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Household determinants of delayed MMR vaccination: longitudinal analysis using electronic health records

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Abstract

Background

There is a lack of information about household factors associated with delayed Measles Mumps and Rubella (MMR) vaccination. We examined whether delay in first MMR (MMR1) receipt is associated with sharing a household with an older child with delayed MMR1 receipt and whether this is independent of household composition and number of children.

Methods

We conducted a longitudinal study using the primary care electronic health records of children registered with general practices in north east London and eligible to receive MMR1 between 1st January 2020 and 28th February 2020. The primary outcome was MMR1 receipt – between age 12 and 24 months. The explanatory variable was non-receipt of MMR1 between age 12 and 24 months in the oldest child sharing the same household. We used Poisson regression to calculate MMR1 prevalence ratios (PR) and 95% confidence intervals (CI) for index children sharing a household with an older child with non-receipt of MMR1 before and after adjustment for individual-, household-, and area-level covariates. We carried out a sensitivity analysis excluding households where the age interval between oldest and youngest child was > five years.

Findings

The index cohort comprised 71,509 children (51.0% males), of whom 59,851 (83.6%) received MMR1 by age 24 months. MMR1 receipt was less likely in index cohort members sharing a household with an older child with non-receipt of MMR1 by age 24 months: PR: 0.67 (95% CI: 0.66,0.68) in the fully adjusted model. This association strengthened when households with an age interval > five years were excluded: PR: 0.57 (0.57,0.58)

Interpretation

There is a strong concordance within households of delay in MMR1 receipt independent of household size and composition. Lack of timely protection within households increases the risk of measles outbreaks. There is a need for household-based interventions to improve MMR1 timeliness.

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Strengths and limitations

- The strengths of our study include the use of a novel method to create households securely while maintaining privacy, as well as having access to a large population with EHRs, for a geographically contiguous area.
- Additionally, we have access to high quality MMR data, that is recorded accurately in the EHR through data recording templates.[1] The codeset used to identify MMR1 in the EHR was validated.
- We used robust statistical methods to assess relationships between the exposure and outcome variables, and we selected a time period before lockdowns due to the Coronavirus pandemic disrupted access to health care in England (March 2020).
- We were not able to confirm whether the processes of decision-making about vaccines differed between the linked index and older children.
- However, we were able to see a strengthening of association between the vaccination status of a younger and linked older child in the sensitivity analyses when excluding children with an age gap of over 5 years. This finding will need to be explored further with research exploring the decision-making around vaccination for multiple young children in a household.

Introduction

Childhood vaccinations form an essential part of public health interventions provided by primary care.[2] In England and Wales, it is recommended that children receive a first dose of Measles, Mumps and Rubella (MMR) vaccine by age 12 months[3]: currently only 89% receive a first dose by age 24 months, and only 84% a second dose by age five years.[4] This countrywide statistic conceals marked geographic inequalities linked to deprivation. The World Health Organization (WHO) recommends that 95% of the population are given two MMR doses toachieve herd immunity and eliminate measles.[5] The United Kingdom (UK) lost measles elimination status in 2018 and while this was reinstated in 2021, measles outbreaks in areas with high measles susceptibility in young children in England suggest that this will not be sustained.[6] Clusters of inequalities in MMR coverage

exacerbate existing outbreaks – a large proportion have been in London, an area with both low and profoundly inequitable coverage.[4]

In light of these public health concerns, there has been increasing emphasis on the importance of timely receipt of MMR, with the first dose conferring 93% protection against infection.[7] In the UK, national targets to ensure receipt of first MMR (MMR1) between 12 and 24 months of age have been recently replaced by a 12-18 month target reflecting this emphasis on timeliness.[8]

It is known that equity in vaccination coverage is impacted by social determinants such as deprivation, ethnicity and area-level variation in healthcare services.[9, 10] There is strong evidence demonstrating that children from more deprived areas are less likely to receive MMR vaccination compared to those living in affluent areas.[11] We and others [12] have previously shown that family size is an important determinant of partial or non-immunisation with MMR, suggesting that access to services may play an important role.[13] [14]

Identifying factors at a household level can create actionable insights into how services might be tailored to improve receipt of vaccinations.[15] We used electronic health records (EHRs) for an ethnically diverse and disadvantaged population, with among the lowest proportion of children receiving MMR1 by 24 months of age in the UK, to investigate whether non-receipt of MMR1 by 24 months of age is clustered in households. Specifically, we hypothesised that children with non-receipt of MMR1 by age 24 months were more likely to share a household with an older child with non-receipt of MMR1 by age 24 months, independently of the number of children in the household and household composition.

Methods

Study design and setting

We conducted a longitudinal study using primary care EHRs from 266 general practices in seven North-East London (NEL) localities: Barking & Dagenham, City & Hackney, Havering, Newham, Redbridge, Tower Hamlets, and Waltham Forest.

Data Sources

Pseudonymised data were provided from the NEL Discovery Data Service (DDS), which receives primary care EHR data in near-real time for all general practices (GPs) in NEL. [16] Unique Property Reference Numbers (UPRNs) are allocated to all GP-recorded patient addresses in DDS using a quality-assured and validated address-matching algorithm.[17] UPRNs are pseudonymised into Residential Anonymous Linking Fields (RALF)[18] using a study-specific encryption key. We used RALFs to link children in households for address records and registrations from 2014 onwards, when data flow for address registrations into NEL DDS commenced. Data were extracted on 23rd November 2021.

Study population

The study population comprised 159,300 children registered with a NEL GP at the time of their second birthday and eligible to receive MMR1 between 1st January 2014 and 28th February 2020. We excluded 17,038 children without a RALF, with a non-residential RALF, with a poor-quality RALF match, or with more than one RALF at time of MMR1 or second birthday, leaving 142,262 children eligible for inclusion (see flow chart S1).

Identifying children sharing a household

We identified older children sharing a household with the 142,262 index children at the index child's MMR1 date or 24 months of age, whichever is the earliest. Index and older children sharing a RALF at index child's MMR1 date, or at the index child's second birthday were considered to share a household. We identified all children in DDS based on the index children's RALFs and excluded 52,693 children without an older child in the household, and 15,516 older children who were already included as index children, leaving 71,509 index children with at least one older child sharing their household at the index child's MMR1 date or second birthday (see flow chart S2). These 71,509 children are henceforth referred to as the "linked index cohort" and the older children with whom they share a household as the "linked older children's cohort".

The study methodology has been reported against both the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) and the REporting of studies Conducted using

Observational Routinely-collected health Data (RECORD) statement (see supplementary files S3 & S4).[19, 20]

Primary outcome

The primary outcome is receipt of MMR1 between 12 and 24 months of age, which is consistent with the Cover of Vaccination Evaluated Rapidly (COVER) measures in place during the study period.[21]

We extracted sociodemographic and area-level data for the linked index and linked older child cohorts, together with all clinical events relating to MMR1 procedures (see Table S1s). We derived a proxy date of birth from calendar week, month and year of birth by combining the date of the first day of the week of the calendar week of birth with month and year of birth. We excluded duplicated events, and events without correct clinical codes. We assumed MMR1 was not given if there was no record of MMR1 being given in the primary care EHR. If a child did not have a record of a MMR1 vaccination, they were linked to a RALF at the time of their second birthday, and were defined as children with non-receipt of MMR1.

Explanatory variable

The main explanatory variable was non-receipt of MMR1 in the linked older child defined as no record of MMR1 given between 12 and 24 months of age.

Covariates

Individual-level

Individual-level covariates were sex and ethnic group. We categorised ethnic group of the index children using the NHS 5+1 classification using information recorded in the EHR.[22] We created five mutually exclusive ethnic groups: white ('white British', 'white Irish' or 'any other white background'); black ('black African', 'black Caribbean' or 'any other black background'); South Asian ('Indian', 'Pakistani', 'Bangladeshi' or 'Sri Lankan'); mixed/other ('any other ethnic background', 'mixed ethnicity', 'Chinese' or 'Asian other'); and missing category (ethnicity code in the primary care record missing or 'not stated' category selected).

Household-level

All household members sharing a household at the index child's MMR1 date were identified. We excluded households with more than ten members, only one child, or no adults aged ≥18.0 years. Household information was available for 65,308 households containing index and linked older children.

We categorised household composition using an adapted Harper and Mayhew method[23] into one of three mutually exclusive categories: working-age adults (aged 18-64 years) with children; single working-age adult with children, or at least one working-age and one older adult (aged >65 years) with children (three-generation household). We included households with at least one older adult with children but no working-age adult (skipped generation households) in the three-generation household group.

We calculated the total number of household members, as well as the number of children within a household at the index child's MMR1 date or 24 months of age for those with no MMR1 date.

Area-level

We merged 2019 Index of Multiple Deprivation (IMD) decile[24] into the datafile using the 2011 Lower layer Super Output Area (LSOA), an area with an average population of 1,500 people or 650 households, as the linkage field. IMD deciles were concatenated into quintiles from most (1) to least deprived (5).

We compared the linked index cohort (n=71,509) with the cohort of eligible children (*n*=70,753) not linked to another older child (Table S2). The linked sample had a lower proportion with receipt of MMR1 by 24 months of age, were less likely to be from a white ethnic background, from smaller households, or from households with two or more working age adults.

Statistical Methods

We calculated the proportion of the index and linked older child cohorts receiving MMR1 by 24 months of age. We examined variation in MMR1 receipt in the index cohort by individual-, household-, and area-level characteristics, as well as by MMR1 receipt in the linked older children's cohort.

We estimated the likelihood of MMR1 vaccination by 24 months in the index cohort using Poisson regression and calculated prevalence ratios (PR) and 95% confidence intervals (CI) for those sharing a household with a linked older child with non-receipt of MMR1 by 24 months of age, before and after adjustment for individual-, household-, and area-level covariates. Covariates with of $p<0.1$ in the univariable Poisson regressions were included in a multivariable Poisson regression model following a step-wise model selection strategy. Variables were retained in the final multivariable model if $p \leq 0.05$.

We performed three sensitivity analyses. In the first, we changed the definition of the primary outcome to receipt of MMR1 between 12 and 18 months of age in line with the recently introduced Quality and Outcomes Framework targets introduced in 2021.[25] In the second, we excluded households containing index and linked older children with an age gap of more than five years. In the third, we extended the age range for MMR1 receipt in the index children from 12-24 months to 11-25 months to allow for potential misclassification of ages related to method for assigning date of birth. We performed post-hoc power calculations to determine an appropriate sample size to power our study for the primary outcome. All analyses were conducted using R Studio.[26]

Patient and public involvement

We involved patients and the public in the communication of study results and dissemination within the local community, using accepted principles from the UK Standards for Public Involvement.[27] The aim was to raise awareness of the importance of inequalities in timely childhood vaccinations. We established a patient advisory group, comprising six parents, to co-produce dissemination materials. The patient and public involvement group reflected on vaccination inequalities, the study design and how results were delivered. Participants expressed reservations about the categorisation of ethnic group and whether more granular categories could be used in future research. They discussed communication and visualisation of results. The results have been disseminated in the form of a short film, informed by advice about accessing seldom-heard as well as and existing community groups.

Results

The index cohort comprised 71,509 children (51% males) of whom 11,658 (16.4%) had not received MMR1 vaccine by 24 months of age. Children in the index cohort who did not receive MMR1 by 24 months of age were more likely to live with a linked older child who similarly had not received MMR1 by 24 months of age (Table 1). Index children receiving MMR1 by 24 months of age were more likely to be from South Asian ethnic groups, and living in households with fewer adults and fewer children, and in households with two or more working age adults or three generation households. Children in single adult households or in households with a larger number of children were less likely to receive MMR1 by 24 months. There was a marked gradient in MMR1 receipt by IMD quintile with an absolute difference of 7.3% in MMR1 receipt by 24 months between the least and most deprived quintiles.

In the unadjusted model, MMR1 receipt by 24 months of age was less likely in the index cohort sharing a household with a linked older child with no MMR1 receipt by 24 months of age (PR: 0.66, 95% CI: 0.65,0.67). The PR did not change after stepwise introduction of individual-, household-, and area-level covariates resulting in a PR of 0.67 (0.66,0.68) in the fully adjusted model (Figure 1; Table S2).

The proportion of index children with MMR1 receipt by age 18 months was, as expected, lower than the proportion with MMR1 receipt by age 24 months: 79.2%, 95% CI: 78.9,79.5. Sensitivity analyses using this measure as the primary outcome did not alter PR estimates (PR: 0.67; 0.66,0.68). Exclusion of households containing index children and linked older cohort children with an age gap of more than five years strengthened the association: PR: 0.57 (0.57,0.58). Extension of the age range for MMR1 receipt from 12-24 months to 11-25 months did not change the main findings: PR: 0.67 (0.66,0.68) (Figure 2, supplementary file Tables S4-S7).

While our study focussed on MMR1 receipt within the UK recommended age range at the time of the study, it is possible that children were vaccinated at older ages. We searched for MMR1 dates for those with no MMR1 date within the 12-24 month age range. Of the 11,658 index children with no MMR1 receipt by 24 months, 516 (4.4%) had a MMR1 record before 12 months, 2,893 (24.8%) had received MMR1 vaccination by 40 months or 3 years and 4 months (when children become eligible for the second dose), 749 (6.4%) received MMR1 after 40 months of age, and 7,500 (64.3%) had no

record of MMR1 receipt in the EHR by November 2021 when data were extracted (Table 2). This suggests that just over one third of index children did eventually receive MMR1 but significantly later than the recommended age. Almost half (47%) of the linked older children without MMR1 receipt between 12 and 24 months of age also eventually received MMR1 and this was also significantly later than the recommended age.

Post-hoc power calculations demonstrated that a sample size of 52,000 in the index cohort would provide 90% power to detect a 2 percentage point difference significant at the 1% level in MMR1 receipt by 24 months of age in the index child between those with and without a linked older child with no MMR1 receipt by 24 months.

