Swansea University
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Assessing equity and effectiveness of vaccination programmes in Wales, utilising linkage of administrative datasets

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Abstract

Vaccinations have been extremely successful in reducing the burden of infectious disease and a number of disease elimination goals rely on sustaining high vaccination coverage. Generating evidence demonstrating gaps in coverage is key to tailoring vaccination programmes, and ongoing vaccine effectiveness studies are needed to improve vaccine confidence and guide public health policy. Using the Secure Anonymised Information Linkage Databank, this project aimed to develop methods for evaluating equity and effectiveness of vaccination programmes through linkage of routine administrative datasets. These methods were put into practice with the roll-out of novel vaccines against COVID-19 in adults, and the longstanding childhood programme against Measles, Mumps and Rubella. Through linkage of ten demographic, education and public health datasets this work has contributed to the evidence base via three peer-reviewed publications, with a fourth under review, and other dissemination activities within policy. Using multivariable logistic regression, factors associated with lower vaccine coverage were identified, including ethnicity, birth order and place of birth. Using Cox regression in a robust cohort design, encouraging effectiveness estimates against severe COVID-19 infection were available in the first few months of the campaign. It was possible for the first time to quantify vaccine waning against mumps and demonstrate that vaccination against measles remains highly effective, improving confidence in elimination targets. Strengths and limitations of using routine administrative datasets for evaluating vaccine programmes are discussed, alongside recommendations and considerations for public health policy. Data linkage provides the opportunity to produce a wealth of evidence to support vaccine programme evaluation. The methodology developed here should be considered by other public health organisations, potentially through the development of strong academic links. More focus is needed on how evidence is disseminated to the general public, as well as those involved in vaccine policy or delivery.

Declaration and Statements

Statement 1

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed: [redacted] (candidate)

Date: 16/02/2026

Statement 2

This thesis is the result of my own work, except where otherwise stated and that other sources are acknowledged by giving explicit references which are provided at the end of the document.

Signed: [redacted] (candidate)

Date: 16/02/2026

Statement 3

If accepted, I agree for the metadata and abstract to be made automatically available in the University repository to outside organisations.

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Date: 16/02/2026

Statement 4

I confirm that the Swansea University's ethical procedures were followed throughout this project.

Signed: [redacted] (candidate)

Date: 16/02/2026

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List of Abbreviations

aHR	Adjusted Hazard Ratio
aVE	Adjusted Vaccine Effectiveness
ADDE	Annual District Death Extract
ALF	Anonymised Linkage Field
AR	Attack Rate
BCG	Bacillus Calmette–Guérin
CDDS	Consolidated Death Data Source
CEV	Clinically Extremely Vulnerable
CI	Confidence Interval
COB	Country of Birth
COVER	Cover of Vaccination Evaluated Rapidly
CVB	COVID-19 Vaccination Board
CVVD	COVID-19 Vaccination Data
CYPrIS	Children and Young Persons Integrated System
DHCW	Digital Health Care Wales
DPIA	Data Protection Impact Assessment
EDUW	Wales Schools and Pupils Dataset
EHR	Electronic Health Record
ESCAIDE	European Scientific Conference on Applied Infectious Disease Epidemiology
GLM	Generalised Linear Model
GP	General Practice
GVAP	Global Vaccine Action Plan
HDR	Health Data Research
HR	Hazard Ratio
HPT	Health Protection Team
HPV	Human Papillomavirus
IGRP	Information Governance Review Panel
IRR	Incidence Rate Ratio

IPW	Inverse Propensity Score Weighting
JCVI	Joint Committee on Vaccination and Immunisation
LHB	Local Health Board
LMIC	Low and Middle Income Country
LSOA	Lower Super Output Area
MVC	Mass Vaccination Centre
MMR	Measles Mumps Rubella
MR	Measles and Rubella
NCCHD	National Community Child Health Database
NHS	National Health Service
ONS	Office for National Statistics
OR	Odds Ratio
PATD	Pathology COVID-19 Daily data
PCR	Polymerase Chain Reaction
PCV	Proportion of Cases Vaccinated
PEDW	Patient Episode Dataset for Wales
PHW	Public Health Wales
PPV	Proportion of Population Vaccinated
RR	Relative Risk
RSV	Respiratory Syncytial Virus
SAIL	Secure Anonymised Information Linkage
SAR	Secondary Attack Rate
TB	Tuberculosis
THB	Teaching Health Board
TNCC	Test Negative Case Control
TRE	Trusted Research Environment
UHB	University Health Board
VEC	Vaccine Equity Committee
UK	United Kingdom
UKHSA	UK Health Security Agency

VE	Vaccine Effectiveness
VPDP	Vaccine Preventable Disease Programme
WDSD	Welsh Demographic Service Dataset
WG	Welsh Government
WHO	World Health Organisation
WIMD	Welsh Index of Multiple Deprivation
WIS	Welsh Immunisation System

Chapter 1 - Introduction

1.0 Background

Vaccination programmes have been extremely successful in reducing or eliminating infectious diseases (1,2). The World Health Organisation (WHO) Immunisation Agenda 2030, in support of the 2030 Sustainable Development Goals, contains a number of disease specific targets that rely on successful dissemination and administration of vaccines (3,4). To ensure ongoing progress towards elimination goals, it is important that robust methods for monitoring and evaluating vaccination programmes are in place.

