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Identifying inequalities in childhood immunisation uptake and timeliness in southeast Scotland, 2008–2018: A retrospective cohort study

Eram A. Haider [a,*], Lorna J. Willocks [b], Niall Anderson [a]

[a] Usher Institute of Population Health Sciences and Informatics, Old Medical School, Teviot Place, University of Edinburgh, Scotland EH8 9AG, UK
[b] NHS Lothian, Directorate of Public Health and Health Policy, National Health Service Scotland, 2-4 Waterloo Place, Edinburgh EH1 3EG, UK

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ABSTRACT

Background: In 2018, there was a record incidence of measles and other vaccine-preventable diseases across developed countries. Declining childhood immunisation uptake in southeast Scotland—an area with a large, highly mobile, and socioeconomically diverse population—threatens regional herd immunity and warrants investigation of suboptimal coverage. As deprivation of social and material resources increases risk of non-vaccination, we examined here the relationship between deprivation, uptake, and timeliness for four routine childhood vaccines and identified trends over the past decade.
Methods: This retrospective cohort study analysed immunisation data from the Scottish Immunisation Recall System (SIRS) for four routine childhood vaccines in the UK: the third dose of the primary vaccine (TPV), both doses of measles, mumps, rubella (MMR 1 and MMR 2), and the preschool booster (PSB). Immunisations (N = 329,897) were administered between 2008 and 2018. Deprivation was measured via the Scottish Index of Multiple Deprivation (SIMD), ranking postcodes by deprivation decile. Chi-squared tests and cox proportional hazards models assessed the relationship between uptake, timeliness, and deprivation.
Results: There is strong evidence for an association between deprivation, uptake, and timeliness. Uptake for all childhood immunisations are very high, especially for TPV and MMR 1 (>98.0%), though certain deprivation deciles exhibit increased risks of non-vaccination for all vaccines. Delay was pronounced for the 40% most deprived population and for immunisations scheduled at later ages. Absolute PSB and MMR 2 uptake has improved since 2008; however, disparities in uptake have increased for all vaccines since the 2006 birth cohort.
Conclusion: Both timeliness and uptake are strongly associated with deprivation. While absolute uptake was high for all vaccines, relative uptake and timeliness has been worsening for most groups; the reason for this decline is unclear. Here we identified subgroups that may require targeted interventions to facilitate uptake and timeliness for essential childhood vaccines.

1. Introduction

Vaccines have resulted in a steady decline in child morbidity and mortality and subsequent improvements in global health [1]. The World Health Organisation (WHO) recommends that 95% of vaccine-eligible people are immunized against diphtheria, tetanus, pertussis (whooping cough), polio, Hib, measles, mumps, and rubella to effectively control these deadly infectious diseases. However, unvaccinated and under-vaccinated children (those with incomplete or delayed vaccinations) are susceptible to these diseases if exposed [2]. Delay in immunisations may play a role in outbreaks of infectious disease since vaccines delivered outside the immunisation schedule leave temporal gaps in immunity in which children are vulnerable to infection [3]. Table 1 outlines the UK schedule for the immunisations included in this analysis, with recommended ages for each dose. These diseases are the most serious vaccine-preventable illnesses for young children and the schedule is designed with age-specific risk of each disease in mind [4].

Research from Scotland, the UK, Australia, and other OECD countries report that deprivation—lack of essential social and material resources such as income, employment, and healthcare [5]—is associated with uptake and timeliness of childhood vaccines

* Corresponding author at: Usher Institute of Population Health Sciences and Informatics, Old Medical School, Teviot Place, University of Edinburgh, Edinburgh EH8 9AG, UK.

E-mail address: Eram.Haider@glasgow.ac.uk (E.A. Haider).

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Table 1
UK routine immunisation schedule (2002—). UK immunisation schedule for the third primary vaccine (TPV), pre-school booster (PSB), and both doses of MMR (MMR 1 and 2).

Recommended age	Uptake calculated At[a]	Dose	Diseases targeted	Vaccine AKA[b]
2 months	12 months	First	Diptheria Tetanus Pertussis Polio *H. influenzae*	DTaP/IPV/Hib Four/Five-in one[c] Primary vaccine DTP
3 months	12 months	Second	Diptheria Tetanus Pertussis Polio *H. influenzae*	DTaP/IPV/Hib Four/Five-in one Primary vaccine DTP
4 months	12 months	Third (completed routine)	Diptheria Tetanus Pertussis Polio *H. influenzae*	DTaP/IPV/Hib Four/Five-in one Third primary vaccine (TPV) DTP
12–13 months	24 months	First	Measles Mumps Rubella	MMR1
40 months	60 months	Second (completed routine)	Measles Mumps Rubella	MMR2
40 months	60 months	Booster	Diptheria Tetanus Pertussis Polio	DTaP/IPV DTP Pre-school booster (PSB)

[a] Age when most immunisations should have been administered by.
[b] AKA: also known as.
[c] 4-in-1 from 2002 to 2004; Polio added in 2004; 6-in-1 after 2017 addition of Hepatitis B immunisation [18].

[6,7,8,9,10,11,12,13]. Risk factors related to access to immunisation information or vaccination clinics impact uptake and timeliness [14,15,9,10]; these factors disproportionately affect deprived families, particularly migrant children and children with multiple risk factors of deprivation [16]. On a national scale, absolute health inequalities have declined in Scotland since 2003, however, relative health inequalities continue to widen [17]. Scottish publications show national uptake consistently surpass 95% though more deprived groups have lower uptake than those less deprived [18]. Timeliness is not discussed in these reports.

This study investigates the relationships between deprivation, uptake, and timeliness and how these relationships have changed over time for four established childhood vaccines: the third dose of the primary vaccine (TPV), both doses of MMR (MMR 1 and 2), and the pre-school booster (PSB), with the objective of assessing the extent of any disparities in uptake or timeliness in southeast Scotland and identifying trends over the past decade. With a growing and increasingly migrant population (NHS [19], southeastern Scotland requires high uptake and timely vaccination across every birth cohort to attain herd immunity and to prevent future outbreaks.

2. Methods

2.1. Study population

The cohort included all vaccinated and unvaccinated children in southeast Scotland, an area with >800,000 residents with a range of deprivation scores across urban and rural areas—including the Scottish capital Edinburgh—over the ten-year period from 2008 to end 2017. TPV (n = 82,434) and MMR 1 (n = 82,539) cohorts consisted of children two years of age born between 2006 and 2015, while PSB (n = 82,382) and MMR 2 (n = 82,542) cohorts included children six years of age born between 2002 and 2011. The chosen vaccines represent completed routines of four established childhood immunisations; they remain relatively unchanged since 2002, ensuring each cohort was subject to the same schedule for these vaccines.

