Characteristics of five year olds who catch-up with MMR: findings from the UK Millennium Cohort Study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-003152
Article Type:	Research
Date Submitted by the Author:	02-May-2013
Complete List of Authors:	Pearce, Anna; UCL Institute of Child Health, Mindlin, Miranda; Kent, Surrey, Sussex Public Health England Centre, Cortina Borja, Mario; UCL, Institute of Child Health Bedford, Helen; UCL, Institute of Child Health
Primary Subject Heading:	Public health
Secondary Subject Heading:	Health policy, Infectious diseases
Keywords:	Socio-economic factors, immunisation, measles-mumps-rubella vaccine, measles, child health services

SCHOLARONE™
Manuscripts

For peer review only

Characteristics of five year olds who catch-up with MMR: findings from the UK Millennium Cohort Study

Anna Pearce (Research Fellow) [1]; Miranda Mindlin (Consultant in Communicable Disease Control)[2;1]; Mario Cortina-Borja (Senior Lecturer)[1]; Helen Bedford (Senior Lecturer)[1]*

[1]MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK

[2] Kent, Surrey, Sussex Public Health England Centre, County Hall North, Chart Way, Horsham, West Sussex, RH12 1XA, UK

*corresponding author and guarantor to the paper. h.bedford@ucl.ac.uk. T 0207 905 2333; F 020 7905 2793

Key words:

Socio-economic factors, immunisation, measles, measles-mumps-rubella vaccine, child health services

Word count: 2999

For peer review only

Abstract

Objectives

To examine predictors of partial and full MMR catch-up between three and five years

Design

Secondary data analysis of the nationally representative Millennium Cohort Study (MCS)

Setting

Children born in the UK, 2000-2

Participants

751 MCS children who were unimmunised against measles, mumps and rubella at age three, with immunisation information at age five

Main outcome measures

Catch-up status: unimmunised (received no MMR), partial catch-up (received one MMR), or full catch-up (received two MMRs)

Results

At age five, 60.3% (*n*=440) children remained unvaccinated, 16.1% (*n*=127) had partially, and 23.6% (*n*=184) had fully caught-up. Children from families who did not speak English at home were five times as likely to partially catch-up than children living in homes where only English was spoken (risk ratio: 4.68 [95% CI, 3.63-6.03]). Full catch-up was also significantly more likely in those did not speak English at home (adjusted risk ratio: 1.90 [1.08-3.32]). In addition, those from Pakistani /Bangladeshi (2.40 [1.38-4.18]) or 'other' ethnicities (such as Chinese) (1.88 [1.08-3.29]) were more likely to fully catch-up than White British. Those living in socially rented (1.86 [1.34-2.56]) or 'Other' (2.52 [1.23-5.18]) accommodations were more likely to fully catch-up than home owners, and families were more likely to catch-up if they lived outside London (1.95 [1.32-2.89]). Full catch-up was less likely if parents reported medical reasons (0.43 [0.25-0.74]), a conscious decision (0.33

For peer review only

[0.23-0.48]), or 'other' reasons (0.46 [0.29-0.73]) for not immunising at age three (compared to 'practical' reasons).

Conclusions

Parents who partially or fully catch-up with MMR experience practical barriers and tend to come from disadvantaged or ethnic minority groups. Families who continue to reject MMR tend to have more advantaged backgrounds and make a conscious decision to not immunise early on. Health professionals should consider these findings in light of the characteristics of their local populations.

Article summary:

Article focus

- Areas of the UK are currently experiencing measles outbreaks, and a MMR national catch-up programme has just been launched
- Individual-level predictors of MMR catch-up are unknown
- We explore a range of risk factors for partial and full catch-up between age three and five years in the nationally representative UK Millennium Cohort Study

Key messages

- Of 751 children who were unimmunised at age three, 60% remained unimmunised at age five, 16% had partially caught-up, and 24% had fully caught-up
- Two distinct groups of parents emerged:
    - those who experienced practical barriers and were from more disadvantaged groups – these groups eventually caught-up
    - those who consciously rejected MMR and were from more advantaged circumstances – these groups tended to remain unimmunised

For peer review only

- Health professionals should consider these findings in light of the characteristics of their local populations when designing programmes to increase and maintain uptake

Strengths and limitations of this study

- This is the first study to examine individual level characteristics of MMR catch-up in the UK; we do this using data from a cohort of children who were born at the height of the MMR scare and are currently being targeted by the national catch-up programme
- We were unable to investigate exact timing of vaccination; therefore our analyses focus on children who were unimmunised at age three (so approximately 2 years after the recommended age of administration), and we were unable to detect how long children who had partially or fully caught-up by age five had been left susceptible
- Our analyses refer to predictors of catch-up during a period when the incidence of measles was relatively low; during times of measles outbreaks the perceived risk-benefit balance of the vaccine shifts, particularly for advantaged families.

For peer review only

Introduction

The combined measles, mumps and rubella vaccination (MMR) has been used routinely in the UK since 1988. Coverage at 2 years of age peaked in 1995[1]at 92%. A two-dose schedule was introduced in 1996, the first dose recommended at soon after the age of 12/13 months[2] (affording 90% protection), with a second at three years four months[2] (99% protection). In 1998, a Lancet article [3] was widely interpreted as suggesting MMR was linked with autism and bowel problems. Although the paper was eventually discredited and retracted by the Lancet in 2010[4], widespread adverse media coverage in the intervening years led to a dramatic fall in MMR uptake, to a low of 79% (of the first dose by age two) in 2003[5]. By 2006-7, 85% of two year olds had received at least one MMR, although only 73% had received the recommended two doses by age five, and levels were particularly low in some geographical areas, such as London[6]. As a result, the Health Protection Agency announced that in 2008 measles was again endemic in England and Wales.

Although coverage has continued to rise (in 2011-12, 91.2% of two year olds had received one and 86% of five year olds two doses of MMR[7]), levels remain below those needed for herd immunity, particularly in some geographical areas and in children who were born in the late 1990s and early 2000s. Consequently, measles outbreaks are currently occurring across some areas of the UK, and young teenagers are being disproportionately affected (one quarter of measles cases in 2011-12 were in 10-14 year olds[8]). In response to this, Public Health England, NHS England and the Department of Health announced a national MMR catch-up programme to vaccinate as many partially or unimmunised 10-16 year olds as possible by the start of the next school year (September 2013)[9]. This lays out aims to strengthen current routine immunisation strategies and in particular to target hard to reach populations; GPs and schools will play a central role. A better understanding of the social and demographic characteristics associated with catching-up (or not),

For peer review only

and the reasons reported by parents for their child's immunisation status, is essential if the aims of the new framework are to be achieved and maintained. Cross-sectional evidence indicates that, at age three, being unimmunised against MMR, or receiving the single antigen vaccines, was socially distributed[10]. However little is known about the factors which influence the propensity of families with unimmunised children to catch-up. We examine the social correlates of partial and full catch-up with MMR between the age of three and five years, in a nationally representative cohort of children born at the height of the MMR scare.

Methods

Participants

We analysed data from the Millennium Cohort Study (MCS), a longitudinal study of children eligible for Child Benefit and born in the UK between September 2000 and January 2002. The sample was derived from a random sample of electoral wards which were disproportionately stratified to ensure an adequate representation of all four UK countries, deprived areas and, in the case of England, areas with high proportions of families from ethnic minority groups[11]. At the first contact, when the MCS children were aged 9 months, data were collected on 18,296 singleton babies (72% of those approached); with subsequent data collections at three and five years. 71% of the initial cohort responded to all three sweeps (*n*= 12,989). Participants in the second and third sweeps were less likely to be from ethnic or deprived wards[12 13], although due to the sampling design these proportions remained higher than the general population.

Our analyses focus on the subsample of MCS singleton children who were unimmunised against measles, mumps or rubella at age three years. Of the 804 children who were unimmunised at age three, 777 (96.6%) had a recorded MMR outcome at five years, and 26 (3.3%) of them were

For peer review only

excluded because they were reported to have received at least one single antigen vaccine by age five, leaving 751 eligible participants in our analyses.

Measures

Measures were reported by the main respondent (usually the mother) during survey interviews, which were carried out by trained interviewers in the home.

Outcome measure: MMR status at age five was classified as unimmunised (received no combined MMR vaccines), partially caught-up (received one combined MMR), or fully caught-up (received two combined MMRs).

Covariates: We explored socio-economic and demographic factors that were found to be associated with immunisation status in earlier sweeps of the MCS[10 14 15], or that were pertinent to immunisation policy. We examined social class (based on National Statistics Socio-economic Classification (NS-SEC)), ethnicity, maternal age at birth (in five-year age bands), maternal education, and child gender. These measures were all captured at age nine months because they were unlikely to have changed in later sweeps. In addition, we explored the following time-variant measures, captured at age three (the beginning of the potential catch-up period): UK country of residence, ward type ('advantaged', 'disadvantaged', 'ethnic'), number of children in the household, maternal employment status, lone parenthood, household income, housing tenure, whether resident in London, whether the family had changed residential address since age three, and whether the parents reported the child having natural measles infection. Income data were missing for 14% (122) children at age three; we supplemented this with information captured at

For peer review only

age nine months, reducing the level of missingness to 24. Missing data were very low for all other measures (listed at the foot of Table 1).

We also investigated reasons given for not having had MMR at age three, classified in a previous analysis [10] as 'practical' (such as missing an appointment), 'medical' (e.g. child had asthma), 'conscious decision' (including fear of links with autism) or 'other' (which included don't know). The mean age of the MCS children at the third survey was 61 months, with a range between 52 and 72 months, meaning that some children had more time to catch-up than others. We therefore explored age as a potential confounder, but as it was not found to be associated with immunisation status (p=0.28) we did not include it in our models. There were no *a priori* hypotheses for interactions so none were explored.

Analysis

We estimated the prevalence of MMR status (unimmunised, partially caught-up, and fully caught-up) at age five, overall and according to the potential explanatory factors. We then fitted Poisson regression models to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for partial and full catch-up (in two separate models, because previous research indicates that the social correlates of partial and full immunisation are likely to differ[14]). The models were built as follows: first we explored univariable associations between the outcome and each of the explanatory variables. Variables, which were associated with the outcome (p<0.10) using Wald tests for trend, were entered into a multivariable model using a forward stepwise model selection strategy. Residence in London was forced into the multivariable models, due to its potential significance for policy. Only measures which remained significantly associated with the outcome after adjustment were retained.

For peer review only

Data were downloaded from the UK Data Archive, University of Essex in May 2010. Analyses were carried out in Stata 12 (Stata Corporation, TX) using survey and response weights to allow for the sample design and attrition between sweeps[12 16].

Results

Of the 751 MCS children who were unimmunised at age three, 60.3% (440) remained unvaccinated, 16.1% (127) had partially caught-up, and 23.6% (184) had fully caught-up. Table 1 presents the proportion of children who were partially, fully, or unimmunised, according to the various predictor measures.

Table 1: Weighted percentage (*n*) of children who remained unimmunised or who partially for fully caught-up with MMR, according to social, demographic and other characteristics

	Total	Full catch-up	Partial catch-up	Unimmunised
Language spoken at home				
English only	91.6 (658)	20.4 (130)	15.8 (11.5)	67.8 (413)
English and other language(s)	5.7 (64)	53.0 (29)	15.0 (9)	32.0 (26)
No - other language(s) only	2.7 (29)	70.2 (25)	27.7 (3)	2.1 (1)
Ward type				
Advantaged	56.5 (290)	20.3 (60)	13.6 (43)	66.1 (187)
Disadvantaged	38.5 (5.0)	24.1 (79)	20.1 (73)	55.8 (227)
Ethnic	5.0 (82)	57.6 (45)	13.3 (11)	29.2 (26)
Ethnicity				
British white	87.5 (644)	20.3 (126)	15.8 (111)	63.9 (407)
Other white	2.2 (13)	10.3 (2)	15.6 (2)	74.1 (9)
Mixed	1.4 (10)	33.5 (3)	15.1 (2)	51.4 (5)
Indian	1.0 (12)	76.9 (9)	5.5 (1)	17.5 (2)
Pakistani or Bangladeshi	3.8 (39)	74.7 (28)	9.8 (3)	15.5 (8)
Black or Black British	2.7 (18)	24.7 (7)	35.1 (5)	40.2 (6)
Other	1.4 (14)	65.2 (9)	19.6 (2)	15.2 (3)
Lone parent/carer				
Two parents/carers	79.2 (597)	21.9 (142)	15.3 (97)	62.9)
One parent/carer	20.8 (154)	30.2 (42)	19.3 (30)	50.5 (82)
Maternal age at birth of cohort child				
14 - 19y	8.1 (60)	37.7 (21)	21.8 (14)	40.6 (25)
20-24y	15.9 (130)	34.3 (40)	19.4 (27)	46.3 (63)

For peer review only

25-29y	23.5 (174)	25.8 (52)	18.2 (27)	55.9 (95)
30-34y	27.6 (205)	17.0 (36)	13.0 (30)	70.0 (13.9)
35-39y	20.4 (145)	15.8 (25)	14.3 (24)	70.0 (96)
40plus	4.5 (36)	24.2 (9)	10.6 (5)	65.1 (22)
Maternal education				
Degree	20.8 (152)	18.8 (32)	10.4 (15)	70.7 (105)
Diploma	8.9 (64)	13.9 (9)	14.9 (9)	71.1 (46)
A or AS levels	11.3 (85)	22.7 (19)	17.0 (20)	60.2 (46)
GCSE A*-C	32.2 (238)	20.4 (48)	19.6 (50)	60.0 (140)
GCSE D-G	8.4 (64)	18.1 (13)	23.9 (16)	58.0 (35)
Other	1.9 (15)	25.1 (6)	7.7 (1)	67.2 (8)
None	16.4 (133)	44.5 (57)	13.4 (16)	42.1 (60)
Housing tenure age 3				
Owned	58.7 (451)	18.1 (92)	15.6 (77)	66.3 (282)
Privately rented	9.8 (71)	29.8 (18)	11.5 (8)	58.6 (45)
Socially rented	27.7 (199)	30.4 (65)	19.8 (37)	49.8 (16)
Other	3.8 (30)	43.4 (9)	8.1 (5)	48.6 (16)
Household income (£ pa)				
0-11000	23.7 (186)	32.1 (57)	18.7 (34)	49.2 (95)
11 000-22 000	30.4 (228)	23.4 (56)	18.2 (41)	58.4 (131)
22 000-33 000	19.9 (142)	12.6 (21)	18.3 (34)	69.1 (87)
33 000-55 000	17.4 (123)	20.6 (28)	6.8 (8)	72.6 (87)
55 000+	8.9 (48)	23.5 (11)	15.9 (8)	60.6 (29)
Social class (9 months)				
Managerial & professional	30.2 (222)	20.8 (42)	12.7 (34)	66.5 (14.6)
Intermediate	16.7 (119)	17.5 (22)	17.6 (18)	65.0 (79)
Small employer/self-employed	8.0 (53)	10.1 (10)	11.9 (8)	78.0 (35)
Lower supervisory & technical	4.0 (33)	33.4 (10)	9.6 (4)	57.1 (19)
Semi-routine & routine	32.0 (248)	24.4 (61)	20.6 (53)	54.9 (134)
Never worked/unemployed	9.2 (73)	47.8 (37)	15.6 (10)	36.6 (26)
Number of children in household (age 3)				
One child	22.5 (180)	26.2 (43)	20.0 (38)	53.8 (99)
Two or three children	63.1 (459)	21.3 (104)	15.5 (73)	63.2 (282)
Four or more children	14.4 (112)	29.9 (37)	12.6 (16)	57.6 (59)
Maternal employment (age 3)				
FT	11.2 (93)	23.8 (21)	11.5 (17)	64.7 (55)
PT	25.2 (191)	22.1 (41)	19.6 (37)	58.3 (113)
On leave	3.9 (28)	26.8 (8)	3.9 (1)	69.4 (19)
Self employed	9.3 (60)	17.1 (13)	13.0 (10)	69.9 (37)
Not employed/student	50.4 (379)	25.3 (101)	16.9 (62)	57.8 (216)
Sex of child				
Male	55.1 (404)	20.6 (95)	17.7 (70)	61.7 (239)
Female	44.9 (347)	27.3 (89)	14.1 (57)	58.6 (201)
Parental report of measles disease by age 3				
Yes	3.5 (22)	19.2 (5)	13.2 (3)	67.6 (14)
No	96.5 (721)	23.7 (176)	16.1 (123)	60.2 (422)
Residence in London				
London	16.2 (102)	17.7 (23)	20.0 (19)	62.3 (60)
Not London	83.8 (649)	24.8 (161)	15.3 (108)	60.0 (380)
Country of residence				
England	58.6 (462)	23.3 (122)	15.7 (74)	61.0 (266)

For Peer Review Only

Wales	21.6 (160)	22.1 (31)	20.1 (31)	57.7 (98)
Scotland	12.9 (87)	26.7 (21)	15.6 (14)	57.5 (52)
Northern Ireland	6.9 (42)	25.3 (10)	17.8 (8)	60.0 (24)
Smoked during pregnancy				
No	63.2 (465)	23.4 (121)	15.1 (76)	61.6 (268)
Yes	36.8 (283)	23.8 (62)	18.0 (51)	58.2 (170)
Changed address since 3				
No	85.6 (647)	23.8 (161)	16.6 (112)	59.6 (374)
Yes	14.4 (104)	22.4 (23)	13.1 (15)	64.5 (66)
Reasons given for not having had MMR (aged 3)				
Practical	6.2 (51)	54.5 (30)	15.3 (7)	30.3 (14)
Medical	15.2 (107)	17.9 (82)	25.5 (26)	56.7 (57)
Conscious decision	66.7 (486)	17.8 (82)	16.0 (85)	66.2 (31.9)
Other	11.7 (76)	35.3 (26)	9.9 (9)	54.9 (41)

Missing: Social class 3, smoked during pregnancy 3, income 24, ethnicity 1, reason 31, age at birth 1.