Wales is one of the four nations of the United Kingdom (UK) with a population of approximately 3.1 million. The National Health Service (NHS) in Wales provides health care for the population, with provision spread across seven geographically defined Local Health Board (LHB) areas and a small number of national NHS Trusts. The Vaccine Preventable Disease Programme (VPDP) was established as part of Public Health Wales (PHW) NHS Trust in 2005 and is responsible for national vaccine surveillance, in addition to supporting LHBs to deliver immunisation services and providing strategic direction to the Welsh Government (WG) to aid service development. Although health is a devolved matter from the UK government, routine vaccination policy is closely aligned across all the UK nations, with central expert advice provided by the UK Joint Committee on Vaccinations and Immunisations (JCVI), the UK's national immunisation technical advisory group. Routine vaccinations are given for free by the NHS.

There is a well-established routine childhood vaccination schedule which, at the time of writing, advises universal immunisation for children against seventeen different infectious diseases between eight weeks and 14 years of age (5). Additionally, annual influenza vaccination is recommended for all children aged two to 16 years, as well as a selective Bacillus Calmette–Guérin (BCG) programme for Tuberculosis (TB). Childhood vaccinations are mainly delivered through General Practices (GPs) where they are recorded on the patients' record. Vaccinations given to older children are mainly delivered by nursing teams in schools, apart from Cardiff and Vale University Health Board (UHB) where currently the Meningococcal ACWY and '3in1' Diphtheria-Tetanus-Pertussis booster vaccinations are delivered by GPs. Routine immunisation services in Wales are underpinned by universal invitations, and recall for missed appointments. Call and recall is managed by each health board through a centrally provided child health information system, called the Children and Young Persons Integrated System (CYPrIS). This system also acts as a record of vaccination history for all children resident in each health board area of Wales, from birth up to 16 years of age. CYPrIS automatically generates invitations for parents to bring their children for each appointment of the routine vaccination schedule and also provides vaccinators with scheduled lists of children who are due their immunisations. For adolescents in areas with school vaccination programmes, similar lists are provided to school nursing services. GPs and school nursing services are required to send notification of any vaccination administered to the local child health office, where the vaccination record is entered into CYPrIS. Transfer of this information is currently a manual process completed using paper forms. Unscheduled or opportunistic vaccinations given by GPs may not make it on to CYPrIS and the completeness of CYPrIS data is not known. Data from child health offices are extracted from CYPrIS monthly, then combined and deduplicated to form the National Community Child Health Database (NCCHD) (Figure 1.1). Anonymised person level data from the NCCHD are used to produce routine childhood vaccination coverage statistics which are published in quarterly Cover of Vaccination Evaluated Rapidly (COVER) reports. These reports are published alongside GP and school level dashboards that are available for health care professionals via the NHS intranet (6).

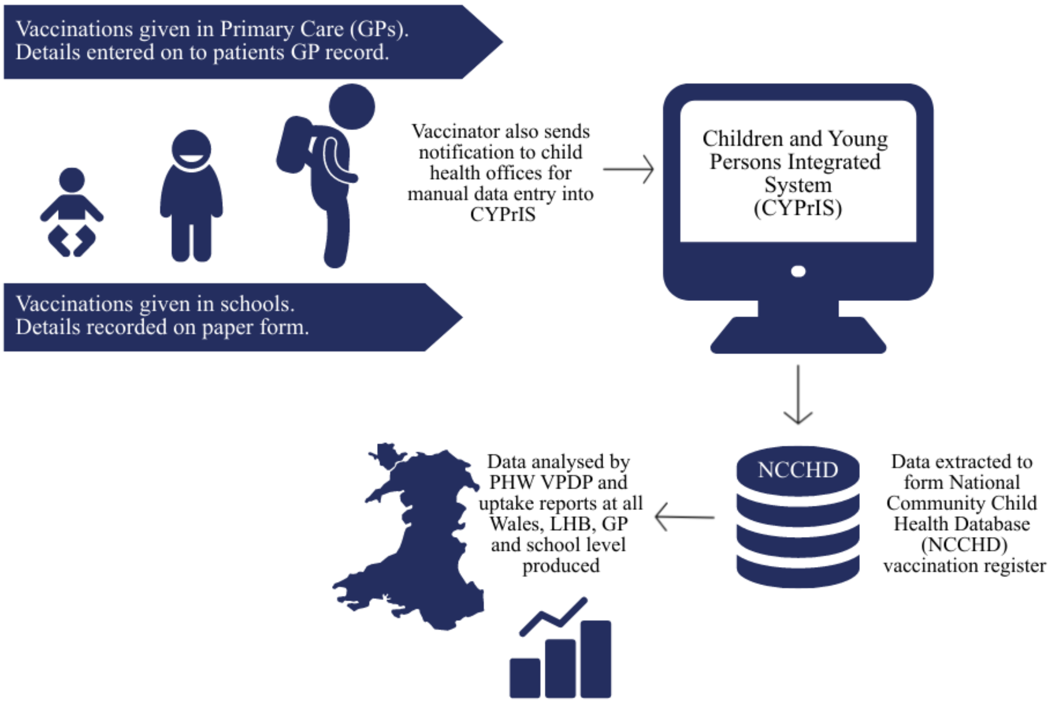


Figure 1.1. Process for recording and reporting on vaccinations given in childhood, Wales, UK. (Original figure cc by Malorie Perry)

Adults who are at risk due to age, clinical vulnerability and other factors are eligible for shingles, pneumococcal and annual seasonal influenza vaccination. Vaccination against pneumococcal and influenza are also available for select at risk groups of all ages. These vaccinations are routinely given in primary care or can be delivered by community pharmacies. Vaccination details are entered on to the patients' primary care GP record and PHW VPDP receive regular extracts of aggregated coverage data from GP systems (Figure 1.2). These extracts are used for routine uptake reporting from national level down to GP level, however, as the data are aggregated there is limited scope for further surveillance outputs.

