences of chronic alcohol abuse[2]. Indicators of one-off intoxication and screening tools were not included.	F10–11 F19
Timing of maternal mental illness (for CMD only)		
History of CMD	Latest record of CMD before start of pregnancy in pregnancy register or at least 40 weeks before recorded delivery date if pregnancy register entry missing	
Antenatal CMD	Latest record of CMD between delivery date and recorded start of pregnancy in pregnancy register or no more than 40 weeks before recorded delivery date if pregnancy register entry missing	
Postnatal CMD	Latest record of CMD between delivery date and before age of 1 year (or due date of vaccination if under one year)	
CMD during the baby's childhood	Latest record of CMD between age of one year and age of 18 months (earliest possible date of second MMR vaccine)	

[1] Any condition had to be recorded before the eligibility age for the vaccine of interest. Mothers could have more than one of these conditions which were then combined into categories as described below.

[2] This entails conditions such liver cirrhosis due to alcohol, alcoholic hepatitis, Korsakoff syndrome, Wernicke disease, and more. All conditions can be found in the code list online [31].

order and ethnicity were considered as confounders based on existing literature [9].

The sex and geographical region of residency of the child, and maternal age at birth, were obtained directly from the provided demographics. Maternal ethnicity was obtained applying an algorithm described by Mathur et al. [21], using the following five categories: South Asian, Black, Mixed, White, Other, or unknown/missing. Missing ethnicity was supplemented with HES data where available. The quintile of the Index of Multiple Deprivation (IMD) [24] was derived from the linked data set based on the mother's postcode and if missing ($N = 284$) substituted with IMD derived from the practice's postcode.

Birth order was defined based on all children linked to the same mother, including siblings born outside of the study period, using the MBL.

As we hypothesized a different attitude towards vaccination for women who receive regular invitations and reminders for vaccinations, we included mothers with a health conditions outside of pregnancy which qualified them as eligible for the flu vaccine as a covariate [32].

2.6. Statistical analysis

All analyses were conducted using R version 4.2.2.

Recording patterns of all maternal mental health issues were explored visually.

A complete case analysis was performed, excluding children with no assigned gender and children of mother with unknown ethnicity.

For vaccination coverage at years 1, 2, and 5 we estimated the odds of being vaccinated using a generalised linear model (GLM) with binomial distribution and a priori-selected confounders based on the literature. We fitted a crude mode and a minimally adjusted model adjusting for region, deprivation, and ethnic group of the mother. In a next step, we added maternal age at birth as a categorical variable, birth order, flu risk group of the mother and sex of the child as potential confounders or effect modifiers. We tested for a potential interaction between maternal mental health and deprivation, and maternal mental health and maternal ethnicity with a Loglikelihood-ratio test.

Kaplan-Meier curves were used to describe vaccination receipt over time by MMI exposure for each of the three vaccines.

For modelling vaccine timeliness, we used accelerated failure time (AFT) models with underlying loglogistic distribution. We followed the same procedure of adding potential confounders in two steps as for the GLM described above. We presented the time ratio, which is the inverse of the acceleration factor and can be interpreted intuitively, e.g., a time ratio of 0.5 means that median time to vaccination for the exposed group is 0.5 times the median time to vaccination for the control group.

2.7. Sensitivity analyses

Firstly, we explored the impact of two different methods for defining mental health. These were (i) using only diagnostic codes for defining exposure categories; (ii) only using a symptom to define CMD if there was a relevant prescription (e.g., antidepressants, anxiolytics) within three months.

Secondly, we explored the role of temporal trends by stratifying the children into two birth cohorts, born 2006–2010 and born in 2011 or after. In a second step, we also adjusted for calendar year in the fully adjusted models.

Thirdly, as recording of vaccines and mental health issues can vary between GPs and several children of a mother could be included into the study, we considered random effects by GP practice, by mother and a nested random effect of mothers within a GP practice (see supplementary methods).

Finally, we included all children with missing maternal ethnicity or gender.