Partial catch-up (compared to remaining unimmunised)

Table 2 (column A) shows unadjusted RRs for partial catch-up, according to each of the predictor measures. Partial catch-up was more likely in families who spoke a language other than English at home (particularly if English was not spoken at home at all), compared to those who only spoke English at home, and in those who lived in a ward classified as 'disadvantaged' or 'ethnic', compared to advantaged wards. No significant associations were seen with any of the other measures. When language, ward type and London residence (due to its policy significance) were entered into the multivariable model, only language remained significantly associated with the likelihood of being partially immunised, with an RR of 4.68 (3.63 to 6.03) in families who did not speak English at home (Table 2, Column B).

Table 2: Unadjusted and adjusted odds ratios (ORs) for partial catch-up with the combined MMR vaccine (baseline unimmunised) by age five

	Partial catch-up		Full catch-up	
	A: uRR (95% CI)	**B: aRR (95% CI)**	**C: uRR (95% CI)**	**D: aRR (95% CI)**
Language spoken at home				
English only	1	1	1	1
English and other language(s)	1.61 (0.96, 2.70)	1.61 (0.96, 2.70)	2.57 (2.00, 3.32)*	1.54 (0.91, 2.63)
Other language(s) only	4.68 (3.63, 6.03)*	4.68 (3.63, 6.03)*	4.00 (3.37, 4.76)*	1.90 (1.08, 3.32)*

For peer review only

p-value	<0.001	<0.001	<0.001	0.0811
Ward type				
Advantaged	1		1	
Disadvantaged	1.55 (1.05, 2.27)*		1.29 (0.92, 1.80)	
Ethnic	1.83 (1.18, 2.83)*		2.83 (2.19, 3.65)*	
p-value	0.0146		<0.001	
Ethnicity				
British white	1		1	1
Other white	0.88 (0.22, 3.54)		0.51 (0.13, 2.06)	0.37 (0.10, 1.34)
Mixed	1.15 (0.29, 4.59)		1.64 (0.57, 4.74)	1.83 (0.65, 5.17)
Indian	1.21 (0.19, 7.82)		3.38 (2.40, 4.76)*	2.01 (0.75, 5.41)
Pakistani or Bangladeshi	1.96 (0.84, 4.54)		3.44 (2.79, 4.23)*	2.40 (1.38, 4.18)*
Black or Black British	2.35 (0.99, 5.57)		1.58 (0.73, 3.43)	1.12 (0.35, 3.63)
Other	2.84 (1.12, 7.22)*		3.36 (2.42, 4.67)*	1.88 (1.08, 3.29)*
p-value	0.0126		<0.001	0.0950
Lone parent/carer				
Two parents/carers	1		1	
One parent/carer	1.42 (0.92, 2.17)		1.45 (1.06, 1.99)*	
p-value	0.1110		0.0208	
Maternal age at birth of cohort child				
14 - 19y	1.42 (0.80, 2.51)		1.52 (0.98, 2,37)	
20-24y	1.20 (0.68, 2.12)		1.35 (0.89, 2.03)	
25-29y	1		1	
30-34y	0.63 (0.37, 1.08)		0.62 (0.40, 0.97)*	
35-39y	0.69 (0.40, 1.20)		0.58 (0.37, 0.92)*	
40plus	0.57 (0.23, 1.43)		0.86 (0.42, 1.74)	
p-value	0.0259		<0.001	
Maternal education				
Degree	1		1	
Diploma	1.35 (0.54, 3.36)		0.78 (0.35, 1.72)	
A or AS levels	1.72 (0.79, 3.74)		1.30 (0.71, 2.38)	
Gcse a*-c	1.91 (1.05, 3.49)*		1.21 (0.75, 1.96)	
Gcse d-g	2.27 (1.07, 4.80)*		1.13 (0.55, 2.34)	
Other	0.80 (0.11, 5.93)		1.29 (0.49, 3.39)	
None	1.88 (0.87, 4.03)		2.44 (1.63, 3.66)*	
p-value	0.2420		<0.001	
Housing tenure age 3				
Owned	1		1	1
Privately rented	0.86 (0.32, 2.34)		1.57 (0.96, 2.59)	1.51 (0.91, 2.48)
Socially rented	1.49 (0.96, 2.32)		1.77 (1.29, 2.43)*	1.86 (1.34, 2.56)*
Other	0.75 (0.27, 2.09)		2.20 (1.27, 3.79)*	2.52 (1.23, 5.18)*
p-value	0.0936		0.0014	<0.001
Household income (£ pa)				
0-11000	1		1	
11 000-22 000	0.86 (0.53, 1.41)		0.72 (0.52, 1.02)	
22 000-33 000	0.76 (0.44, 1.31)		0.39 (0.23, 0.66)	
33 000-55 000	0.31 (0.14, 0.70)*		0.56 (0.36, 0.87)	
55 000+	0.76 (0.36, 1.61)		0.71 (0.39, 1.29)	
p-value	0.0816		0.0028	
Social class (9 months)				
Managerial & professional	1		1	

For peer review only

Intermediate	1.33 (0.73, 2.42)		0.89 (0.52, 1.53)	
Small employer/self-employed	0.83 (0.38, 1.79)		0.48 (0.20, 1.16)	
Lower supervisory & technical	0.90 (0.30, 2.67)		1.55 (0.80, 3.00)	
Semi-routine & routine	1.71 (1.11, 2.64)*		1.29 (0.87, 1.92)	
Never worked/unemployed	1.87 (0.96, 3.64)		2.38 (1.62, 3.49)*	
p-value	0.0989		<0.001	
Number of children in household (age 3)				
One child	1		1	
Two or three children	0.73 (0.47, 1.12)		0.77 (0.52, 1.14)	
Four or more children	0.66 (0.34, 1.29)		1.04 (0.67, 1.63)	
p-value	0.2807		0.1832	
Maternal employment (age 3)				
Full-time	1		1	
Part-time	1.67 (0.84, 3.33)		1.02 (0.58, 1.79)	
On leave	0.35 (0.05, 2.48)		1.04 (0.46, 2.33)	
Self employed	1.04 (0.41, 2.66)		0.73 (0.37, 1.45)	
Not employed/student	1.50 (0.88, 2.57)		1.13 (0.71, 1.80)	
p-value	0.1836		0.6517	
Sex of child				
Male	1		1	
Female	0.87 (0.60, 1.27)		1.27 (0.94, 1.71)	
p-value	0.4755		0.1171	
Parental report of measles disease by age 3				
Yes	1		1	
No	1.29 (0.48, 3.49)		1.28 (0.52, 3.16)	
p-value	0.6163		0.5970	
Residence in London				
London	1		1	1
Not London	0.84 (0.50, 1.41)		1.32 (0.86, 2.02)	1.95 (1.32, 2.89)*
p-value	0.5078		0.2012	<0.001
Country of residence				
England	1		1	
Wales	1.26 (0.86, 1.84)		1.00 (0.69, 1.46)	
Scotland	1.04 (0.60, 1.83)		1.16 (0.71, 1.88)	
Northern Ireland	1.16 (0.55, 2.44)		1.11 (0.66, 1.88)	
p-value	0.6802		0.9272	
Smoked during pregnancy				
No	1		1	
Yes	1.20 (0.73, 1.74)		0.05 (0.76, 1.46)	
p-value	0.3202		0.7481	
Changed address since 3				
No	1			
Yes	0.90 (0.62, 1.32)		0.77 (0.42, 1.43)	
p-value	0.6031		0.4112	
Reasons given for not having had MMR (aged 3)				
Practical	1		1	
Medical	0.93 (0.44, 1.93)		0.37 (0.20, 0.68)*	0.43 (0.25, 0.74)*
Conscious decision	0.58 (0.27, 1.22)		0.33 (0.23, 0.47)*	0.33 (0.23, 0.48)*
Other	0.45 (0.16, 1.30)		0.61 (0.40, 0.93)*	0.46 (0.29, 0.73)*
p-value	0.1357		<0.001	<0.001

For peer review only

Full catch-up (compared to remaining unimmunised)

Table 2 also presents unadjusted and adjusted RRs for fully catching up. In the univariable analysis (Column C), children whose parents spoke a language other than English in the home (as opposed to only speaking English), who were from ethnic minority groups (compared to White British), or living in 'ethnic' wards (compared to 'advantaged' wards) were more likely to fully catch-up. Catch-up was also significantly more likely in children who mother had no educational qualifications (compared to a degree), in lone parent families (compared to two parent families), and in those living in 'socially rented' or 'other' tenure types (compared to own/mortgage). Catch-up was significantly less likely in children with a mother in her thirties (compared to 24-29 years), and in children living in higher income households. Children whose parents had reported a non-practical reason ('medical', 'conscious decision', or 'other') for not having their child immunised with the combined MMR at age three were also less likely to have fully caught-up than those reporting practical reasons. Living in London was not associated with immunisation status, although due to its policy significance was included in the multivariable model reported below.

In the multivariable analysis (Column D), full catch-up remained significantly more likely in those who only spoke a non-English language at home (1.90 [1.08 to 3.32]), when compared to those who only spoke English. Those from Pakistani or Bangladeshi (2.40 [1.38 to 4.18]), and 'Other' (1.88 [1.08 to 3.29]) ethnic groups were more likely to have caught-up than White British groups, as were those living in 'socially rented' (1.86 [1.34 to 2.56]) or 'other' (2.52 [1.23 to 5.18]) tenure types (compared to own/mortgage). Full catch-up was also more likely in families living outside London (1.95 [1.32 to 2.89]). Compared to those reporting practical reasons for not having been immunised at age three, children whose parents reported medical reasons (0.43 [0.25 to 0.74]), a

For peer review only

conscious decision (0.33 [0.23 to 0.48]), or 'other' reasons (0.46 [0.29 to 0.73]) were considerably less likely to have fully caught-up.

Discussion

Just over 40% of children who were unimmunised with MMR vaccine at age three had either partially or fully caught-up by age five (of which more than caught-up fully). The likelihood of catching-up varied markedly with a number of social factors, and more so for full than partial catch-up. Some families, particularly those from ethnic minority groups, appear to have difficulty accessing the vaccination schedule in a timely fashion. Advantaged families and those citing non-practical reasons for non-vaccination at age three are more likely to persist in not immunising their child against MMR.

We used sample and response weights to account for the survey design and attrition between the first, second, and third sweeps. However the non-response weights are unlikely to have entirely accounted for differential response; for example 95.7% children who were included in the age three and five surveys were fully immunised with the primary vaccines (at age 9 months) compared to 92.7% in children who did not take part in both of the later surveys (p<0.001). Information bias may occur when using parental report to measure immunisation status, however there is no gold standard measure and studies have found disagreement between parental report and health records to be low[17] and not socially distributed[18]. Parents were given the opportunity to consult the Personal Child Health Record (or 'red book'). Of the 751 families included in our analysis, 19% (137) consulted the book and found the relevant information, 1% (11) checked the book and did not find the relevant information, and 79% (603) chose not to consult the book. There was no association between catch-up status and whether the parent consulted the red book (p=0.18), and the

For peer review only

associations reported in this paper remained the same when analyses were repeated excluding children where the parent had looked but not found information (data not shown). A small number (26) of children who were unimmunised at age three had received at least one single antigen vaccine by age five. Due to low numbers we were unable to explore the characteristics of this group.

The intense negative media attention around MMR vaccine peaked in 2002/3 when the MCS children were toddlers. These findings therefore provide important information on the barriers to catch-up, in a cohort of children who are currently experiencing measles outbreaks throughout the UK[8], and are a central focus of the newly launched national catch-up programme. We measured catch-up across the period 2003/5 to 2006/7, when the incidence of measles was low, although beginning to increase. It is likely that some of the barriers we report for more advantaged families are reduced during times of measles outbreaks, as the perceived risk-benefit balance of the vaccine shifts. Nonetheless, this paper provides important information on the barriers experienced by advantaged families during times of no outbreak to improve and sustain the current MMR programme, which is also a central aim of the catch-up programme. The recommended age of the first dose of MMR is 12/13 months; however information on uptake was not collected in the MCS until the children were age three years. Our analysis is unable to address those children who were immunised by age three but who had not been immunised on time. Similarly, we were unable to investigate the timing of catch-up between the age of three and five, and therefore how long children who partially or fully caught-up were left susceptible.

Before the scare, MMR uptake was generally lower in more deprived areas and households[19 20]. Since 1998, rates declined faster in more advantaged areas[21 22] and more slowly in areas with lower

For peer review only

proportions of highly educated residents[21] and in minority ethnic groups[23]. Earlier cross-sectional findings from the MCS demonstrated that the likelihood of being unimmunised against measles, mumps and rubella tended to be greater in more disadvantaged families, while children living in more affluent households were more likely to receive single antigen vaccines (indicating conscious rejection of combined MMR) [10]. However there is a dearth of longitudinal research exploring the social correlates of catch-up with MMR. The only study, to our knowledge, which has explored the social correlates of MMR catch-up was an ecological study of one million children born between 1987 and 2004 in Scotland. The authors found that children living in more affluent areas were either immunised with MMR on time or not at all, whereas children living in deprived areas were more likely to be immunised late[22]. Our findings not only reflect this, but add to the evidence base by demonstrating that individual-level predictors of catch-up are strongly related to catch-up. We have also found that remaining unvaccinated with MMR at age five was associated with non-practical reasons for not immunising with MMR at three, reflecting other research which has shown that more affluent families are more likely to consciously reject MMR[22 24].