From December 2020 a new vaccination programme was introduced to protect the population against SARS-CoV-2, almost one year after the COVID-19 pandemic began. A new all Wales vaccination register was developed, known locally as the Welsh Immunisation System (WIS), to support invitations and the delivery and recording of COVID-19 vaccination through Mass Vaccination Centres (MVCs). Since implementation, PHW VPDP have received a near real-time view of COVID-19 data from WIS enabling timely reporting of vaccination uptake at various levels.

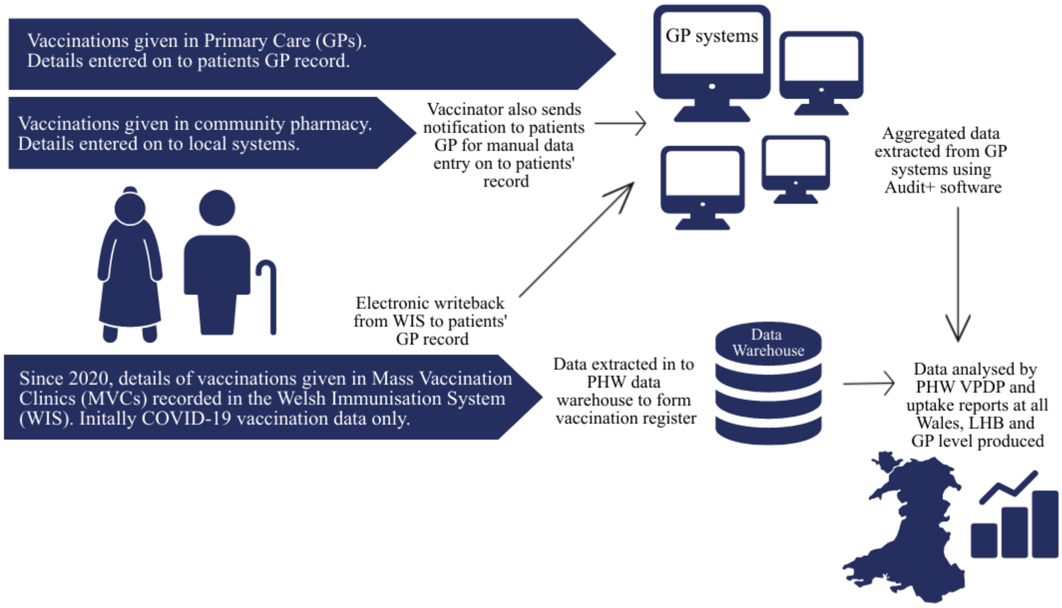


Figure 1.2. Process for recording and reporting on vaccinations given to older adults, Wales, UK. (Original figure cc by Malorie Perry)

Although reporting vaccine uptake at a granular level is now routine in Wales, there are developments needed with regards to the other aspects of vaccine programme monitoring and evaluation. Implementation of methods to regularly assess equity, effectiveness, impact and safety can be achieved through improved surveillance systems and development of robust epidemiological studies.

1.1 Vaccine equity

The WHO Immunisation Agenda 2030: a global strategy to leave no one behind, encourages the systematic collection of disaggregated data on underserved groups and the creation of data-driven evidence to introduce targeted interventions to reduce inequity (3). This follows on from a decade of implementation of the WHO Global Vaccine Action Plan 2011-20 (GVAP) that included equitable vaccine access as one of its guiding principles (7). Unfortunately, although progress was made in a number of countries, many of the GVAP targets were unmet at the end of the decade (8).

At the time of conceptualisation of this thesis in 2020, evaluation of equity in vaccination coverage in Wales was limited. In 2016, published data showed that socioeconomic inequalities in immunisation exist at an ecological level, and these inequalities increase as children get older (9). This work led to development of an annual report using NCCHD data to report the difference in uptake of routine childhood vaccinations by quintile of deprivation of Lower Super Output Area (LSOA) of residence (10). Although this report has shown a consistent gap in equity between children residing in the most and least deprived areas of Wales, there was limited information regarding specific factors associated with lower vaccination uptake.

Measuring deprivation at a geographical level through the use of indices, such as deprivation quintiles, can be useful for identifying areas to focus catch-up campaigns. The WHO's Health Equity Assessment Toolkit (HEAT) is an open access software that supports countries to analyse and report on health inequalities (11). This toolkit contains a variety of measures for high level comparisons of health outcomes across equity indicators and can be used to summarise inequalities in vaccination coverage. These summary measures are useful for comparing situations across time and place, however, this kind of analysis can be subject to ecological fallacy, and it is not possible to identify specific areas or populations that would benefit from improved accessibility or tailored information.

A broad literature search was conducted for peer-reviewed articles that looked at the association between vaccine uptake and social, economic or demographic determinants, published during the period 2000-20. Titles and abstracts were searched using the below terms. The search was optimised for each database (Scopus and PubMed).