Table 1: MMR1 receipt in linked index children by individual, household and area-level characteristics

	Vaccinated			**Non- Vaccinated**			**All Index cohort**		
	N=59,851 **(84.1%)**			**N =** 11,658 **(15.9%)**			**N=71,509**		
	Received first MMR between 12 and 24 months of age			*Did not receive first MMR between 12 and 24 months age*					
	N	%	95% CI	*n*	%	95% CI	*n*	%	95% CI
MMR1 Status of Oldest Child									
Vaccinated	53198	88.4	88.1, 88.6	6987	11.6	11.3, 11.9	60185	84.2	83.9 , 84.4
Non-vaccinated	6653	58.8	57.8, 59.7	4671	41.2	40.3, 42.2	11324	15.8	15.6, 16.1
Individual covariates									
Ethnic Background									
South Asian	16963	88.0	87.6, 88.5	2305	12.0	11.5, 12.4	19268	25.5	25.1, 25.8
White	16625	83.8	83.3, 84.3	3219	16.2	15.8,16.7	19844	28.3	27.9-28.6
Black or Black British	5703	82.2	81.2,83.1	1238	17.8	16.9,18.7	6941	10.0	9.8,10.2
Mixed and Other	4847	78.8	77.8,79.8	1303	21.2	20.2,22.2	6150	8.5	8.3,8.7
Missing**	15713	81.4	80.8,81.9	3593	18.6	18.1,19.2	19306	27.7	27.4,28.1
Sex									
Female	29399	84.0	83.6,84.3	5614	16.0	15.6,16.4	35013	48.9	48.5,49.3

Male	30452	83.4	83,83.8	6044	16.6	16.3,16.9	36496	51.1	50.7,51.4
Household-level covariates									
Household size									
3-4	18695	86.1	85.7-86.6	2976	13.9	13.5,14.3	21671	30.3	30 ,30.6
5 to 7	26867	84.0	83.6,84.4	5097	16.0	15.6,16.4	31964	44.8	44.4,45.2
8 to 10	9397	80.6	79.9,81.3	2264	19.4	18.7,20.1	11661	16.3	16,16.6
Missing**	4881	78.7	77.7,79.7	1320	21.3	20.3,22.3	6201	8.6	8.4,8.8
Household Composition									
Two working age adults with children	42380	84.6	84.3,84.9	7713	15.4	15.1,15.7	50093	76.7	76.4,77
Single working age adult with children	7699	81.5	80.7,82.3	1747	18.5	17.7,19.3	9446	14.5	14.2,14.7
Three-generational household	4891	84.8	83.8, 85.7	878	15.5	14.5,16.4	5769	8.8	8.6,9
Missing**	4881	78.7	77.7,79.7	1320	21.3	20.3,22.3	6201	8.6	8.4,8.8
No. of children in the household									
2 to 3	43968	85.4	85.0,85.7	7527	14.6	14.3,14.9	51495	72	71.7,72.3
4 to 6	10669	80.2	79.5,80.8	2629	19.8	19.2,20.5	13298	18.7	18.4,19
7 to 9	333	64.7	60.4,68.8	182	35.3	31.2,39.6	515	0.7	0.6,0.8
Missing**	4881	78.7	77.7,79.7	1320	21.3	20.3,22.3	6201	8.6	8.4,8.8
Area level covariates									
Index of Multiple Deprivation Quintile									
1 (most deprived)	23861	83.9	83.5,84.3	4587	16.1	15.7,16.5	28448	40	39.7,40.3

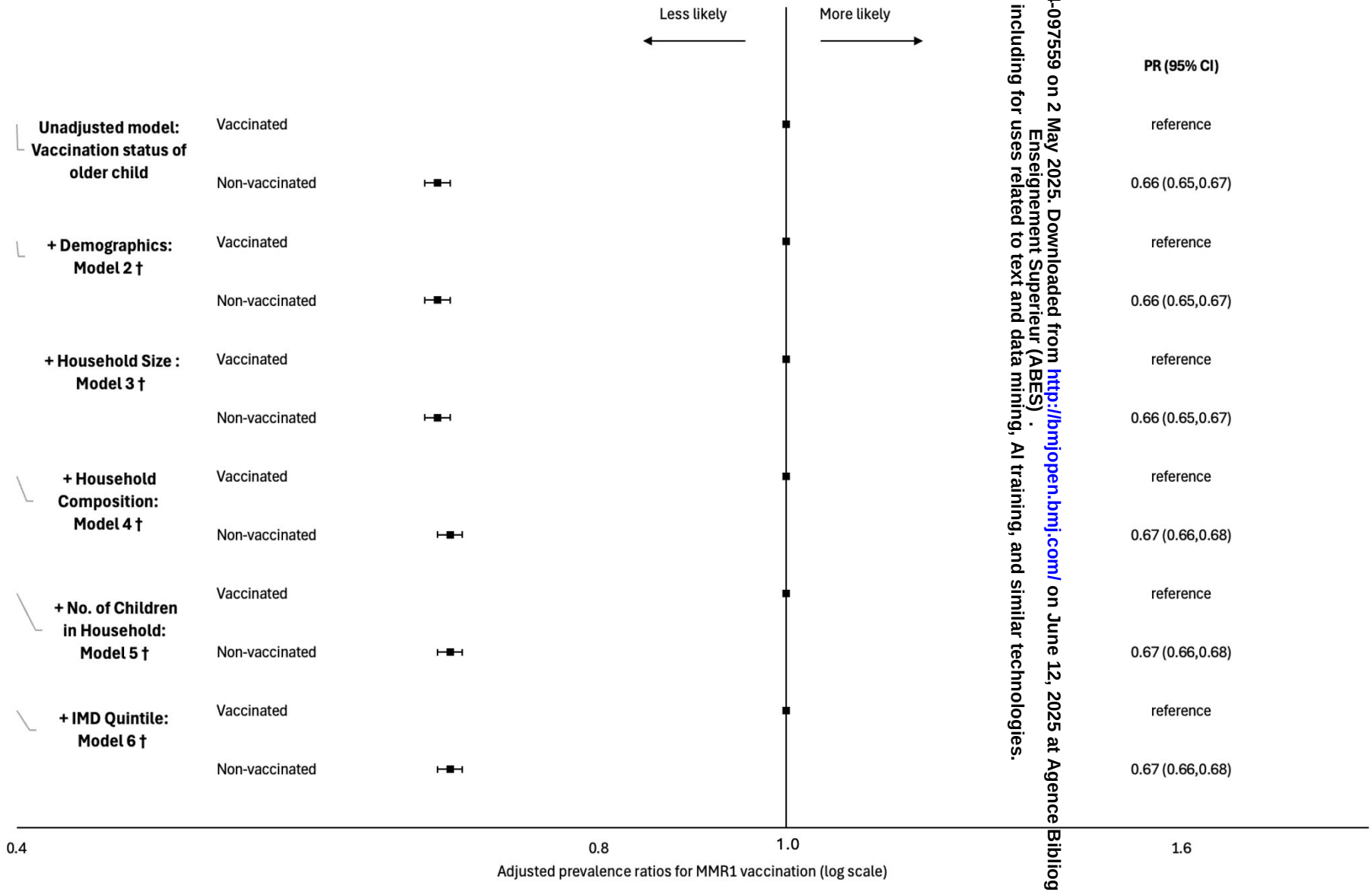
2	23512	82.3	81.7,82.8	5052	17.7	17.2,18.1	28564	39.8	39.5,40.1
3	7600	83.9	83.2,84.7	1454	16.1	15.3,16.8	9054	12.6	12.4,12.8
4	3345	88.9	87.9,89.9	417	11.1	10.1,12.1	3762	5.2	5,5.4
5 (least deprived)	1533	91.2	89.7,92.5	148	8.8	7.5,10.2	1681	2.3	2.2,2.4

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

Table 2. MMR1 receipt in Index and Older Children without MMR1 receipt between 12 and 24 months of age.

Non-vaccinated groups	Index Child (N = 11658)	%	Older Child (N=11324)	%
MMR1 receipt <12 months of age	516	4.4	993	8.8
MMR1 receipt between 24 and 2y40 months of age	2893	24.8	2642	23.3
MMR1 receipt > 40 months of age	749	6.4	1689	14.9
No record of MMR1 receipt in period of follow-up	7500	64.3	6000	53.0
Total	11658	100.0	11324	100.0

Figure 1. Forest Plot of MMR1* Vaccination Prevalence Ratios by 24 months of age using stepwise Poisson Regression

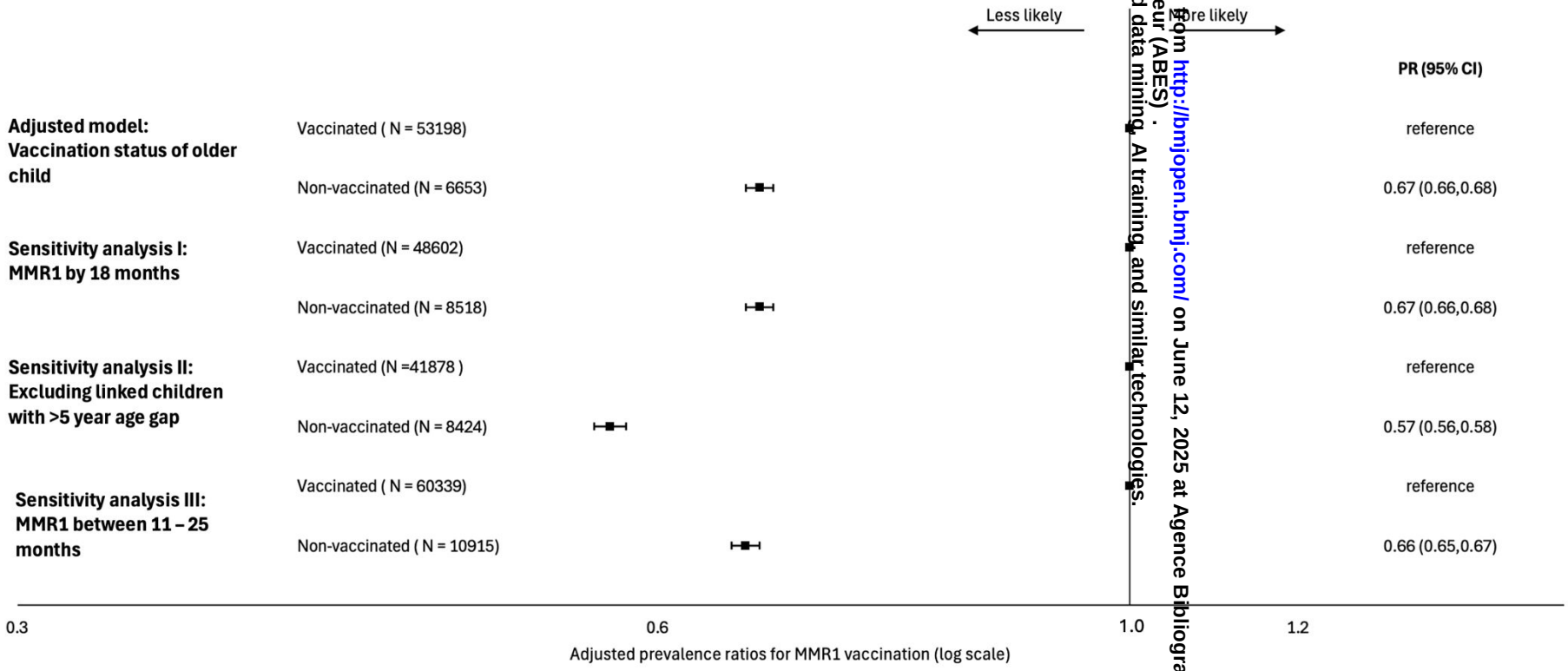


† Model 1: Vaccination status of older child sharing household with index child
Model 2: Model 1 + Sex + Ethnicity of index child
Model 3: Model 2 + Household size
Model 4: Model 3 + Household composition
Model 5: Model 4 + Number of children in the household
Model 6: Model 5 + Index of Multiple Deprivation quintile

†Vaccinated signifies receipt of MMR1 by 24 months of age

*MMR1: first Measles, Mumps and Rubella dose

Figure 2. Forest Plot comparing MMR1* Prevalence ratios from main model and from specified sensitivity analyses



†Vaccinated signifies receipt of MMR1 by 24 months of age

*MMR1: first Measles, Mumps and Rubella dose

Discussion

We have shown that 16% of children from an English urban, disadvantaged, and multi-ethnic population with low MMR1 coverage do not receive MMR1 by age 24 months, and that they are less likely to do so if they share a household with an older child who did not receive MMR1 by age 24 months. This association was independent of ethnic group, number of children in the household, household composition, and area-level deprivation, and was strengthened when analyses were confined to household children with an age gap of less than five years. We also found that children in single adult households or in households with a larger number of children are less likely to receive MMR1, confirming findings from previous studies reporting household characteristics of children with delayed MMR1 receipt. These findings suggest that caregivers' actions related to attendance for child vaccinations may be consistent across children in the household, particularly among children who are close in age.

While our study focused on MMR1 receipt within the UK recommended age range at the time of the study, we were able to show that one third of index children did receive MMR1 at both younger and older ages. There are a number of explanations for this. UK vaccine guidance states that MMR1 may be given under 12 months of age in the context of outbreaks or exposure to measles. However, as there is evidence that this doesn't produce a strong antibody response, it is recommended that MMR1 must be given again within the scheduled age range.[3] Parents may not agree to a second MMR1, especially if this was given close to the first birthday. Furthermore, a proportion of MMR1 events under 12 months of age were assigned an implausible date (e.g. given at birth date), and we are aware that GP practices may use this to record vaccines given in other countries for which the caregiver is unable to provide a date. London includes a significant proportion of children who are non-UK born and who migrate after the age of primary immunisations, many of whom anecdotally also spend periods back in their country of birth.[28, 29] This complicates administration and recording of vaccines, and may create different expectations among parents or caregivers regarding vaccine schedules. Opportunistic catch up of MMR1 has also been initiated on a number of occasions, and appointments for the second dose may be the opportunity to give the first dose: almost one quarter of index and linked older children were given MMR1 between 24 and 40 months of age. So while we

were unable to confirm MMR1 receipt in two thirds of index and one half of linked older children, a significant proportion were delayed rather than never immunised.

This is to our knowledge the first study to examine associations within households of MMR1 coverage, so direct comparisons with existing literature are not possible. Previous studies have found that vaccine coverage is lower in families with larger numbers of children and in single-parent households.[30] [31] It has been suggested that the main drivers of vaccination delay in these households are access-based, with vaccination services and appointments less suitable for families with larger numbers of children, or for parents requiring more flexible clinic appointments.[13] [32] Vaccination delay may also be non-intentional; parents may delay vaccinations due to a child's illness.[33] This may explain some of the factors driving delayed MMR1 receipt in our study.

There may be other reasons for delayed MMR1 receipt. Qualitative research around reasons for delayed, partial or non-vaccination of children highlight the importance for parents of shared decision-making with clinicians, and the strong association between trust in healthcare professionals and vaccine hesitancy in parents or caregivers. Parents or caregivers who have some trust in the information given by healthcare professionals may delay rather than completely refuse a child's vaccination, and this may be a consistent factor for all children in the household.[34] One study looking at decision-making in a household between adults and adolescents for the Men ACWY vaccination found that information gathering outside of a healthcare setting even prior to invitation for vaccination significantly impacted the decision made.[35]

Vaccinations can also be delayed by parents if they feel that data around the safety of a vaccine is insufficient, or if they have concerns about overburdening a child's immune system.[36, 37] Parental or caregiver disagreement around childhood vaccination may also contribute to delay.[14]

Further qualitative research is needed to tease out the likely heterogenous reasons for MMR1 delay at a household level and to understand household factors that interact with access and the decision-making process.[38] Delay in primary vaccinations against diphtheria, pertussis, polio, tetanus and

Haemophilus influenza has been shown to be associated with an incomplete vaccination schedule by 24 months of age.[39] We were not able to examine this in our study.

Implications for practice

Our study has demonstrated that delay in MMR1 receipt is strongly clustered within households. This lack of timely protection or any protection within households increases the risk of measles outbreaks. This suggests the need for household-based interventions to improve vaccination coverage and timeliness. Knowing the household composition of children with delayed or non-vaccination can allow a healthcare professional (HCP) to tailor their approach to organising vaccination appointments. For example, if it is known that there is more than one child in the household needing vaccination, a HCP can arrange an appropriate appointment for two children at one time. In England, the EHR in GPs allows a HCP to view the household of a selected patient.

Household-based interventions could also be considered by public health and service commissioners. Setting up services tailored to households with non- or partially-vaccinated children aligns with documented interventions recommended to improve vaccination coverage.[40] The same principle applies to providing wider public health education about vaccination for these households:- the interventions can be more targeted when non- or partially-vaccinated households are identified. Emerging interventions using enhanced information and educational programmes and vaccination delivery by health visitors could be tailored to target more vulnerable households.[41] Evidence from adolescent/adult decision making about vaccines in a household reinforces the importance of giving parents relevant information before the offer of vaccination from a healthcare provider.[35]

Existing literature cites multi-component interventions as the most effective interventions for increasing vaccination coverage in deprived communities with intersectional inequalities – these would include information, education and re-call measures.[38] Robust re-call methods are cited as an effective way to vaccinate children with delayed vaccinations.[42] We are evaluating a quality improvement programme that aims to improve timeliness and equity of pre-school immunisations in NEL, focussing on data-enabled call and recall for immunisation.[43]

Future research

We have shown that non-receipt of MMR1 by 24 months of age is clustered in households. However, a significant proportion of children do ultimately receive MMR1 in the preschool years and later childhood, with no clear evidence of MMR1 receipt in the remainder. Qualitative research is needed to understand the decision-making processes underlying this heterogenous group. Similar research in demographically different areas of the UK may help understand the extent to which these findings are generalisable to households in a different socioeconomic context.