3. Results

3.1. Sample characteristics

The final study population consisted of 397,519 children born between 2006 and 2014 to 330,199 linked mothers. The median follow up time was 1805 days (IQR 1790-1815) for the children and 15 years (IQR 10–22) for the mothers. At the due date of the first childhood immunisation, 28.06 % of children ($N = 111,529$) had a mother with a record of any prior mental illness. At 18 months, 96,161 children (32.11 %) had a mother with any CMD recorded of which 20.40 % were postnatal depression (Table S.1).

Baseline characteristics were similar for children followed to ages 1, 2 and 5 (Table 3) and did not differ significantly by length of follow up.

3.2. Vaccine coverage and timeliness

Vaccine coverage was high for all vaccines and MMI exposures but decreased for vaccines later in the schedule. Most doses of the second MMR dose were given within the regular schedule after 3 years and four months with only a very small peak representing the delivery of an accelerated schedule (Fig. 1).

Figs. S2-S8 show more detailed visual descriptions of vaccine uptake over time by different MMI.

For the first dose of the DTP vaccine we found no evidence for differences in vaccine coverage at age one by MMI (Table 4). At two years, there was 5 % lower odds of being vaccinated for children of mothers with CMD (fully adjusted OR: 0.95, 95 % CI: 0.93–0.98) and 22 % lower

Table 3
The study population for children with differing length of follow up.