Outbreaks of measles are currently being experienced across the UK, leading to the launch of a national catch-programme in April 2013. Approaches to optimise uptake of MMR will need to be tailored to the needs of local populations, both now and into the future. Our study has identified two distinct groups of families that do not immunise their child with MMR in a timely fashion (during periods of low measles incidence). The first comprises those who partially or fully catch-up, amounting to 40% of those who were unimmunised at age three. These families tend to experience practical barriers to immunisation, and are socially disadvantaged or from ethnic minority groups. The second group, which continues to reject MMR and makes up the remaining 60%, consists of parents who consciously reject MMR from the start, and are from more advantaged backgrounds.

For peer review only

Steps are required to minimise time to uptake in those families who do eventually catch-up, through the reduction of practical barriers. NICE guidance outlines actions to reduce inequalities in immunisation[25], including provision of information in multiple languages, offering immunisation checks and administration in alternative settings, and sending out reminder invitations from GPs[26]. In addition, alleviating any lingering fears and concerns of families who consciously reject MMR is essential. This should include discussion of concerns about 'medical' reasons for not giving MMR, as there are very few true contraindications for MMR vaccination. NICE recommends offering parents opportunities to discuss their concerns with health professionals; receiving such information from health professionals has been found to be the decisive factor for parents who have changed their minds about previously rejected or delayed vaccines[27]. In addition training is recommended for health care professionals to equip them with the skills and information needed to communicate effectively with parents about immunisation. Finally, joint working between the health sector and childcare providers, nurseries, and schools is essential[25].

Conclusions

Children born at the height of the MMR scare are being disproportionately affected by current measles outbreaks and are the target of a newly launched national catch-up programme. Our findings refer to children of this age and have identified the characteristics of two distinct groups of parents who do not immunise their children with MMR on time. Health professionals should consider their local populations in light of our findings, and tailor the local roll-out of the catch-up programme accordingly.

For peer review only

The new national immunisation framework not only aims to facilitate catch-up but also to strengthen routine approaches to immunisation[9]. Findings from this study should be used to inform longer-term local and national planning to improve and maintain timely uptake. While uptake of the first dose of MMR in younger age groups has increased, levels remains below those required for herd immunity and uptake of the second dose is lower. Measles outbreaks remain a risk, particularly in areas of the country with low uptake.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, Institute of Education, University of London. We would also like to thank the MCS user group at the MRC Centre of Epidemiology for Child Health: Catherine Law, Carol Dezateux, Lucy Griffiths, Tim Cole, Phillippa Cumberland, Jamie Fagg, Francesco Sera, Steven Hope, Hannah Lewis and Marco Geraci; also David Elliman, for his advice early on in the project.

Funding

The Centre for Paediatric Epidemiology and Biostatistics is supported in part by the Medical Research Council in its capacity as the MRC Centre of Epidemiology for Child Health (Grant reference G0400546). Research at the UCL Institute of Child Health and Great Ormond Street Hospital for Children receives a proportion of the funding from the Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme. All researchers were independent of the funders and the funders played no part in the study design, analysis or interpretation of the data, writing of the report or the decision to submit for publication.

Contributors: MM and HB contributed to the study conception. All authors contributed to the design of the analysis. AP, MM and MC-B carried out the analyses. AP and MM drafted the paper.

For peer review only

All authors revised the paper. All authors had full access to the data and take responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval: Research ethics approval was not required for this study as it was a secondary data analysis of the UK Millennium Cohort Study. The first sweep of the Millennium Cohort Study received ethics approval from National Health Service Ethical Authority in February 2001 (MREC/01/6/19), and the second and third received approval from the London Multi-Centre Research Ethics Committee in September 2004 (MREC/03/2/022) and December 2005 (05/MRE02/46).

Data sharing: The Millennium Cohort Study is available at: http://www.esds.ac.uk/findingData/mcs.asp

Competing interests

All authors have completed the ICMJE uniform disclosure form at ww.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; MCB has received research grants from the Health Protection Agency; no other relationships or activities that could appear to have influenced the submitted work.

Copyright/licence for publication

I, Helen Bedford, the Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs, other illustrative material, video, film or any other material howsoever submitted by the Contributor(s) at any time and related to the Contribution ("the Contribution") have the right to grant on behalf of all authors and do grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licensees, to permit this Contribution (if accepted) to be published in BMJ Open an d any other BMJ Group products and to exploit all subsidiary rights, as set out in the licence at: http://group.bmj.com/products/journals/instructions-for-authors/BMJOpen_licence.pdf

For peer review only

Reference List

1. Communicable Disease Surveillance Centre. COVER/Korner July to September 1995. *CDR weekly* 1995;5:301.
2. Salisbury D, Ramsay M, Noakes K. Immunisation against infectious disease: the green book. In: England PH, editor, 2013.
3. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998;351 (9103):637-41.
4. Lancet. Retraction--Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. 2010 Feb *Lancet.* 2010;375(9713):445.
5. Health Protection Agency. COVER programme: January to March 2003. *CDR weekly* 2003;91(6):465-68.
6. The Information Centre. NHS Immunisation Statistics: England 2006-07, 2007.
7. The Health and Social Care Information Centre Screening and Immunisations team. NHS Immunisation Statistics, England: 2011-12 In: Centre TI, editor, 2012.
8. Health Protection Agency. Confirmed cases of measles by region and age: 1996-2012. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733778332: Public Health England, 2013.
9. Public Health England. MMR catch-up programme 2013. . https://www.gov.uk/government/organisations/public-health-england/series/MMR-catch-up-programme-2013#publications: GOV.UK, 2013.
10. Pearce A, Law C, Elliman D, Cole TJ, Bedford H, the Millennium Cohort Study Child Health G. Factors associated with uptake of measles, mumps and rubella vaccine (MMR) and use of single antigen vaccines in a comtemporary UK cohort: prospective cohort study. *British Medical Journal* 2008;336:754-60.
11. Centre for Longitudinal Studies. Millennium Cohort Study: Survey design: Institute of Education, 2007.
12. Plewis I, Ketende S. Millennium Cohort Study: technical report on response. 1st ed. London Centre for Longitudinal Studies, 2006.
13. Hansen K, Joshi H. Millennium Cohort Study Third Survey: A User's Guide to Initial Findings. London: Institute of Education 2008.
14. Samad L, Bedford H, Tate AR, Dezateux C, Peckham C, Butler N, et al. Differences in risk factors for partial and no immunisation in the first year of life. *British Medical Journal* 2006;332 1312-13.
15. Pearce A, Elliman D, Bedford H, Law C. Residential mobility and uptake of childhood immunisations: findings from the UK Millennium Cohort Study. *Vaccine* 2008;26:1675-80.
16. Plewis I. Millennium Cohort Study: technical report on sampling. 3rd ed. . London: Centre for Longitudinal Studies, 2004.
17. AbdelSalam HHM, Sokal MM. Accuracy of parental reporting of immunization. *Clinical Pediatrics* 2004;43 (1):83-85.
18. Suarez L, Simpson DM, Smith DR. Errors and correlates in parental recall of child immunizations: effects on vaccination coverage estimates. *Pediatrics* 1997;99 (5):E3.
19. Sharland M, Atkinson P, Maguire H, Begg N. Lone parent families are an independent risk factor for lower rates of childhood immunisation in London. *Communicable Disease Report.CDR Review* 1997;7 (11):R196-R72.

For peer review only

20. Li J, Taylor B. Factors affecting uptake of measles, mumps, and rubella immunisation. *British Medical Journal* 1993;307 168-71.
21. Middleton E, Baker D. Comparison of social distribution of immunisation with measles, mumps, and rubella vaccine, England, 1991-2001. *British Medical Journal* 2003;326 854-54.
22. Friederichs V, Cameron JC, Robertson C. Impact of adverse publicity on MMR vaccine uptake: a population based analysis of vaccine uptake records for one million children, born 1987-2004. *Archives of Disease in Childhood* 2006;91 465-68.
23. Hawker J, Olowokure B, Wood A, Wilson R, Johnson R. Widening inequalities in MMR vaccine uptake rates among ethnic groups in an urban area of the UK during a period of vaccine controversy (1994-2000). *Vaccine* 2007;25:7516-9.
24. MacDonald H, Henderson R, Oates K. Low uptake of immunisation: contributing factors. *Community Practioner* 2004;77 (3):95-100.
25. National Institute for Health and Clinical Excellence. Reducing differences in the uptake of immunisations. *NICE public health guidance 21*, 2009.
26. Jacobson Vann J, Szilagyi P. Patient reminder and patient recall systems to improve immunization rates. . *Cochrane Database Syst Rev.* 2005;Jul 20(3).
27. Gust D, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics* 2008;1227(4):18-25.

For peer review only

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
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	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 6
Methods			
Study design	4	Present key elements of study design early in the paper	2, 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	9, 11
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	7-8, 9
		(*d*) If applicable, explain how loss to follow-up was addressed	9
		(*e*) Describe any sensitivity analyses	
Results			

For peer review only

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	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2
		(b) Indicate number of participants with missing data for each variable of interest	Table 2
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	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	Table 3
		(*b*) Report category boundaries when continuous variables were categorized	Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
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	15

*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.

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.

For peer review only

Characteristics of five year olds who catch-up with MMR: findings from the UK Millennium Cohort Study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-003152.R1
Article Type:	Research
Date Submitted by the Author:	14-Jun-2013
Complete List of Authors:	Pearce, Anna; UCL Institute of Child Health, Mindlin, Miranda; Kent, Surrey, Sussex Public Health England Centre, Cortina Borja, Mario; UCL, Institute of Child Health Bedford, Helen; UCL, Institute of Child Health
Primary Subject Heading:	Public health
Secondary Subject Heading:	Infectious diseases, Health policy
Keywords:	Socio-economic factors, immunisation, measles-mumps-rubella vaccine, measles, child health services

SCHOLARONE™
Manuscripts

For peer review only

Characteristics of five year olds who catch-up with MMR: findings from the UK Millennium Cohort Study

Anna Pearce (Research Fellow) [1]; Miranda Mindlin (Consultant in Communicable Disease Control)[2;1]; Mario Cortina-Borja (Senior Lecturer)[1]; Helen Bedford (Senior Lecturer)[1]*

[1]MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK

[2] Kent, Surrey, Sussex Public Health England Centre, County Hall North, Chart Way, Horsham, West Sussex, RH12 1XA, UK

*corresponding author and guarantor to the paper. h.bedford@ucl.ac.uk. T 0207 905 2333; F 020 7905 2793

Key words:

Socio-economic factors, immunisation, measles, measles-mumps-rubella vaccine, child health services

Word count: 3441

For peer review only

Abstract

Objectives

To examine predictors of partial and full MMR catch-up between three and five years

Design

Secondary data analysis of the nationally representative Millennium Cohort Study (MCS)

Setting

Children born in the UK, 2000-2

Participants

751 MCS children who were unimmunised against measles, mumps and rubella at age three, with immunisation information at age five

Main outcome measures

Catch-up status: unimmunised (received no MMR), partial catch-up (received one MMR), or full catch-up (received two MMRs)

Results

At age five, 60.3% (*n*=440) children remained unvaccinated, 16.1% (*n*=127) had partially, and 23.6% (*n*=184) had fully caught-up. Children from families who did not speak English at home were five times as likely to partially catch-up than children living in homes where only English was spoken (risk ratio: 4.68 [95% CI, 3.63-6.03]). Full catch-up was also significantly more likely in those did not speak English at home (adjusted risk ratio: 1.90 [1.08-3.32]). In addition, those from Pakistani /Bangladeshi (2.40 [1.38-4.18]) or 'other' ethnicities (such as Chinese) (1.88 [1.08-3.29]) were more likely to fully catch-up than White British. Those living in socially rented (1.86 [1.34-2.56]) or 'Other' (2.52 [1.23-5.18]) accommodations were more likely to fully catch-up than home owners, and families were more likely to catch-up if they lived outside London (1.95 [1.32-2.89]). Full catch-up was less likely if parents reported medical reasons (0.43 [0.25-0.74]), a conscious decision (0.33

For peer review only

[0.23-0.48]), or 'other' reasons (0.46 [0.29-0.73]) for not immunising at age three (compared to 'practical' reasons).

Conclusions

Parents who partially or fully catch-up with MMR experience practical barriers and tend to come from disadvantaged or ethnic minority groups. Families who continue to reject MMR tend to have more advantaged backgrounds and make a conscious decision to not immunise early on. Health professionals should consider these findings in light of the characteristics of their local populations.

Article summary:

Article focus

- Areas of the UK are currently experiencing measles outbreaks, and a MMR national catch-up programme has just been launched
- Individual-level predictors of MMR catch-up are unknown
- We explore a range of risk factors for partial and full catch-up between age three and five years in the nationally representative UK Millennium Cohort Study

Key messages

- Of 751 children who were unimmunised at age three, 60% remained unimmunised at age five, 16% had partially caught-up, and 24% had fully caught-up
- Two distinct groups of parents emerged:
    - those who experienced practical barriers and were from ethnic minority backgrounds – these groups eventually caught-up
    - those who consciously rejected MMR and were from more advantaged circumstances – these groups tended to remain unimmunised

For peer review only

- Health professionals should consider these findings in light of the characteristics of their local populations when designing programmes to increase and maintain uptake

Strengths and limitations of this study

- This is the first study to examine individual-level characteristics of MMR catch-up in the UK; we do this using data from a nationally representative cohort of children who were born at the height of the MMR scare and are currently being targeted by the national catch-up programme
- Our analyses refer to predictors of catch-up during a period when parental concerns around the safety of the vaccine were relatively high, and the incidence of measles relatively low; predictors of catch- up in families with young children today may be different .
- We were unable to investigate exact timing of vaccination; therefore our analyses focus on children who were unimmunised at age three (so approximately 2 years after the recommended age of administration), and we were unable to detect how long children who had partially or fully caught-up by age five had been left susceptible

For peer review only

Introduction

The combined measles, mumps and rubella vaccination (MMR) has been used routinely in the UK since 1988. Coverage at 2 years of age peaked in England in 1995, at 92% [1]. A two-dose schedule was introduced in 1996, the first dose recommended at soon after the age of 12/13 months[2] (affording 90-95% protection against measles), with a second at three years four months[2] (99% protection). In 1998, a Lancet article[3] was widely interpreted as suggesting MMR was linked with autism and bowel problems. Although the paper was eventually discredited and retracted by the Lancet in 2010[4], widespread adverse media coverage in the intervening years led to a dramatic fall in MMR uptake, to a low of 80% in England (of the first dose by age two) in 2003[1]. By 2006-7, 85% of two year olds had received at least one MMR, although only 73% had received the recommended two doses by age five, and levels were particularly low in some geographical areas, such as London[1]. Measles cases started to rise and in 2008 the Health Protection Agency announced that measles was again endemic in England and Wales.

Although coverage has continued to rise (in England in 2011-12, 91% of two year olds had received one and 86% of five year olds two doses of MMR[5]), levels remain below those needed for herd immunity, particularly in some geographical areas and in children who were born in the late 1990s and early 2000s. Consequently, measles outbreaks are currently occurring across some areas of the UK, with young teenagers disproportionately affected (one quarter of measles cases in 2011-12 were in 10-14 year olds[6]). In response to this, Public Health England, NHS England and the Department of Health announced a national MMR catch-up programme to vaccinate as many partially or unimmunised 10-16 year olds as possible by the start of the next school year (September 2013)[7]. The catch-up programme outlines aims to strengthen current routine immunisation strategies and in particular to target hard to reach populations; GPs and schools will

For peer review only

play a central role. A better understanding of the social and demographic characteristics associated with catching-up (or not), and the reasons reported by parents for their child's immunisation status, is essential if the aims of the new framework are to be achieved and maintained. Cross-sectional evidence indicates that, at age three, being unimmunised against MMR, or receiving the single antigen vaccines, was socially distributed[8]. However little is known about the factors which influence the propensity of families with unimmunised children to catch-up. We examine the social correlates of partial and full catch-up with MMR between the age of three and five years, in a nationally representative cohort of children born at the height of the MMR scare.