2.2. Ethical approval and data obtainment

Childhood vaccination records were obtained from the Scottish Immunisation and Recall System (SIRS), a national record of immunisation and demographic information for children in Scotland from 2002 onwards, updated daily [20]. Data included the vaccines given, the age when each vaccination was given, the cohort year, and Scottish Index of Multiple Deprivation (SIMD) score. The SIMD is a measure of relative deprivation, used to monitor long-term inequalities and inform healthcare policy; the index ranks 6505 data zones across Scotland by indicators of income, employment, health, education, access, crime, and housing for various geographic levels [22]. Deciles were preferred over quintiles as they allowed for greater stratification of the deprivation score amongst the population; large and complete deciles meant all SIMD groups were appropriate for statistical analysis. We used the 2016 SIMD, the most recent update, at the postcode level. The study did not include any patient identifiable data.

2.3. Outcomes

Vaccination status with vaccinated and unvaccinated categories was used to calculate uptake, the primary outcome of interest. Children immunised outside of Scotland may not have immunisation details in SIRS; however, consent to immunisation is required and recorded for all children [21]. Therefore, subjects without vaccination data but with a record of immunisation consent were excluded from the cohort; those with all other consent statuses (e.g. withdrawn, delayed, etc.) were defined as unvaccinated. Timeliness, determined via the age the vaccine was given, was the secondary outcome.

2.4. Timeliness

Timely vaccination was defined as receiving the vaccine at the scheduled age, as shown in Table 1. Data were analysed using time to vaccination, so any vaccine administered beyond the scheduled age was considered untimely. The following criteria based on minimum vaccination age restrictions excluded some early vaccinations: <3.5 months for TPV (n = 836), <12 months for MMR 1 (n = 203), and <39.5 months for PSB (n = 8862) and MMR 2 (n = 713). These exclusion criteria leave a margin for travel or other circumstances requiring vaccination before the minimum recommended age. Data not meeting these age restrictions were treated as data-entry mistakes.

2.5. Statistical analysis

All analyses were conducted using SPSS (V24.0.0.2, IBM, NY, USA).

Missing data analysis was conducted for each vaccine using chi-squared tests of homogeneity with a null hypothesis (H_0) of equal proportions across vaccination cohorts of the missing values. Since missing data accounted for a very small percentage of the cohorts (0.2%) and the tests were nonsignificant, case-wise deletion was used for all analyses.

Two-sided chi-squared tests for trend ($\alpha = 0.05$) with H_0 of no association between SIMD score and vaccination status were performed to determine if deprivation score was associated with vaccination status for each immunisation. Non-parametric one-sample Wilcoxon signed rank tests compared the vaccinated cohort's median age against the age for timely vaccination (4 months for TPV, 12.5 months for MMR1, and 40 months for PSB and MMR2) to test the association of the age when the vaccine was given (positively-skewed distribution) with SIMD deciles per vaccine.

Survival analyses using Kaplan-Meier hazard curves were used to model time to vaccination. Cox proportional hazards (CPH) regression models with SIMD decile and birth cohort as factors provided magnitudes of risk for delayed vaccination for deprivation groups and birth cohorts via hazard ratios (HR). CPH model interactions between SIMD-birth cohort were graphed to analyse the relationship of timeliness and deprivation over the past decade. Log minus log (log-log) plots validated the CPH model.

3. Results

3.1. Uptake

The ten-year averages for all vaccinations were high, especially for TPV (99.2%, n = 82,108) and MMR 1 (98.0%, n = 81,706). Average uptake for PSB was 95.6% (n = 79,123), and MMR 2 was 94.2% (n = 78,851). When uptake was stratified by SIMD decile (Fig. 1), the middle class (deciles 4–7) generally had the lowest uptake for PSB and both doses of MMR. Stratified PSB and TPV uptake rates were very high (>99%) for all groups with only the least deprived decile revealing TPV uptake below 99%. More children were vaccinated for PSB and TPV regardless of deprivation decile compared to the MMR vaccines and the range between highest and lowest vaccination rates for deprivation groups was still relatively small for all vaccines: 0.9% for TPV; 0.5% for MMR 1; 0.4% for PSB; and 1.1% for MMR 2 (data not shown).

Chi-squared tests for trend show very strong associations ($p < 0.0005$) between deprivation and uptake for TPV and MMR 1, and a significant association between uptake and deprivation for MMR 2 ($p = 0.03$) (Table 2). PSB uptake was not found to be significantly associated with deprivation.

3.2. Timeliness

The median age that each vaccine was administered was significantly different ($p < 0.0005$, Wilcoxon signed-rank test, data not shown) from the scheduled vaccination age, suggesting lack of timeliness.

Table 2
Chi-squared test for trend results. Chi-squared test for trend results testing association for uptake across SIMD deciles.

Vaccine	N	∑2 (df)	P-value
TPV	82,108	14.94 (1)	<0.0005
MMR 1	81,706	12.23 (1)	<0.0005
PSB	79,123	0.09 (1)	0.77
MMR 2	78,851	4.78 (1)	0.03