((vaccin* OR immuni?ation) AND (inequalit* OR inequit* OR equalit* OR equit*)) OR ("low vaccination" OR "low immuni?ation" OR "low vaccine") OR ("suboptimal vaccination" OR "suboptimal immuni?ation" OR "suboptimal vaccine")

A total of 3 192 unique articles were returned (Figure 1.3). Articles were screened to exclude reviews, studies from less developed countries (2023 Human Development Index < 0.8), where vaccination was not provided for free or reimbursed through insurance, studies which looked at sub-populations i.e. pregnant women or those with a specific chronic disease, studies which looked at views on potential receipt of a vaccine if offered in the future, ecological studies or studies where the vaccination history was based on surveys using parent/patient recall only. These exclusion criteria were applied to identify studies that would supplement previously published reviews; Bocquier A *et al.* (childhood immunisations 2017) (12), Fisher H *et al.* (HPV 2013)

(13), de Casadevante VF *et al.* (HPV 2015) (14) and Jain A *et al.* (adult immunisations 2017) (15).

A total of 25 studies were identified (Table 1.1). A greater number of studies were published relating to childhood vaccinations, compared to adult vaccinations. A large number of studies in adults are completed using surveys which involve patient recall. Many countries have vaccination registers for children, but not necessarily adults. Additionally, studies that involve surveys for childhood vaccinations are often more robust as many countries distribute a vaccination record book or card to parents which can be checked to confirm vaccination history.

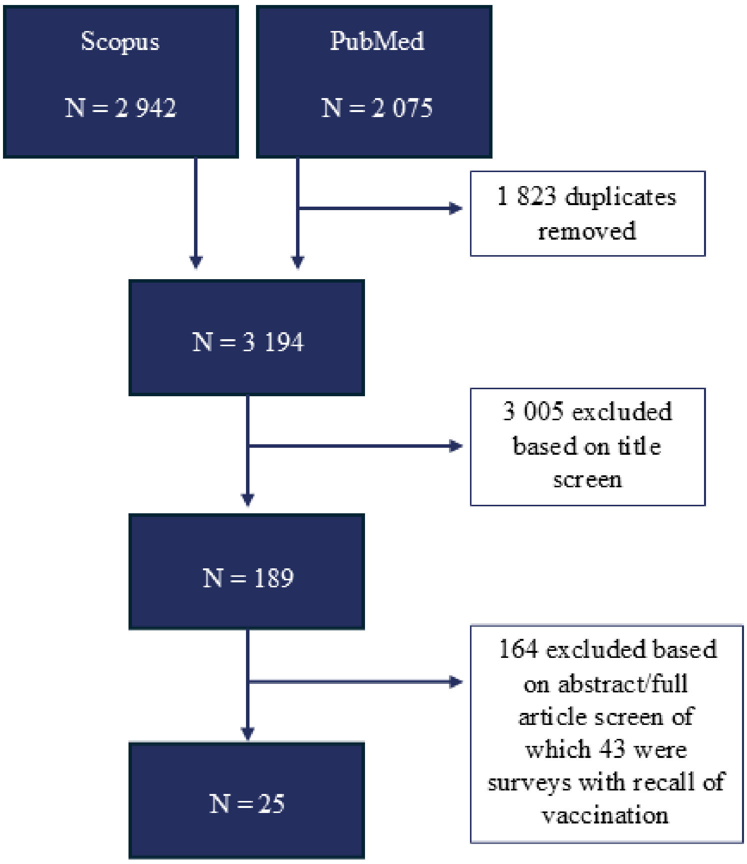


Figure 1.3. Article screening process for vaccine equity literature review.

Table 1.1. Summary of factors explored in vaccine equity studies published 2000-20 identified through a search of PubMed and Scopus literature databases.

First author	Year	Country	Population size	Age group (years)	Vaccine (s)	Social and/or demographic determinants explored	Factors associated with coverage
Baker D (16)	2011	UK (England)	20 203	0 to 2	Diphtheria-containing vaccine and MMR	Ethnic group Mothers age Single parent Parity	White ethnic groups lower coverage. Sub-analysis within ethnic groups: White ethnic individuals in larger families with younger mothers had lower coverage.
Bois C (17)	2013	France	1 227	3 to 4	BCG and Hepatitis B	Bilingual Parents' occupation Daycare attendance Active father Attended free check-up	Those who did not attend their free child health check-up had lower coverage for both vaccinations. BCG coverage lower if child did not attend daycare. Hepatitis B coverage lower if child bilingual.
Byrne L (18)	2018	UK (England)	459 074	1	Rotavirus	Ethnic group	Lower coverage in all ethnic groups compared to White British.
Gilbert NL (19)	2017	Canada	5 477	2	Various childhood vaccinations	COB Parents' income Parents' education Marital status	Lower coverage if; child born outside of Canada, lower parental income, lower education or unmarried.
Guthmann JP (20)	2014	France	710	0 to 5	Pneumococcal conjugate vaccine	Income Insurance type	Lower income associated with lower uptake of first dose.
Hawker J (21)	2007	UK (England)	83 487	2	MMR	Ethnic group	Asian ethnic group (excluding Chinese) had persistently higher coverage than White or Black ethnic groups over time.
Koller D (22)	2009	Germany	9 353	6	Up to date	Parents' mother tongue Daycare attendance	Lower coverage if parents' mother tongue is German or child did not attend daycare.
Morgenroth H (23)	2005	Germany	8 457	2 to 3	Up to date	Single parent Number of siblings Distance to practice Insurance type Parents' education	Lower coverage if parents not living together, more siblings, longer distance to practice, mother having high school education (MMR).
Müller S (24)	2012	New Zealand	161 230	1	Up to date	Ethnic group	Lower coverage in Maori and 'other' ethnic groups.