Methods

Participants

We analysed data from the Millennium Cohort Study (MCS), a longitudinal study of children eligible for Child Benefit and born in the UK between September 2000 and January 2002. The sample was derived from a random sample of electoral wards which were disproportionately stratified to ensure an adequate representation of all four UK countries, deprived areas and, in the case of England, areas with high proportions of families from ethnic minority groups[9]. At the first contact, when the MCS children were aged 9 months, data were collected on 18,296 singleton babies (72% of those approached); with subsequent data collections at three and five years. 71% of the initial cohort responded to all three sweeps (*n*= 12,989). Participants in the second and third sweeps were less likely to be from ethnic or deprived wards[10;11], although due to the sampling design these proportions remained higher than the general population.

Our analyses focus on the subsample of MCS singleton children who were unimmunised against measles, mumps or rubella at age three years. Of the 804 children who were unimmunised at age

For peer review only

three, 777 (96.6%) had a recorded MMR outcome at five years, and 26 (3.3%) of them were excluded because they were reported to have received at least one single antigen vaccine by age five, leaving 751 eligible participants in our analyses. Compared to the unimmunised children (who are the focus of this analysis), children who had been immunised with MMR at age three were: less likely to have a mother with a degree or A-levels, and more likely to have a mother in her twenties or early thirties or who did not smoke during pregnancy; they were also less likely to be living in a lone parent family and more likely to be an only child. The socio-economic and demographic characteristics of children according to MMR status at age three is described in greater detail elsewhere[8].

Measures

Measures were reported by the main respondent (usually the mother) during survey interviews, which were carried out by trained interviewers in the home.

Outcome measure: MMR status at age five was classified as unimmunised (received no combined MMR vaccines), partially caught-up (received one combined MMR), or fully caught-up (received two combined MMRs).

Covariates: We explored socio-economic and demographic factors that were found to be associated with immunisation status in earlier sweeps of the MCS[8;12;13], or that were pertinent to immunisation policy. We examined maternal social class (based on National Statistics Socio-economic Classification (NS-SEC)), ethnicity, maternal age at birth (in five-year age bands), maternal education, and child gender. These measures were all captured at age nine months because they were unlikely to have changed in later sweeps. In addition, we explored the following time-variant

For peer review only

measures, captured at age three (the beginning of the potential catch-up period): UK country of residence, ward type ('advantaged', 'disadvantaged', 'ethnic'), number of children in the household, maternal employment status, lone parenthood, household income, housing tenure, whether resident in London, whether the family had changed residential address since age three, and whether the parents reported the child having natural measles infection. Income data were missing for 14% (122) children at age three; we supplemented this with information captured at age nine months, reducing the level of missingness to 24. Missing data were very low for all other measures (listed at the foot of Table 1).

We also investigated reasons given for not having had MMR at age three, classified in a previous analysis[10] as 'practical' (such as missing an appointment), 'medical' (e.g. child had asthma), 'conscious decision' (including fear of links with autism) or 'other' (which included don't know). The mean age of the MCS children at the third survey was 61 months, with a range between 52 and 72 months, meaning that some children had more time to catch-up than others. We therefore explored age as a potential confounder, but as it was not found to be associated with immunisation status (p=0.28) we did not include it in our models. There were no *a priori* hypotheses for interactions so none were explored.

Analysis

We estimated the prevalence of MMR status (unimmunised, partially caught-up, and fully caught-up) at age five, overall and according to the potential explanatory factors. We then fitted Poisson regression models to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for partial and full catch-up (in two separate models, because previous research indicates that the social correlates of partial and full immunisation are likely to differ[12]). The models were built as follows: first we

For peer review only

explored univariable associations between the outcome and each of the explanatory variables. Variables, which were associated with the outcome (p<0.10) using Wald tests for trend, were entered into a multivariable model using a forward stepwise model selection strategy. Residence in London was forced into the multivariable models, due to its potential significance for policy. Only measures which remained significantly associated with the outcome after adjustment were retained.

Data were downloaded from the UK Data Archive, University of Essex in May 2010. Analyses were carried out in Stata 12 (Stata Corporation, TX) using survey and response weights to allow for the sample design and attrition between sweeps[10;14].

Results

Of the 751 MCS children who were unimmunised at age three, 60.3% (440) remained unvaccinated, 16.1% (127) had partially caught-up, and 23.6% (184) had fully caught-up. Table 1 presents the proportion of children who were partially, fully, or unimmunised, according to the various predictor measures.

Table 1: Weighted percentage (*n*) of children who remained unimmunised or who partially for fully caught-up with MMR, according to social, demographic and other characteristics

	Total	Full catch-up (2 doses)	Partial catch-up (1 dose)	Unimmunised
Language spoken at home				
English only	91.6 (658)	20.4 (130)	15.8 (11.5)	67.8 (413)
English and other language(s)	5.7 (64)	53.0 (29)	15.0 (9)	32.0 (26)
No - other language(s) only	2.7 (29)	70.2 (25)	27.7 (3)	2.1 (1)
Ward type				
Advantaged	56.5 (290)	20.3 (60)	13.6 (43)	66.1 (187)
Disadvantaged	38.5 (5.0)	24.1 (79)	20.1 (73)	55.8 (227)
Ethnic	5.0 (82)	57.6 (45)	13.3 (11)	29.2 (26)
Ethnicity				
British white	87.5 (644)	20.3 (126)	15.8 (111)	63.9 (407)

For peer review only

Other white	2.2 (13)	10.3 (2)	15.6 (2)	74.1 (9)
Mixed	1.4 (10)	33.5 (3)	15.1 (2)	51.4 (5)
Indian	1.0 (12)	76.9 (9)	5.5 (1)	17.5 (2)
Pakistani or Bangladeshi	3.8 (39)	74.7 (28)	9.8 (3)	15.5 (8)
Black or Black British	2.7 (18)	24.7 (7)	35.1 (5)	40.2 (6)
Other	1.4 (14)	65.2 (9)	19.6 (2)	15.2 (3)
Lone parent/carer				
Two parents/carers	79.2 (597)	21.9 (142)	15.3 (97)	62.9)
One parent/carer	20.8 (154)	30.2 (42)	19.3 (30)	50.5 (82)
Maternal age at birth of cohort child				
14 - 19y	8.1 (60)	37.7 (21)	21.8 (14)	40.6 (25)
20-24y	15.9 (130)	34.3 (40)	19.4 (27)	46.3 (63)
25-29y	23.5 (174)	25.8 (52)	18.2 (27)	55.9 (95)
30-34y	27.6 (205)	17.0 (36)	13.0 (30)	70.0 (13.9)
35-39y	20.4 (145)	15.8 (25)	14.3 (24)	70.0 (96)
40plus	4.5 (36)	24.2 (9)	10.6 (5)	65.1 (22)
Maternal education				
Degree	20.8 (152)	18.8 (32)	10.4 (15)	70.7 (105)
Diploma	8.9 (64)	13.9 (9)	14.9 (9)	71.1 (46)
A or AS levels	11.3 (85)	22.7 (19)	17.0 (20)	60.2 (46)
GCSE A*-C	32.2 (238)	20.4 (48)	19.6 (50)	60.0 (140)
GCSE D-G	8.4 (64)	18.1 (13)	23.9 (16)	58.0 (35)
Other	1.9 (15)	25.1 (6)	7.7 (1)	67.2 (8)
None	16.4 (133)	44.5 (57)	13.4 (16)	42.1 (60)
Housing tenure age 3				
Owned	58.7 (451)	18.1 (92)	15.6 (77)	66.3 (282)
Privately rented	9.8 (71)	29.8 (18)	11.5 (8)	58.6 (45)
Socially rented	27.7 (199)	30.4 (65)	19.8 (37)	49.8 (16)
Other	3.8 (30)	43.4 (9)	8.1 (5)	48.6 (16)
Household income (£ pa)				
0-11000	23.7 (186)	32.1 (57)	18.7 (34)	49.2 (95)
11 000-22 000	30.4 (228)	23.4 (56)	18.2 (41)	58.4 (131)
22 000-33 000	19.9 (142)	12.6 (21)	18.3 (34)	69.1 (87)
33 000-55 000	17.4 (123)	20.6 (28)	6.8 (8)	72.6 (87)
55 000+	8.9 (48)	23.5 (11)	15.9 (8)	60.6 (29)
Social class (9 months)				
Managerial & professional	30.2 (222)	20.8 (42)	12.7 (34)	66.5 (14.6)
Intermediate	16.7 (119)	17.5 (22)	17.6 (18)	65.0 (79)
Small employer/self-employed	8.0 (53)	10.1 (10)	11.9 (8)	78.0 (35)
Lower supervisory & technical	4.0 (33)	33.4 (10)	9.6 (4)	57.1 (19)
Semi-routine & routine	32.0 (248)	24.4 (61)	20.6 (53)	54.9 (134)
Never worked/unemployed	9.2 (73)	47.8 (37)	15.6 (10)	36.6 (26)
Number of children in household (age 3)				
One child	22.5 (180)	26.2 (43)	20.0 (38)	53.8 (99)
Two or three children	63.1 (459)	21.3 (104)	15.5 (73)	63.2 (282)
Four or more children	14.4 (112)	29.9 (37)	12.6 (16)	57.6 (59)
Maternal employment (age 3)				
FT	11.2 (93)	23.8 (21)	11.5 (17)	64.7 (55)
PT	25.2 (191)	22.1 (41)	19.6 (37)	58.3 (113)
On leave	3.9 (28)	26.8 (8)	3.9 (1)	69.4 (19)
Self employed	9.3 (60)	17.1 (13)	13.0 (10)	69.9 (37)

For peer review only

Not employed/student	50.4 (379)	25.3 (101)	16.9 (62)	57.8 (216)
Sex of child				
Male	55.1 (404)	20.6 (95)	17.7 (70)	61.7 (239)
Female	44.9 (347)	27.3 (89)	14.1 (57)	58.6 (201)
Parental report of measles disease by age 3				
Yes	3.5 (22)	19.2 (5)	13.2 (3)	67.6 (14)
No	96.5 (721)	23.7 (176)	16.1 (123)	60.2 (422)
Residence in London				
London	16.2 (102)	17.7 (23)	20.0 (19)	62.3 (60)
Not London	83.8 (649)	24.8 (161)	15.3 (108)	60.0 (380)
Country of residence				
England	58.6 (462)	23.3 (122)	15.7 (74)	61.0 (266)
Wales	21.6 (160)	22.1 (31)	20.1 (31)	57.7 (98)
Scotland	12.9 (87)	26.7 (21)	15.6 (14)	57.5 (52)
Northern Ireland	6.9 (42)	25.3 (10)	17.8 (8)	60.0 (24)
Smoked during pregnancy				
No	63.2 (465)	23.4 (121)	15.1 (76)	61.6 (268)
Yes	36.8 (283)	23.8 (62)	18.0 (51)	58.2 (170)
Changed address since 3				
No	85.6 (647)	23.8 (161)	16.6 (112)	59.6 (374)
Yes	14.4 (104)	22.4 (23)	13.1 (15)	64.5 (66)
Reasons given for not having had MMR (aged 3)				
Practical	6.2 (51)	54.5 (30)	15.3 (7)	30.3 (14)
Medical	15.2 (107)	17.9 (82)	25.5 (26)	56.7 (57)
Conscious decision	66.7 (486)	17.8 (82)	16.0 (85)	66.2 (31.9)
Other	11.7 (76)	35.3 (26)	9.9 (9)	54.9 (41)

Missing: Social class 3, smoked during pregnancy 3, income 24, ethnicity 1, reason 31, age at birth 1.

Partial catch-up (compared to remaining unimmunised)

Table 2 (column A) shows unadjusted RRs for partial catch-up, according to each of the predictor measures. Partial catch-up was more likely in families who spoke a language other than English at home (particularly if English was not spoken at home at all), compared to those who only spoke English at home, and in those who lived in a ward classified as 'disadvantaged' or 'ethnic', compared to advantaged wards. No significant associations were seen with any of the other variables. When language, ward type and London residence (due to its policy significance) were entered into the multivariable model, only language remained significantly associated with the likelihood of being partially immunised, with an adjusted RR of 4.68 (3.63 to 6.03) in families who did not speak English at home (Table 2, Column B).

For peer review only

Table 2: Unadjusted and adjusted odds ratios (ORs) for partial catch-up with the combined MMR vaccine (baseline unimmunised) by age five

	Partial catch-up (1 dose)		Full catch-up (2 doses)	
	A: uRR (95% CI)	**B: aRR (95% CI)**	**C: uRR (95% CI)**	**D: aRR (95% CI)**
Language spoken at home				
English only	1	1	1	1
English and other language(s)	1.61 (0.96, 2.70)	1.61 (0.96, 2.70)	2.57 (2.00, 3.32)*	1.54 (0.91, 2.63)
Other language(s) only	4.68 (3.63, 6.03)*	4.68 (3.63, 6.03)*	4.00 (3.37, 4.76)*	1.90 (1.08, 3.32)*
p-value	<0.001	<0.001	<0.001	0.0811
Ward type				
Advantaged	1		1	
Disadvantaged	1.55 (1.05, 2.27)*		1.29 (0.92, 1.80)	
Ethnic	1.83 (1.18, 2.83)*		2.83 (2.19, 3.65)*	
p-value	0.0146		<0.001	
Ethnicity				
British white	1		1	1
Other white	0.88 (0.22, 3.54)		0.51 (0.13, 2.06)	0.37 (0.10, 1.34)
Mixed	1.15 (0.29, 4.59)		1.64 (0.57, 4.74)	1.83 (0.65, 5.17)
Indian	1.21 (0.19, 7.82)		3.38 (2.40, 4.76)*	2.01 (0.75, 5.41)
Pakistani or Bangladeshi	1.96 (0.84, 4.54)		3.44 (2.79, 4.23)*	2.40 (1.38, 4.18)*
Black or Black British	2.35 (0.99, 5.57)		1.58 (0.73, 3.43)	1.12 (0.35, 3.63)
Other	2.84 (1.12, 7.22)*		3.36 (2.42, 4.67)*	1.88 (1.08, 3.29)*
p-value	0.0126		<0.001	0.0950
Lone parent/carer				
Two parents/carers	1		1	
One parent/carer	1.42 (0.92, 2.17)		1.45 (1.06, 1.99)*	
p-value	0.1110		0.0208	
Maternal age at birth of cohort child				
14 - 19y	1.42 (0.80, 2.51)		1.52 (0.98, 2,37)	
20-24y	1.20 (0.68, 2.12)		1.35 (0.89, 2.03)	
25-29y	1		1	
30-34y	0.63 (0.37, 1.08)		0.62 (0.40, 0.97)*	
35-39y	0.69 (0.40, 1.20)		0.58 (0.37, 0.92)*	
40plus	0.57 (0.23, 1.43)		0.86 (0.42, 1.74)	
p-value	0.0259		<0.001	
Maternal education				
Degree	1		1	
Diploma	1.35 (0.54, 3.36)		0.78 (0.35, 1.72)	
A or AS levels	1.72 (0.79, 3.74)		1.30 (0.71, 2.38)	
GCSE A*-C	1.91 (1.05, 3.49)*		1.21 (0.75, 1.96)	
GCSE D-G	2.27 (1.07, 4.80)*		1.13 (0.55, 2.34)	
Other	0.80 (0.11, 5.93)		1.29 (0.49, 3.39)	
None	1.88 (0.87, 4.03)		2.44 (1.63, 3.66)*	
p-value	0.2420		<0.001	
Housing tenure age 3				
Owned	1		1	1