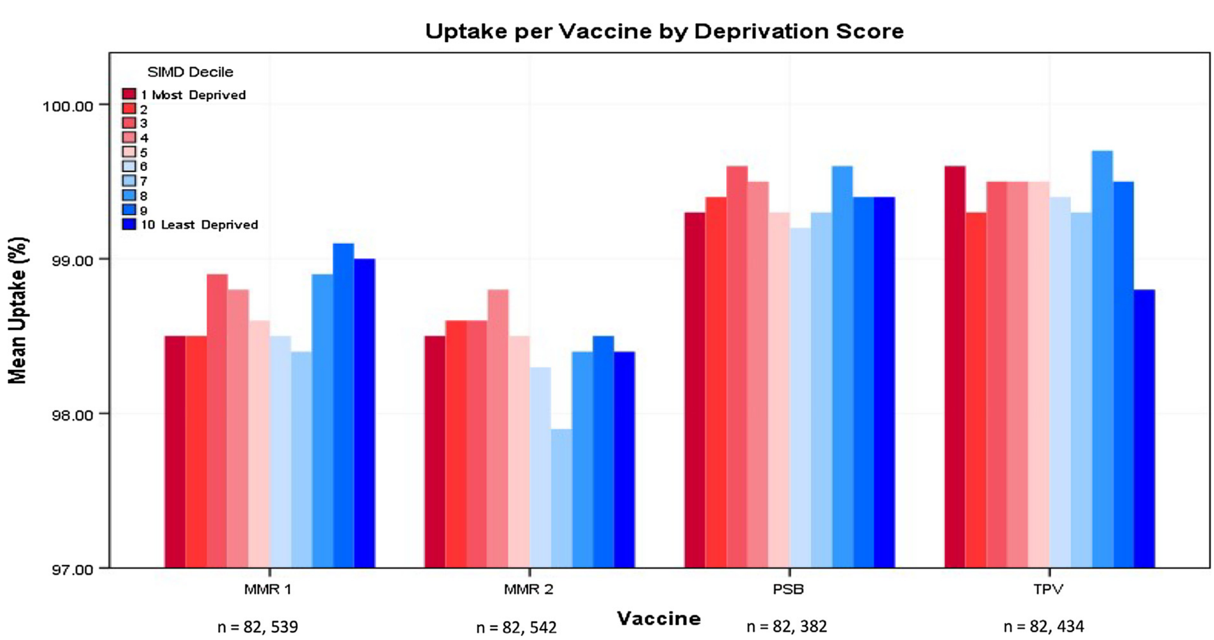

Fig. 1. Uptake stratified by SIMD decile for all vaccines (N = 329,897). Uptake by SIMD decile and birth cohort. PSB and MMR 2 data are from 2002 to 2011 while TPV and MMR 1 data are from 2006 to 2015.

Kaplan-Meier plots (Fig. 2) show clear separation in hazard curves across SIMD deciles though differences in timeliness vary between vaccines. All graphs show greater delays for more deprived deciles. TPV exhibits the greatest difference between the two subpopulations, with a gap of nearly 14% (n = 11,423) between the most and least deprived deciles at the median age when the vaccine was administered; by the time uptake is calculated for TPV at 12 months, there is still an 8% gap (n = 6527) between the most deprived and least deprived groups. This trend is similar across all vaccines with more deprived groups taking longer to reach the 95% WHO recommended target uptake rate.

In Table 3, HR < 1 is an increased hazard of delayed vaccination. Consistently, the 40% most deprived population ($30{,}816 \le n \le 32{,}639$) demonstrate a significant ($p < 0.0005$) relative risk of delayed vaccinations. The greatest disparity was seen in the most deprived group which had an average 31% increased risk of delay for TPV compared to SIMD 10; there were also significant ($p < 0.0005$) disparities in timeliness up to the 8th decile for TPV.

3.3. Time trends

Uptake over time is clearly declining for TPV and MMR 1, with the least deprived group demonstrating a 2.4% decrease in TPV uptake over the last decade (Fig. 3). Though MMR 1 uptake fluctuates for all groups across the decade, SIMD 1 and 2 suffered nearly 3% reductions in uptake between the 2008 and 2018. PSB and MMR 2 cohorts experienced a dramatic rise in uptake across all deprivation scores followed by a gradual decline after the 2006 birth cohort. However, MMR 2 uptake rates for all deciles were still higher in 2018 than in 2008.

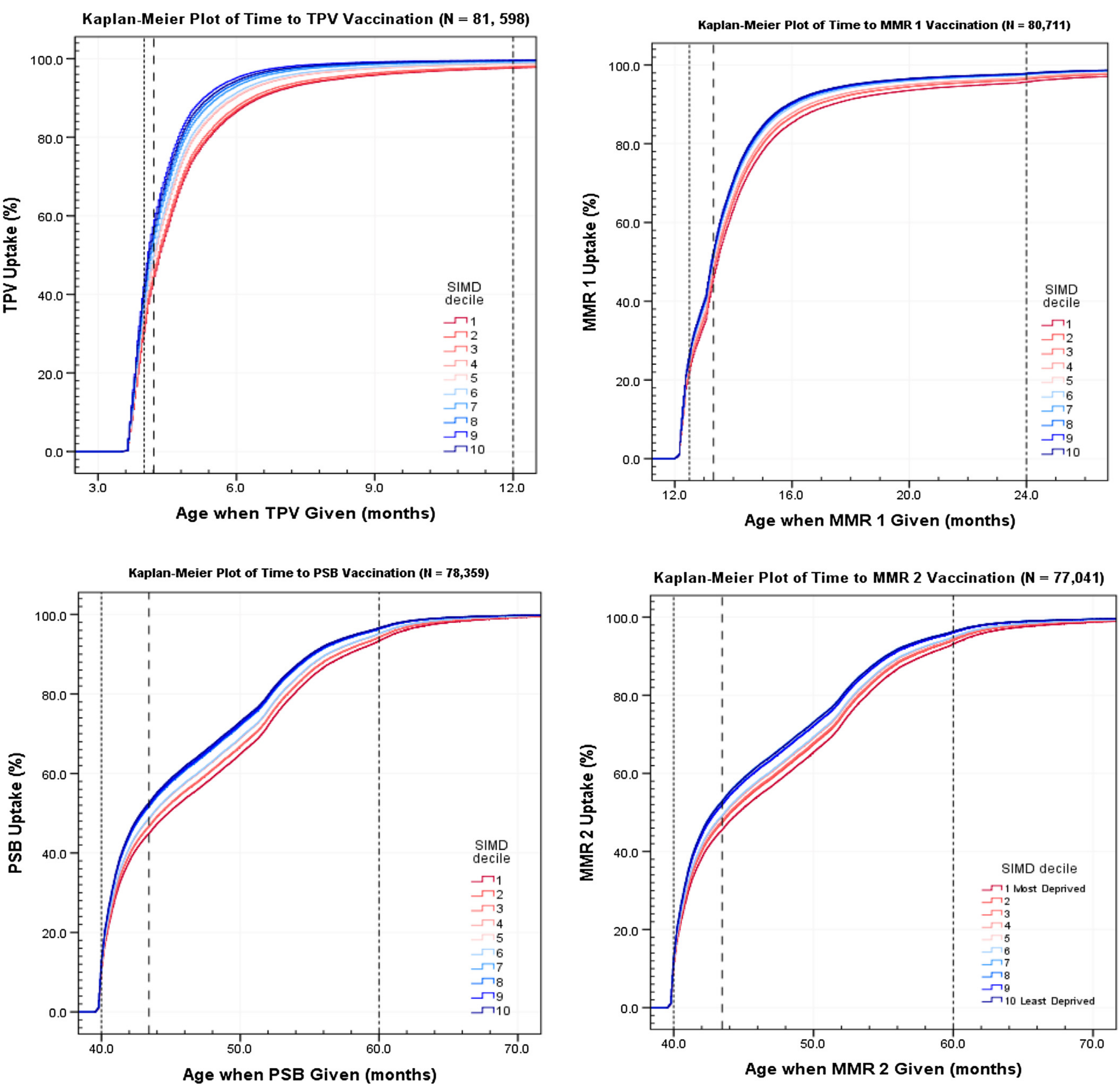

Fig. 2. Time to vaccination by deprivation score per vaccine. Inverse Kaplan-Meier curves of time-to-vaccination for each vaccine by SIMD decile. Dashed lines are (from left to right): recommended age, median age, age of uptake calculation.