Conclusion

Our study suggests a strong concordance in MMR1 vaccine delay between children sharing the same household in a region with the lowest MMR vaccination coverage in the UK.[4] These findings have implications for the planning and delivery of vaccination services that consider children in their household context.

Acknowledgements

We are grateful to colleagues within the Clinical Effectiveness Group for access to and expertise in using general practice data. This work uses data provided by patients and collected by the NHS as part of their care and support. We would also like to acknowledge our PPI participants for their invaluable insight into patient perspectives around dissemination of our research to the wider community.

Funding

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Contributions

As per CrEdit accreditation, significant contributions to: Conceptualisation (MM, CD, NF, MW), Methodology (MM, CD, MW, NF), Resources (CD, AG), Data Curation (MM, AG, NF, MW, KS), Data Analysis (MM, NF, CD), Writing-Original Draft (MM, CD), Review and Editing (MM, AG, NF, MW, KS, CD), Formal Analysis (MM, CD), Validation (AG, MM), Visualisation (MM), Supervision (CD), Funding Acquisition (MM, CD).

Competing interests declaration

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval

Access to general practice data is enabled by data sharing agreements between the Discovery Data Service and general practice data controllers. The Discovery Programme Board has approved data access by the REAL Child Health programme.

Data sharing

The senior author (CD) was granted access to de-identified data by the data controllers for this work and onward sharing of data is not permitted. The R codes used in the analyses are available at https://github.com/mmarszalek1991/mmarszalek1991households/tree/main1.

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Figure 1. Forest Plot of MMR1* Vaccination Prevalence Ratios by 24 months of age using stepwise Poisson regression

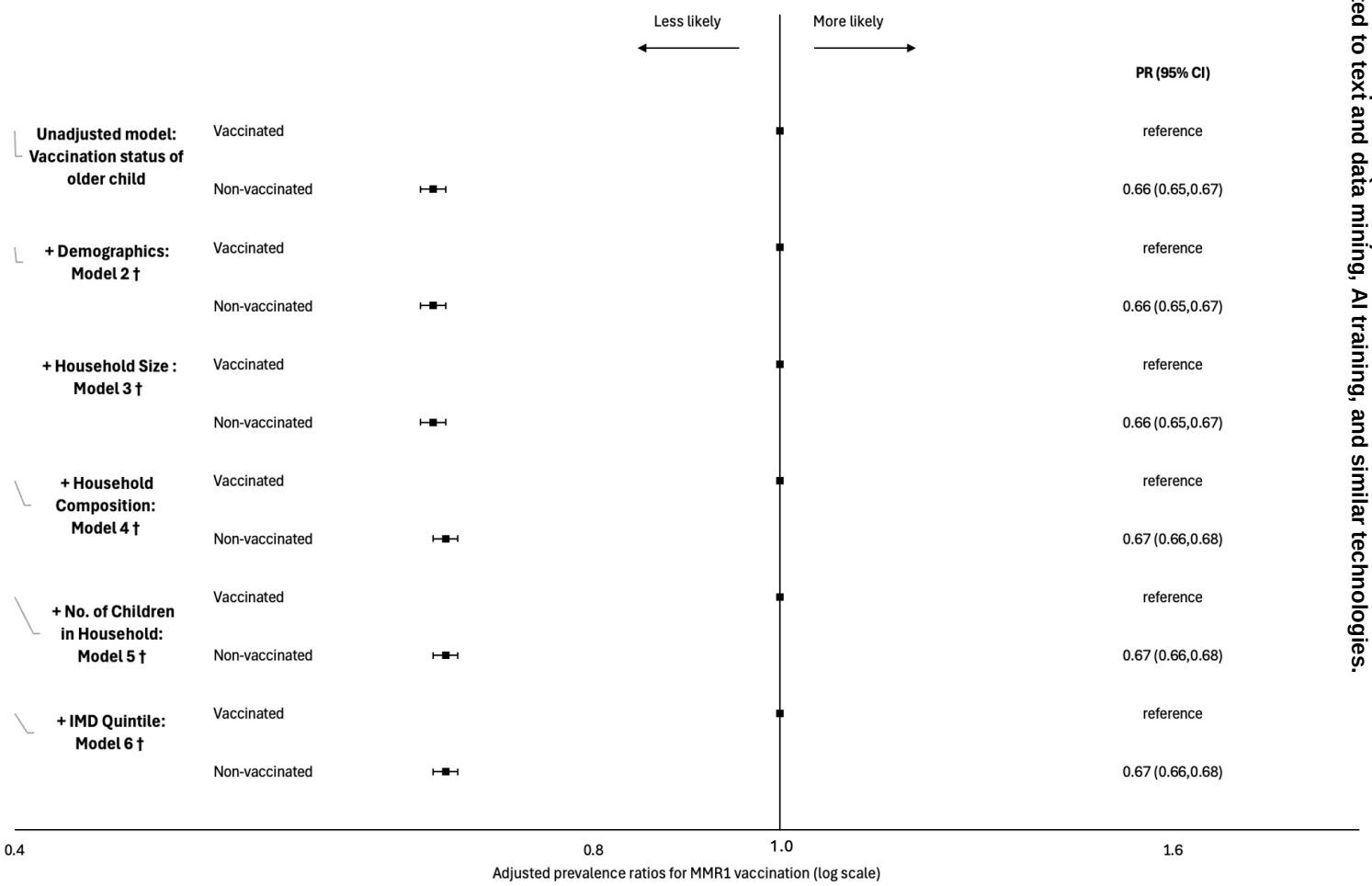

Figure 2. Forest Plot comparing MMR1* Prevalence ratios from main model and from specified sensitivity analyses

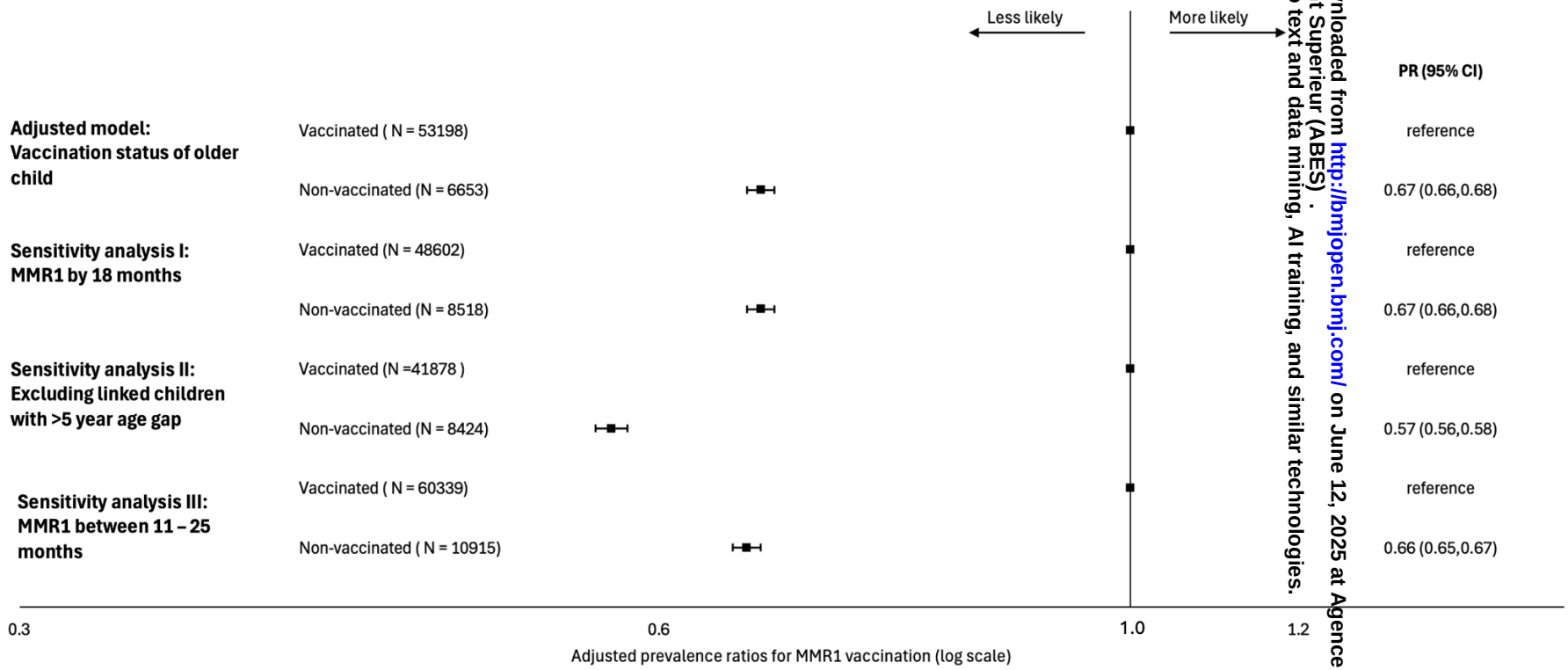

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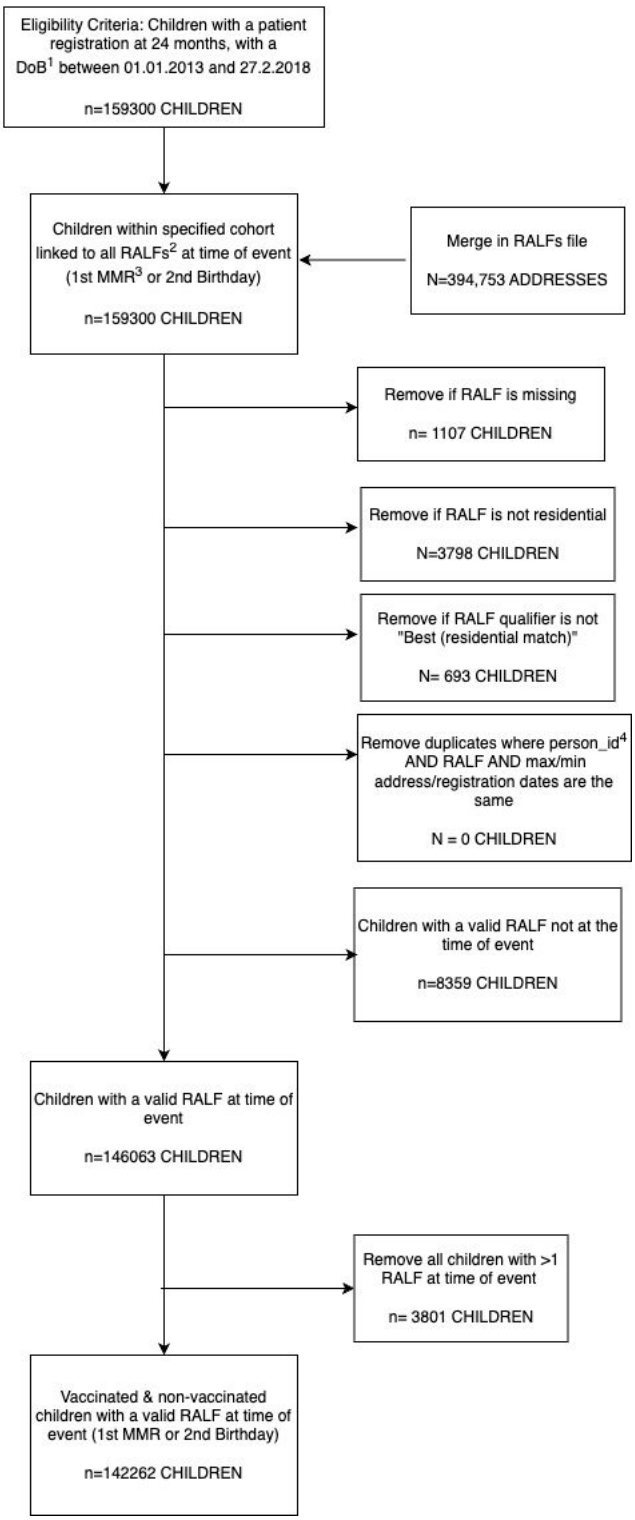
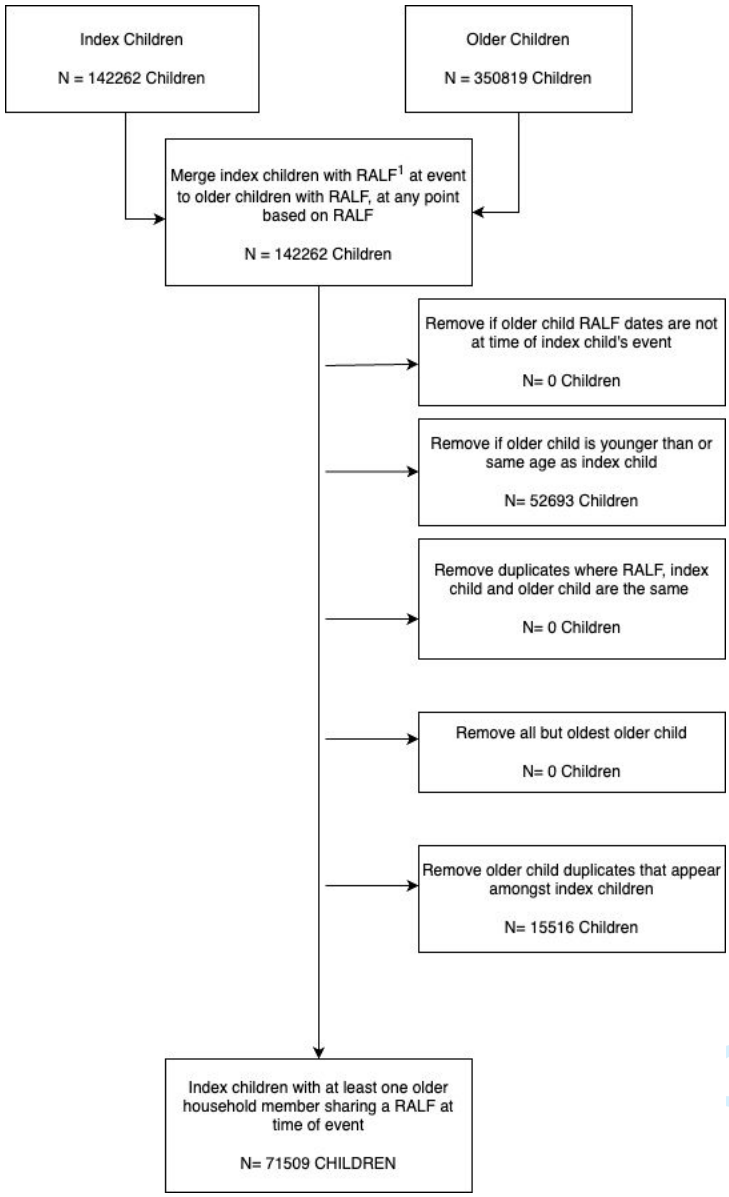
Figure S1- Inclusion and Exclusion Criteria for Sample population with a valid Residential Anonymised Linkage Field (RALF)



1 Date of Birth
2 Residential Anonymised Linkage Field
3 Measles, Mumps & Rubella vaccination
4 Individual person identifier

Figure S2- Inclusion and Exclusion criteria for linking index and older children



[1] Residential Anonymised Linkage Field

Supplementary file 3 (S3)- STROBE Checklist

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3	
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4	
Methods				
Study design	4	Present key elements of study design early in the paper	4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-7	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-7	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-7	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7	
Bias	9	Describe any efforts to address potential sources of bias	6	

Study size	10	Explain how the study size was arrived at	4-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Supplementary file
		(b) Give reasons for non-participation at each stage	Supplementary file
		(c) Consider use of a flow diagram	Supplementary file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	9
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	3 + Supplementary file

		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10 + supplementary file
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

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

Supplementary file 4 (S4) - RECORD checklist

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Abstract- Separate File
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			2
Objectives	3	State specific objectives, including any prespecified hypotheses			2-3

Methods					
Study Design	4	Present key elements of study design early in the paper			3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			3
Participants	6	*(a)* *Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b)* *Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	4

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Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	5
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			3-4
Bias	9	Describe any efforts to address potential sources of bias			4
Study size	10	Explain how the study size was arrived at			7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			6

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			6-7
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	3
				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	3

Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	4
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for nonparticipation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons should be described in the text and/or by means of the study flow diagram.	3-5
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			7

Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure			7-9
		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounderadjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			7-10
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			10-14
Discussion					
Key results	18	Summarise key results with reference to study objectives			15

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives,			15
		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			17
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			18-19
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	19

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

Table S1- Systematized Nomenclature of Medicine (SNOMED) clinical codes for first Measles, Mumps and Rubella vaccination procedures

Events recorded in the primary care electronic heath record using another clinical coding system (e.g. Read v2 or EMIS local codes) have been mapped to relevant SNOMED codes within the Discovery Data Service. This ensures that searching the database using SNOMED codes captured all events regardless of the clinical coding system used.