For peer review only

Privately rented	0.86 (0.32, 2.34)		1.57 (0.96, 2.59)	1.51 (0.91, 2.48)
Socially rented	1.49 (0.96, 2.32)		1.77 (1.29, 2.43)*	1.86 (1.34, 2.56)*
Other	0.75 (0.27, 2.09)		2.20 (1.27, 3.79)*	2.52 (1.23, 5.18)*
p-value	0.0936		0.0014	<0.001
Household income (£ per annum)				
0-11000	1		1	
11 000-22 000	0.86 (0.53, 1.41)		0.72 (0.52, 1.02)	
22 000-33 000	0.76 (0.44, 1.31)		0.39 (0.23, 0.66)	
33 000-55 000	0.31 (0.14, 0.70)*		0.56 (0.36, 0.87)	
55 000+	0.76 (0.36, 1.61)		0.71 (0.39, 1.29)	
p-value	0.0816		0.0028	
Social class (9 months)				
Managerial & professional	1		1	
Intermediate	1.33 (0.73, 2.42)		0.89 (0.52, 1.53)	
Small employer/self-employed	0.83 (0.38, 1.79)		0.48 (0.20, 1.16)	
Lower supervisory & technical	0.90 (0.30, 2.67)		1.55 (0.80, 3.00)	
Semi-routine & routine	1.71 (1.11, 2.64)*		1.29 (0.87, 1.92)	
Never worked/unemployed	1.87 (0.96, 3.64)		2.38 (1.62, 3.49)*	
p-value	0.0989		<0.001	
Number of children in household (age 3)				
One child	1		1	
Two or three children	0.73 (0.47, 1.12)		0.77 (0.52, 1.14)	
Four or more children	0.66 (0.34, 1.29)		1.04 (0.67, 1.63)	
p-value	0.2807		0.1832	
Maternal employment (age 3)				
Full-time	1		1	
Part-time	1.67 (0.84, 3.33)		1.02 (0.58, 1.79)	
On leave	0.35 (0.05, 2.48)		1.04 (0.46, 2.33)	
Self employed	1.04 (0.41, 2.66)		0.73 (0.37, 1.45)	
Not employed/student	1.50 (0.88, 2.57)		1.13 (0.71, 1.80)	
p-value	0.1836		0.6517	
Sex of child				
Male	1		1	
Female	0.87 (0.60, 1.27)		1.27 (0.94, 1.71)	
p-value	0.4755		0.1171	
Parental report of measles disease by age 3				
Yes	1		1	
No	1.29 (0.48, 3.49)		1.28 (0.52, 3.16)	
p-value	0.6163		0.5970	
Residence in London				
London	1		1	1
Not London	0.84 (0.50, 1.41)		1.32 (0.86, 2.02)	1.95 (1.32, 2.89)*
p-value	0.5078		0.2012	<0.001
Country of residence				
England	1		1	
Wales	1.26 (0.86, 1.84)		1.00 (0.69, 1.46)	
Scotland	1.04 (0.60, 1.83)		1.16 (0.71, 1.88)	
Northern Ireland	1.16 (0.55, 2.44)		1.11 (0.66, 1.88)	
p-value	0.6802		0.9272	
Smoked during pregnancy				
No	1		1	

For peer review only

Yes	1.20 (0.73, 1.74)		0.05 (0.76, 1.46)	
p-value	0.3202		0.7481	
Changed address since 3				
No	1			
Yes	0.90 (0.62, 1.32)		0.77 (0.42, 1.43)	
p-value	0.6031		0.4112	
Reasons given for not having had MMR (aged 3)				
Practical	1		1	
Medical	0.93 (0.44, 1.93)		0.37 (0.20, 0.68)*	0.43 (0.25, 0.74)*
Conscious decision	0.58 (0.27, 1.22)		0.33 (0.23, 0.47)*	0.33 (0.23, 0.48)*
Other	0.45 (0.16, 1.30)		0.61 (0.40, 0.93)*	0.46 (0.29, 0.73)*
p-value	0.1357		<0.001	<0.001

uRR = unadjusted risk ratio; aRR = adjusted risk ratio. * *p*=<0.05

Full catch-up (compared to remaining unimmunised)

Table 2 also presents unadjusted and adjusted RRs for fully catching up. In the univariable analyses (Column C), children whose parents spoke a language other than English at home (as opposed to only speaking English), who were from ethnic minority groups (compared to White British), or lived in 'ethnic' wards (compared to 'advantaged' wards) were more likely to fully catch-up. Catch-up was also significantly more likely in children who mother had no educational qualifications (compared to a degree), in lone parent families (compared to two parent families), and in those living in 'socially rented' or 'other' tenure types (compared to own/mortgage). Catch-up was significantly less likely in children with a mother in her thirties (compared to 24-29 years), and in children living in higher income households. Children whose parents had reported a non-practical reason ('medical', 'conscious decision', or 'other') for not having their child immunised with the combined MMR at age three were also less likely to have fully caught-up than those reporting practical reasons. Living in London was not associated with immunisation status, although due to its policy significance was included in the multivariable model reported below.

In the multivariable analysis (Column D), full catch-up remained significantly more likely in those who only spoke a non-English language at home (1.90 [1.08 to 3.32]), when compared to those who

For peer review only

only spoke English. Those from Pakistani or Bangladeshi (2.40 [1.38 to 4.18]), and 'Other' (1.88 [1.08 to 3.29]) ethnic groups were more likely to have caught-up than White British groups, as were those living in 'socially rented' (1.86 [1.34 to 2.56]) or 'other' (2.52 [1.23 to 5.18]) tenure types (compared to own/mortgage). Full catch-up was also more likely in families living outside London (1.95 [1.32 to 2.89]). Compared to those reporting practical reasons for not having been immunised at age three, children whose parents reported medical reasons (0.43 [0.25 to 0.74]), a conscious decision (0.33 [0.23 to 0.48]), or 'other' reasons (0.46 [0.29 to 0.73]) were considerably less likely to have fully caught-up.

Parents from Asian and "other White" backgrounds were 2-3 times more likely to experience practical barriers to immunisation than those from White British, Mixed or Black backgrounds. Similarly, families who spoke a non-English language in the home were two-three times as likely to experience practical barriers as families who only spoke English at home (data not shown).

Discussion

Just over 40% of children who were unimmunised with MMR vaccine at age three had either partially or fully caught-up by age five. The likelihood of catching-up varied markedly with a number of social factors, and more so for full than partial catch-up. Some families, particularly those from ethnic minority groups, appear to have difficulty accessing vaccination in a timely fashion. Advantaged families and those citing non-practical reasons for non-vaccination at age three are more likely to persist in not immunising their child against MMR.

We used sample and response weights to account for the survey design and attrition between the first, second, and third sweeps of the MCS. However the non-response weights are unlikely to have entirely accounted for differential response; for example 95.7% children who were included in the age three and five surveys were fully immunised with the primary vaccines (at age 9 months)

For peer review only

compared to 92.7% in children who did not take part in both of the later surveys (p<0.001). A limitation of the study is that we utilised parental report of immunisation status, and it was not possible to validate report of immunisation status against health system records. However there is no gold standard measure of immunisation status and studies have found disagreement between parental report and health records to be low[15] and not socially distributed[16]. Parents were given the opportunity to consult the Personal Child Health Record (or 'red book'). Of the 751 families included in our analysis, 19% (137) consulted the book and found the relevant information, 1% (11) checked the book and did not find the relevant information, and 79% (603) chose not to consult the book and relied on their memory. There was no association between catch-up status and whether the parent consulted the red book (p=0.18), and the associations reported in this paper remained the same when analyses were repeated excluding children where the parent had looked but not found information (data not shown). A small number (26) of children who were unimmunised at age three had received at least one single antigen vaccine by age five. Due to low numbers we were unable to explore the characteristics of this group.

The intense negative media attention around the safety of the MMR vaccine peaked in 2002/3 when the MCS children were toddlers. These findings therefore provide important information on the barriers to catch-up, in a cohort of children who are currently experiencing measles outbreaks throughout the UK[6], and are a central focus of the newly launched national catch-up programme. However we measured catch-up across the period 2003/5 to 2006/7, when the MMR scare was at its height and the incidence of measles was relatively low (although with some indications of a rise). Concerns around the safety of the MMR have diminished over recent years and therefore the characteristics of families who catch-up with the vaccine today may be different. It is also likely that some of the barriers we report for more advantaged families are reduced during times of measles

For peer review only

outbreaks, as the perceived risk-benefit balance of the vaccine shifts. Nonetheless, this paper provides important information on the barriers experienced by advantaged families during times of no outbreak to improve and sustain the current MMR programme, which is also a central aim of the catch-up programme. The recommended age of the first dose of MMR is 12/13 months; however information on uptake was not collected in the MCS until the children were age three years. Our analysis is unable to address those children who were immunised by age three but who had not been immunised on time. Similarly, we were unable to investigate the timing of catch-up between the age of three and five, and therefore how long children who partially or fully caught-up were left susceptible. Finally, the MCS consists only of children who were born in the UK. The barriers experienced by families from ethnic minority groups or who speak other may be different and/or greater in families where the child was born outside the UK.

Before the scare, MMR uptake was generally lower in more deprived areas and households[17;18]. Since 1998, rates declined faster in more advantaged areas[19;20] and more slowly in areas with lower proportions of highly educated residents[20] and in minority ethnic groups[21]. Earlier cross-sectional findings from the MCS demonstrated that the likelihood of being unimmunised against measles, mumps and rubella tended to be greater in more disadvantaged families, while children living in more affluent households were more likely to receive single antigen vaccines (indicating conscious rejection of combined MMR)[8]. However there is a dearth of longitudinal research exploring the social correlates of catch-up with MMR. The only study, to our knowledge, which has explored the social correlates of MMR catch-up was an ecological study of one million children born between 1987 and 2004 in Scotland. The authors found that children living in more affluent areas were either immunised with MMR on time or not at all, whereas children living in deprived areas were more likely to be immunised late[20]. Our findings not only reflect this, but add to the evidence base

For peer review only

by demonstrating that individual-level predictors of catch-up are strongly related to catch-up. We have also found that remaining unvaccinated with MMR at age five was associated with non-practical reasons for not immunising with MMR at three, reflecting other research which has shown that more affluent families are more likely to consciously reject MMR[20;22].

Outbreaks of measles are currently being experienced across the UK, leading to the launch of a national catch-programme in April 2013. Approaches to optimise uptake of MMR will need to be tailored to the needs of local populations, both now and in the future. Our study has identified two distinct groups of families that do not immunise their child with MMR in a timely fashion (during periods of low measles incidence). The first comprises those who partially or fully catch-up, amounting to 40% of those who were unimmunised at age three. These families tend to experience practical barriers to immunisation, and are socially disadvantaged or from ethnic minority groups. The second group, which continues to reject MMR and makes up the remaining 60%, consists of parents who consciously reject MMR from the start, and are from more advantaged backgrounds.

Steps are required to minimise time to uptake in those families who do eventually catch-up, through the reduction of practical barriers. NICE guidance outlines actions to reduce inequalities in immunisation[23], including provision of information in multiple languages, offering immunisation checks and administration in alternative settings, and sending out reminder invitations from GPs[24]. In addition, alleviating any lingering fears and concerns of families who consciously reject MMR is essential. This should include discussion of concerns about 'medical' reasons for not giving MMR. Mythical contraindications to MMR have circulated amongst the health professional community and parents for some time[25] despite there being few true contraindications for MMR vaccination. 'Medical reasons' reported by parent for not immunising in the MCS (at age five) included: "child is

For peer review only

not able to have it for health reasons" and "other medical problems or bad reactions". It is not possible to ascertain whether any of these were true contraindications, although there are very few genuine contraindications to MMR[2] and these tend to be very rare. It was possible to look at longstanding illness however, and children who had not been immunised for 'medical reasons' had a higher prevalence of longstanding illness (38%) than overall prevalence in the cohort (15%). Conditions reported for children who had not been immunised and who had a long standing illness included asthma, epilepsy, dermatitis/eczema and cerebral palsy, and although none appeared to be true contraindications, some may have been incorrectly considered to be at that time, either by the health professional or the parents themselves. NICE recommends offering parents opportunities to discuss their concerns about vaccines or vaccine safety with health professionals; receiving such information from health professionals has been found to be the decisive factor for parents who have changed their minds about previously rejected or delayed vaccines[26]. In addition training is recommended for health care professionals to equip them with the skills and information needed to communicate effectively with parents about immunisation, to allay any fears over the safety of the vaccine and any misinformation about medical contraindications. Finally, joint working between the health sector and childcare providers, nurseries, and schools is essential[23].

Conclusions

Children born at the height of the MMR scare are being disproportionately affected by current measles outbreaks and are the target of a newly launched national catch-up programme. Our findings refer to children of this age and have identified the characteristics of two distinct groups of parents who do not immunise their children with MMR on time. Health professionals should consider their local populations in light of our findings, and tailor the local roll-out of the catch-up programme accordingly.

For peer review only

The new national immunisation framework not only aims to facilitate catch-up but also to strengthen routine approaches to immunisation[7]. Findings from this study should be used to inform longer-term local and national planning to improve and maintain timely uptake. While uptake of the first dose of MMR in younger age groups has increased, levels remains below those required for herd immunity and uptake of the second dose is lower still. Measles outbreaks remain a risk, particularly in areas of the country with low uptake.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, Institute of Education, University of London. We would also like to thank the MCS user group at the MRC Centre of Epidemiology for Child Health: Catherine Law, Carol Dezateux, Lucy Griffiths, Tim Cole, Phillippa Cumberland, Jamie Fagg, Francesco Sera, Steven Hope, Hannah Lewis and Marco Geraci; also David Elliman, for his advice early on in the project.

Funding

The Centre for Paediatric Epidemiology and Biostatistics is supported in part by the Medical Research Council in its capacity as the MRC Centre of Epidemiology for Child Health (Grant reference G0400546). Research at the UCL Institute of Child Health and Great Ormond Street Hospital for Children receives a proportion of the funding from the Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme. AP is funded by a Medical Research Council fellowship (grant reference MR/J012351/1). All researchers were independent of the funders and the funders played no part in the study design, analysis or interpretation of the data, writing of the report or the decision to submit for publication.

For peer review only

Contributors: MM and HB contributed to the study conception. All authors contributed to the design of the analysis. AP, MM and MC-B carried out the analyses. AP and MM drafted the paper. All authors revised the paper. All authors had full access to the data and take responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval: Research ethics approval was not required for this study as it was a secondary data analysis of the UK Millennium Cohort Study. The first sweep of the Millennium Cohort Study received ethics approval from National Health Service Ethical Authority in February 2001 (MREC/01/6/19), and the second and third received approval from the London Multi-Centre Research Ethics Committee in September 2004 (MREC/03/2/022) and December 2005 (05/MRE02/46).

Data sharing: The Millennium Cohort Study is available at: http://www.esds.ac.uk/findingData/mcs.asp

Competing interests

All authors have completed the ICMJE uniform disclosure form at ww.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; MCB has received research grants from the Health Protection Agency; no other relationships or activities that could appear to have influenced the submitted work.