Table 1.1. continued. Summary of factors explored in vaccine equity studies published 2000-20 identified through a search of PubMed and Scopus literature databases.

First author	Year	Country	Population size	Age group (years)	Vaccine (s)	Social and/or demographic determinants explored	Factors associated with coverage
Sakou II (25)	2011	Greece	1 005	11 to 19	Up to date	Ethnic group Parents' education Marital status Rural/urban residence	Lower coverage if non-Greek or resident in a rural area.
Stein-Zamir C (26)	2019	Israel	3 098	2	Up to date	Ethnic group Birth weight Birth order Marital status Month of birth	Lower coverage if Ultra-Orthodox Jew, large number of siblings (>=4), born Jan- March compared to Oct-Dec.
Tiley KS (27)	2018	UK (England)	343 844	1 and 5	Diphtheria-containing vaccines	Ethnic group	Lower coverage in Polish ethnic group, and Black ethnic groups compared to White British.
van der Wal MF (28)	2001	Netherlands	83 217	2 to 12	Diphtheria-containing vaccine and MMR	Parents' COB Childs' COB Type of school attended	Mixed picture depending on COB of child. Lower coverage if attending anthroposophical school.
van der Wal MF (29)	2005	Netherlands	57 382	5 to 12	Diphtheria-containing vaccine and MMR	Parents' COB Childs' COB Type of school attended	Lower coverage if child born overseas or attends anthroposophical school.
Wagner KS (30)	2014	UK (England)	315 381	2 to 5	Diphtheria-containing vaccines	Ethnic group	Lower coverage in Polish ethnic group, unknown and minority ethnic groups compared to White British. Higher coverage in Indian and Bangladeshi ethnic groups.
Hansen BT (31)	2015	Norway	90 842 girls	12 to 13	HPV	Parents' age Marital status Parents' education Parents' income Parents' occupation Parents' COB Number of siblings Mothers cervical screening status MMR status	Mixed picture depending on COB of parent. Mothers cervical screening attendance and negative result associated with higher coverage. Lower coverage if older mother, higher education level of mother, lower income of mother or mother unemployed. Higher in girls who received previous MMR vaccine. Associations similar but not as strong when looking at fathers characteristics.
Lefevere E (32)	2015	Belgium	66 664 girls	12 to 15	HPV	Social benefits	Lower coverage in those who receive social benefits.

Table 1.1. continued. Summary of factors explored in vaccine equity studies published 2000-20 identified through a search of PubMed and Scopus literature databases.

First author	Year	Country	Population size	Age group (years)	Vaccine (s)	Social and/or demographic determinants explored	Factors associated with coverage
Poole T (33)	2012	New Zealand	8 665 girls	11 to 17	HPV	Ethnic group	Lower coverage in New Zealand Europeans and those with missing ethnic group.
Slåttelid Schreiber SM (34)	2015	Denmark	61 162 girls	12 to 13	HPV	Ethnic group Parents' education Parents' income Parents' occupation Marital status.	Lower coverage those born overseas or low education status and low income of mother, those with unmarried mothers.
Wang J (35)	2019	Sweden	689 676 girls	11 to 24	HPV	Parents' COB Parents' education Parents' income	Lower coverage if mother born outside Sweden has lower income or lower education level.
Anandappa M (36)	2018	USA	98 186	1 to 3	Influenza	Ethnic group Mothers age Parents' education Marital status Number of siblings Health insurance Parents' income	Lover coverage in smaller families, Hispanic ethnic groups, where parents' have lower education level.
Bielecki K (37)	2019	UK (Scotland)	922	5 to 12	Influenza	Ethnic group	Lower coverage in Polish ethnic group.
Stefanati A (38)	2018	Italy	All Municipality residents	65+	Influenza	Martial status Education Family size Employment 'foreigners' House ownership	Lower coverage if member of a larger family, married, unemployed, poor education. Differences in factors associated with coverage between males and females.
Jain A (39)	2018	UK (England)	18 669	70 and 79	Shingles	Ethnic group Immigration status Marital status Living alone Care home resident	Lower coverage in non-White ethnic groups, care home residents, those living alone.
Ward C (40)	2017	UK (England)	178 808	70+	Shingles	Ethnic group	Lower coverage in all ethnic groups compared to White British, apart from Indian, Bangladeshi and Mixed: Other.

A 2017 review by Bocquier *et al*. focused on specifics of socioeconomic determinants (income, education, employment) in association with uptake of childhood vaccinations in developed countries (12). Lower coverage among groups with lower socioeconomic status was a common theme, although in some populations no difference was observed. Specifically relating to MMR in the UK and Germany, lower coverage was seen in those with a higher income or education level (12). However, these studies were all conducted pre-2010 and there is limited up to date evidence relating to specific socioeconomic indicators. A previous meta-analysis showed little evidence of association of HPV vaccination coverage with income or education level (13), in contrast to a review looking at European studies only and articles published since where lower socioeconomic indicators have been associated with lower coverage (14,31,32,34,35). Lower income and education level has been associated with lower uptake of seasonal influenza vaccine in adults (15).

In the UK, data suggests variation in vaccination coverage by ethnic group in both children (14,16,21,27,30,37) and adults (39–41). Coverage has previously been seen to be lowest in Black ethnic groups or Polish ethnic groups (14,18,27,30,37,39,40). However, depending on vaccine, year of study and population, sometimes this finding is reversed (16,42). Coverage is often highest in South Asian ethnic groups (21,30,40,43). Many studies look at parents Country of Birth (COB), with coverage varying by country, and uptake generally lower in those born overseas compared to current country of residence (15,19,28,29,31,35).