SNOMED concept ID	Other code	Clinical coding scheme	Code description
38598009	38598009	SNOMED	Measles-mumps-rubella vaccination (procedure)
	65M1.	Read v2	Measles/mumps/rubella vaccn.
	^ESCT1405772	EMIS local	Administration of measles and mumps and rubella vaccine
47435007	47435007	SNOMED	Measles vaccination (procedure)
	65A..	Read v2	Measles vaccination
	65A1.	Read v2	Measles vaccination
	ZV042	Read v2	[V]Measles vaccination
	^ESCT1405845	EMIS local	Administration of measles vaccine
50583002	50583002	SNOMED	Mumps vaccination (procedure)
	65F5.	Read v2	Mumps vaccination
	ZV046	Read v2	[V]Mumps vaccination
	^ESCT1405876	EMIS local	Administration of mumps vaccine
82314000	65B..	Read v2	Rubella vaccination
	ZV043	Read v2	[V]Rubella vaccination
	^ESCT1406118	EMIS local	Administration of rubella vaccine
170364006	65A2.	Read v2	Measles vaccin.+immunoglobulin
432636005	^ESCT1408534	EMIS local	Administration of measles and mumps and rubella and varicella virus vaccine
871909005	^ESCT1397548	EMIS local	Administration of first dose of measles and mumps and rubella and varicella virus vaccine
150971000119104	ZV064	Read v2	[V]Measles-mumps-rubella (MMR) vaccination
308081000000105	65M10	Read v2	First MMR (measles mumps and rubella) vaccination
	Xaeec	Read v3	First MMR (measles mumps and rubella) vaccination
	^ESCTME809974	EMIS local	Measles mumps and rubella vaccination - first dose

505001000000109	9ki1.	Read v2	MMR catch-up vaccination - enhanced services administration
	XaQPr	Read v3	Measles mumps rubella catch-up vaccination
571591000119106	^ESCT1409651	EMIS local	Administration of live attenuated measles mumps and rubella vaccine
1037251000000100	65M11	Read v2	First MMR vaccination given by other healthcare provider
	Xaeeq	Read v3	First MMR vaccination given by other healthcare provider

We included clinical codes relating to administration of mono-components of the first MMR vaccination. After removal of duplicate data entries and merging to the study cohort, 584989 children had a clinical code for measles vaccination, and two for mumps vaccination, as opposed to a combined MMR vaccination.

Table S2. Demographics of linked and unlinked cohorts by individual-, household- and area-level variables

	Linked cohort (n = 71509)			Unlinked cohort (n = 70753)		
	N	%	95% CI	N	%	95% CI
Individual Variables						
MMR status						
Vaccinated	59851	83.6	83.3-83.9	60512	85.5	85.3-85.8
Non-Vaccinated	11658	16.4	16.1-16.6	10240	14.5	14.2-14.7
Sex						
Female	35013	48.9	48.5-49.3	34885	49.3	48.9-49.7
Male	36496	51.1	50.7-51.4	35867	50.7	50.3-51.1
Ethnic Background						
Asian or Asian British	19268	25.5	25.1-25.8	16073	22.7	22.4-23
White	19844	28.3	27.9-28.6	23536	33.3	32.9-33.6
Missing	19306	27.7	27.4-28.1	18807	26.6	26.3-26.9
Black or Black British	6941	10.0	9.8-10.2	5467	7.7	7.5-7.9
Mixed and Other	6150	8.5	8.3-8.7	6869	9.7	9.5-9.9
Household-level Variables						
Number of Children per household						
2 to 3	51495	72.0	71.7-72.3	59151	83.6	83.3-83.9
4 to 6	13298	18.7	18.4-19	4486	6.3	6.1-6.5
7 to 9	515	0.7	0.6-0.8	270	0.4	0.3-0.5
Missing	6201	8.6	8.4-8.8	6845	9.7	9.4-10
Household size						
3 to 4	21683	30.3	30 -30.6	37417	52.9	52.5-53.3
5 to 7	31964	44.7	44.3-45.1	18976	26.8	26.5-27.1
8 to 10	11661	16.3	16-16.6	7514	10.6	10.4-10.8
Missing	6201	8.7	8.5-8.9	6845	9.7	9.4-10
Household composition						
Two adults with children	50093	70.0	69.7-70.3	46906	66.3	66-66.6
Single adult with children	9446	13.2	13-13.4	10356	14.6	14.4-14.9
Three generational household	5769	8.1	7.9-8.3	6645	9.4	9.2-9.6
Missing	6201	8.7	8.5-8.9	6845	9.7	9.5-9.9
Area-level Variables						
IMD Quintile						
IMD1 (Most deprived)	28448	40.0	39.7-40.3	26062	36.8	36.5-37.2
IMD2	28564	39.8	39.5-40.1	28972	40.9	40.5-41.3
IMD3	9054	12.6	12.4-12.8	9602	13.6	13.3-13.8
IMD4	3762	5.2	5-5.4	4311	6.1	5.9-6.3
IMD5 (Least deprived)	1681	2.3	2.2-2.4	1805	2.5	2.4-2.6

Table S3. Unadjusted and adjusted prevalence ratios for 1st Measles, Mumps and Rubella vaccination by 24 months of age, by individual-, household-, and area-level characteristics:

	PR[1]	95% CI[1]	p-value	PR[1]	95% CI[1]	p-value
Individual characteristics						
Vaccination status of older child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.66	0.66, 0.67	<0.001	0.67	0.67, 0.68	<0.001
Sex						
Male	Reference			Reference		
Female	0.99	0.99, 1.00	0.073	0.99	0.99,1.00	0.07
Ethnic background						
Asian or Asian British	1.04	1.03, 1.05	<0.001	1.05	1.04, 1.06	<0.001
White	Reference			Reference		
Missing	0.97	0.96, 0.98	<0.001	0.98	0.97, 0.99	<0.001
Black or Black British	0.98	0.97, 0.99	0.001	1.00	0.98, 1.01	0.4
Mixed and Other	0.95	0.94, 0.97	<0.001	0.97	0.95, 0.98	<0.001
Household-level Variables						
Number of children per household						
2 to 3	Reference			Reference		
4 to 6	0.95	0.94,0.96	<0.001	0.97	0.96,0.98	<0.001
7 to 9	0.82	0.78,0.85	<0.001	0.85	0.82,0.89	<0.001
Missing	0.94	0.93,0.96	<0.001	NA	NA	NA
Household size						
3 to 4	Reference			Reference		
5 to 7	0.98	0.98,0.99	<0.001	0.97	0.96,0.98	<0.001
8 to 10	0.96	0.95,0.97	<0.001	0.96	0.94,0.97	<0.001
Missing	0.94	0.93,0.95	<0.001	NA	NA	NA
Household composition						
Two adults with children	Reference			Reference		
Single adult with children	0.97	0.96,0.97	<0.001	0.95	0.94,0.96	<0.001
Three generational household	1.00	0.98,1.01	0.7	1.00	0.99,1.01	0.7
Missing	0.95	0.94,0.96	<0.001	0.92	0.90,0.93	<0.001
Area-level Variables						
IMD Quintile						
IMD1 (Most deprived)	Reference			Reference		
IMD2	0.99	0.98,1.00	0.002	0.99	0.98,0.99	<0.001
IMD3	1.00	0.99,1.01	0.8	0.99	0.98,1.00	0.13
IMD4	1.04	1.03,1.06	<0.001	1.03	1.02,1.05	<0.001
IMD5 (Least deprived)	1.07	1.04,1.09	<0.001	1.05	1.03,1.08	<0.001

[1] PR = Prevalence Ratio, CI = Confidence Interval

Table S4- Sensitivity analysis: timely Measles, Mumps and Rubella vaccination status at 18 months of age, by individual-, household-, and area-level characteristics

	Vaccinated			**Non- Vaccinated**			**All Index cohort**		
	N= 56641 (79.2%)			**N = 14889 (20.8%)**			**N=71530**		
	Received first MMR between 12 and 18 months of age			*Did not receive first MMR between 12 and 18 months of age*					
	n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI
Individual-level									
Ethnic Background									
Asian or Asian British	16214	84.3	83.8-84.9	3007	15.6	15.1-16.2	19221	26.9	26.5-27.2
White	15834	79.9	79.3-80.5	3978	20.1	19.5-20.6	19812	27.7	27.4-28
Missing	14803	76.5	75.9-77.1	4554	23.5	22.9-24.1	19357	27.1	26.7-27.4
Black or Black British	5342	76.9	75.9-77.9	1605	23.1	22.1-24.1	6947	9.7	9.5-9.9
Mixed and Other	4448	71.8	70.7-72.9	1745	28.2	27.1-29.3	6193	8.7	8.5-8.9
Sex									
Female	27814	79.4	79-79.8	7206	20.6	20.2-21	35020	49.0	48.6-49.3
Male	28827	79	78.5-79.4	7683	21	20.6-21.5	36510	51.0	50.6-51.4
Household -level									
MMR vaccination status of older household child									
Vaccinated	48602	85.8	85.5-86.1	8039	14.2	13.9-14.5	56641	79.2	78.9-79.5
Non-vaccinated	8518	57.2	56.4-58.0	6371	42.8	42-43.6	14889	20.8	20.5-21.1
Total number of adults and children per household									
0-4	17848	82.4	81.9-82.9	3819	17.6	17.1-18.1	21655	30.3	29.9-30.6
5 to 7	25460	79.7	79.2-80.1	6492	20.3	19.9-20.8	31952	44.7	44.3-45
8 to 10	8806	75.5	74.7-76.3	2849	24.4	23.7-25.2	11655	16.3	16-16.6
Missing	4527	72.4	71.2-73.5	1729	27.6	26.5-28.8	6256	8.7	8.5-8.9
Household composition									
Two adults with children	40292	80.5	80.1-80.8	9773	19.5	19.3-19.9	50065	70	69.6-70.4
Single adult with children	7187	76.1	75.2-77.0	2256	23.9	23.0-24.8	9443	13.2	13-13.4
Three generational household	4625	80.3	79.5-81.6	1131	19.7	18.7-20.8	5766	8.1	7.9-8.3
Missing	4527	72.4	71.2-73.5	1729	27.6	26.5-28.8	6256	8.7	8.5-8.9
Number of Children in household									
2 to 3	41973	81.6	81.2-81.9	9494	18.4	18.1-18.8	51467	71.9	71.6-72.2
4 to 6	9875	74.2	73.5-75.0	3422	25.7	25.0-26.5	13297	18.6	18.3-18.9
7 to 9	266	52.1	47.7-56.5	244	47.8	43.4-52.3	510	0.7	0.6-0.8

Missing	4527	72.4	71.2-73.5	1729	27.6	26.5-28.8	6256	8.7	8.5-8.9
Area-level characteristics									
Index of Multiple Deprivation quintile									
IMD 1 (most deprived)	22451	78.9	78.4-79.4	5998	21.0	20.6-21.6	28449	39.8	39.4-40.1
IMD 2	22180	77.6	77.1-78.1	6390	22.4	21.9-22.9	28570	39.9	39.6-40.3
IMD 3	7273	80.3	79.4-81.1	1786	19.7	18.9-20.5	9059	12.7	12.4-12.9
IMD 4	3238	85.9	84.8-87	530	14	13-15.2	3768	5.3	5.1-5.4
IMD 5 (least deprived)	1499	89	87.4-90.5	185	11	9.5-12.5	1684	2.3	2.3-2.4

Table S5- Sensitivity analyses I- unadjusted and adjusted prevalence ratios for 1st Measles, Mumps and Rubella vaccination receipt by 18 months of age

	PR[1]	95% CI[1]	p-value	PR[1]	95% CI[1]	p-value
	Unadjusted Variable			**Adjusted Variable**		
Individual characteristics						
Vaccination status of older child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.66	0.65,0.66	<0.001	0.67	0.66,0.68	<0.001
Sex						
Female	Reference			Reference		
Male	1.00	0.99,1.00	0.2	1.00	0.99,1.00	0.13
Ethnic Background						
Asian or Asian British	1.04	1.03,1.05	<0.001	1.06	1.05,1.07	<0.001
White	Reference			Reference		
Missing	0.96	0.95,0.97	<0.001	0.97	0.96,0.98	<0.001
Black or Black British	0.96	0.95,0.98	<0.001	0.99	0.97,1.00	0.042
Mixed and Other	0.92	0.95,0.97	<0.001	0.94	0.96,0.98	<0.001
Household-level variables						
Household size						
3 to 4	Reference			Reference		
5 to 7	0.98	0.97,0.99	<0.001	0.97	0.96,0.98	<0.001
8 to 10	0.95	0.94,0.96	<0.001	0.96	0.94,0.97	<0.001
Number of children per household						
2 to 3	Reference			Reference		
4 to 6	0.93	0.92,0.94	<0.001	0.95	0.94,0.96	<0.001
7 to 9	0.72	0.68,0.76	<0.001	0.75	0.71,0.80	<0.001
Household composition						
Two adults with children	Reference			Reference		
Single adult with children	0.95	0.94,0.96	<0.001	0.94	0.93,0.95	<0.001
Three generational household	0.99	0.98,1.01	0.3	0.99	0.98,1.01	0.4
Area-level variables						
IMD Quintile						
IMD1 (Most deprived)	Reference			Reference		
IMD2	0.99	0.98,1.00	0.013	0.99	0.98,0.99	0.001
IMD3	1.01	1.00,1.02	0.062	1.00	0.99,1.01	>0.9
IMD4	1.06	1.04,1.08	<0.001	1.05	1.03,1.07	<0.001
IMD5 (Least deprived)	1.10	1.07,1.12	<0.001	1.08	1.05,1.11	<0.001

[1] PR = Prevalence Ratio, CI = Confidence Interval

Table S6- Sensitivity analyses II- Unadjusted and adjusted prevalence ratios in multivariable analysis: Index and linked older cohort children with an age gap greater than five years excluded