	All included children (*N* = 397,518)	Children followed up to age 1 (*N* = 373,107)	Children followed up to age 2 (*N* = 349,013)	Children followed up to age 5 (*N* = 299,438)
Number of linked mothers	330,119	309,114	288,224	245,003
Maternal age				
Median maternal age at birth (IQR)	31 (27–35)	31 (27–35)	31 (27–35)	31 (27–35)
<20 years, N(%)	11,023 (2.77)	10,084 (2.70)	9282 (2.66)	7628 (2.55)
20–29 years, N (%)	152,091 (38.26)	141,587 (37.95)	131,697 (37.73)	111,893 (37.37)
30–39 years, N (%)	212,540 (53.47)	200,572 (53.76)	188,163 (53.91)	162,212 (54.17)
> 40 years, N(%)	21,864 (5.50)	20,864 (5.59)	19,871 (5.69)	17,705 (5.91)
Siblings and birth order				
Median number of siblings (IQR)	1 (0–1)	1 (0–1)	1 (0–1)	1 (0–1)
First child, N(%)	247,854 (62.35)	228,539 (61.25)	209,846 (60.13)	174,795 (58.37)
Second child, N (%)	118,076 (29.70)	113,593 (30.45)	108,879 (31.20)	96,596 (32.26)
Third child, N(%)	25,361 (6.38)	24,832 (6.66)	24,251 (6.95)	22,371 (7.47)
At least fourth child, N(%)	6227 (1.57)	6143 (1.65)	6037 (1.73)	5676 (1.90)
Sex of the child				
Female, N(%)	193,498 (48.68)	181,845 (48.74)	170,173 (48.76)	145,927 (48.73)
Indeterminate, N (%)	<5 (<0.01)	<5 (<0.01)	<5 (<0.01)	<5 (<0.01)
Maternal ethnicity				
White, N(%)	317,179 (79.79)	29,8412 (79.98)	280,013 (80.23)	242,263 (80.91)
South Asian, N (%)	32,289 (8.12)	30,484 (8.17)	28,597 (8.19)	24,330 (8.13)
Black, N(%)	15,665 (3.94)	14,253 (3.82)	12,854 (3.68)	10,151 (3.39)
Other, N(%)	7137 (1.80)	6525 (1.75)	5909 (1.69)	4664 (1.56)
Mixed, N(%)	15,070 (3.79)	13,938 (3.74)	12,865 (3.69)	10,607 (3.54)
Unknown/ Missing, N(%)	10,178 (2.56)	9495 (2.54)	8775 (2.51)	7423 (2.48)
IMD quintile of mother				
1 (Least deprived), N (%)	81,499 (20.50)	77,613 (20.80)	73,764 (21.14)	65,167 (21.76)
2, N(%)	75,520 (19.00)	71,468 (19.15)	67,241 (19.27)	58,381 (19.50)
3, N(%)	73,172 (18.41)	68,460 (18.35)	63,719 (18.26)	54,223 (18.11)
4, N(%)	79,866 (20.09)	74,226 (19.89)	68,706 (19.69)	57,534 (19.21)
5 (Most deprived), N (%)	87,461 (22.00)	81,340 (21.80)	75,583 (21.66)	64,133 (21.42)
Region of residency				
North East, N(%)	15,656 (3.94)	14,821 (3.97)	14,105 (4.04)	12,541 (4.19)
North West, N(%)	76,985 (19.37)	73,179 (19.61)	69,563 (19.93)	62,007 (20.71)
Yorkshire & The Humber, N(%)	13,748 (3.46)	13,045 (3.50)	12,386 (3.55)	10,968 (3.66)
East Midlands, N (%)	7169 (1.80)	6806 (1.82)	6447 (1.85)	5703 (1.90)
West Midlands, N (%)	64,937 (16.34)	61,306 (16.43)	57,882 (16.58)	50,656 (16.92)
East of England, N (%)	18,734 (4.71)	17,633 (4.73)	16,506 (4.73)	14,344 (4.79)
London, N(%)	70,520 (17.74)	64,224 (17.21)	57,861 (16.58)	44,666 (14.92)
South East, N(%)	80,761 (20.32)	75,964 (20.36)	71,045 (20.36)	60,906 (20.34)
South West, N(%)	49,008 (12.33)	46,129 (12.36)	43,218 (12.38)	37,647 (12.57)
Number of mothers with chronic conditions eligible for regular flu vaccination[1]				
Any record of flu risk condition, N(%)	71,138 (17.90)	66,838 (17.91)	62,740 (18.00)	54,189 (18.10)
Maternal mental health issue – recorded before child's age of 8 weeks[2]				
No MMI, N(%)	285,989 (71.94)	268,773 (72.04)	251,596 (72.09)	215,647 (72.02)
CMD, N(%)	103,722 (26.09)	97,244 (26.06)	90,941 (26.06)	78,483 (26.21)
CMD & SUD, N (%)	4164 (1.05)	3774 (1.01)	3465 (0.99)	2895 (0.97)
SUD, N(%)	3231 (0.81)	2942 (0.79)	2664 (0.76)	2120 (0.71)
Any SMI, N(%)	412 (0.10)	374 (0.10)	347 (0.10)	293 (0.10)
Maternal mental health issue – recorded before child's age of 1 year[2]				
No MMI, N(%)	–	255,222 (68.4)	238,971 (68.47)	204,837 (68.41)
CMD, N(%)	–	110,388 (29.59)	103,197 (29.57)	88,993 (29.72)
CMD & SUD, N (%)	–	4250 (1.14)	3896 (1.12)	3241 (1.08)
SUD, N(%)	–	2850 (0.76)	2583 (0.74)	2058 (0.69)
Any SMI, N(%)	–	397 (0.11)	366 (0.10)	309 (0.10)
Maternal mental health issue – recorded before child's age of 18 months[2]				
No MMI, N(%)	–	–	234,247 (67.12)	200,880 (67.09)
CMD, N(%)	–	–	107,639 (30.84)	92,711 (30.96)
CMD & SUD, N (%)	–	–	4141 (1.19)	3450 (1.15)
SUD, N(%)	–	–	2599 (0.74)	2070 (0.69)
Any SMI, N(%)	–	–	387 (0.11)	327 (0.11)

[1] Chronic conditions which qualify adults under 65 for a regular flu vaccine considered for this covariate includes respiratory conditions (e.g., asthma, chronic obstructive pulmonary disease), heard conditions (e.g., coronary heart disease, heart failure), a body mass index of 40 and above, chronic kidney disease, liver disease (e.g., cirrhosis, hepatitis), neurological conditions (e.g., Parkinson's disease, motor neurone disease, multiple sclerosis or cerebral palsy), learning disability, sickle cell disease or asplenia.