Copyright/licence for publication

I, Helen Bedford, the Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs, other illustrative material, video, film or any other material howsoever submitted by the Contributor(s) at any time and related to the Contribution ("the Contribution") have the right to grant on behalf of all authors and do grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licensees, to permit this Contribution (if accepted) to be published in BMJ Open an d any other BMJ Group products and to exploit all

For peer review only

subsidiary rights, as set out in the licence at: http://group.bmj.com/products/journals/instructions-for-authors/BMJOpen_licence.pdf

References

1. The Information Centre. NHS Immunisation Statistics: England 2006-07, 2007.
2. Salisbury D, Ramsay M, Noakes K. Immunisation against infectious disease: the green book. In: England PH, editor, 2013. https://www.gov.uk/government/organisations/public-health-england/series/immunisation-against-infectious-disease-the-green-book
3. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998;351 (9103):637-41.
4. Lancet. Retraction--Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. 2010 Feb *Lancet.* 2010;375(9713):445.
5. The Health and Social Care Information Centre Screening and Immunisations team. NHS Immunisation Statistics, England: 2011-12 In: Centre TI, editor, 2012.
6. Health Protection Agency. Confirmed cases of measles by region and age: 1996-2012. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733778332: Public Health England, 2013.
7. Public Health England. MMR catch-up programme 2013. . https://www.gov.uk/government/organisations/public-health-england/series/MMR-catch-up-programme-2013#publications: GOV.UK, 2013.
8. Pearce A, Law C, Elliman D, Cole TJ, Bedford H, the Millennium Cohort Study Child Health G. Factors associated with uptake of measles, mumps and rubella vaccine (MMR) and use of single antigen vaccines in a comtemporary UK cohort: prospective cohort study. *British Medical Journal* 2008;336:754-60.
9. Centre for Longitudinal Studies. Millennium Cohort Study: Survey design: Institute of Education, 2007.
10. Plewis I, Ketende S. Millennium Cohort Study: technical report on response. 1st ed. London Centre for Longitudinal Studies, 2006.
11. Hansen K, Joshi H. Millennium Cohort Study Third Survey: A User's Guide to Initial Findings. London: Institute of Education 2008.
12. Samad L, Bedford H, Tate AR, Dezateux C, Peckham C, Butler N, et al. Differences in risk factors for partial and no immunisation in the first year of life. *British Medical Journal* 2006;332 1312-13.
13. Pearce A, Elliman D, Bedford H, Law C. Residential mobility and uptake of childhood immunisations: findings from the UK Millennium Cohort Study. *Vaccine* 2008;26:1675-80.
14. Plewis I. Millennium Cohort Study: technical report on sampling. 3rd ed. . London: Centre for Longitudinal Studies, 2004.
15. AbdelSalam HHM, Sokal MM. Accuracy of parental reporting of immunization. *Clinical Pediatrics* 2004;43 (1):83-85.
16. Suarez L, Simpson DM, Smith DR. Errors and correlates in parental recall of child immunizations: effects on vaccination coverage estimates. *Pediatrics* 1997;99 (5):E3.

For peer review only

17. Sharland M, Atkinson P, Maguire H, Begg N. Lone parent families are an independent risk factor for lower rates of childhood immunisation in London. *Communicable Disease Report.CDR Review* 1997;7 (11):R196-R72.
18. Li J, Taylor B. Factors affecting uptake of measles, mumps, and rubella immunisation. *British Medical Journal* 1993;307 168-71.
19. Middleton E, Baker D. Comparison of social distribution of immunisation with measles, mumps, and rubella vaccine, England, 1991-2001. *British Medical Journal* 2003;326 854-54.
20. Friederichs V, Cameron JC, Robertson C. Impact of adverse publicity on MMR vaccine uptake: a population based analysis of vaccine uptake records for one million children, born 1987-2004. *Archives of Disease in Childhood* 2006;91 465-68.
21. Hawker J, Olowokure B, Wood A, Wilson R, Johnson R. Widening inequalities in MMR vaccine uptake rates among ethnic groups in an urban area of the UK during a period of vaccine controversy (1994-2000). *Vaccine* 2007;25:7516-9.
22. MacDonald H, Henderson R, Oates K. Low uptake of immunisation: contributing factors. *Community Practioner* 2004;77 (3):95-100.
23. National Institute for Health and Clinical Excellence. Reducing differences in the uptake of immunisations. *NICE public health guidance 21*, 2009.
24. Jacobson Vann J, Szilagyi P. Patient reminder and patient recall systems to improve immunization rates. . *Cochrane Database Syst Rev.* 2005;Jul 20(3).
25 Bedford, H; Elliman, D. Concerns about immunisation. *British Medical Journal* 2000;320;7229: 240.
26. Gust D, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics* 2008;1227(4):18-25.

For peer review only

Characteristics of five year olds who catch-up with MMR: findings from the UK Millennium Cohort Study

Anna Pearce (Research Fellow) [1]; Miranda Mindlin (Consultant in Communicable Disease Control)[2;1]; Mario Cortina-Borja (Senior Lecturer)[1]; Helen Bedford (Senior Lecturer)[1]*

[1]MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK

[2] Kent, Surrey, Sussex Public Health England Centre, County Hall North, Chart Way, Horsham, West Sussex, RH12 1XA, UK

*corresponding author and guarantor to the paper. h.bedford@ucl.ac.uk. T 0207 905 2333; F 020 7905 2793

Key words:

Socio-economic factors, immunisation, measles, measles-mumps-rubella vaccine, child health services

Word count: 3441

For peer review only

Abstract

Objectives

To examine predictors of partial and full MMR catch-up between three and five years

Design

Secondary data analysis of the nationally representative Millennium Cohort Study (MCS)

Setting

Children born in the UK, 2000-2

Participants

751 MCS children who were unimmunised against measles, mumps and rubella at age three, with immunisation information at age five

Main outcome measures

Catch-up status: unimmunised (received no MMR), partial catch-up (received one MMR), or full catch-up (received two MMRs)

Results

At age five, 60.3% (*n*=440) children remained unvaccinated, 16.1% (*n*=127) had partially, and 23.6% (*n*=184) had fully caught-up. Children from families who did not speak English at home were five times as likely to partially catch-up than children living in homes where only English was spoken (risk ratio: 4.68 [95% CI, 3.63-6.03]). Full catch-up was also significantly more likely in those did not speak English at home (adjusted risk ratio: 1.90 [1.08-3.32]). In addition, those from Pakistani /Bangladeshi (2.40 [1.38-4.18]) or 'other' ethnicities (such as Chinese) (1.88 [1.08-3.29]) were more likely to fully catch-up than White British. Those living in socially rented (1.86 [1.34-2.56]) or 'Other' (2.52 [1.23-5.18]) accommodations were more likely to fully catch-up than home owners, and families were more likely to catch-up if they lived outside London (1.95 [1.32-2.89]). Full catch-up was less likely if parents reported medical reasons (0.43 [0.25-0.74]), a conscious decision (0.33

For peer review only

[0.23-0.48]), or 'other' reasons (0.46 [0.29-0.73]) for not immunising at age three (compared to 'practical' reasons).

Conclusions

Parents who partially or fully catch-up with MMR experience practical barriers and tend to come from disadvantaged or ethnic minority groups. Families who continue to reject MMR tend to have more advantaged backgrounds and make a conscious decision to not immunise early on. Health professionals should consider these findings in light of the characteristics of their local populations.

Article summary:

Article focus

- Areas of the UK are currently experiencing measles outbreaks, and a MMR national catch-up programme has just been launched
- Individual-level predictors of MMR catch-up are unknown
- We explore a range of risk factors for partial and full catch-up between age three and five years in the nationally representative UK Millennium Cohort Study

Key messages

- Of 751 children who were unimmunised at age three, 60% remained unimmunised at age five, 16% had partially caught-up, and 24% had fully caught-up
- Two distinct groups of parents emerged:
    - those who experienced practical barriers and were from ~~more disadvantaged groups~~ethnic minority backgrounds – these groups eventually caught-up
    - those who consciously rejected MMR and were from more advantaged circumstances – these groups tended to remain unimmunised

For peer review only

- Health professionals should consider these findings in light of the characteristics of their local populations when designing programmes to increase and maintain uptake

Strengths and limitations of this study

- This is the first study to examine individual-level characteristics of MMR catch-up in the UK; we do this using data from a nationally representative cohort of children who were born at the height of the MMR scare and are currently being targeted by the national catch-up programme
- Our analyses refer to predictors of catch-up during a period when parental concerns around the safety of the vaccine were relatively high, and the incidence of measles ~~was~~ relatively low; predictors of catch- up in families with young children today may be different ~~during times of measles outbreaks the perceived risk-benefit balance of the vaccine shifts, particularly for advantaged families~~.
- We were unable to investigate exact timing of vaccination; therefore our analyses focus on children who were unimmunised at age three (so approximately 2 years after the recommended age of administration), and we were unable to detect how long children who had partially or fully caught-up by age five had been left susceptible

For peer review only

Introduction

The combined measles, mumps and rubella vaccination (MMR) has been used routinely in the UK since 1988. Coverage at 2 years of age peaked in England in 1995, at 92% [1]. A two-dose schedule was introduced in 1996, the first dose recommended at soon after the age of 12/13 months[2] (affording 90-95% protection against measles), with a second at three years four months[2] (99% protection). In 1998, a Lancet article[3] was widely interpreted as suggesting MMR was linked with autism and bowel problems. Although the paper was eventually discredited and retracted by the Lancet in 2010[4], widespread adverse media coverage in the intervening years led to a dramatic fall in MMR uptake, to a low of 80% in England (of the first dose by age two) in 2003[1]. By 2006-7, 85% of two year olds had received at least one MMR, although only 73% had received the recommended two doses by age five, and levels were particularly low in some geographical areas, such as London[1]. Measles cases started to rise and in 2008 the Health Protection Agency announced that measles was again endemic in England and Wales.

Although coverage has continued to rise (in England in 2011-12, 91% of two year olds had received one and 86% of five year olds two doses of MMR[5]), levels remain below those needed for herd immunity, particularly in some geographical areas and in children who were born in the late 1990s and early 2000s. Consequently, measles outbreaks are currently occurring across some areas of the UK, with young teenagers disproportionately affected (one quarter of measles cases in 2011-12 were in 10-14 year olds[6]). In response to this, Public Health England, NHS England and the Department of Health announced a national MMR catch-up programme to vaccinate as many partially or unimmunised 10-16 year olds as possible by the start of the next school year (September 2013)[7]. The catch-up programme outlines aims to strengthen current routine immunisation strategies and in particular to target hard to reach populations; GPs and schools will

For peer review only

play a central role. A better understanding of the social and demographic characteristics associated with catching-up (or not), and the reasons reported by parents for their child's immunisation status, is essential if the aims of the new framework are to be achieved and maintained. Cross-sectional evidence indicates that, at age three, being unimmunised against MMR, or receiving the single antigen vaccines, was socially distributed[8]. However little is known about the factors which influence the propensity of families with unimmunised children to catch-up. We examine the social correlates of partial and full catch-up with MMR between the age of three and five years, in a nationally representative cohort of children born at the height of the MMR scare.

Methods

Participants

We analysed data from the Millennium Cohort Study (MCS), a longitudinal study of children eligible for Child Benefit and born in the UK between September 2000 and January 2002. The sample was derived from a random sample of electoral wards which were disproportionately stratified to ensure an adequate representation of all four UK countries, deprived areas and, in the case of England, areas with high proportions of families from ethnic minority groups[9]. At the first contact, when the MCS children were aged 9 months, data were collected on 18,296 singleton babies (72% of those approached); with subsequent data collections at three and five years. 71% of the initial cohort responded to all three sweeps (*n*= 12,989). Participants in the second and third sweeps were less likely to be from ethnic or deprived wards[10;11], although due to the sampling design these proportions remained higher than the general population.

Our analyses focus on the subsample of MCS singleton children who were unimmunised against measles, mumps or rubella at age three years. Of the 804 children who were unimmunised at age

For peer review only

three, 777 (96.6%) had a recorded MMR outcome at five years, and 26 (3.3%) of them were excluded because they were reported to have received at least one single antigen vaccine by age five, leaving 751 eligible participants in our analyses. Compared to the unimmunised children (who are the focus of this analysis), children who had been immunised with MMR at age three were: less likely to have a mother with a degree or A-levels, and more likely to have a mother in her twenties or early thirties or who did not smoke during pregnancy; they were also less likely to be living in a lone parent family and more likely to be an only child. The socio-economic and demographic characteristics of children according to MMR status at age three is described in greater detail elsewhere[8].

Measures

Measures were reported by the main respondent (usually the mother) during survey interviews, which were carried out by trained interviewers in the home.

Outcome measure: MMR status at age five was classified as unimmunised (received no combined MMR vaccines), partially caught-up (received one combined MMR), or fully caught-up (received two combined MMRs).

Covariates: We explored socio-economic and demographic factors that were found to be associated with immunisation status in earlier sweeps of the MCS[8;12;13], or that were pertinent to immunisation policy. We examined maternal social class (based on National Statistics Socio-economic Classification (NS-SEC)), ethnicity, maternal age at birth (in five-year age bands), maternal education, and child gender. These measures were all captured at age nine months because they were unlikely to have changed in later sweeps. In addition, we explored the following time-variant

For peer review only

measures, captured at age three (the beginning of the potential catch-up period): UK country of residence, ward type ('advantaged', 'disadvantaged', 'ethnic'), number of children in the household, maternal employment status, lone parenthood, household income, housing tenure, whether resident in London, whether the family had changed residential address since age three, and whether the parents reported the child having natural measles infection. Income data were missing for 14% (122) children at age three; we supplemented this with information captured at age nine months, reducing the level of missingness to 24. Missing data were very low for all other measures (listed at the foot of Table 1).

We also investigated reasons given for not having had MMR at age three, classified in a previous analysis[10] as 'practical' (such as missing an appointment), 'medical' (e.g. child had asthma), 'conscious decision' (including fear of links with autism) or 'other' (which included don't know). The mean age of the MCS children at the third survey was 61 months, with a range between 52 and 72 months, meaning that some children had more time to catch-up than others. We therefore explored age as a potential confounder, but as it was not found to be associated with immunisation status (p=0.28) we did not include it in our models. There were no *a priori* hypotheses for interactions so none were explored.

Analysis

We estimated the prevalence of MMR status (unimmunised, partially caught-up, and fully caught-up) at age five, overall and according to the potential explanatory factors. We then fitted Poisson regression models to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for partial and full catch-up (in two separate models, because previous research indicates that the social correlates of partial and full immunisation are likely to differ[12]). The models were built as follows: first we

For peer review only

explored univariable associations between the outcome and each of the explanatory variables. Variables, which were associated with the outcome (p<0.10) using Wald tests for trend, were entered into a multivariable model using a forward stepwise model selection strategy. Residence in London was forced into the multivariable models, due to its potential significance for policy. Only measures which remained significantly associated with the outcome after adjustment were retained.

Data were downloaded from the UK Data Archive, University of Essex in May 2010. Analyses were carried out in Stata 12 (Stata Corporation, TX) using survey and response weights to allow for the sample design and attrition between sweeps[10;14].

Results

Of the 751 MCS children who were unimmunised at age three, 60.3% (440) remained unvaccinated, 16.1% (127) had partially caught-up, and 23.6% (184) had fully caught-up. Table 1 presents the proportion of children who were partially, fully, or unimmunised, according to the various predictor measures.