	PR[1]	95% CI[1]	p-value	PR[1]	95% CI[1]	p-value
	Unadjusted			Adjusted		
Individual Characteristics						
Vaccination status of older child						
Vaccinated	Reference	—		Reference		
Non-vaccinated	0.56	0.56, 0.57	<0.001	0.57	0.57,0.58	<0.001
Ethnicity						
White	Reference	—		Reference		
Asian or Asian British	1.03	1.02, 1.04	<0.001	1.04	1.03,1.06	<0.001
Black or Black British	0.98	0.96, 0.99	0.006	1.00	0.98,1.01	>0.9
Mixed and Other	0.96	0.94, 0.97	<0.001	0.97	0.95,0.98	<0.001
Missing	0.97	0.96, 0.98	<0.001	0.98	0.97,0.99	<0.001
Sex						
Male	Reference	—		Reference		
Female	1.0	0.99, 1.00	0.2	1.0	0.99,1.00	0.2
Household characteristics						
Household composition						
Two adults with children	Reference	—		Reference		
Single adult with children	0.97	0.96, 0.98	<0.001	0.95	0.94,0.97	<0.001
Three generational household	1.00	0.98, 1.01	0.6	1.00	0.98,1.01	>0.9
Missing	0.96	0.95, 0.97	<0.001	NA	NA	NA
No of children in household						
2 to 3	Reference	—		Reference		
4 to 6	0.94	0.93, 0.95	<0.001	0.96	0.95, 0.97	<0.001
7 to 9	0.85	0.81, 0.89	<0.001	0.88	0.84, 0.93	<0.001
Missing	0.95	0.94, 0.96	<0.001	NA	NA	NA
Area level characteristics						
IMD Quintile						
IMD 1 (Most deprived)	Reference	—		Reference		
IMD 2	0.99	0.98, 1.00	0.2	0.99	0.98,1.00	0.019
IMD 3	1.01	1.00, 1.03	0.041	1.00	0.99,1.02	0.5
IMD 4	1.05	1.03, 1.07	<0.001	1.04	1.02,1.06	<0.001
IMD 5 (Least deprived)	1.08	1.05, 1.10	<0.001	1.06	1.03,1.09	<0.001

[1] PR = Prevalence Ratio, CI = Confidence Interval

Table S7- Sensitivity analyses III- Unadjusted and adjusted prevalence ratios in multivariable analysis: 1st Measles, Mumps and Rubella vaccination receipt between 11–25 months of age

Characteristic	PR[1]	95% CI[1]	p-value	PR[1]	95% CI[1]	p-value
	Univariable			Multivariable		
Individual Characteristics						
Vaccination status of older child						
Vaccinated	Reference	—		Reference		
Non-vaccinated	0.65	0.64, 0.65	<0.001	0.66	0.65, 0.66	<0.001
Ethnicity						
White	Reference	—		Reference		
Asian or Asian British	1.03	1.02, 1.04	<0.001	1.05	1.04, 1.05	<0.001
Black or Black British	0.98	0.97, 0.99	0.003	1.00	0.98, 1.01	0.3
Mixed and Other	0.96	0.95, 0.97	<0.001	0.97	0.96, 0.98	<0.001
Missing	0.97	0.97, 0.98	<0.001	0.98	0.97, 0.99	<0.001
Sex						
Male	Reference	—		Reference		
female	1.0	0.99, 1.00	0.1	1.0	0.99, 1.00	0.2
Household Characteristics						
Household Composition						
Two adults with children	Reference	—		Reference		
Single adult with children	0.97	0.96, 0.98	<0.001	0.97	0.96, 0.98	<0.001
Three generational household	1.00	0.98, 1.01	0.4	0.99	0.98, 1.00	0.042
Missing	0.94	0.92, 0.95	<0.001	0.92	0.91,0.93	<0.001
No of Children in Household						
2 to 3	Reference	—		Reference		
4 to 6	0.96	0.95, 0.96	<0.001	0.96	0.95, 0.96	<0.001
7 to 9	0.83	0.80, 0.86	<0.001	0.84	0.81, 0.88	<0.001
Missing	0.93	0.92, 0.94	<0.001	NA	NA	NA
Area level characteristics						
IMD Quintile						
IMD 1 (Most deprived)	Reference	—		Reference		
IMD 2	0.99	0.98, 1.00	0.001	0.99	0.98, 0.99	<0.001
IMD 3	1.00	0.99, 1.01	0.8	0.99	0.98, 1.00	0.2
IMD 4	1.03	1.02, 1.05	<0.001	1.03	1.01, 1.04	<0.001
IMD 5 (Least deprived)	1.06	1.04,1.08	<0.001	1.06	1.03, 1.08	<0.001
[1] PR = Prevalence Ratio, CI = Confidence Interval						

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Household determinants of delayed MMR vaccination: longitudinal analysis using electronic health records in north east London, United Kingdom

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The authors declare no competing financial interests.

Abstract

Objectives

There is a lack of information about household factors associated with delayed Measles Mumps and Rubella (MMR) vaccination. We examined whether timeliness of first MMR (MMR1) receipt is associated with sharing a household with an older child with non-receipt of MMR1 independent of household composition and size.

Design

Longitudinal observational study using linked electronic health records

Setting:

North east London, United Kingdom

Participants:

The index cohort comprised 71,509 children (51.0% males) eligible to receive MMR1 between 1st January 2014 and 28th February 2020.

Methods

The primary outcome was MMR1 receipt between age 12 and 24 months. The explanatory variable was non-receipt of MMR1 between age 12 and 24 months in the oldest child sharing the same household. We examined the likelihood of MMR1 receipt in index children sharing a household with an older child with non-receipt of MMR1 between 12 and 24 months using logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) before and after adjustment for individual-, household-, and area-level covariates. We carried out sensitivity analyses excluding households with an age interval between oldest and youngest child greater than five years.

Results

59,851 (83.6%) index children received MMR1 between age 12 and 24 months. After adjustment for household composition and size, MMR1 receipt was less likely in index children sharing a household with an older child with non-receipt of MMR1 between age 12 and 24 months: OR: 0.19 (95% CI: 0.18,0.20). This association strengthened after excluding households with an age interval greater than five years: OR: 0.14 (0.13,0.15)

Conclusions

There is strong concordance within households of delay in MMR1 receipt independent of household size and composition. Lack of timely protection within households increases the risk of measles outbreaks. There is a need for household-based interventions to improve MMR1 timeliness.

Strengths and limitations

- We used a novel method to link individuals into households while maintaining privacy and confidentiality using electronic health records (EHRs) for a large population.
- We obtained high quality, accurately coded and validated MMR data in the EHR.
- We used robust statistical methods to assess relationships between the exposure and outcome variables.
- Processes of, and influences on, decision-making about vaccines between the linked younger and older children may have differed. We were not able to examine associations with delayed receipt of primary vaccinations against diphtheria, pertussis, polio, tetanus and Haemophilus influenza.
- More granular categorisation of ethnic groups, as suggested by our patient and public involvement group, was not possible due to limited sample size.

Introduction

Childhood vaccinations form an essential part of public health interventions provided by primary care.[1] In England and Wales, it is recommended that children receive a first dose of Measles, Mumps and Rubella (MMR) vaccine between age 12 and 13 months[2]: currently only 89% receive a first dose by age 24 months, and only 84% a second dose by age five years.[3] This countrywide statistic conceals marked geographic inequalities linked to deprivation. The World Health Organization (WHO) recommends that 95% of the population are given two MMR doses to achieve herd immunity and eliminate measles.[4] The United Kingdom (UK) lost measles elimination status in 2018 and while this was reinstated in 2021, measles outbreaks in areas with high measles susceptibility in young children in England suggest that this will not be sustained.[5] Clusters of inequalities in MMR coverage exacerbate existing outbreaks – a large proportion have been in London, an area with both low and profoundly inequitable coverage.[3]

In light of these public health concerns, and with the first dose conferring 93% protection against infection, there has been increasing emphasis on the importance of timely receipt of MMR1.[6] In the UK, national targets to ensure receipt of first MMR (MMR1) between 12 and 24 months of age have been recently replaced by a 12-18 month target reflecting this emphasis on timeliness.[7]

It is known that equity in vaccination coverage is impacted by social determinants such as deprivation, ethnicity and area-level variation in healthcare services.[8, 9] There is strong evidence demonstrating that children from more deprived areas are less likely to receive MMR vaccination compared to those living in affluent areas.[10] We and others 11 have previously shown that family size is an important determinant of partial or non-immunisation with MMR, suggesting that access to services may play an important role.[12 13]

Identifying factors at a household level can create actionable insights into how services might be tailored to improve receipt of vaccinations.[14] The current pressures on the UK National Health Service have significantly impacted the delivery of vaccinations in primary care- therefore new ways of working to vaccinate the most vulnerable children in a resource-tight setting are needed. [15, 16] We used electronic health records (EHRs) for an ethnically diverse and disadvantaged population, with

among the lowest proportion of children receiving MMR1 by 24 months of age in the UK, to investigate whether non-receipt of MMR1 between 12 and 24 months of age is clustered in households. Specifically, we hypothesised that children with non-receipt of MMR1 between 12 and 24 months were more likely to share a household with an older child with non-receipt of MMR1 at these ages, independently of the number of children in the household and household composition.

Methods

Study design and setting

We conducted a longitudinal observational study using primary care EHRs from 266 general practices in seven north east London (NEL) localities: Barking & Dagenham, City & Hackney, Havering, Newham, Redbridge, Tower Hamlets, and Waltham Forest.

Data Sources

Pseudonymised data were provided from the NEL Discovery Data Service (DDS), which receives primary care EHR data in near-real time for all general practices (GPs) in NEL. [17] Unique Property Reference Numbers (UPRNs) are allocated to all GP-recorded patient addresses in DDS using a quality-assured and validated address-matching algorithm.[18] UPRNs are pseudonymised into Residential Anonymous Linking Fields (RALF)[19] using a study-specific encryption key. We used RALFs to link children in households for address records and registrations from 2014 onwards, when data flow for address registrations into NEL DDS commenced. Data were extracted on 23rd November 2021.

Study population

The study population comprised 159,300 children registered with a NEL GP at the time of their second birthday and eligible to receive MMR1 between 1st January 2014 and 28th February 2020. We excluded 17,038 children without a RALF, with a non-residential RALF, with a poor-quality RALF match, or with more than one RALF at time of MMR1 or second birthday, leaving 142,262 children eligible for inclusion (supplementary file 1 figure S1).

Identifying children sharing a household

We identified older children sharing a household with the 142,262 index children at the index child's MMR1 date or 24 months of age, whichever is the earliest. Index and older children sharing a RALF at index child's MMR1 date, or at the index child's second birthday were considered to share a household. We identified all children in DDS based on the index children's RALFs and excluded 52,693 children without an older child in the household, and 15,516 older children who were already included as index children, leaving 71,509 index children with at least one older child sharing their household at the index child's MMR1 date or second birthday (supplementary file 1 figure S2). These 71,509 children are henceforth referred to as the "linked index cohort" and the older children with whom they share a household as the "linked older children's cohort".

The study methodology has been reported against the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement (supplementary file 2).[20, 21]

Primary outcome

The primary outcome is receipt of MMR1 between 12 and 24 months of age, which is consistent with the Cover of Vaccination Evaluated Rapidly (COVER) measures in place during the study period.[22]

We extracted sociodemographic and area-level data for the linked index and linked older child cohorts, together with all clinical events relating to MMR1 procedures (supplementary file 1 Table S1). We derived a proxy date of birth from calendar week, month and year of birth by combining the date of the first day of the week of the calendar week of birth with month and year of birth. We excluded duplicated events, and events without correct clinical codes. We assumed MMR1 was not given if there was no record of MMR1 being given in the primary care EHR. If a child did not have a record of a MMR1 vaccination, they were linked to a RALF at the time of their second birthday, and were defined as children with non-receipt of MMR1.

Explanatory variable

The main explanatory variable was non-receipt of MMR1 in the linked older child defined as no record of MMR1 given between 12 and 24 months of age.

Covariates

Individual-level

Individual-level covariates were sex and ethnic group. We categorised ethnic group of the index children using the NHS 5+1 classification using information recorded in the EHR.[23] We created five mutually exclusive ethnic groups: white ('white British', 'white Irish' or 'any other white background'); black ('black African', 'black Caribbean' or 'any other black background'); South Asian ('Indian', 'Pakistani', 'Bangladeshi' or 'Sri Lankan'); mixed/other ('any other ethnic background', 'mixed ethnicity', 'Chinese' or 'Asian other'); and missing category (ethnicity code in the primary care record missing or 'not stated' category selected).

Household-level

All household members sharing a household at the index child's MMR1 date were identified. We excluded households with more than ten members, only one child, or no adults aged ≥18.0 years. Household information was available for 65,308 households containing index and linked older children.

We categorised household composition using an adapted Harper and Mayhew method[24] into one of three mutually exclusive categories: working-age adults (aged 18-64 years) with children; single working-age adult with children, or at least one working-age and one older adult (aged >65 years) with children (three-generation household). We included households with at least one older adult with children but no working-age adult (skipped generation households) in the three-generation household group.

We calculated the total number of household members, as well as the number of children within a household at the index child's MMR1 date or 24 months of age for those with no MMR1 date.

Area-level

We merged 2019 Index of Multiple Deprivation (IMD) decile[25] into the datafile using the 2011 Lower layer Super Output Area (LSOA), an area with an average population of 1,500 people or 650 households, as the linkage field. IMD deciles were concatenated into quintiles from most (1) to least deprived (5).

We compared the linked index cohort (n=71,509) with the cohort of eligible children (*n*=70,753) not linked to another older child (supplementary file 1 Table S2). The linked sample had a lower

proportion with receipt of MMR1 between 12 and 24 months of age, were less likely to be from a white ethnic background, from smaller households, or from households with two or more working age adults.

Statistical Methods

We calculated the proportion of the linked index and older child cohorts receiving MMR1 between 12 and 24 months of age. We examined variation in MMR1 receipt in the linked index cohort by individual-, household-, and area-level characteristics, as well as by MMR1 receipt in the linked older children's cohort.

We estimated the likelihood of MMR1 vaccination between age 12 and 24 months in the linked index cohort using binary logistic regression and estimated odds ratios (OR) and 95% confidence intervals (CI) for those sharing a household with a linked older child with non-receipt of MMR1 between 12 and 24 months of age, before and after adjustment for individual-, household-, and area-level covariates. Covariates with of $p<0.1$ in the univariable logistic regression models were included in a multivariable logistic regression model following a step-wise model selection strategy. Variables were retained in the final multivariable model if $p\leq0.05$.

We performed three sensitivity analyses. In the first, we changed the definition of the primary outcome to receipt of MMR1 between 12 and 18 months of age in line with the recently introduced Quality and Outcomes Framework targets introduced in 2021.[26] In the second, we excluded households containing index and linked older children with an age gap of more than five years. In the third, we extended the age range for MMR1 receipt in the index children from 12-24 months to 11-25 months to allow for potential misclassification of ages related to method for assigning date of birth. We performed post-hoc power calculations to determine an appropriate sample size to power our study for the primary outcome. All analyses were conducted using R Studio.[27]

Post-hoc power calculations demonstrated that a sample size of 52,000 in the index cohort would provide 90% power to detect a two percentage point difference significant at the 1% level in MMR1

receipt between 12 and 24 months of age in the index child between those with and without a linked older child with no MMR1 receipt between 12 and 24 months.

Patient and public involvement

We involved patients and the public in the communication of study results and dissemination within the local community, in line with accepted principles from the UK Standards for Public Involvement.[28] The aim was to raise awareness of the importance of inequalities in timely childhood vaccinations. We established a patient advisory group, comprising six parents, to co-produce dissemination materials. The patient and public involvement group reflected on vaccination inequalities, the study design and how results were delivered. Participants expressed reservations about the categorisation of ethnic group and whether more granular categories could be used in future research. They discussed communication and visualisation of results. Dissemination of results is ongoing and informed by advice about accessing seldom-heard as well as and existing community groups.