[2] MMI: Maternal mental illness. CMD: Common mental disorder. SUD: substance use disorder. SMI: Severe mental illness. The exposure of children to maternal CMD by timing of record can be found in the supplementary table S.1.

odds for children of mothers with combined CMD and SUD (fully adjusted OR 0.78, 95 % CI: 0.71–0.87). There was no evidence for any difference in coverage for children of mothers with SUD only or SMI. At the age of five, children of mothers with CMD had 14 % lower adjusted

Fig. 1. Vaccination coverage of the three vaccines of interest by different ages and maternal illness exposure of the child.
Yearly vaccination uptake after birth. MHI: Mental health issue. CMD: Common mental disorder. SUD: Substance use disorder. SMI: Severe mental illness. Earlier years of MMR2 coverage were presented to reflect the proportion of children receiving MMR as part of an accelerated vaccination schedule.

odds (OR 0.86, 95 % CI: 0.84–0.89) of having received the second dose of the MMR vaccine and children of mothers with both CMD and SUD had 30 % lower adjusted odds (OR 0.70, 95 % CI: 0.62–0.78) compared to children of mothers with no MMI. Once again, we found no differences for children of mothers with SMI or SUD only.

There was no meaningful difference in timing of vaccinations for children of mothers with or without MMI (Table 4).

The Loglikelihood-ratio test showed no significant evidence for an interaction between deprivation or ethnicity and maternal mental health for any of the three outcomes.

Furthermore, vaccine coverage was lower from the age of two in children of mothers from black, mixed and other ethnic minorities and living in more deprived areas (see Table S2).

3.3. *Timing of the mental health recording*

There was a consistent fall in recorded MMI diagnosis or symptoms during pregnancy for all types of MMI, and a peak in recorded MMI in the month of birth (fig. S12).

Children of mothers with a history of CMD had a higher vaccination uptake at the age of one year but a lower uptake at ages two and five years (Table 4). For children of women with CMD recorded during pregnancy, there was no difference in uptake at the ages of one and two years, but 19 % lower odds (95 % CI: 0.73–0.90) of being vaccinated at

Table 4
Odds ratios and time ratios of being vaccinated by type of maternal mental health issue, and by timings of latest recording for common mental disorders (CMD).