Table 3
Cox proportional hazards results per vaccine. CPH results testing the effect of SIMD decile group on time-to-vaccination. Hazard ratio (HR) < 1 is increased risk of delayed vaccination relative to SIMD 10.

Vaccine	SIMD Decile[a]	N	∑2 (df)	Significance	HR (95% CI)
TPV	**1**	**10,775**	**564.41** (1)	**<0.0005**	**0.69 (0.67, 0.72)**
	2	**8773**	**474.52** (1)	**<0.0005**	**0.71 (0.68, 0.73)**
	3	**8189**	**380.29** (1)	**<0.0005**	**0.73 (0.71, 0.75)**
	4	**7583**	**164.53** (1)	**<0.0005**	**0.81 (0.78, 0.84)**
	5	**7002**	**144.60** (1)	**<0.0005**	**0.82 (0.79, 0.84)**
	6	**8499**	**105.09** (1)	**<0.0005**	**0.85 (0.82, 0.88)**
	7	**7898**	**24.74** (1)	**<0.0005**	**0.92 (0.89, 0.95)**
	8	8449	5.27 (1)	0.022	0.96 (0.93, 1.00)
	9	7226	8.02 (1)	0.005	0.96 (0.93, 1.00)
	10[a]	7074	–	–	–
MMR 1	**1**	**5001**	**159.69 (1)**	**<0.0005**	**0.81 (0.79, 0.84)**
	2	**8008**	**121.23** (1)	**<0.0005**	**0.86 (0.84, 0.88)**
	3	**8871**	**124.29** (1)	**<0.0005**	**0.86 (0.84, 0.88)**
	4	**8125**	**70.41** (1)	**<0.0005**	**0.89 (0.87, 0.92)**
	5	5906	2.26 (1)	0.13	0.98 (0.95, 1.01)
	6	6989	12.08 (1)	0.001	0.95 (0.92, 0.98)
	7	7272	0.05 (1)	0.83	1.00 (0.97, 1.03)
	8	6944	3.12 (1)	0.08	0.98 (0.95, 1.00)
	9	8378	0.68 (1)	0.41	0.99 (0.96, 1.02)
	10[a]	15,087	–	–	–
PSB	**1**	**4385**	**173.43 (1)**	**<0.0005**	**0.80 (0.78, 0.83)**
	2	**7497**	**153.01** (1)	**<0.0005**	**0.84 (0.82, 0.87)**
	3	**8524**	**158.27** (1)	**<0.0005**	**0.84 (0.82, 0.87)**
	4	**7654**	**69.81** (1)	**<0.0005**	**0.89 (0.97. 0.92)**
	5	5670	2.99 (1)	0.08	0.97 (0.94, 1.00)
	6	6762	59.40 (1)	**<0.0005**	**0.89 (0.87, 0.92)**
	7	6832	0.31 (1)	0.58	0.99 (0.95, 1.02)
	8	6810	3.69 (1)	0.06	0.97 (0.95, 1.00)
	9	8392	1.53 (1)	0.22	0.98 (0.96, 1.01)
	10[a]	15,707	–	–	–
MMR 2	**1**	**4337**	**151.64** (1)	**<0.0005**	**0.81 (0.78, 0.84)**
	2	**7404**	**124.48** (1)	**<0.0005**	**0.85 (0.83, 0.88)**
	3	**8393**	**114.75** (1)	**<0.0005**	**0.86 (0.84, 0.89)**
	4	**7573**	**63.62** (1)	**<0.0005**	**0.89 (0.87, 0.92)**
	5	5592	1.34 (1)	0.25	0.98 (0.95, 1.01)
	6	**6667**	**49.27** (1)	**<0.0005**	**0.90 (0.88, 0.93)**
	7	6700	0.05 (1)	0.82	1.00 (0.98, 1.03)
	8	6681	2.34 (1)	0.13	0.98 (0.95, 1.01)
	9	8242	3.73 (1)	0.05	0.97 (0.95, 1.00)
	10[a]	15,330	–	–	–

[a] Reference Category is SIMD Decile 10.

Table 4 demonstrates that, excepting TPV, absolute timeliness across birth cohorts for all vaccines improved significantly between 2008 and 2018 ($p < 0.0005$). The greatest improvement was for the 2011 MMR 2 cohort which was, on average, >4 times as likely to be vaccinated on time than the 2002 cohort (95% CI: 3.93–4.19). Similarly, HRs for timeliness steadily increased each year for PSB to 3.86 (95% CI: 3.74–3.99) by 2018. Though some birth cohorts were significant for TPV, the 2013 cohort showed the greatest difference from the earliest cohort with a 12% increased hazard of being vaccinated.

The Kaplan-Meier hazard curves of the time to vaccination (Fig. 4) show that for all vaccines except TPV, uptake and timeliness has been improving; greater proportions of the population adhered to the schedule over time. The rise in uptake improves considerably for the first dose of MMR between the 2009 and 2010 birth cohorts (years 2011 and 2012). The primary vaccine shows relatively stable rates of uptake and timeliness for each birth cohort. For PSB and MMR 2, the average uptake by 60 months is around 80% for the 2002 birth cohort but by 2006, the uptake for PSB and MMR 2 surpass 95% and continues to remain above this target uptake rate. This is approximately a 15% increase in uptake and timeliness between the years 2008–2012 for both the PSB and the second dose of MMR.

The graphs of HR (Fig. 5) for delay across deprivation groups for each vaccine (except TPV) illustrate a general downward trend. Some deprivation groups, such as the 9th decile, improve timeliness by approximately 10% for PSB and MMR 2 immunisations between the 2005 and 2006 birth cohorts. Other more deprived groups show a decline in timeliness for both MMR doses and the pre-school booster. There is a pronounced separation in the hazard ratios for more deprived groups (deciles 1–4) in the PSB and MMR 2 relative to the least deprived decile. For all but TPV, more deprived groups are at a higher risk of delayed vaccination, with the hazards gradually increasing over the past decade.