Results

The index cohort comprised 71,509 children (51% males) of whom 11,658 (16.4%) had not received MMR1 vaccine between 12 and 24 months of age. Children in the index cohort who did not receive MMR1 between 12 and 24 months of age were more likely to live with a linked older child who similarly had not received MMR1 between 12 and 24 months of age (Table 1). Index children receiving MMR1 between 12 and 24 months of age were more likely to be from South Asian ethnic groups, or living in households with fewer adults and fewer children, or in households with two or more working age adults or three generation households. Children in single adult households or in households with a larger number of children were less likely to receive MMR1 between 12 and 24 months. There was a marked gradient in timely MMR1 receipt by IMD quintile with an absolute difference of 7.3% in MMR1 receipt between 12 and 24 months of age between the least and most deprived quintiles.

In the unadjusted model, MMR1 receipt between 12 and 24 months of age was less likely among children in the linked index cohort sharing a household with a linked older child with no MMR1 receipt between 12 and 24 months of age (OR: 0.19, 95% CI: 0.18,0.20). The effect size and direction did not

change after stepwise introduction of individual-, household-, and area-level covariates resulting in an adjusted OR of 0.20 (0.19,0.21) in the final model (Figure 1; supplementary file 1 Table S3).

In sensitivity analyses (Figure 2), the proportion of index children with MMR1 receipt between age 12 and 18 months (79.2%; 95% CI: 78.9,79.5) was, as expected, lower than the proportion with MMR1 receipt between 12 and 24 months (83.6%; 95% CI: 83.3,83.9) (supplementary file 1 Table S4). Associations were weaker in sensitivity analyses using this measure as the primary outcome (OR: 0.24; 0.23,0.25) (supplementary 2 file Table S5). By contrast, associations were stronger in sensitivity analyses restricted to households containing index children and linked older cohort children with an age gap of less than five years: OR: 0.14 (0.13,0.15) (supplementary file 1 Table S6). Sensitivity analyses extending the age range for MMR1 receipt to 11-25 months did not change the main findings: OR: 0.18 (0.17,0.19) (supplementary file 1 Table S7).

While our study focussed on MMR1 receipt within the UK recommended age range at the time of the study, it is possible that children were vaccinated before or after the recommended age range. We searched for MMR1 dates for those with no MMR1 date within the 12-24 month age range. Of the 11,658 index children with no MMR1 receipt between 12- 24 months, 516 (4.4%) had a MMR1 record before age 12 months, 2,893 (24.8%) between age 25 and 40 months (equivalent to 3 years and 4 months when children become eligible for the second dose), 749 (6.4%) received MMR1 after 40 months of age, and 7,500 (64.3%) had no record of MMR1 receipt in the EHR by November 2021 when data were extracted (Table 2). This suggests that just over one third of index children did eventually receive MMR1 but significantly later than the recommended age. Almost half (47%) of the linked older children without MMR1 receipt between 12 and 24 months of age also eventually received MMR1 and this was also significantly later than the recommended age.

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276 Table 1: MMR1 receipt in linked index children by individual, household and area-level characteristics

	Vaccinated			Non-vaccinated			All linked index children		
	N=59,851 (83.6%)			N=11,658 (16.4%)			N=71,509		
	Received first MMR between 12 and 24 months of age			*Did not receive first MMR between 12 and 24 months of age*					
	N	%	95% CI	*N*	%	95% CI	*n*	%	95% CI
MMR1 status of oldest child									
Vaccinated	53198	88.4	88.1, 88.6	6987	11.6	11.4, 11.9	60185	84.2	83.9, 84.4
Non-vaccinated	6653	58.8	57.8, 59.7	4671	41.2	40.3, 42.2	11324	15.8	15.6,16.1
Individual covariates									
Ethnic background									
South Asian	16963	88.0	87.6, 88.5	2305	12.0	11.5, 12.4	19268	25.5	25.1, 25.8
White	16625	83.8	83.3, 84.3	3219	16.2	15.7,16.7	19844	28.3	27.9, 28.6
Black or Black British	5703	82.2	81.2, 83.1	1238	17.8	16.9,18.7	6941	10.0	9.8,10.2
Mixed and Other	4847	78.8	77.8, 79.8	1303	21.2	20.8, 22.2	6150	8.5	8.3, 8.7
Missing**	15713	81.4	80.8, 81.9	3593	18.6	18.1,19.2	19306	27.7	27.4, 28.1
Sex									
Female	29399	84.0	83.6, 84.3	5614	16.0	15.7,16.4	35013	48.9	48.5, 49.3
Male	30452	83.4	83.0, 83.8	6044	16.6	16.2,16.9	36496	51.1	50.7, 51.4
Household-level covariates									
Household size									
3-4	18695	86.1	85.7, 86.6	2976	13.9	13.4,14.3	21671	30.3	30.0, 30.6
5 to 7	26867	84.0	83.6, 84.4	5097	16.0	15.6,16.4	31964	44.8	44.4, 45.2
8 to 10	9397	80.6	79.9, 81.3	2264	19.4	18.7, 20.1	11661	16.3	16.0,16.6
Missing**	4881	78.7	77.7, 79.7	1320	21.3	20.3, 22.3	6201	8.6	8.4, 8.8
Household composition									
Two working age adults with children	42380	84.6	84.3, 84.9	7713	15.4	15.1,15.7	50093	76.7	76.4, 77.0
Single working age adult with children	7699	81.5	80.7, 82.3	1747	18.5	17.7,19.3	9446	14.5	14.2,14.7

Three-generational household	4891	84.8	83.8, 85.7	878	15.5	14.5, 16.4	5769	8.8	8.6, 9.0
Missing**	4881	78.7	77.7, 79.7	1320	21.3	20.3, 22.3	6201	8.6	8.4, 8.8
Number of children in household									
2 to 3	43968	85.4	85.0, 85.7	7527	14.6	14.3, 15.0	51495	72	71.7, 72.3
4 to 6	10669	80.2	79.5, 80.8	2629	19.8	19.2, 20.5	13298	18.7	18.4,19.0
7 to 9	333	64.7	60.4, 68.8	182	35.3	31.2, 39.6	515	0.7	0.6, 0.8
Missing**	4881	78.7	77.7, 79.7	1320	21.3	20.3, 22.3	6201	8.6	8.4, 8.8
Area level covariates									
Index of Multiple Deprivation (IMD) Quintile									
1 (most deprived)	23861	83.9	83.5, 84.3	4587	16.1	15.7, 16.5	28448	40	39.7, 40.3
2	23512	82.3	81.7, 82.8	5052	17.7	17.2, 18.3	28564	39.8	39.5, 40.1
3	7600	83.9	83.2, 84.7	1454	16.1	15.3, 16.8	9054	12.6	12.4,12.8
4	3345	88.9	87.9, 89.9	417	11.1	10.1, 12.1	3762	5.2	5.0, 5.4
5 (least deprived)	1533	91.2	89.7, 92.5	148	8.8	7.5, 10.2	1681	2.3	2.2, 2.4

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

Table 2: MMR1 receipt in linked Index and Older Children without MMR1 receipt between 12 and 24 months of age

Non-vaccinated groups	Index Child (N = 11658)	%	Older Child (N=11324)	%
MMR1 receipt <12 months of age	516	4.4	993	8.8
MMR1 receipt between 24 and 40 months of age	2893	24.8	2642	23.3
MMR1 receipt >40 months of age	749	6.4	1689	14.9
No record of MMR1 receipt in period of follow-up	7500	64.3	6000	53.0
Total	11658	100.0	11324	100.0

Discussion

We have shown that 16% of children from an English urban, disadvantaged, and multi-ethnic population with low MMR1 coverage do not receive MMR1 between the recommended age interval of 12 and 24 months, and that they are less likely to do so if they share a household with an older child who did not receive MMR1 between age 12 and 24 months. This association was independent of ethnic group, number of children in the household, household composition, and area-level deprivation, and was strengthened when analyses were confined to household children with an age gap of less than five years. We also found that children in single adult households or in households with a larger number of children are less likely to receive MMR1 between 12 and 24 months of age, consistent with findings from previous studies reporting household characteristics of children with delayed or non-MMR1 receipt. These findings suggest that caregivers' actions related to attendance for child vaccinations may be consistent across children in the household, particularly among children who are close in age.

While we examined MMR1 receipt within the UK recommended age range of 12 to 24 months in place at the time of our study, we were able to show that one third of index children did receive MMR1 at both younger and older ages. There are a number of explanations for this. UK vaccine guidance states that MMR1 may be given under 12 months of age in the context of outbreaks or exposure to measles. However, as there is evidence that this doesn't produce a strong antibody response, it is recommended that MMR1 must be given again within the scheduled age range.[2] Parents may not agree to a second MMR1, especially if this was given close to the first birthday. Furthermore, a proportion of MMR1 events under 12 months of age were assigned an improbable date (e.g. given at birth date), and we are aware that GP practices may use this to record vaccines given in other countries for which the caregiver is unable to provide a date. London includes a significant proportion of children who are non-UK born and who migrate after the age of primary immunisations, many of whom anecdotally also spend periods back in their country of birth.[29, 30] This complicates administration and recording of vaccines, and may create different expectations among parents or caregivers regarding vaccine schedules. Opportunistic catch up of MMR1 has also been initiated on a number of occasions, and appointments for the second dose may be the opportunity to give the first dose: almost one quarter of index and linked older children were given MMR1 between 24 and 40

months of age. So, while we were unable to confirm MMR1 receipt in two thirds of index and one half of linked older children, a significant proportion were delayed rather than never immunised.

This is to our knowledge the first study to examine associations within households of MMR1 timeliness, so direct comparisons with existing literature are not possible. Previous studies have found that vaccine coverage is lower in families with larger numbers of children and in single-parent households.[31 32] It has been suggested that the main drivers of vaccination delay in these households are access-based, with vaccination services and appointments less suitable for families with larger numbers of children, or for parents requiring more flexible clinic appointments.[12 33] Vaccination delay may also be non-intentional: parents may delay vaccinations due to a child's illness.[34] This may explain some of the factors driving delayed MMR1 receipt in our study.

There may be other reasons for delayed MMR1 receipt. Qualitative research around reasons for delayed, partial or non-vaccination of children highlight the importance for parents of shared decision-making with clinicians, and the strong association between trust in healthcare professionals and vaccine hesitancy in parents or caregivers. Parents or caregivers who have some trust in the information given by healthcare professionals may delay rather than completely refuse a child's vaccination, and this may be a consistent factor for all children in the household.[35] One study looking at decision-making between adults and adolescents in a household for the Men ACWY vaccination found that information gathering outside of a healthcare setting, even prior to invitation for vaccination, significantly impacted the decision made.[36]

Vaccinations can also be delayed by parents if they feel that information around the safety of a vaccine is insufficient, or if they have concerns about overburdening a child's immune system.[37, 38] Parental or caregiver disagreement around childhood vaccination may also contribute to delay.[13]

Further qualitative research is needed to tease out the likely heterogenous reasons for MMR1 delay or non-receipt at a household level and to understand household factors that interact with access and the decision-making process.[39] Delay in primary vaccinations against diphtheria, pertussis, polio,

tetanus and Haemophilus influenza has been shown to be associated with an incomplete vaccination schedule by 24 months of age.[40] We were not able to examine this in our study.

Implications for practice

Our study has demonstrated that delay in MMR1 receipt is strongly clustered within households. This lack of timely protection or any protection within households increases the risk of measles outbreaks. This suggests the need for household-based interventions to improve vaccination coverage and timeliness. Knowing the household composition of children with delayed or non-vaccination can allow a healthcare professional (HCP) to tailor their approach to organising vaccination appointments. For example, if it is known that there is more than one child in the household needing vaccination, a HCP can arrange an appropriate appointment for two children at one time. In England, the EHR in GPs allows a HCP to view other patients registered at the same address as the selected patient.

Household-based interventions could also be considered by public health and service commissioners. Setting up services tailored to households with non- or partially-vaccinated children aligns with documented interventions recommended to improve vaccination coverage.[41] The same principle applies to providing wider public health education about vaccination for these households: interventions can be more targeted when non- or partially-vaccinated households are identified. Emerging interventions using enhanced information and educational programmes and vaccination delivery by health visitors could be tailored to target more vulnerable households.[42] Evidence from adolescent/adult decision making about vaccines in a household reinforces the importance of giving parents relevant information before the offer of vaccination from a healthcare provider.[36]

Existing literature cites multi-component interventions as the most effective interventions for increasing vaccination coverage in deprived communities with intersectional inequalities, including information, education and re-call measures.[39] Robust re-call methods are cited as an effective way to vaccinate children with delayed vaccinations.[43] We have shown that a quality improvement programme that aims to improve timeliness and equity of pre-school immunisations in NEL, focussing on data-enabled call and recall for immunisation is effective.[44]

Future research

We have shown that non-receipt of MMR1 between 12 and 24 months of age is clustered in households. However, a significant proportion of children in our study ultimately received MMR1 in the preschool years and later childhood, with no clear evidence of MMR1 receipt in the remainder. Qualitative research is needed to understand the decision-making processes underlying this heterogenous group. Similar research in demographically different areas of the UK may help understand the extent to which these findings are generalisable to households in a different socioeconomic context.

Strengths and limitations

The strengths of our study include the use of a novel method to create households securely while maintaining privacy, as well as having access to a large population with EHRs for a geographically contiguous area. Additionally, we have access to high quality MMR data, that is recorded accurately in the EHR through data recording templates.[45] The codeset used to identify MMR1 in the EHR was validated. We used robust statistical methods to assess relationships between the exposure and outcome variables, and we selected a time period before lockdowns due to the Coronavirus pandemic disrupted access to health care in England (March 2020).

We were not able to examine associations with delayed receipt of primary vaccinations against diphtheria, pertussis, polio, tetanus and Haemophilus influenza. More granular categorisation of ethnic groups, as suggested by our patient and public involvement group, was not possible due to limited sample size. Processes of decision-making about vaccines may have differed between the linked index and older children. However, associations between the vaccination status of a younger and linked older child strengthened when restricted to children with an age interval of less than five years.

Conclusion

There is strong concordance in MMR1 vaccine delay or non-receipt between children sharing the same household in a region with the lowest MMR vaccination coverage in the UK.[3] These findings

have implications for the planning and delivery of vaccination services that consider children in their household context.

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Contributions

As per CrEdit accreditation, significant contributions to: Conceptualisation (MM, CD, NF, MW), Methodology (MM, CD, MW, NF), Resources (CD, AG), Data Curation (MM, AG, NF, MW, KS), Data Analysis (MM, NF, CD), Writing-Original Draft (MM, CD), Review and Editing (MM, AG, NF, MW, KS, CD), Formal Analysis (MM, CD), Validation (AG, MM), Visualisation (MM), Supervision (CD), Funding Acquisition (MM, CD). CD is the guarantor for this research.

Competing interests declaration

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous

three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethics approval

Access to general practice data is enabled by data sharing agreements between the Discovery Data Service and general practice data controllers. The Discovery Programme Board has approved data access by the REAL Child Health programme.

Data sharing

The senior author (CD) was granted access to de-identified data by the data controllers for this work and onward sharing of data is not permitted. The R codes used in the analyses are available at https://github.com/mmarszalek1991/mmarszalek1991households/tree/main1.