Table 1: Weighted percentage (*n*) of children who remained unimmunised or who partially for fully caught-up with MMR, according to social, demographic and other characteristics

	Total	Full catch-up (2 doses)	Partial catch-up (1 dose)	Unimmunised
Language spoken at home				
English only	91.6 (658)	20.4 (130)	15.8 (11.5)	67.8 (413)
English and other language(s)	5.7 (64)	53.0 (29)	15.0 (9)	32.0 (26)
No - other language(s) only	2.7 (29)	70.2 (25)	27.7 (3)	2.1 (1)
Ward type				
Advantaged	56.5 (290)	20.3 (60)	13.6 (43)	66.1 (187)
Disadvantaged	38.5 (5.0)	24.1 (79)	20.1 (73)	55.8 (227)
Ethnic	5.0 (82)	57.6 (45)	13.3 (11)	29.2 (26)
Ethnicity				
British white	87.5 (644)	20.3 (126)	15.8 (111)	63.9 (407)

For peer review only

Other white	2.2 (13)	10.3 (2)	15.6 (2)	74.1 (9)
Mixed	1.4 (10)	33.5 (3)	15.1 (2)	51.4 (5)
Indian	1.0 (12)	76.9 (9)	5.5 (1)	17.5 (2)
Pakistani or Bangladeshi	3.8 (39)	74.7 (28)	9.8 (3)	15.5 (8)
Black or Black British	2.7 (18)	24.7 (7)	35.1 (5)	40.2 (6)
Other	1.4 (14)	65.2 (9)	19.6 (2)	15.2 (3)
Lone parent/carer				
Two parents/carers	79.2 (597)	21.9 (142)	15.3 (97)	62.9)
One parent/carer	20.8 (154)	30.2 (42)	19.3 (30)	50.5 (82)
Maternal age at birth of cohort child				
14 - 19y	8.1 (60)	37.7 (21)	21.8 (14)	40.6 (25)
20-24y	15.9 (130)	34.3 (40)	19.4 (27)	46.3 (63)
25-29y	23.5 (174)	25.8 (52)	18.2 (27)	55.9 (95)
30-34y	27.6 (205)	17.0 (36)	13.0 (30)	70.0 (13.9)
35-39y	20.4 (145)	15.8 (25)	14.3 (24)	70.0 (96)
40plus	4.5 (36)	24.2 (9)	10.6 (5)	65.1 (22)
Maternal education				
Degree	20.8 (152)	18.8 (32)	10.4 (15)	70.7 (105)
Diploma	8.9 (64)	13.9 (9)	14.9 (9)	71.1 (46)
A or AS levels	11.3 (85)	22.7 (19)	17.0 (20)	60.2 (46)
GCSE A*-C	32.2 (238)	20.4 (48)	19.6 (50)	60.0 (140)
GCSE D-G	8.4 (64)	18.1 (13)	23.9 (16)	58.0 (35)
Other	1.9 (15)	25.1 (6)	7.7 (1)	67.2 (8)
None	16.4 (133)	44.5 (57)	13.4 (16)	42.1 (60)
Housing tenure age 3				
Owned	58.7 (451)	18.1 (92)	15.6 (77)	66.3 (282)
Privately rented	9.8 (71)	29.8 (18)	11.5 (8)	58.6 (45)
Socially rented	27.7 (199)	30.4 (65)	19.8 (37)	49.8 (16)
Other	3.8 (30)	43.4 (9)	8.1 (5)	48.6 (16)
Household income (£ pa)				
0-11000	23.7 (186)	32.1 (57)	18.7 (34)	49.2 (95)
11 000-22 000	30.4 (228)	23.4 (56)	18.2 (41)	58.4 (131)
22 000-33 000	19.9 (142)	12.6 (21)	18.3 (34)	69.1 (87)
33 000-55 000	17.4 (123)	20.6 (28)	6.8 (8)	72.6 (87)
55 000+	8.9 (48)	23.5 (11)	15.9 (8)	60.6 (29)
Social class (9 months)				
Managerial & professional	30.2 (222)	20.8 (42)	12.7 (34)	66.5 (14.6)
Intermediate	16.7 (119)	17.5 (22)	17.6 (18)	65.0 (79)
Small employer/self-employed	8.0 (53)	10.1 (10)	11.9 (8)	78.0 (35)
Lower supervisory & technical	4.0 (33)	33.4 (10)	9.6 (4)	57.1 (19)
Semi-routine & routine	32.0 (248)	24.4 (61)	20.6 (53)	54.9 (134)
Never worked/unemployed	9.2 (73)	47.8 (37)	15.6 (10)	36.6 (26)
Number of children in household (age 3)				
One child	22.5 (180)	26.2 (43)	20.0 (38)	53.8 (99)
Two or three children	63.1 (459)	21.3 (104)	15.5 (73)	63.2 (282)
Four or more children	14.4 (112)	29.9 (37)	12.6 (16)	57.6 (59)
Maternal employment (age 3)				
FT	11.2 (93)	23.8 (21)	11.5 (17)	64.7 (55)
PT	25.2 (191)	22.1 (41)	19.6 (37)	58.3 (113)
On leave	3.9 (28)	26.8 (8)	3.9 (1)	69.4 (19)
Self employed	9.3 (60)	17.1 (13)	13.0 (10)	69.9 (37)

For peer review only

Not employed/student	50.4 (379)	25.3 (101)	16.9 (62)	57.8 (216)
Sex of child				
Male	55.1 (404)	20.6 (95)	17.7 (70)	61.7 (239)
Female	44.9 (347)	27.3 (89)	14.1 (57)	58.6 (201)
Parental report of measles disease by age 3				
Yes	3.5 (22)	19.2 (5)	13.2 (3)	67.6 (14)
No	96.5 (721)	23.7 (176)	16.1 (123)	60.2 (422)
Residence in London				
London	16.2 (102)	17.7 (23)	20.0 (19)	62.3 (60)
Not London	83.8 (649)	24.8 (161)	15.3 (108)	60.0 (380)
Country of residence				
England	58.6 (462)	23.3 (122)	15.7 (74)	61.0 (266)
Wales	21.6 (160)	22.1 (31)	20.1 (31)	57.7 (98)
Scotland	12.9 (87)	26.7 (21)	15.6 (14)	57.5 (52)
Northern Ireland	6.9 (42)	25.3 (10)	17.8 (8)	60.0 (24)
Smoked during pregnancy				
No	63.2 (465)	23.4 (121)	15.1 (76)	61.6 (268)
Yes	36.8 (283)	23.8 (62)	18.0 (51)	58.2 (170)
Changed address since 3				
No	85.6 (647)	23.8 (161)	16.6 (112)	59.6 (374)
Yes	14.4 (104)	22.4 (23)	13.1 (15)	64.5 (66)
Reasons given for not having had MMR (aged 3)				
Practical	6.2 (51)	54.5 (30)	15.3 (7)	30.3 (14)
Medical	15.2 (107)	17.9 (82)	25.5 (26)	56.7 (57)
Conscious decision	66.7 (486)	17.8 (82)	16.0 (85)	66.2 (31.9)
Other	11.7 (76)	35.3 (26)	9.9 (9)	54.9 (41)

Missing: Social class 3, smoked during pregnancy 3, income 24, ethnicity 1, reason 31, age at birth 1.

Partial catch-up (compared to remaining unimmunised)

Table 2 (column A) shows unadjusted RRs for partial catch-up, according to each of the predictor measures. Partial catch-up was more likely in families who spoke a language other than English at home (particularly if English was not spoken at home at all), compared to those who only spoke English at home, and in those who lived in a ward classified as 'disadvantaged' or 'ethnic', compared to advantaged wards. No significant associations were seen with any of the other variables. When language, ward type and London residence (due to its policy significance) were entered into the multivariable model, only language remained significantly associated with the likelihood of being partially immunised, with an adjusted RR of 4.68 (3.63 to 6.03) in families who did not speak English at home (Table 2, Column B).

For peer review only

Table 2: Unadjusted and adjusted odds ratios (ORs) for partial catch-up with the combined MMR vaccine (baseline unimmunised) by age five

	Partial catch-up (1 dose)		Full catch-up (2 doses)	
	A: uRR (95% CI)	**B: aRR (95% CI)**	**C: uRR (95% CI)**	**D: aRR (95% CI)**
Language spoken at home				
English only	1	1	1	1
English and other language(s)	1.61 (0.96, 2.70)	1.61 (0.96, 2.70)	2.57 (2.00, 3.32)*	1.54 (0.91, 2.63)
Other language(s) only	4.68 (3.63, 6.03)*	4.68 (3.63, 6.03)*	4.00 (3.37, 4.76)*	1.90 (1.08, 3.32)*
p-value	<0.001	<0.001	<0.001	0.0811
Ward type				
Advantaged	1		1	
Disadvantaged	1.55 (1.05, 2.27)*		1.29 (0.92, 1.80)	
Ethnic	1.83 (1.18, 2.83)*		2.83 (2.19, 3.65)*	
p-value	0.0146		<0.001	
Ethnicity				
British white	1		1	1
Other white	0.88 (0.22, 3.54)		0.51 (0.13, 2.06)	0.37 (0.10, 1.34)
Mixed	1.15 (0.29, 4.59)		1.64 (0.57, 4.74)	1.83 (0.65, 5.17)
Indian	1.21 (0.19, 7.82)		3.38 (2.40, 4.76)*	2.01 (0.75, 5.41)
Pakistani or Bangladeshi	1.96 (0.84, 4.54)		3.44 (2.79, 4.23)*	2.40 (1.38, 4.18)*
Black or Black British	2.35 (0.99, 5.57)		1.58 (0.73, 3.43)	1.12 (0.35, 3.63)
Other	2.84 (1.12, 7.22)*		3.36 (2.42, 4.67)*	1.88 (1.08, 3.29)*
p-value	0.0126		<0.001	0.0950
Lone parent/carer				
Two parents/carers	1		1	
One parent/carer	1.42 (0.92, 2.17)		1.45 (1.06, 1.99)*	
p-value	0.1110		0.0208	
Maternal age at birth of cohort child				
14 - 19y	1.42 (0.80, 2.51)		1.52 (0.98, 2,37)	
20-24y	1.20 (0.68, 2.12)		1.35 (0.89, 2.03)	
25-29y	1		1	
30-34y	0.63 (0.37, 1.08)		0.62 (0.40, 0.97)*	
35-39y	0.69 (0.40, 1.20)		0.58 (0.37, 0.92)*	
40plus	0.57 (0.23, 1.43)		0.86 (0.42, 1.74)	
p-value	0.0259		<0.001	
Maternal education				
Degree	1		1	
Diploma	1.35 (0.54, 3.36)		0.78 (0.35, 1.72)	
A or AS levels	1.72 (0.79, 3.74)		1.30 (0.71, 2.38)	
GCSE A*-C	1.91 (1.05, 3.49)*		1.21 (0.75, 1.96)	
GCSE D-G	2.27 (1.07, 4.80)*		1.13 (0.55, 2.34)	
Other	0.80 (0.11, 5.93)		1.29 (0.49, 3.39)	
None	1.88 (0.87, 4.03)		2.44 (1.63, 3.66)*	
p-value	0.2420		<0.001	
Housing tenure age 3				
Owned	1		1	1

For peer review only

Privately rented	0.86 (0.32, 2.34)		1.57 (0.96, 2.59)	1.51 (0.91, 2.48)
Socially rented	1.49 (0.96, 2.32)		1.77 (1.29, 2.43)*	1.86 (1.34, 2.56)*
Other	0.75 (0.27, 2.09)		2.20 (1.27, 3.79)*	2.52 (1.23, 5.18)*
p-value	0.0936		0.0014	<0.001
Household income (£ per annum)				
0-11000	1		1	
11 000-22 000	0.86 (0.53, 1.41)		0.72 (0.52, 1.02)	
22 000-33 000	0.76 (0.44, 1.31)		0.39 (0.23, 0.66)	
33 000-55 000	0.31 (0.14, 0.70)*		0.56 (0.36, 0.87)	
55 000+	0.76 (0.36, 1.61)		0.71 (0.39, 1.29)	
p-value	0.0816		0.0028	
Social class (9 months)				
Managerial & professional	1		1	
Intermediate	1.33 (0.73, 2.42)		0.89 (0.52, 1.53)	
Small employer/self-employed	0.83 (0.38, 1.79)		0.48 (0.20, 1.16)	
Lower supervisory & technical	0.90 (0.30, 2.67)		1.55 (0.80, 3.00)	
Semi-routine & routine	1.71 (1.11, 2.64)*		1.29 (0.87, 1.92)	
Never worked/unemployed	1.87 (0.96, 3.64)		2.38 (1.62, 3.49)*	
p-value	0.0989		<0.001	
Number of children in household (age 3)				
One child	1		1	
Two or three children	0.73 (0.47, 1.12)		0.77 (0.52, 1.14)	
Four or more children	0.66 (0.34, 1.29)		1.04 (0.67, 1.63)	
p-value	0.2807		0.1832	
Maternal employment (age 3)				
Full-time	1		1	
Part-time	1.67 (0.84, 3.33)		1.02 (0.58, 1.79)	
On leave	0.35 (0.05, 2.48)		1.04 (0.46, 2.33)	
Self employed	1.04 (0.41, 2.66)		0.73 (0.37, 1.45)	
Not employed/student	1.50 (0.88, 2.57)		1.13 (0.71, 1.80)	
p-value	0.1836		0.6517	
Sex of child				
Male	1		1	
Female	0.87 (0.60, 1.27)		1.27 (0.94, 1.71)	
p-value	0.4755		0.1171	
Parental report of measles disease by age 3				
Yes	1		1	
No	1.29 (0.48, 3.49)		1.28 (0.52, 3.16)	
p-value	0.6163		0.5970	
Residence in London				
London	1		1	1
Not London	0.84 (0.50, 1.41)		1.32 (0.86, 2.02)	1.95 (1.32, 2.89)*
p-value	0.5078		0.2012	<0.001
Country of residence				
England	1		1	
Wales	1.26 (0.86, 1.84)		1.00 (0.69, 1.46)	
Scotland	1.04 (0.60, 1.83)		1.16 (0.71, 1.88)	
Northern Ireland	1.16 (0.55, 2.44)		1.11 (0.66, 1.88)	
p-value	0.6802		0.9272	
Smoked during pregnancy				
No	1		1	

For peer review only

Yes	1.20 (0.73, 1.74)		0.05 (0.76, 1.46)	
p-value	0.3202		0.7481	
Changed address since 3				
No	1			
Yes	0.90 (0.62, 1.32)		0.77 (0.42, 1.43)	
p-value	0.6031		0.4112	
Reasons given for not having had MMR (aged 3)				
Practical	1		1	
Medical	0.93 (0.44, 1.93)		0.37 (0.20, 0.68)*	0.43 (0.25, 0.74)*
Conscious decision	0.58 (0.27, 1.22)		0.33 (0.23, 0.47)*	0.33 (0.23, 0.48)*
Other	0.45 (0.16, 1.30)		0.61 (0.40, 0.93)*	0.46 (0.29, 0.73)*
p-value	0.1357		<0.001	<0.001

uRR = unadjusted risk ratio; aRR = adjusted risk ratio. * p=<0.05

Full catch-up (compared to remaining unimmunised)

Table 2 also presents unadjusted and adjusted RRs for fully catching up. In the univariable analyses (Column C), children whose parents spoke a language other than English at home (as opposed to only speaking English), who were from ethnic minority groups (compared to White British), or lived in 'ethnic' wards (compared to 'advantaged' wards) were more likely to fully catch-up. Catch-up was also significantly more likely in children who mother had no educational qualifications (compared to a degree), in lone parent families (compared to two parent families), and in those living in 'socially rented' or 'other' tenure types (compared to own/mortgage). Catch-up was significantly less likely in children with a mother in her thirties (compared to 24-29 years), and in children living in higher income households. Children whose parents had reported a non-practical reason ('medical', 'conscious decision', or 'other') for not having their child immunised with the combined MMR at age three were also less likely to have fully caught-up than those reporting practical reasons. Living in London was not associated with immunisation status, although due to its policy significance was included in the multivariable model reported below.