4. Discussion

In exploring the relationship between deprivation, uptake, and timeliness for four essential and established childhood vaccines, we found that despite high uptake rates for each vaccine, deprivation was strongly associated with both uptake and timeliness. While all vaccines surpassed the 95% WHO recommended target rate, differences in uptake across deprivation groups were not only significant but were greatest for middle class children (SIMD deciles 4–7) for all vaccines except the primary vaccine. The 40% most deprived population experienced significantly reduced timeliness relative to

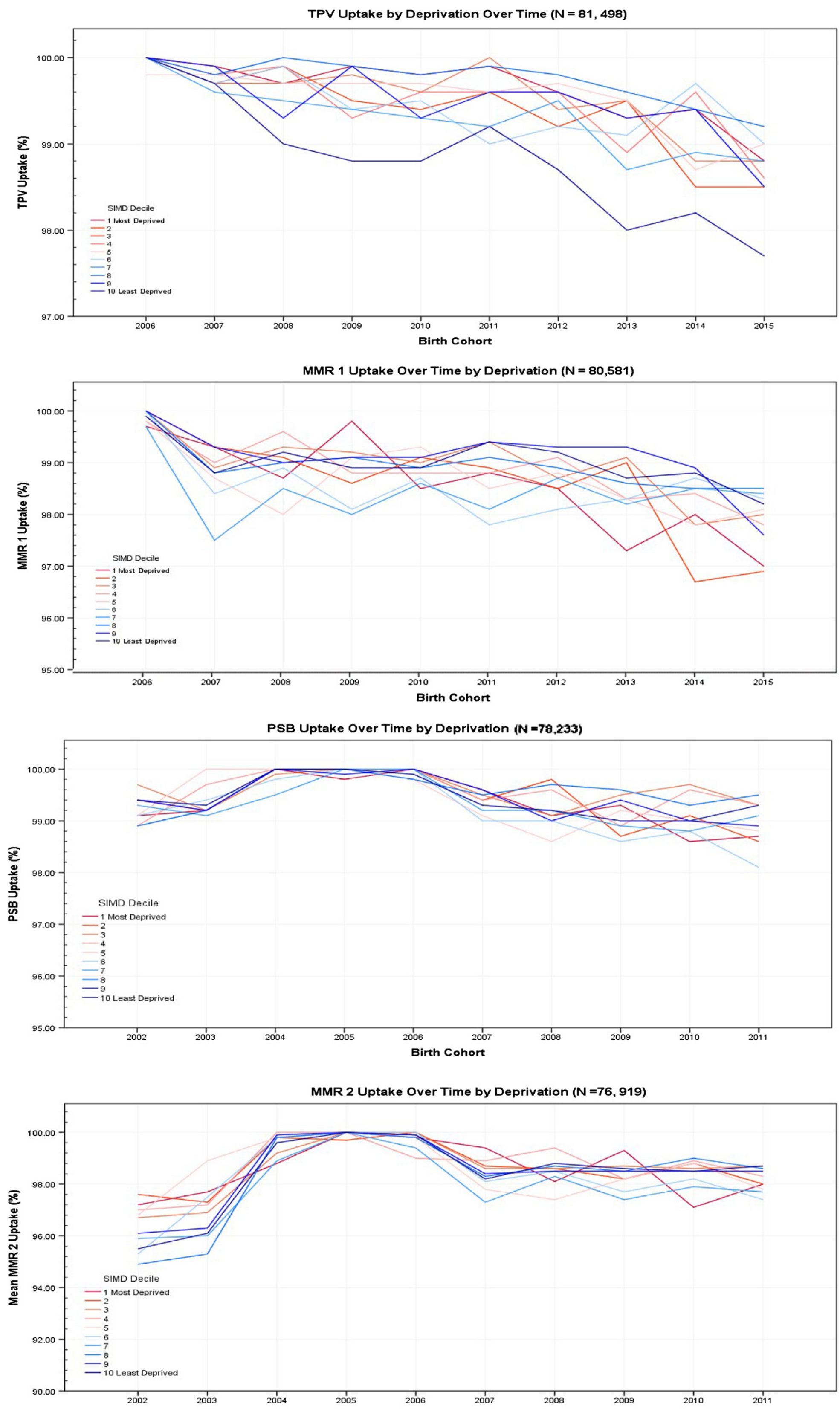

Fig. 3. Gradients of uptake over time by deprivation score. Average uptake for each vaccine over the past decade by SIMD decile.

the least deprived group. In the last decade, the gradient of uptake has worsened and though timeliness seems to have improved, stratifying by deprivation decile revealed increasing disparities in timeliness; the most deprived group was at a nearly 50% increased risk of delayed vaccination relative to the least deprived decile for both doses of MMR and the pre-school booster.

Table 4
Results of cox proportional hazards model on birth cohort. Chi-squared test for trend results testing association for uptake across SIMD deciles. Hazard ratio (HR) > 1 is reduced risk of delayed vaccination relative to first birth cohort (2002 for PSB/MMR2 and 2006 for TPV/MMR1).