			Coverage at specified age (Odds ratio (95 % CI))			Timeliness of uptake (Time ratio (95 %-CI))		
			Crude Model	Adj. Model 1	Adj. Model 2	Crude Model	Adj. Model 1	Adj. Model 2
DTP vaccine due at 8 weeks	*No MMI*		1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
	CMD	*CMD Overall*	1.04 (1.02–1.07)	1.09 (1.07–1.12)	1.10 (1.07–1.13)	0.99 (0.99–1.00)	1.00 (0.99–1.00)	1 (0.99–1.00).00
		CMD & SUD	1.06 (0.95–1.19)	1.12 (1.00–1.25)	1.15 (1.03–1.28)	0.96 (0.94–0.98)	0.97 (0.95–0.99)	0.97 (0.95–0.99)
		History of CMD	1.07 (1.04–1.10)	1.12 (1.09–1.15)	1.13 (1.10–1.16)	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (1.00–1.01)
		Antenatal CMD	0.96 (0.90–1.02)	1.01 (0.95–1.07)	1.02 (0.96–1.08)	0.96 (0.95–0.98)	0.97 (0.96–0.98)	0.97 (0.96–0.98)
		Postnatal CMD	0.94 (0.89–1.00)	0.99 (0.93–1.05)	1.00 (0.94–1.06)	0.97 (0.96–0.99)	0.98 (0.97–0.99)	0.98 (0.97–0.99)
	SUD		1.22 (1.07–1.39)	1.17 (1.03–1.34)	1.19 (1.04–1.36)	0.98 (0.96–1.00)	0.98 (0.96–1.00)	0.98 (0.96–1.00)
	SMI		0.91 (0.65–1.26)	0.87 (0.62–1.21)	0.88 (0.63–1.22)	0.95 (0.90–1.01)	0.96 (0.90–1.02)	0.96 (0.90–1.02)
PCV due at one year	*No MMI*		1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
	CMD	*CMD Overall*	0.97 (0.95–1.00)	0.91 (0.89–0.94)	0.95 (0.93–0.98)	1.00 (1.00–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
		CMD & SUD	0.75 (0.68–0.83)	0.71 (0.64–0.78)	0.78 (0.7–0.87)	0.98 (0.97–0.99)	0.98 (0.98–0.99)	0.98 (0.98–0.99)
		History of CMD	0.99 (0.96–1.02)	0.93 (0.90–0.97)	0.96 (0.93–1.00)	1.00 (1.00–1.00)	1.00 (0.99–1.00)	1.00 (1.00–1.00)
		Antenatal CMD	0.97 (0.89–1.06)	0.93 (0.85–1.01)	0.99 (0.91–1.08)	1.00 (0.99–1.00)	0.99 (0.99–0.99)	1.00 (0.99–1.00)
		Postnatal CMD	0.92 (0.88–0.95)	0.85 (0.82–0.89)	0.91 (0.88–0.95)	0.99 (0.99–0.99)	0.99 (0.99–1.00)	0.99 (0.99–0.99)
	SUD		0.93 (0.81–1.07)	0.96 (0.84–1.00)	1.00 (0.87–1.15)	1.01 (1.00–1.02)	1.01 (1.01–1.02)	1.01 (1.00–1.02)
	SMI		0.66 (0.48–0.91)	0.69 (0.50–0.95)	0.71 (0.52–0.98)	0.97 (0.95–1.00)	0.98 (0.95–1.00)	0.98 (0.95–1.00)
MMR vaccine due at three years and four months	*No MMI*		1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
	CMD	*CMD Overall*	1.00 (0.97–1.03)	0.84 (0.82–0.87)	0.87 (0.84–0.89)	0.99 (0.99–1.00)	0.99 (0.99–0.99)	0.99 (0.99–1.00)
		CMD & SUD	0.74 (0.66–0.83)	0.63 (0.56–0.70)	0.69 (0.62–0.77)	0.98 (0.98–0.99)	0.98 (0.98–0.99)	0.98 (0.98–0.99)
		History of CMD	0.98 (0.95–1.02)	0.84 (0.81–0.87)	0.86 (0.83–0.89)	1.00 (0.99–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
		Antenatal CMD	0.89 (0.80–0.98)	0.78 (0.70–0.86)	0.81 (0.73–0.90)	0.99 (0.99–0.99)	0.99 (0.99–0.99)	0.99 (0.99–0.99)
		Postnatal CMD	0.97 (0.92–1.02)	0.81 (0.77–0.85)	0.85 (0.80–0.89)	0.99 (0.99–1.00)	0.99 (0.99–1.00)	0.99 (0.99–1.00)
		CMD after child's first birthday	1.03 (0.98–1.09)	0.83 (0.78–0.88)	0.86 (0.82–0.92)	0.99 (0.99–0.99)	0.99 (0.99–0.99)	0.99 (0.99–0.99)
	SUD		0.87 (0.75–1.02)	1.00 (0.85–1.17)	1.06 (0.9–1.24)	0.99 (0.99–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
	SMI		0.73 (0.51–1.04)	0.79 (0.55–1.14)	0.81 (0.56–1.17)	0.98 (0.97–0.99)	0.98 (0.97–1)	0.98 (0.97–0.99)

DTP: diphtheria, tetanus, pertussis. PCV: Pneumococcal conjugate vaccine. MMR: measles, mumps, rubella. MHI: Mental health issue. CMD: Common mental disorder. SUD: Substance use disorder. SMI: Severe mental illness. Uptake of the DTP, PCV and MMR vaccine was measured at child's first, second and fifth birthday. The recommended ages for each vaccine can be found in Table 1.

five years.