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Figure legends:

Figure 1. Forest Plot of MMR1* vaccination odds ratios (OR) and 95% Confidence Intervals (CI) between 12 and 24 months of age using stepwise binary logistic regression

† Model 1: Vaccination status of older child sharing household with index child
Model 2: Model 1 + Sex + Ethnicity of index child
Model 3: Model 2 + Household size
Model 4: Model 3 + Household composition
Model 5: Model 4 + Number of children in the household
Model 6: Model 5 + Index of Multiple Deprivation quintile

†Vaccinated signifies receipt of MMR1 between 12 and 24 months of age

*MMR1: first Measles, Mumps and Rubella dose

Figure 2. Forest Plot of MMR1* vaccination odds ratios (OR) and 95% Confidence Intervals (CI) from main model and from sensitivity analyses

†Vaccinated signifies receipt of MMR1 between 12 and 24 months of age

*MMR1: first Measles, Mumps and Rubella dose

615

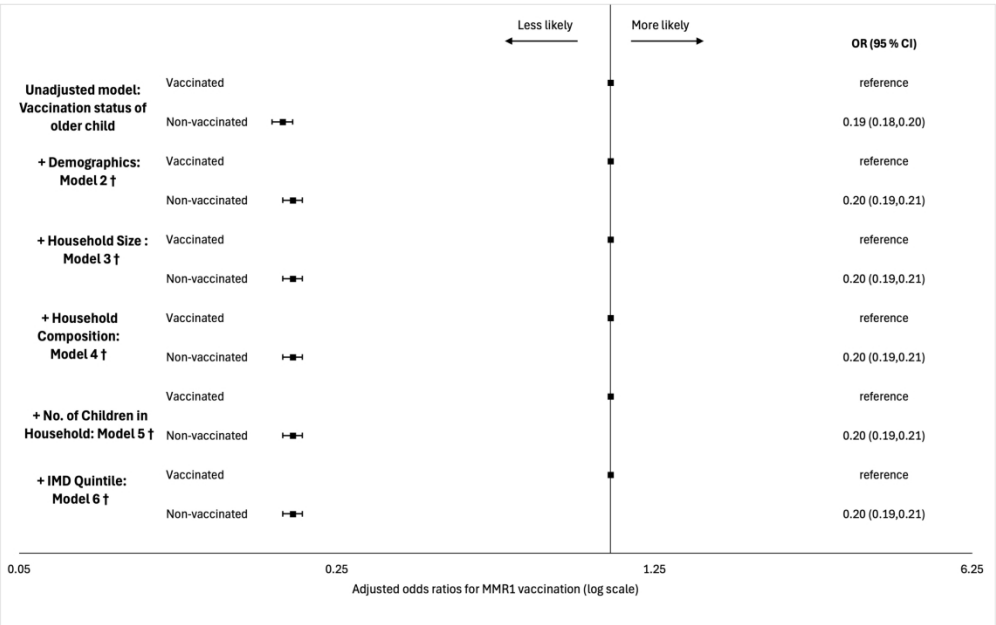

Figure 1. Forest Plot of MMR1* vaccination odds ratios (OR) and 95% Confidence Intervals (CI) between 12 and 24 months of age using stepwise binary logistic regression

286x179mm (300 x 300 DPI)

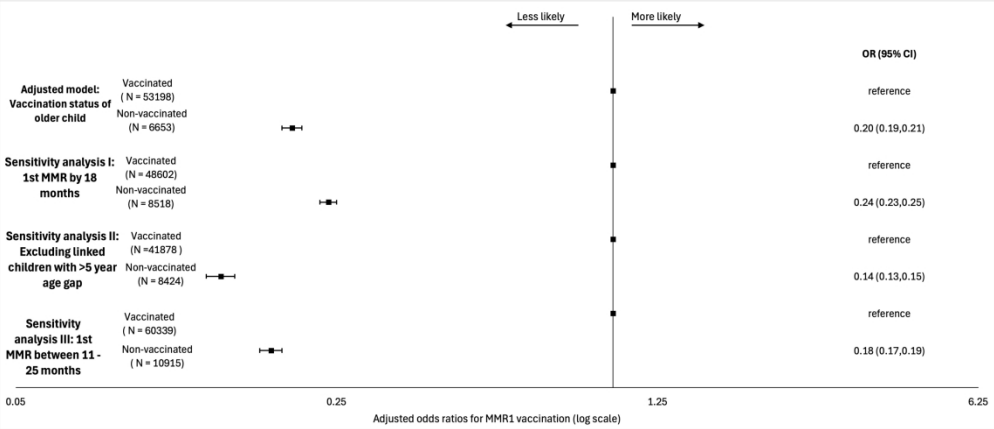

Figure 2. Forest Plot of MMR1* vaccination odds ratios (OR) and 95% Confidence Intervals (CI) from main model and from sensitivity analyses

331x142mm (300 x 300 DPI)

Household determinants of delayed MMR vaccination: longitudinal analysis using electronic health records in north east London, United Kingdom

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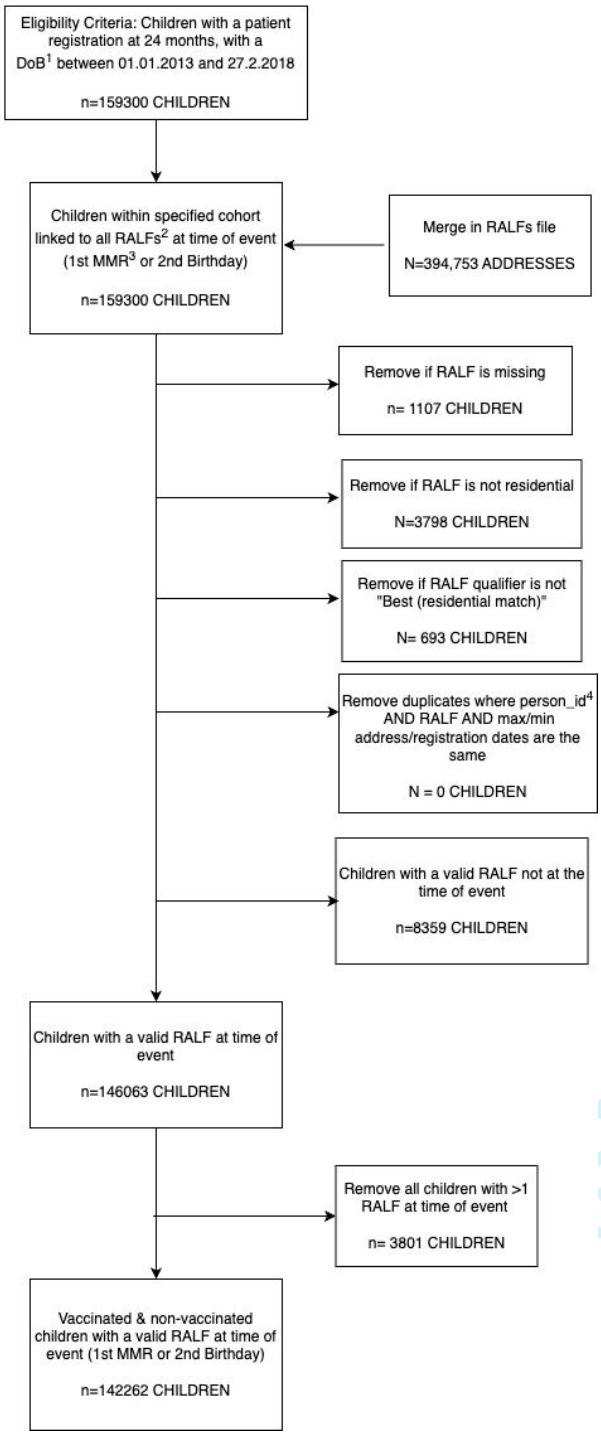
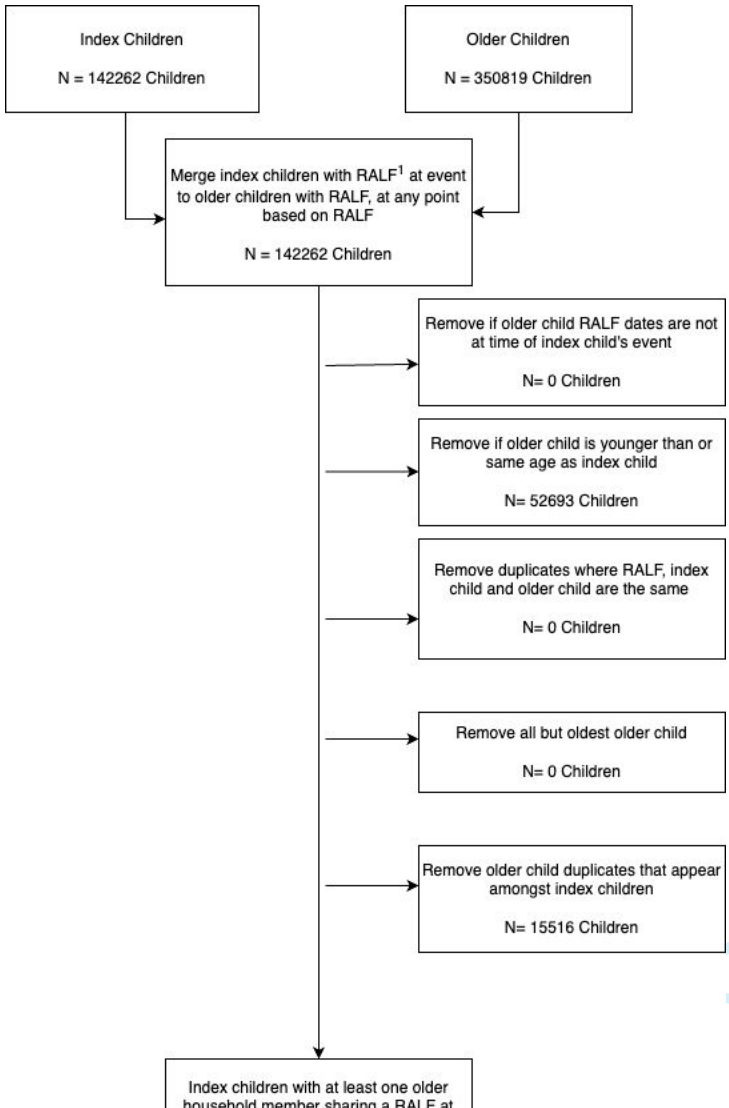
Supplementary file 1 – additional tables and figures

Figure S1-Inclusion and exclusion criteria for sample population with a valid Residential Anonymised Linkage Field (RALF)



1 Date of Birth
2 Residential Anonymised Linkage Field
3 Measles, Mumps & Rubella vaccination
4 Individual person identifier

Figure S2- Inclusion and exclusion criteria for linking index and older children



[1] Residential Anonymised Linkage Field

Table S1- Systematized Nomenclature of Medicine (SNOMED) clinical codes for first Measles, Mumps and Rubella vaccination procedures

Events recorded in the primary care electronic heath record using another clinical coding system (e.g. Read v2 or EMIS local codes) have been mapped to relevant SNOMED codes within the Discovery Data Service. This ensures that searching the database using SNOMED codes captured all events regardless of the clinical coding system used.

SNOMED concept ID	Other code	Clinical coding scheme	Code description
38598009	38598009	SNOMED	Measles-mumps-rubella vaccination (procedure)
	65M1.	Read v2	Measles/mumps/rubella vaccn.
	^ESCT1405772	EMIS local	Administration of measles and mumps and rubella vaccine
47435007	47435007	SNOMED	Measles vaccination (procedure)
	65A..	Read v2	Measles vaccination
	65A1.	Read v2	Measles vaccination
	ZV042	Read v2	[V]Measles vaccination
	^ESCT1405845	EMIS local	Administration of measles vaccine
50583002	50583002	SNOMED	Mumps vaccination (procedure)
	65F5.	Read v2	Mumps vaccination
	ZV046	Read v2	[V]Mumps vaccination
	^ESCT1405876	EMIS local	Administration of mumps vaccine
82314000	65B..	Read v2	Rubella vaccination
	ZV043	Read v2	[V]Rubella vaccination
	^ESCT1406118	EMIS local	Administration of rubella vaccine
170364006	65A2.	Read v2	Measles vaccin.+immunoglobulin
432636005	^ESCT1408534	EMIS local	Administration of measles and mumps and rubella and varicella virus vaccine
871909005	^ESCT1397548	EMIS local	Administration of first dose of measles and mumps and rubella and varicella virus vaccine
150971000119104	ZV064	Read v2	[V]Measles-mumps-rubella (MMR) vaccination
308081000000105	65M10	Read v2	First MMR (measles mumps and rubella) vaccination
	Xaeec	Read v3	First MMR (measles mumps and rubella) vaccination
	^ESCTME809974	EMIS local	Measles mumps and rubella vaccination first dose
505001000000109	9ki1.	Read v2	MMR catch-up vaccination - enhanced services administration
	XaQPr	Read v3	Measles mumps rubella catch-up vaccination
571591000119106	^ESCT1409651	EMIS local	Administration of live attenuated measles mumps and rubella vaccine
1037251000000100	65M11	Read v2	First MMR vaccination given by other healthcare provider
	Xaeeq	Read v3	First MMR vaccination given by other healthcare provider

We included clinical codes relating to administration of mono-components of the first MMR vaccination. After removal of duplicate data entries and merging to the study cohort, 584989 children had a clinical code for measles vaccination, and two for mumps vaccination, as opposed to a combined MMR vaccination.

Table S2- Characteristics of linked and unlinked cohorts by individual-, household- and area level variables

	Linked cohort (n = 71509)			Unlinked cohort (n = 70753)		
	N	%	95% CI[1]	N	%	95% CI[1]
MMR1[2] status of oldest child						
Vaccinated	59851	83.6	83.3,83.9	60512	85.5	85.3,85.8
Non-vaccinated	11658	16.4	16.1,16.6	10240	14.5	14.2,14.7
Individual covariates						
Ethic Background						
South Asian	19268	25.5	25.1,25.8	16073	22.7	22.4,23
White	19844	28.3	27.9,28.6	23536	33.3	32.9,33.6
Black or Black British	6941	10.0	9.8,10.2	5467	7.7	7.5,7.9
Mixed and Other	6150	8.5	8.3,8.7	6869	9.7	9.5,9.9
Missing**	19306	27.7	27.4,28.1	18807	26.6	26.3,26.9
Sex						
Female	35013	48.9	48.5,49.3	34885	49.3	48.9,49.7
Male	36496	51.1	50.7,51.4	35867	50.7	50.3,51.1
Household-level covariates						
Household size						
3 to 4	21683	30.3	30.0 ,30.6	37417	52.9	52.5,53.3
5 to 7	31964	44.7	44.3,45.1	18976	26.8	26.5,27.1
8 to 10	11661	16.3	16,16.6	7514	10.6	10.4,10.8
Missing**	6201	8.7	8.5,8.9	6845	9.7	9.4,10.0
Household composition						
Two working age adults with children	50093	70.0	69.7,70.3	46906	66.3	66,66.6
Single working age adult with children	9446	13.2	13,13.4	10356	14.6	14.4,14.9

Three-generational household	5769	8.1	7.9,8.3	6645	9.[illegible]	9.2,9.6
Missing**	6201	8.7	8.5,8.9	6845	9.[illegible]	9.5,9.9
Number of children in household						
2 to 3	51495	72.0	71.7,72.3	59151	83.[illegible]	83.3,83.9
4 to 6	13298	18.7	18.4,19	4486	6.[illegible]	6.1,6.5
7 to 9	515	0.7	0.6,0.8	270	0.[illegible]	0.3,0.5
Missing	6201	8.6	8.4,8.8	6845	9.[illegible]	9.4,10.0
Area level covariates						
Index of Multiple Deprivation (IMD) quintile						
IMD 1 (Most deprived)	28448	40.0	39.7,40.3	26062	36.[illegible]	36.5,37.2
IMD 2	28564	39.8	39.5,40.1	28972	40.[illegible]	40.5,41.3
IMD 3	9054	12.6	12.4,12.8	9602	13.[illegible]	13.3,13.8
IMD 4	3762	5.2	5.0,5.4	4311	6.[illegible]	5.9,6.3
IMD 5 (Least deprived)	1681	2.3	2.2,2.4	1805	2.[illegible]	2.4,2.6