Vaccine	Covariate	N	∑2 (df)	Significance	HR (95% CI)
TPV	2006[a]	6924	–	–	–
	2007	7479	0.79 (1)	0.37	0.98 (0.95, 1.02)
	2008	**7776**	**13.76 (1)**	**<0.0005**	**1.06 (1.03, 1.10)**
	2009	7851	0.08 (1)	0.77	1.00 (0.96, 1.03)
	2010	8063	0.09 (1)	0.76	1.00 (0.96. 1.03)
	2011	8306	3.65 (1)	0.06	1.03 (1.04, 1.11)
	2012	**8299**	**17.69 (1)**	**<0.0005**	**1.07 (1.04, 1.07)**
	2013	**8714**	**51.21 (1)**	**<0.0005**	**1.12 (1.09, 1.16)**
	2014	**9059**	**22.31 (1)**	**<0.0005**	**1.08 (1.05, 1.13)**
	2015	8997	2.59 (1)	0.11	1.03 (0.99, 1.06)
MMR 1	2006	6825	–	–	–
	2007	**7387**	**35.28 (1)**	**<0.0005**	**1.11 (1.07, 1.14)**
	2008	**7709**	**104.47 (1)**	**<0.0005**	**1.19 (1.15, 1.23)**
	2009	**7794**	**110.48 (1)**	**<0.0005**	**1.19 (1.15, 1.23)**
	2010	**8011**	**1911.43 (1)**	**<0.0005**	**2.06 (1.99, 2.13)**
	2011	**8230**	**3192.44 (1)**	**<0.0005**	**2.53 (2.45, 2.62)**
	2012	**8221**	**3433.51 (1)**	**<0.0005**	**2.62 (2.54, 2.71)**
	2013	**8640**	**3493.97 (1)**	**<0.0005**	**2.62 (2.54, 2.71)**
	2014	**8926**	**3411.32 (1)**	**<0.0005**	**2.57 (2.49, 2.65)**
	2015	**8838**	**3333.96 (1)**	**<0.0005**	**2.55 (2.50, 2.63)**
PSB	2002	6539	–	–	–
	2003	6829	0.05 (1)	0.82	1.00 (0.86, 1.03)
	2004	**6925**	**469.31 (1)**	**<0.0005**	**1.46 (1.01, 1.51)**
	2005	**7204**	**2011.70 (1)**	**<0.0005**	**2.17 (2.10, 2.24)**
	2006	**7478**	**3878.45 (1)**	**<0.0005**	**2.89 (2.80, 2.99)**
	2007	**8129**	**5212.83 (1)**	**<0.0005**	**3.37 (3.26, 3.48)**
	2008	**8563**	**5846.46 (1)**	**<0.0005**	**3.57 (3.45, 3.68)**
	2009	**8589**	**6594.53 (1)**	**<0.0005**	**3.87 (3.74, 4.00)**
	2010	**8899**	**6622.10 (1)**	**<0.0005**	**3.84 (3.72, 3.97)**
	2011	**9078**	**6725.65 (1)**	**<0.0005**	**3.86 (3.74, 3.99)**
MMR 2	2002	6345	–	–	–
	2003	6627	0.89 (1)	0.35	1.02 (0.98, 1.05)
	2004	**6788**	**491.64 (1)**	**<0.0005**	**1.48 (1.43, 1.53)**
	2005	**7057**	**2103.92 (1)**	**<0.0005**	**2.23 (2.16, 2.31)**
	2006	**7316**	**4084.23 (1)**	**<0.0005**	**3.02 (2.92, 3.13)**
	2007	**8024**	**5346.03 (1)**	**<0.0005**	**3.48 (3.36, 3.59)**
	2008	**8493**	**6087.11 (1)**	**<0.0005**	**3.72 (3.59, 3.84)**
	2009	**8505**	**6852.87 (1)**	**<0.0005**	**4.04 (3.91, 4.17)**
	2010	**8786**	**6958.78 (1)**	**<0.0005**	**4.05 (3.92, 4.18)**
	2011	**8978**	**7044.95 (1)**	**<0.0005**	**4.06 (3.93, 4.19)**

[a] Reference category is the first birth cohort (2006/2002).

This study fulfills a need for an updated and detailed understanding of disparities in immunisation uptake and timeliness in one of the largest and most socioeconomically diverse areas in Scotland. Moreover, the findings concur with recent literature on deprivation and uptake and timeliness in developed countries [23,8,24,25]. The large, comprehensive, and complete population-based data from the Scottish Immunisation and Recall System provides an advantage over ecological study designs.

4.1. Uptake and timeliness

Ten-year average uptake was highest for the primary vaccine (99.2%) and lowest for the second dose of MMR (94.2%). These high average uptake rates are near or above the 95% WHO recommended target for controlling infectious diseases; however, these excellent immunisation rates may be undermined by the uptake-by-deprivation relationship. Uptake was significantly associated with deprivation for all vaccines except the pre-school booster though there are differences in uptake for PSB when stratified by deprivation, especially for the middle class (deciles 4–7). Similar inequities in uptake were seen for the other vaccines. Though the differences in uptake for the middle class are <1% for certain groups, the disparities may be locally clustered, as Busby and Chesterley found in Canadian provinces (2015). This increases the risk of outbreaks in certain areas that could result in more widespread infections in the southeastern Scotland. Moreover, Edinburgh, the capital, has a highly mobile population that includes tourists and international students, making imported cases of measles and other infections a hazard in an undervaccinated population [2]. Similarly, in response to a record number of measles incidence in Europe in 2018, the WHO pointed to sub-national coverage despite high national uptake rates as the culprit of these outbreaks [26]. Therefore, not only should Scotland and other countries reach the 95% uptake rate for herd immunity, but groups with suboptimal coverage—such as those we have identified in this research—should be targeted to minimise the risk of outbreaks.

The findings on deprivation are consistent with several studies that investigated deprivation as a factor of differential uptake [23,27,9,6,7,15,10,12]. Scottish publications from the height of the MMR controversy found that more affluent groups were less likely to vaccinate for MMR [12] and DTP [7]. More than a decade later, affluent groups (deciles 8–10) exhibit relatively high uptake rates (>98%) and are more likely to vaccinate for the first dose of MMR than the rest of the cohort. Surprisingly, coverage for the primary vaccine and the second dose of MMR was greater for more deprived groups (>96%), surpassing affluent groups' uptake. However, despite high uptake, all vaccine cohorts exhibited substantial