Children of women with CMD recorded after birth had lower vaccination uptake than children with no maternal CMD at the age of two and five (OR: 0.91, 95 % CI: 0.88–0.95 at age two, and OR 0.85, 95 % CI: 0.81–0.89 at age five) which was very similar to mothers with CMD recorded when the child was over the age of one year (OR 0.86, 95 % CI: 0.81–0.91).

We found no difference in the timeliness of uptake of any vaccination dependent on when the CMD was recorded (Table 4, figs. S.9–11).

3.4. Sensitivity analysis

Using diagnostic codes only significantly reduced the numbers of woman with record of CMD and SUD (Table S1). There was only a small difference when including prescriptions. Children of mothers with a diagnosis of SUD had 45 % lower odds of being vaccinated at age 2 (aOR 0.55, 95 % CI 0.36–85) and 53 % lower odds of being vaccinated at age five (aOR 0.47, 95 % CI 0.28–0.79, Table S2).

The analysis of vaccine coverage by birth cohort and adjusting for the calendar year when the coverage was measured, showed very similar results (Table S4). Greater differences between birth cohorts were observed for children of mothers with SMI and SUD.

The models with random effects by GP practice, by mother and both together did not show any meaningful differences (Table S5). Similar applied to the models including children with missing maternal ethnicity and missing gender (Table S6).

4. Discussion

In this study of over 300,000 children in England and their mothers,

we found reduced odds of vaccination for children of mothers with CMD or both CMD and SUD in comparison to children of mothers with no MMI at the ages of two and five, but not at the age of one. There was no evidence of difference in coverage for children born to mothers with recorded SMI or SUD alone. At the age of one, vaccine coverage was even higher in children of mothers with CMD and SUD. Among those vaccinated, MMI was not associated with vaccine timeliness.

Our findings for reduced vaccine coverage in children exposed to maternal CMD aligned with two other UK studies [19,33]; one of which also showed a similar age-dependent effect of reduced vaccine uptake with increasing age [33].

In contrast to older ages, we found a higher vaccine uptake for the DTP vaccine at the age of one year for mothers with CMD and SUD. As the first vaccination appointment usually falls into the time when GPs are encouraged to screen women for postnatal mental health issues [34], we hypothesized that these women with mental health issue may receive additional support related to their and the child's health including reminders for the first vaccines of the immunisation schedule.

We additionally explored the impact of timing of the most recent CMD recording, which emphasised that any history of CMD was associated with reduced vaccination uptake. However, the analysis of the timing of CMD recording might have been affected by under-recording in pregnancy in our study: another study showed that the prevalence of depression in pregnancy was comparable to the general population [35].

Other findings around SMI and SUD have been mixed. A Canadian study found a lower vaccination uptake in children of mothers with schizophrenia which did not persist after adjusting for demographic and health-related factors [36] and an English study found lower vaccine uptake in children of mothers with psychosis and substance and alcohol abuse [19]. When using a more conservative approach using diagnostic codes for SUD only in the sensitivity analysis, our study yielded very comparable results. Our main definition of SMI was broader including bipolar disorder and schizophrenia which may impact vaccination coverage differently than postnatal psychosis.

A qualitative study [37] indicated that maternal trauma was linked to greater vaccine hesitancy for the COVID-19 vaccine in their children due to distrust in science and government. Mothers with SUD may experience stigma when interacting with health professionals in primary care which could potentially impact vaccination behaviour [38]. Factors preventing woman with perinatal mental health issues from seeking care include fear of social service involvement when disclosing issues, travel costs and timing of services, communication style of the health professionals and lack of time, and general pressure on 'being a good mum' [39]. More research is needed on the extent to which these issues affect vaccine decision-making for their children.

We found no difference in timing of vaccine receipt between different MMI exposure groups, hence improving overall vaccination coverage rather than timeliness should be a priority for children of women with MMI.