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

[1]CI – Confidence interval
[2] Vaccinated signifies receipt of MMR1 between 12 and 24 months of age

Table S3- Unadjusted and adjusted odds ratios for 1st Measles, Mumps and Rubella (MMR) vaccination between 12 and 24 months of age, by individual-, household-, and area level characteristics:

	OR[1]	95% CI[2]	p-value	OR[1]	95% CI[2]	p-value
	Unadjusted			Adjusted		
MMR1[3] status of oldest child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.19	0.18, 0.20	<0.001	0.20	0.19, 0.21	<0.001
Individual covariates						
Ethnic background						
South Asian	1.34	1.26, 1.42	<0.001	1.46	1.37, 1.55	<0.001
White	Reference			Reference		
Black or Black British	0.88	0.82, 0.95	<0.001	0.97	0.90, 1.04	0.40
Mixed and Other	0.76	0.71, 0.82	<0.001	0.83	0.77, 0.90	<0.001
Missing	0.84	0.79, 0.88	<0.001	0.87	0.82, 0.92	<0.001
Sex						
Male	Reference			Reference		
Female	0.96	0.92, 1.00	0.061	0.96	0.92, 1.00	0.06
Household level covariates						
Household size						
3 to 4	Reference			Reference		
5 to 7	0.88	0.84, 0.93	<0.001	0.81	0.76, 0.86	<0.001
8 to 10	0.74	0.69, 0.79	<0.001	0.71	0.66, 0.77	<0.001
Missing**	0.68	0.63, 0.73	<0.001	NA	NA	NA
Household composition						
Two working age adults with children	Reference			Reference		
Single working age adult with children	0.80	0.75, 0.85	<0.001	0.72	0.67, 0.77	<0.001
Three generational household	0.97	0.90,1.05	0.40	0.98	0.91, 1.07	0.70
Missing**	0.74	0.69, 0.79	<0.001	0.56	0.52, 0.61	<0.001

Number of children in household						
2 to 3	Reference			Reference		
4 to 6	0.73	0.69, 0.77	<0.001	0.82	0.77, 0.87	<0.001
7 to 9	0.42	0.35, 0.52	<0.001	0.57	0.46, 0.70	<0.001
Missing	0.71	0.66, 0.76	<0.001	NA	NA	NA
Area level						
Index of Multiple Deprivation (IMD) quintile						
IMD1 (Most deprived)	Reference			Reference		
IMD2	0.93	0.89, 0.97	<0.001	0.91	0.87, 0.95	<0.001
IMD3	1.01	0.95, 1.08	0.80	0.96	0.89, 1.03	0.20
IMD4	1.40	1.25, 1.56	<0.001	1.33	1.19, 1.48	<0.001
IMD5 (Least deprived)	1.81	1.52, 2.16	<0.001	1.69	1.42, 2.02	<0.001

[1]OR = Odds Ratio, [2]CI = Confidence Interval
[3] Vaccinated signifies receipt of MMR1 between 12 and 24 months of age

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

Table S4- Sensitivity analysis I: timely Measles, Mumps and Rubella (MMR) vaccination status between 12 and 18 months of age, by individual-, household-, and area level characteristics

	Vaccinated			Non-vaccinated			All Index cohort		
	N=56641 (79.2%)			N=14889 (20.8%)			N=71530		
	Received first MMR[1] between 12 and 18 months of age			*Did not receive first MMR between 12 and 18 months of age*					
	n	%	95% CI[2]	n	%	95% CI	n	%	95% CI
MMR1[1] status of oldest child									
Vaccinated	48602	85.8	85.5,86.1	8039	14.2	13.9,14.5	56641	79.2	78.9,79.5
Non-vaccinated	8518	57.2	56.4,58.0	6371	42.8	42.0,43.6	14889	20.8	20.5,21.1
Individual covariates									
Ethnic Background									
South Asian	16214	84.3	83.8,84.9	3007	15.6	15.1,16.2	19221	26.9	26.5,27.2
White	15834	79.9	79.3,80.5	3978	20.1	19.5,20.6	19812	27.7	27.4,28.0
Black or Black British	5342	76.9	75.9,77.9	1605	23.1	22.1,24.1	6947	9.7	9.5,9.9
Mixed and Other	4448	71.8	70.7,72.9	1745	28.2	27.1,29.3	6193	8.7	8.5,8.9
Missing	14803	76.5	75.9,77.1	4554	23.5	22.9,24.1	19357	27.1	26.7,27.4
Sex									
Female	27814	79.4	79.0,79.8	7206	20.6	20.2,21.0	35020	49.0	48.6,49.3
Male	28827	79.0	78.5,79.4	7683	21.0	20.6,21.5	36510	51.0	50.6,51.4
Household-level covariates									
Household size									
3 to 4	17848	82.4	81.9,82.9	3819	17.6	17.1,18.1	21655	30.3	29.9,30.6

5 to 7	25460	79.7	79.2,80.1	6492	20.3	19.9,20.8	31952	44.7	44.3,45
8 to 10	8806	75.5	74.7,76.3	2849	24.4	23.7,25.2	11655	16.3	16,16.6
Missing**	4527	72.4	71.2,73.5	1729	27.6	26.5,28.8	6256	8.7	8.5,8.9
Household composition									
Two working age adults with children	40292	80.5	80.1,80.8	9773	19.5	19.2,19.9	50065	70.0	69.6,70.4
Single working age adult with children	7187	76.1	75.2,77.0	2256	23.9	23.0,24.8	9443	13.2	13,13.4
Three-generational household	4625	80.3	79.5,81.6	1131	19.7	18.4,20.8	5766	8.1	7.9,8.3
Missing**	4527	72.4	71.2,73.5	1729	27.6	26.5,28.8	6256	8.7	8.5,8.9
Number of Children in household									
2 to 3	41973	81.6	81.2,81.9	9494	18.4	18.1,18.8	51467	71.9	71.6,72.2
4 to 6	9875	74.2	73.5,75.0	3422	25.7	25.0,26.5	13297	18.6	18.3,18.9
7 to 9	266	52.1	47.7,56.5	244	47.8	43.4,52.3	510	0.7	0.6,0.8
Missing**	4527	72.4	71.2,73.5	1729	27.6	26.5,28.8	6256	8.7	8.5,8.9
Area level covariates									
Index of Multiple Deprivation (IMD) Quintile									
IMD 1 (Most deprived)	22451	78.9	78.4,79.4	5998	21.0	20.6,21.6	28449	39.8	39.4,40.1
IMD 2	22180	77.6	77.1,78.1	6390	22.4	21.9,22.9	28570	39.9	39.6,40.3
IMD 3	7273	80.3	79.4,81.1	1786	19.7	18.9,20.5	9059	12.7	12.4,12.9
IMD 4	3238	85.9	84.8,87	530	14.0	13.3,15.2	3768	5.3	5.1,5.4
IMD 5 (Least deprived)	1499	89.0	87.4,90.5	185	11.0	9.5,12.5	1684	2.3	2.3,2.4

[1] Vaccinated signifies receipt of MMR1 between 12 and 24 months of age
[2]CI- Confidence interval
** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

Table S5- Sensitivity analysis I- unadjusted and adjusted odds ratios for 1st Measles, Mumps and Rubella vaccination receipt between 12 and 18 months of age

	OR[1]	95% CI[2]	p-value	OR[1]	95% CI[1]	p-value
	Unadjusted			Adjusted		
MMR1[3] status of oldest child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.22	0.21,0.23	<0.001	0.24	0.23,0.25	<0.001
Individual covariates						
Ethnic Background						
South Asian	1.29	1.22,1.36	<0.001	1.41	1.33,1.49	<0.001
White	Reference			Reference		
Black or Black British	0.83	0.78,0.89	<0.001	0.76	0.72,0.81	<0.001
Mixed and Other	0.69	0.64,0.74	<0.001	0.85	0.80,0.89	<0.001
Missing	0.82	0.78,0.86	<0.001	0.92	0.87,0.99	0.027
Sex						
Female	Reference			Reference		
Male	0.97	0.94,1.01	0.20	0.97	0.94,1.01	0.20
Household level covariates						
Household size						
3 to 4	Reference			Reference		
5 to 7	0.90	0.86,0.94	<0.001	0.83	0.79,0.88	<0.001
8 to 10	0.75	0.71,0.79	<0.001	0.75	0.70,0.81	<0.001
Missing**	0.65	0.60,0.69	<0.001	NA	NA	NA
Household composition						
Two adults with children	Reference			Reference		
Single adult with children	0.78	0.74,0.82	<0.001	0.71	0.67,0.76	<0.001
Three generational household	0.96	0.90,1.04	0.30	0.97	0.90,1.04	0.40
Missing**	0.69	0.65,0.74	<0.001	0.53	0.49,0.57	<0.001
Number of children in household						
2 to 3	Reference			Reference		
4 to 6	0.71	0.68,0.74	<0.001	0.79	0.74,0.83	<0.001
7 to 9	0.35	0.29,0.42	<0.001	0.46	0.38,0.56	<0.001
Missing**	0.66	0.62,0.70	<0.001	NA	NA	NA
Area level covariates						

Index of Multiple Deprivation (IMD) quintile						
IMD 1 (Most deprived)	Reference			Reference		
IMD 2	0.95	0.91,0.99	0.012	0.93	0.89,0.97	<0.001
IMD 3	1.06	1.00,1.13	0.050	1.00	0.94,1.07	0.90
IMD 4	1.46	1.32,1.61	<0.001	1.37	1.24,1.52	<0.001
IMD 5 (Least deprived)	1.95	1.67,2.30	<0.001	1.81	1.54,2.13	<0.001

[1] OR = Odds Ratio, [2]CI = Confidence Interval
[3] Vaccinated signifies receipt of MMR1 between 12 and 18 months of age

** Children that could not be linked to other members of the household apart from the oldest child were documented having household demographics as 'Missing'

Table S6-Sensitivity analyses II- Unadjusted and adjusted odds ratios for 1st Measles, Mumps and Rubella vaccination receipt between 12 and 24 months of age: excluding linked index and older cohort children with an age gap greater than five years

	OR[1]	95% CI[2]	p-value	OR[1]	95% CI[2]	p-value
	Unadjusted			Adjusted		
MMR1[3] status of oldest child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.13	0.12, 0.14	<0.001	0.14	0.13,0.15	<0.001
Individual covariates						
Ethnic background						
South Asian	1.27	1.18, 1.36	<0.001	1.41	1.31,1.52	<0.001
White	Reference			Reference		
Black or Black British	0.87	0.79, 0.95	0.003	0.98	0.90,1.08	0.70
Mixed and Other	0.77	0.70, 0.97	<0.001	0.85	0.77,0.93	<0.001
Missing	0.82	0.76, 0.87	<0.001	0.86	0.80,0.92	<0.001
Sex						
Male	Reference			Reference		
Female	0.97	0.92, 1.02	0.20	0.97	0.92,1.02	0.20
Household level covariates						
Household size						
3 to 4	Reference			Reference		
5 to 7	0.83	0.78,0.88	<0.001	0.78	0.73,0.84	<0.001
8 to 10	0.71	0.66,0.77	<0.001	0.71	0.64,0.79	<0.001
Missing**	0.68	0.62,0.74	<0.001	NA	NA	NA
Household composition						

Two working age adults with children	Reference			Reference		
Single working age adult with children	0.80	0.74, 0.86	<0.001	0.71	0.65,0.77	<0.001
Three-generational household	0.98	0.89, 1.07	0.60	0.99	0.89,1.09	0.80
Missing**	0.77	0.72, 0.84	<0.001	0.57	0.52,0.63	<0.001
Number of children in household						
2 to 3	Reference			Reference		
4 to 6	0.70	0.65, 0.74	<0.001	0.83	0.74, 0.86	<0.001
7 to 9	0.49	0.40, 0.60	<0.001	0.65	0.52, 0.81	<0.001
Missing**	0.72	0.67, 0.78	<0.001		NA	NA
Area level covariates						
Index of Multiple Deprivation (IMD) quintile						
IMD 1 (Most deprived)	Reference			Reference		
IMD 2	0.96	0.91, 1.02	0.20	0.93	0.88,0.99	0.018
IMD 3	1.09	1.01, 1.19	0.029	1.03	0.95,1.12	0.50
IMD 4	1.54	1.35, 1.75	<0.001	1.43	1.26,1.64	<0.001
IMD 5 (Least deprived)	1.98	1.63, 2.44	<0.001	1.82	1.49,2.24	<0.001

[1] OR = Odds Ratio, [2]CI = Confidence Interval
[3] Vaccinated signifies receipt of MMR1 between 12 and 24 months of age

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'

Table S7-Sensitivity analyses III- Unadjusted and adjusted odds ratios in multivariable analysis: 1st Measles, Mumps and Rubella vaccination receipt between 11–25 months of age

	OR[1]	95% CI[2]	p-value	OR	95% CI[2]	p-value
	Unadjusted			Adjusted		
MMR1[3] status of oldest child						
Vaccinated	Reference			Reference		
Non-vaccinated	0.16	0.16, 0.17	<0.001	0.18	0.17, 0.19	<0.001
Individual covariates						
Ethnic background						
Asian or Asian British	1.33	1.25, 1.42	<0.001	1.46	1.37, 1.55	<0.001
White	Reference			Reference		
Black or Black British	0.88	0.82, 0.96	0.002	0.96	0.89, 1.04	0.40
Mixed and Other	0.76	0.71, 0.82	<0.001	0.83	0.77, 0.90	<0.001
Missing	0.84	0.80, 0.89	<0.001	0.88	0.83, 0.93	<0.001
Sex						
Male	Reference			Reference		
Female	0.96	0.92, 1.01	0.084	0.96	0.92, 1.01	0.085
Household level covariates						
Household size						
3 to 4	Reference			Reference		
5 to 7	0.90	0.85, 0.94	<0.001	0.81	0.76, 0.87	<0.001
8 to 10	0.74	0.69, 0.79	<0.001	0.71	0.65, 0.77	<0.001
Missing**	0.62	0.57, 0.67	<0.001	N/A	N/A	N/A
Household composition						
Two working age adults with children	Reference			Reference		
Single working age adult with children	0.79	0.74, 0.84	<0.001	0.71	0.66, 0.76	<0.001

Three-generational household	0.96	0.89, 1.05	0.40	0.98	0.90, 1.07	0.60
Missing**	0.67	0.62, 0.71	<0.001	0.51	0.47,0.55	<0.001
Number of Children in household						
2 to 3	Reference			Reference		
4 to 6	0.74	0.70, 0.78	<0.001	0.83	0.78, 0.88	<0.001
7 to 9	0.42	0.34, 0.52	<0.001	0.57	0.46, 0.71	<0.001
Missing**	0.64	0.60, 0.69	<0.001	NA	NA	NA
Area level covariates						
Index of Multiple Deprivation (IMD) quintile						
IMD 1 (Most deprived)	Reference			Reference		
IMD 2	0.92	0.88, 0.97	0.001	0.91	0.87, 0.95	<0.001
IMD 3	0.99	0.92, 1.06	0.70	0.94	0.88, 1.01	0.076
IMD 4	1.34	1.20, 1.50	<0.001	1.27	1.14, 1.43	<0.001
IMD 5 (Least deprived)	1.85	1.54,2.23	<0.001	1.73	1.44, 2.09	<0.001

[1] OR = Odds Ratio, [2]CI = Confidence Interval
[3] Vaccinated signifies receipt of MMR1 between 11 and 25 months of age

** Children that could not be linked to other members of the household apart from the oldest child were documented as having household demographics as 'Missing'