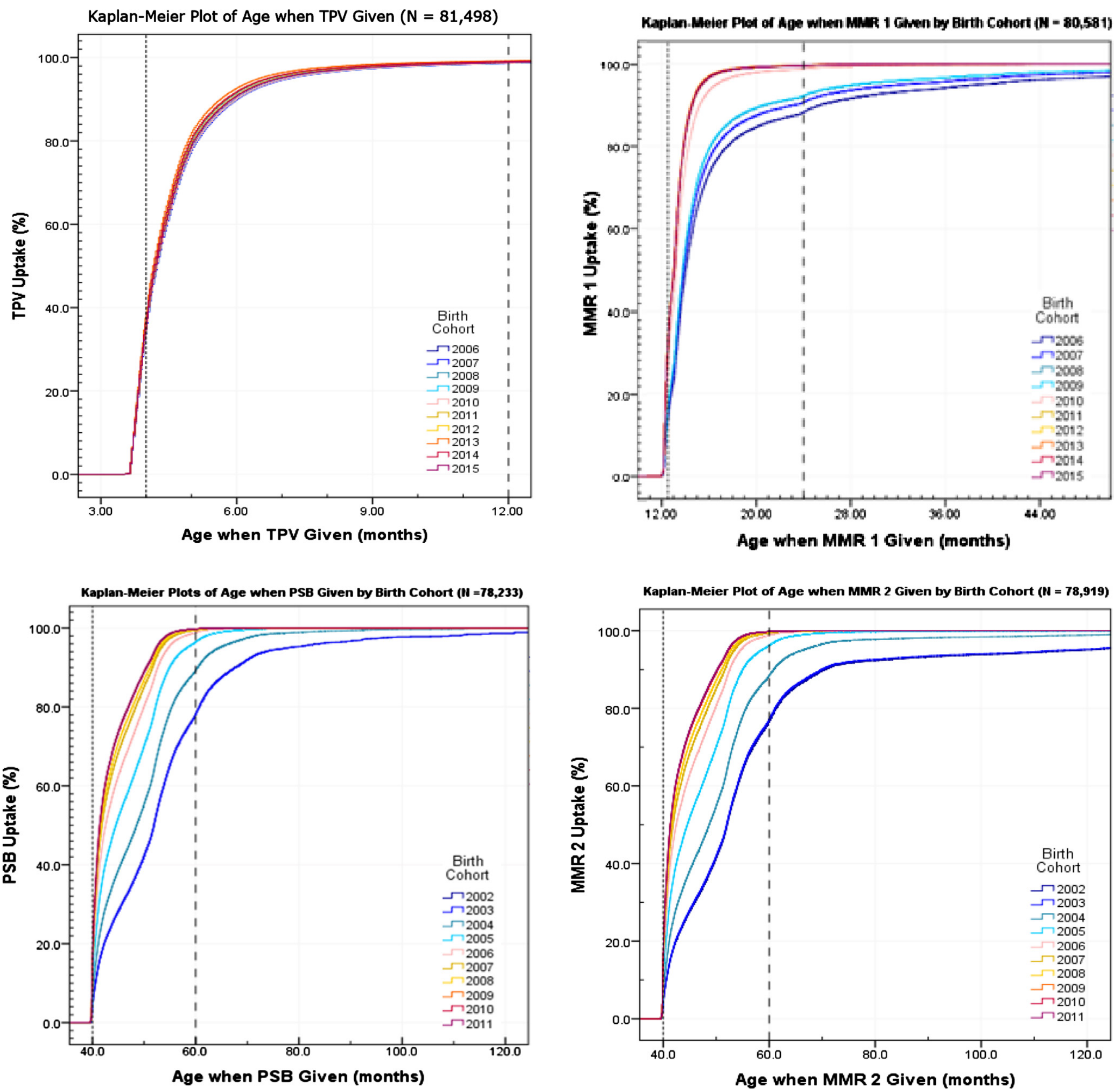

Fig. 4. Time to vaccination for birth cohort per vaccine. Inverse Kaplan-Meier curves of time-to-vaccination for all vaccines by birth cohort. Dashed lines (from left to right) are: recommended age and median age.

delays with more deprived deciles at a significantly higher risk of delayed vaccination. The primary vaccine, in particular, showed a clear difference in timeliness across all deprivation groups with only 28% of the most deprived decile vaccinating on time compared to 43% of the least deprived group. Families within the 40% most deprived population group were at least 10% more likely to not vaccinate on time for both doses of MMR and the pre-school booster; this hazard was doubled for the primary vaccine. As the primary vaccine in this study is the third and final dose of DTaP/IPV/Hib (and so indicates a completed TPV routine) there is presumably a greater portion of children that are incompletely immunized and thus are more vulnerable to acquiring these diseases throughout their lives. All three doses of primary immunizations are required for an effective immune response [28]. Although the least deprived decile was most likely to immunise on time, they also has the lowest uptake; families within this most affluent group are the least likely to complete the TPV routine at all.

For the primary vaccine, administered at 4 months, it took approximately 2 weeks after the scheduled age for half the cohort to be vaccinated. The delay increased to nearly 1 month for the first dose of MMR before half the cohort was immunised, while the pre-school booster and second dose of MMR, both meant to be given at 40 months, saw delays of 3 months. The later the dose was scheduled on the UK routine, the greater the delay. Moreover, delay for all vaccines in our research was always greater for more deprived groups.

This phenomenon has been seen in several other studies [11,29,23,13,8]. As such, there is robust evidence for a direct positive relationship between deprivation and delay. This may be due to more deprived families experiencing access-related barriers to

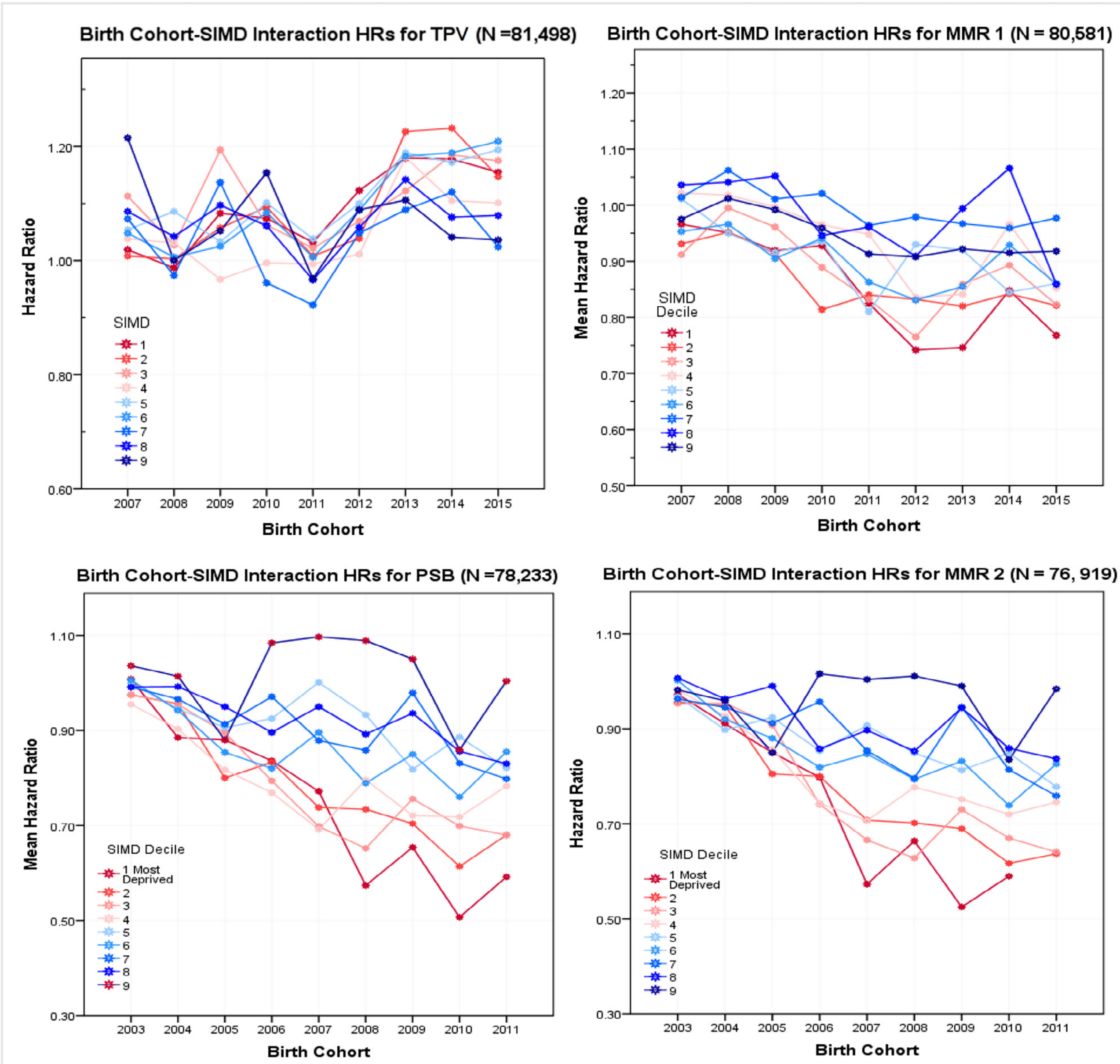

Fig. 5. Hazard ratios of interaction terms from cox model. Risk (hazard ratio) of delayed vaccination for birth cohorts by deprivation for all vaccines. HR < 1 is the relative (to the first birth cohort) reduction in the rate of vaccination for each birth cohort while a HR > 1 is a relative increase in the rate of vaccination for each cohort.