Other independent factors influencing vaccine uptake and timeliness included maternal ethnicity and level of deprivation. This aligned well with findings from other existing literature finding lower vaccine uptake in specific ethnic groups or immigrants [40–44]. Further, a potential interaction between deprivation and mental health issues with respect to vaccine uptake should be explored in future research.

4.1. Strengths and limitations

Strengths of our study include the use of a large, representative primary care dataset, allowing for investigation of current and previous MMI. We provided detailed information on vaccination uptake and precise ages at which vaccinations were delayed. We used a validated algorithm to identify vaccination records in electronic health records and followed children up to the age of five. A paired analysis of vaccination coverage at key ages with survival analysis for timeliness helped to unpick the role of delay of vaccines in reduced vaccination coverage.

Key limitations of our study are missing information on the mental health of fathers or other care givers in the household. The influence of fathers in the decision-making process to vaccinate remains uncertain and could differ when mothers have MMI [45,46]. Due to low numbers, various disorders were grouped together in categories such as SMI or SUD, but there might be significant differences in women with these conditions. Furthermore, many mental health issues are of episodic nature and the impaired functionality of those affected can vary widely, which is not captured sufficiently in primary care data, [47,48]. MMI might be under-recorded in primary care as stigma affects healthcare seeking behaviour [38,49]. Furthermore, MMI recorded in other care settings such as antenatal clinics or hospitals might not be transferred to GP records in a timely manner [50]. This might offer a potential explanation for the apparent drop in recording of CMD during pregnancy. Non-differential exposure misclassification would tend to underestimate the impact of mental health problems on vaccination uptake.

4.2. Policy implications

Our results show that MMI was associated with lower vaccination uptake in children aged two years and above which suggests potential to reduce infectious diseases in childhood for this vulnerable population. The National Institute for Health and Care Excellence already recommends screening questions for mental health in pregnancy and the postpartum period [51]. Health visitors usually visit parents of young children supporting the GP up to the child's first birthday and during preschool only on a targeted basis if in need of additional support [52,53]. However, the workforce of health visitors has declined recently and shows major regional variation with especially low coverage in London [54]. While this study doesn't support specific changes to vaccine policy, we recommend Improving the coverage of health visitors, including extending visits beyond one year and supporting mothers with any history of CMD could help to improve vaccination uptake.

Furthermore, more research is needed on the potential causes of vaccine hesitancy or issues with vaccination access in women with MMI in order to address their concerns around vaccines and improve accessibility. A potential interaction with maternal deprivation should be also explored.

Authors contributions

AS, JW, HM and CWG conceptualised the study and contributed to the study design. AS and HM developed the code lists for the different vaccinations, and AS developed the mental health code lists based on code lists from the UCL Mental Health Data Science Group which were discussed with the same group and clinically reviewed by DO. DG gave feedback and suggestions to the statistical analysis. AS cleaned, analysed and interpreted the data and drafted the first draft of the manuscript. The manuscript was critically revised by all authors. All authors approved the submission of the article.

Ethics statement

We received data governance approval from CPRD (protocol number 22_001706) and ethical approval from the London School of Hygiene and Tropical Medicine's research ethics committee (reference number 27651).

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CRediT authorship contribution statement

Anne M. Suffel: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Helena Carreira:** Writing – review & editing, Conceptualization. **Jemma Walker:** Writing – review & editing, Funding acquisition, Conceptualization. **Daniel Grint:** Writing – review & editing, Methodology. **David Osborn:** Writing – review & editing, Methodology, Conceptualization. **Helen I. McDonald:** Writing – review & editing, Funding acquisition, Conceptualization. **Charlotte Warren-Gash:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

The study uses data from the Clinical Practice Research Datalink (CPRD). CPRD does not allow the sharing of patient-level data. The data specification for the CPRD data set is available at: https://cprd.com/cprd-aurum-may-2022-dataset. The code lists can be found at: https://github.com/Eyedeet/vaccine_methods_ehr_public/tree/main/codelists.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.126529.

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