In the multivariable analysis (Column D), full catch-up remained significantly more likely in those who only spoke a non-English language at home (1.90 [1.08 to 3.32]), when compared to those who

For peer review only

only spoke English. Those from Pakistani or Bangladeshi (2.40 [1.38 to 4.18]), and 'Other' (1.88 [1.08 to 3.29]) ethnic groups were more likely to have caught-up than White British groups, as were those living in 'socially rented' (1.86 [1.34 to 2.56]) or 'other' (2.52 [1.23 to 5.18]) tenure types (compared to own/mortgage). Full catch-up was also more likely in families living outside London (1.95 [1.32 to 2.89]). Compared to those reporting practical reasons for not having been immunised at age three, children whose parents reported medical reasons (0.43 [0.25 to 0.74]), a conscious decision (0.33 [0.23 to 0.48]), or 'other' reasons (0.46 [0.29 to 0.73]) were considerably less likely to have fully caught-up.

Parents from Asian and "other White" backgrounds were 2-3 times more likely to experience practical barriers to immunisation than those from White British, Mixed or Black backgrounds. Similarly, families who spoke a non-English language in the home were two-three times as likely to experience practical barriers as families who only spoke English at home (data not shown).

Discussion

Just over 40% of children who were unimmunised with MMR vaccine at age three had either partially or fully caught-up by age five. The likelihood of catching-up varied markedly with a number of social factors, and more so for full than partial catch-up. Some families, particularly those from ethnic minority groups, appear to have difficulty accessing vaccination in a timely fashion. Advantaged families and those citing non-practical reasons for non-vaccination at age three are more likely to persist in not immunising their child against MMR.

We used sample and response weights to account for the survey design and attrition between the first, second, and third sweeps of the MCS. However the non-response weights are unlikely to have entirely accounted for differential response; for example 95.7% children who were included in the age three and five surveys were fully immunised with the primary vaccines (at age 9 months)

For peer review only

compared to 92.7% in children who did not take part in both of the later surveys (p<0.001).

~~Information bias may occur when~~A limitation of the study is that we utilised ~~using~~ parental report ~~to measure~~of immunisation status, and it was not possible to validate report of immunisation status against health system records. However there is no gold standard measure of immunisation status and studies have found disagreement between parental report and health records to be low[15] and not socially distributed[16]. Parents were given the opportunity to consult the Personal Child Health Record (or 'red book'). Of the 751 families included in our analysis, 19% (137) consulted the book and found the relevant information, 1% (11) checked the book and did not find the relevant information, and 79% (603) chose not to consult the book and relied on their memory. There was no association between catch-up status and whether the parent consulted the red book (p=0.18), and the associations reported in this paper remained the same when analyses were repeated excluding children where the parent had looked but not found information (data not shown). A small number (26) of children who were unimmunised at age three had received at least one single antigen vaccine by age five. Due to low numbers we were unable to explore the characteristics of this group.

The intense negative media attention around the safety of the MMR vaccine peaked in 2002/3 when the MCS children were toddlers. These findings therefore provide important information on the barriers to catch-up, in a cohort of children who are currently experiencing measles outbreaks throughout the UK[6], and are a central focus of the newly launched national catch-up programme. ~~We~~ However we measured catch-up across the period 2003/5 to 2006/7, when the MMR scare was at its height and the incidence of measles was relatively low (although with some indications of a rise). Concerns around the safety of the MMR have diminished over recent years and therefore the characteristics of families who catch-up with the vaccine today may be different. It is also likely that

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

some of the barriers we report for more advantaged families are reduced during times of measles outbreaks, as the perceived risk-benefit balance of the vaccine shifts. Nonetheless, this paper provides important information on the barriers experienced by advantaged families during times of no outbreak to improve and sustain the current MMR programme, which is also a central aim of the catch-up programme. The recommended age of the first dose of MMR is 12/13 months; however information on uptake was not collected in the MCS until the children were age three years. Our analysis is unable to address those children who were immunised by age three but who had not been immunised on time. Similarly, we were unable to investigate the timing of catch-up between the age of three and five, and therefore how long children who partially or fully caught-up were left susceptible. Finally, the MCS consists only of children who were born in the UK. The barriers experienced by families from ethnic minority groups or who speak other may be different and/or greater in families where the child was born outside the UK.

Before the scare, MMR uptake was generally lower in more deprived areas and households[17;18]. Since 1998, rates declined faster in more advantaged areas[19;20] and more slowly in areas with lower proportions of highly educated residents[20] and in minority ethnic groups[21]. Earlier cross-sectional findings from the MCS demonstrated that the likelihood of being unimmunised against measles, mumps and rubella tended to be greater in more disadvantaged families, while children living in more affluent households were more likely to receive single antigen vaccines (indicating conscious rejection of combined MMR)[8]. However there is a dearth of longitudinal research exploring the social correlates of catch-up with MMR. The only study, to our knowledge, which has explored the social correlates of MMR catch-up was an ecological study of one million children born between 1987 and 2004 in Scotland. The authors found that children living in more affluent areas were either immunised with MMR on time or not at all, whereas children living in deprived areas were

For peer review only

more likely to be immunised late[20]. Our findings not only reflect this, but add to the evidence base by demonstrating that individual-level predictors of catch-up are strongly related to catch-up. We have also found that remaining unvaccinated with MMR at age five was associated with non-practical reasons for not immunising with MMR at three, reflecting other research which has shown that more affluent families are more likely to consciously reject MMR[20;22].

Outbreaks of measles are currently being experienced across the UK, leading to the launch of a national catch-programme in April 2013. Approaches to optimise uptake of MMR will need to be tailored to the needs of local populations, both now and in the future. Our study has identified two distinct groups of families that do not immunise their child with MMR in a timely fashion (during periods of low measles incidence). The first comprises those who partially or fully catch-up, amounting to 40% of those who were unimmunised at age three. These families tend to experience practical barriers to immunisation, and are socially disadvantaged or from ethnic minority groups. The second group, which continues to reject MMR and makes up the remaining 60%, consists of parents who consciously reject MMR from the start, and are from more advantaged backgrounds.

Steps are required to minimise time to uptake in those families who do eventually catch-up, through the reduction of practical barriers. NICE guidance outlines actions to reduce inequalities in immunisation[23], including provision of information in multiple languages, offering immunisation checks and administration in alternative settings, and sending out reminder invitations from GPs[24]. In addition, alleviating any lingering fears and concerns of families who consciously reject MMR is essential. This should include discussion of concerns about 'medical' reasons for not giving MMR. Mythical contraindications to MMR have circulated amongst the health professional community and parents for some time[25] despite there being~~there are~~ few true contraindications for MMR

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

vaccination.-'Medical reasons' reported by parent for not immunising in the MCS (at age five) included: "child is not able to have it for health reasons" and "other medical problems or bad reactions". It is not possible to ascertain whether any of these were true contraindications, although there are very few genuine contraindications to MMR[2] and these tend to be very rare[2]. It was possible to look at longstanding illness however, and children who had not been immunised for 'medical reasons' had a higher prevalence of longstanding illness (38%) than overall prevalence in the cohort (15%). Conditions reported for children who had not been immunised and who had a long standing illness included asthma, epilepsy, dermatitis/eczema and cerebral palsy, and although none appeared to be true contraindications, some may have been incorrectly considered to be at that time, either by the health professional or the parents themselves. NICE recommends offering parents opportunities to discuss their concerns about vaccines or vaccine safety with health professionals; receiving such information from health professionals has been found to be the decisive factor for parents who have changed their minds about previously rejected or delayed vaccines[26]. In addition training is recommended for health care professionals to equip them with the skills and information needed to communicate effectively with parents about immunisation, to allay any fears over the safety of the vaccine and any misinformation about medical contraindications. Finally, joint working between the health sector and childcare providers, nurseries, and schools is essential[23].

Conclusions

Children born at the height of the MMR scare are being disproportionately affected by current measles outbreaks and are the target of a newly launched national catch-up programme. Our findings refer to children of this age and have identified the characteristics of two distinct groups of parents who do not immunise their children with MMR on time. Health professionals should

For peer review only

consider their local populations in light of our findings, and tailor the local roll-out of the catch-up programme accordingly.

The new national immunisation framework not only aims to facilitate catch-up but also to strengthen routine approaches to immunisation[7]. Findings from this study should be used to inform longer-term local and national planning to improve and maintain timely uptake. While uptake of the first dose of MMR in younger age groups has increased, levels remains below those required for herd immunity and uptake of the second dose is lower still. Measles outbreaks remain a risk, particularly in areas of the country with low uptake.

Acknowledgements

We would like to thank all the Millennium Cohort families for their participation, and the director of the Millennium Cohort Study and colleagues in the management team at the Centre for Longitudinal Studies, Institute of Education, University of London. We would also like to thank the MCS user group at the MRC Centre of Epidemiology for Child Health: Catherine Law, Carol Dezateux, Lucy Griffiths, Tim Cole, Phillippa Cumberland, Jamie Fagg, Francesco Sera, Steven Hope, Hannah Lewis and Marco Geraci; also David Elliman, for his advice early on in the project.

Funding

The Centre for Paediatric Epidemiology and Biostatistics is supported in part by the Medical Research Council in its capacity as the MRC Centre of Epidemiology for Child Health (Grant reference G0400546). Research at the UCL Institute of Child Health and Great Ormond Street Hospital for Children receives a proportion of the funding from the Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme. AP is funded by a Medical Research Council fellowship. All researchers were independent of the funders and the

For peer review only

funders played no part in the study design, analysis or interpretation of the data, writing of the report or the decision to submit for publication.

Contributors: MM and HB contributed to the study conception. All authors contributed to the design of the analysis. AP, MM and MC-B carried out the analyses. AP and MM drafted the paper. All authors revised the paper. All authors had full access to the data and take responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval: Research ethics approval was not required for this study as it was a secondary data analysis of the UK Millennium Cohort Study. The first sweep of the Millennium Cohort Study received ethics approval from National Health Service Ethical Authority in February 2001 (MREC/01/6/19), and the second and third received approval from the London Multi-Centre Research Ethics Committee in September 2004 (MREC/03/2/022) and December 2005 (05/MRE02/46).

Data sharing: The Millennium Cohort Study is available at:

http://www.esds.ac.uk/findingData/mcs.asp

Competing interests

All authors have completed the ICMJE uniform disclosure form at ww.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; MCB has received research grants from the Health Protection Agency; no other relationships or activities that could appear to have influenced the submitted work.

Copyright/licence for publication

I, Helen Bedford, the Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs, other illustrative material, video, film or any other material howsoever submitted by the Contributor(s) at any time and related to the Contribution ("the Contribution") have the right to grant on behalf of all authors and do grant on behalf of all

For peer review only

authors, a licence to the BMJ Publishing Group Ltd and its licensees, to permit this Contribution (if accepted) to be published in BMJ Open an d any other BMJ Group products and to exploit all subsidiary rights, as set out in the licence at: http://group.bmj.com/products/journals/instructions-for-authors/BMJOpen_licence.pdf

References

1. The Information Centre. NHS Immunisation Statistics: England 2006-07, 2007.
2. Salisbury D, Ramsay M, Noakes K. Immunisation against infectious disease: the green book. In: England PH, editor, 2013. https://www.gov.uk/government/organisations/public-health-england/series/immunisation-against-infectious-disease-the-green-book
3. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998;351 (9103):637-41.
4. Lancet. Retraction--Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. 2010 Feb *Lancet.* 2010;375(9713):445.
5. The Health and Social Care Information Centre Screening and Immunisations team. NHS Immunisation Statistics, England: 2011-12 In: Centre TI, editor, 2012.
6. Health Protection Agency. Confirmed cases of measles by region and age: 1996-2012. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1195733778332: Public Health England, 2013.
7. Public Health England. MMR catch-up programme 2013. . https://www.gov.uk/government/organisations/public-health-england/series/MMR-catch-up-programme-2013#publications: GOV.UK, 2013.
8. Pearce A, Law C, Elliman D, Cole TJ, Bedford H, the Millennium Cohort Study Child Health G. Factors associated with uptake of measles, mumps and rubella vaccine (MMR) and use of single antigen vaccines in a comtemporary UK cohort: prospective cohort study. *British Medical Journal* 2008;336:754-60.
9. Centre for Longitudinal Studies. Millennium Cohort Study: Survey design: Institute of Education, 2007.
10. Plewis I, Ketende S. Millennium Cohort Study: technical report on response. 1st ed. London Centre for Longitudinal Studies, 2006.
11. Hansen K, Joshi H. Millennium Cohort Study Third Survey: A User's Guide to Initial Findings. London: Institute of Education 2008.
12. Samad L, Bedford H, Tate AR, Dezateux C, Peckham C, Butler N, et al. Differences in risk factors for partial and no immunisation in the first year of life. *British Medical Journal* 2006;332 1312-13.
13. Pearce A, Elliman D, Bedford H, Law C. Residential mobility and uptake of childhood immunisations: findings from the UK Millennium Cohort Study. *Vaccine* 2008;26:1675-80.
14. Plewis I. Millennium Cohort Study: technical report on sampling. 3rd ed. . London: Centre for Longitudinal Studies, 2004.
15. AbdelSalam HHM, Sokal MM. Accuracy of parental reporting of immunization. *Clinical Pediatrics* 2004;43 (1):83-85.

For peer review only

16. Suarez L, Simpson DM, Smith DR. Errors and correlates in parental recall of child immunizations: effects on vaccination coverage estimates. *Pediatrics* 1997;99 (5):E3.
17. Sharland M, Atkinson P, Maguire H, Begg N. Lone parent families are an independent risk factor for lower rates of childhood immunisation in London. *Communicable Disease Report.CDR Review* 1997;7 (11):R196-R72.
18. Li J, Taylor B. Factors affecting uptake of measles, mumps, and rubella immunisation. *British Medical Journal* 1993;307 168-71.
19. Middleton E, Baker D. Comparison of social distribution of immunisation with measles, mumps, and rubella vaccine, England, 1991-2001. *British Medical Journal* 2003;326 854-54.
20. Friederichs V, Cameron JC, Robertson C. Impact of adverse publicity on MMR vaccine uptake: a population based analysis of vaccine uptake records for one million children, born 1987-2004. *Archives of Disease in Childhood* 2006;91 465-68.
21. Hawker J, Olowokure B, Wood A, Wilson R, Johnson R. Widening inequalities in MMR vaccine uptake rates among ethnic groups in an urban area of the UK during a period of vaccine controversy (1994-2000). *Vaccine* 2007;25:7516-9.
22. MacDonald H, Henderson R, Oates K. Low uptake of immunisation: contributing factors. *Community Practioner* 2004;77 (3):95-100.
23. National Institute for Health and Clinical Excellence. Reducing differences in the uptake of immunisations. *NICE public health guidance 21*, 2009.
24. Jacobson Vann J, Szilagyi P. Patient reminder and patient recall systems to improve immunization rates. . *Cochrane Database Syst Rev.* 2005;Jul 20(3).
25 Bedford, H; Elliman, D. Concerns about immunisation. *British Medical Journal* 2000;320;7229: 240.
26. Gust D, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics* 2008;1227(4):18-25.

For peer review only

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
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	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 6
Methods			
Study design	4	Present key elements of study design early in the paper	2, 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
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	9, 15-16
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	9, 15-16
		(*d*) If applicable, explain how loss to follow-up was addressed	9, 15-16
		(*e*) Describe any sensitivity analyses	
Results			

For peer review only

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	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	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	Table 2
		(*b*) Report category boundaries when continuous variables were categorized	Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	15-16
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
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	20

*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.

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.

For peer review only