immunisation, resulting in lack of timeliness as other more immediate needs are prioritized over preventative measures such as vaccination [9,30]. Increasing delay for doses scheduled at later ages could be influenced by other factors as well, such as the end of maternity leave or preschool/child-care time commitments; negative experiences or dissatisfaction with immunisation services—which includes difficulty finding available healthcare workers and perceived poor, unreliable, or insufficient information on immunisations from healthcare workers [31]; or lack of timely reminders for appointments [32]. Additionally, known risk factors of deprivation such as single parent families, large households, rural residence, or low educational attainment may affect vaccination timeliness [14]. Many of the factors related to healthcare structure, such as access to clinics and experiences with healthcare workers, represent areas in which policy changes can help reduce disparities in timeliness.

4.2. Time trends

Although there has been a history of controversy surrounding vaccinations [1], in 1998, there was a rise in global concern amongst parents when a publication incorrectly associated the MMR vaccine with autism and gastrointestinal problems; though the study was discredited in 2004, it was not officially retracted until 2010 [33]. This research, spanning from 2008 to the end of 2017, illustrates that the debate continues to affect vaccination trends in Scotland. In 2008, uptake for the first dose of MMR was high (>99%) for all groups; in the same year, however, uptake for the second dose in more affluent groups was below 95% while more deprived groups' uptake remained near 99%. Children receiving the second dose of MMR in 2008 would have received their first dose in 2004 or 2005—amidst peak public concerns. British publications investigating uptake around this time illustrated reductions in MMR uptake

[6,7,12]; therefore, it is understandable that the cohort with low MMR 1 uptake also had relatively low MMR 2 uptake in 2008. Conversely, by 2010, nearly all children born in 2004 were vaccinated for the second dose of MMR.

By the end of the decade, the lowest uptake in 2018 was still >95% for all vaccines, with PSB showing an overall increase from 2008 uptake rates. This suggests high compliance from all deprivation groups to the UK health board recommendations for the vaccines studied here despite possible vaccine hesitancy.

Notably, however, from the 2006 birth cohort onwards, there is a small (<3%) but apparent reduction in uptake for all vaccines. The least deprived group, decile 10, shows a steep decline in uptake for the primary vaccine, decreasing by 2.2% in the last decade. This may be due to the well-established association between affluence and vaccine hesitancy or refusal [34]. Also, the primary vaccine is one of the first childhood vaccines; vaccine hesitant parents would be more likely to refuse this first vaccine altogether.

The primary vaccine shows a slight increase in timeliness over the past decade and there are dramatic improvements in timeliness between 2008 and 2012 for the other vaccines which may be due to improved public opinion of vaccine safety. However, stratification of deprivation-birth cohort interactions illustrates the effects of deprivation for each birth cohort: the most deprived groups have nearly a 50% reduced likelihood of timely vaccination—especially for both doses of MMR and the pre-school booster. This finding emphasizes the importance of investigating relative inequalities; although absolute timeliness has improved, it is evident that more work is necessary to reduce the relative vaccination delay, the brunt of which is carried by more deprived families.

As mentioned, deprived groups are more likely to experience access-related barriers to timely vaccination. Feasible changes which could improve coverage and timeliness include more flexible immunisation clinic hours (Busby and Chesterley); [14], increased contact with and trust in healthcare workers such as health visitors [35,36], streamlined and accessible information on vaccines [9,37], improved access to information in other languages [10,30], better childcare centers or subsidies for childcare [37,38] and programmes for single mothers and mothers of young children [37,9].

4.3. Strengths and limitations

By utilizing the Scottish Immunisation Recall System (SIRS), one of the most comprehensive child immunisation databases, this study assesses a large and comprehensive cohort of children that were immunised in southeast Scotland over the past decade. As most recent literature has used ecological data, the relatively complete data in this study strengthens the validity of the findings herein. This study also assesses uptake, timeliness, and time-trends for four childhood vaccines and as such provides a thorough investigation of benchmarks of the immunisation programme.

While SIRS is one of the most comprehensive immunisation databases in Europe [39], it may not include an entirely accurate denominator of children. As it is updated daily, newer data are prioritized for validation and older data may include overlooked inaccuracies. Due to these inaccuracies, it is possible that the results are not entirely reflective of the true uptake and timeliness of childhood immunisation in southeast Scotland. However, the data are largely complete with approximately 0.2% missing data in any given variable which was not found to be significantly different from the rest of the cohort.

Finally, the SIMD used in this paper was based on postcode. Model of vaccine delivery, population structure and ethnicity, urbanicity, or other factors associated with geographic area may potentially confound uptake and timeliness analyses. Future research investigating these factors along with postcode-based deprivation indices may be able to elucidate the relationship between deprivation, uptake, timeliness, and other confounding factors.

5. Conclusions

In our research, we tested uptake and timeliness associations with deprivation for ten years of vaccinations from one of the most comprehensive immunisation databases in Europe for four routine childhood vaccinations. This study has identified significant findings that could inform key stakeholders for policy and practice, mainly: definitive evidence for deprivation associations with uptake and timeliness; significant delay in vaccination for more deprived groups for all vaccines; and growing disparities in uptake and timeliness over the last decade. These results can be used to target deprived populations and improve access to immunisation, thereby increasing uptake and timeliness and attaining herd immunity; striving for high uptake and timeliness is necessary to control infectious diseases that continue to pose a threat, even to countries surpassing WHO recommended 95% target uptake rates.

Declaration of Competing Interest

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Author contributions

Eram A. Haider conceived and designed the study, analysed and interpreted the data, drafted and revised the manuscript.

Lorna Willocks conceived and designed the study, revised the manuscript, and approved the final manuscript.

Niall Anderson suggested statistical analyses and helped interpret results and revised the manuscript.

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