Another important consideration is household size, especially in the context of avoiding outbreaks and ensuring there are not a large number of unvaccinated children residing in the same household. Children who have more siblings have been shown to have lower vaccination coverage in the UK, Germany, Norway and Denmark (16,23,31,44). There is also evidence that older adults living alone have lower vaccination coverage (15,39).

Other factors that may be predictors of vaccination uptake include religion, childcare usage, mothers age, marital status, parents' smoking status, type of school attended, rural/urban residence, comorbidities, amount of contact with health care providers, attendance at other medical appointments and receipt of previous vaccinations (13–17,19,22,23,25,26,28,29,31,34,36,38–40,45–48).

Vaccine hesitancy is only one reason individuals remain unvaccinated, with many complex social determinants contributing to uptake (49). An important component and first step of the WHO Tailoring Immunisation Programmes (TIP) framework is to identify groups or communities with suboptimal vaccination coverage so that programmes can be adjusted to meet the needs of everyone in society (50). Variation in findings highlights the need for ongoing monitoring and evaluation within countries.

Multivariable regression is a common approach for identifying factors that are associated with vaccine coverage (12–15). Odds ratios (ORs) are a commonly reported measure of association in this area of research for the purpose of comparing groups (51). The underlying reasons for an inequity may be complex and multivariable regression enables a number of different dimensions to be observed in the data. This is a preferable choice of methodology for this project, as it will be easily reproducible across vaccination programmes and can be adapted for use with a wide variety of statistical packages.

Further discussion of literature and methodology for assessing vaccine equity are presented in Chapter 2 and Chapter 4.

1.2 Vaccine effectiveness

Vaccine effectiveness (VE) studies following the implementation of a vaccine programme are important to inform policy and optimise resources. Local evidence can be useful to highlight the importance of vaccines as a public health intervention and increase confidence for both health professionals involved in vaccine delivery and the public. Randomised controlled trails prior to vaccine licensing are often restricted to healthy individuals and are not representative of how effective vaccines are in 'real life' settings. Results from these type of studies, measured under closely monitored scientific conditions, are reported as vaccine *efficacy*. Vaccine *effectiveness* is calculated in 'real life' settings following vaccine roll-out where individuals immune response may be more variable, and operational conditions may impact vaccine performance (52). There is the potential for waning of vaccine induced immunity over time, viruses are continuously evolving, and serotype replacement has been shown to be a concern, specifically in the case of pneumococcal vaccines. All these challenges highlight the need for ongoing VE studies, even when vaccine efficacy prior to licensure is well demonstrated.

Public health authorities in all four UK nations have contributed virological testing data to studies looking at mid-season and end of season influenza VE for a number of years (53,54). In addition, data from Wales has contributed to other UK studies looking at VE for other vaccinations (55–62). VE studies have occasionally been conducted in Wales during outbreak situations (63,64).

There are many methods for calculating effectiveness of vaccinations through observational studies. The choice of method often depends on data availability, completeness and quality, in addition to characteristics of the infection and how patients present. It is common for VE to be calculated opportunistically using attack rates (ARs) during outbreaks to enable prompt public health interventions. In these settings where exposure occurs over a relatively short period of time, the AR (proportion who become cases) in vaccinated individuals is compared to the AR in unvaccinated individuals to produce the Relative Risk (RR) (65,66).

$$VE = 1 - RR = 1 - \frac{Cases_{vaccinated} / Total_{vaccinated}}{Cases_{unvaccinated} / Total_{unvaccinated}}$$

Secondary Attack Rates (SARs) can also be calculated within household studies where the primary case is clearly defined to help eliminate bias in exposure between vaccinated and unvaccinated individuals (65,66). These types of cohort study, that take place in outbreak settings, tend to have smaller sample sizes and may not have significant power.

Although they are called ARs, these measures are a measure of risk, as rates must include a time element. Incidence rate ratios (IRRs) comparing incidence in unvaccinated and vaccinated groups are also a valid method in cohort studies for calculating VE where time exposed may vary between vaccinated and unvaccinated individuals (52).

$$VE = 1 - IRR = 1 - \frac{Cases_{vaccinated} / Person\text{-}time_{vaccinated}}{Cases_{unvaccinated} / Person\text{-}time_{unvaccinated}}$$

Case-control studies can be less resource intensive and can be more rapid to conduct than cohort studies. With the identification of a suitable control group, the odds of vaccination in cases can be compared to the odds of vaccination in controls to calculate VE (67,68)

$$VE = 1 - OR = 1 - \frac{Cases_{vaccinated} \text{ X } Controls_{unvaccinated}}{Cases_{unvaccinated} \text{ X } Controls_{vaccinated}}$$

The test negative design is common, where suspected cases which test negative are used as controls. This helps control for differences in health seeking behaviour between cases and controls. Similarly, the indirect cohort method uses cases that test positive for infection but against serotypes not included in the vaccine as controls, as is possible for pneumococcal and meningococcal disease (69).

Where it is only possible to obtain vaccination status for cases and not a suitable comparison group, estimates of vaccination coverage within the population from which the cases occurred can be used to calculate VE using the screening method (70). This is a crude but efficient way to calculate VE using the Proportion of Cases Vaccinated (PCV) and Proportion of Population Vaccinated (PPV).

$$VE = = 1 - \frac{PCV}{1 - PCV} \text{ X } \frac{1 - PPV}{PPV}$$

Randomisation in pre-licence vaccine efficacy trials reduce bias, which is challenging to account for when evaluating VE using post-licensure observational studies. The methods mentioned above can be adapted through the use of Generalised Linear Models (GLMs) or Poisson models for cohort studies, or logistic regression in case-control studies, to adjust for identified confounders (52,71).

For this project, survival analysis using Cox regression has been chosen to calculate Hazard Ratios (HRs) and in turn VE. Cox regression is a flexible method for following individuals over long time periods, incorporating time-varying exposures such as multiple vaccination states (52).

Further discussion of literature and methodology for assessing VE are presented in Chapter 3 and Chapter 5.

1.3 Epidemiology of COVID-19 in Wales prior to introduction of the vaccination programme

Although this project was initially scoped to focus on childhood immunisations, the project commenced in July 2020 after the first wave of the COVID-19 pandemic when the new vaccines against SARS-CoV-2 were imminent. Due to timeliness and importance of providing feedback on the vaccination programme to the service, as well as the value in producing rapid evidence to the wider scientific community, the scope of the project was amended. The scope would extend to developing methods that would be reproducible across the entire vaccination life course, by focusing on a vaccination given to older adults and a vaccination that is part of the routine childhood schedule.

The first case of SARS-CoV-2 was confirmed in Wales on 28th February 2020, in an individual who had recently returned from Italy (72). By 6th March 2020 COVID-19 was added to the list of legally notifiable conditions, and SARS-CoV-2 was added to the list of legally notifiable causative agents (73). This meant medical professionals/laboratories had the duty to notify the local public health body if they had suspicion of a case and/or confirmed organism from a human sample. However, availability and utilisation of testing varied considerably throughout the pandemic. The first restrictions on social movement ('lockdown') was announced on 23rd March 2020 in line with the rest of the UK and restrictions began to ease at the end of May (72). Between the 28th October and 9th November 2020 a second, shorter restriction on social movements was imposed (the Welsh 'firebreak') (72). The first COVID-19 vaccinations were given on 8th December 2020, the start of an ambitious programme to vaccinate the majority of the population in the face of changing circulating variants of SARS-CoV-2. Figure 1.4 shows the trends in SARS-CoV-2 testing and case numbers from the beginning of February 2020 to the end of July 2021, the timeline relevant for the work presented in Chapter 2 and Chapter 3 of this thesis.

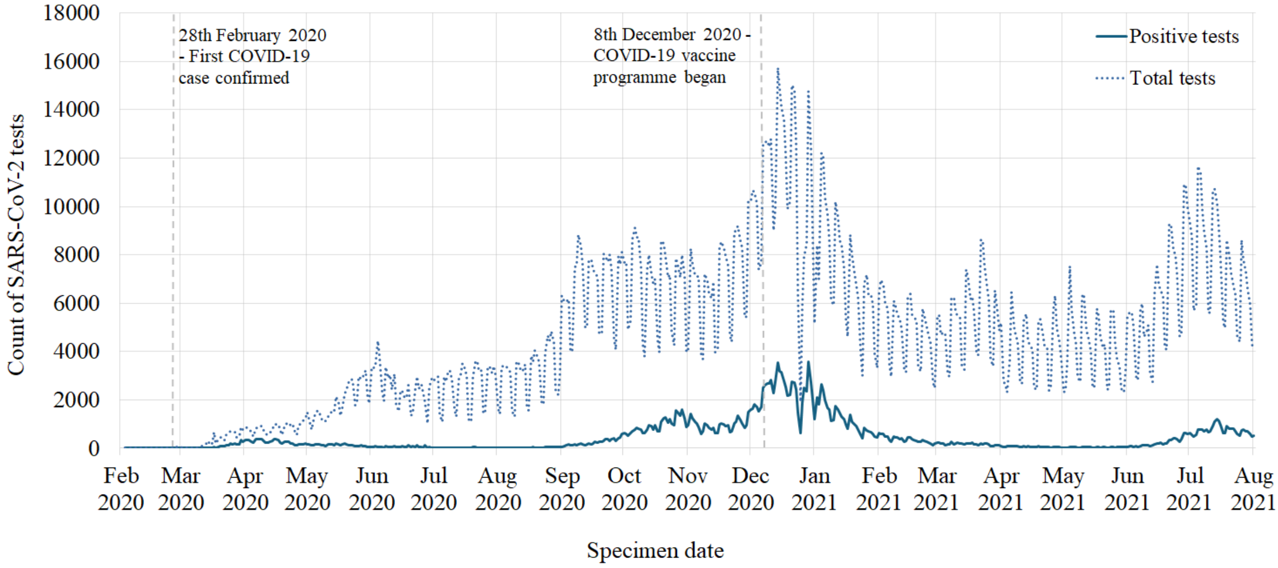


Figure 1.4. Number of tests (and number positive) for SARV-CoV-2 in Welsh residents 1st February 2020 to 31st July 2021, by specimen date. Data sourced from the Public Health Wales Rapid Surveillance Dashboard (74)**.**

1.4 Epidemiology of measles, mumps and rubella in Wales and the measles and rubella elimination programme

As Europe has committed to eliminating measles and rubella as part of the 2015-20 European Vaccine Action Plan, evaluation of the Measles, Mumps and Rubella (MMR) vaccine is particularly timely (75,76).

Measles has been a notifiable disease in the UK since 1940 (Figure 1.5). Vaccination has been available since 1968, however, uptake of the single antigen vaccine was poor and measles cases were frequently seen until the introduction of the MMR vaccine in 1988 (Figure 1.5) (77).

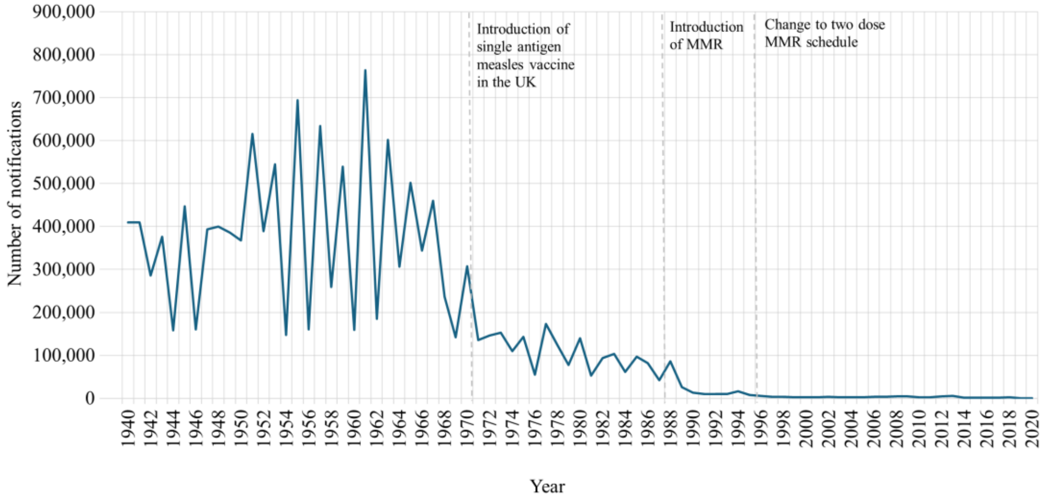


Figure 1.5. Number of notifications of measles in England and Wales 1940 - 2020. Data sourced from UK Health Security Agency (78)**.**

Although one dose of MMR provided fairly high levels of individual protection, population immunity was not sufficient to eliminate measles. The one dose MMR schedule was changed to a two dose schedule in 1996 with the first dose offered at 13 months of age and the second dose at three years and four months of age, as part of the routine UK childhood vaccination schedule. Uptake of both doses of MMR in Wales is generally high, although there are fluctuations over time and regions (Figure 1.6). In 1998 a since debunked article was published, associating the MMR vaccine with autism. This, and the extensive media coverage around it, led to a decline in uptake over the following six years. A national catch-up campaign and a change in policy to ensure children's vaccination status is checked up-on school entry was introduced in 2005 (79). Despite improvements in coverage, a large measles outbreak occurred in Wales in 2013 (Figure 1.7). Since 2013 there have been a number of small, localised measles outbreaks following importation of cases (Figure 1.7) (80–82).

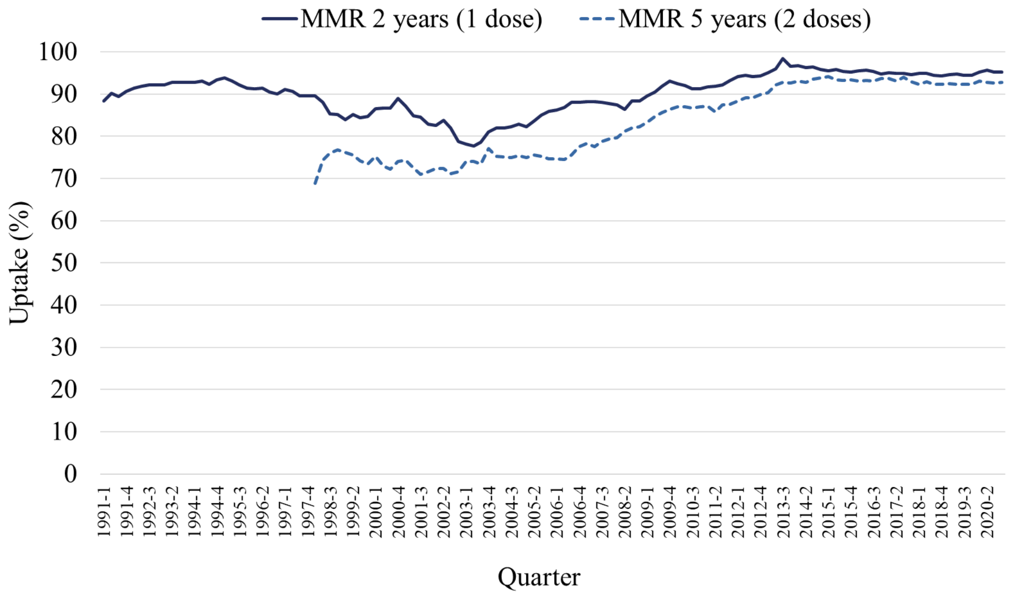


Figure 1.6. Uptake of MMR vaccination 1991-2020, Wales, UK. Data sourced from Public Health Wales COVER reports (6)**.**

Measles is a highly infectious disease and 95% coverage of two doses is recommended to prevent endemic transmission and reduce the chance of outbreaks. This is a key target for the elimination of measles, and rubella (76). There have been no rubella cases in Wales since 2005 (Figure 1.7) and rubella has been considered eliminated in the UK since 2015 (83). Although measles cases have remained low in Wales since the 2013 outbreak, elimination status is assigned at the UK level and endemic measles transmission was considered re-established in 2018 following two years of elimination (83).

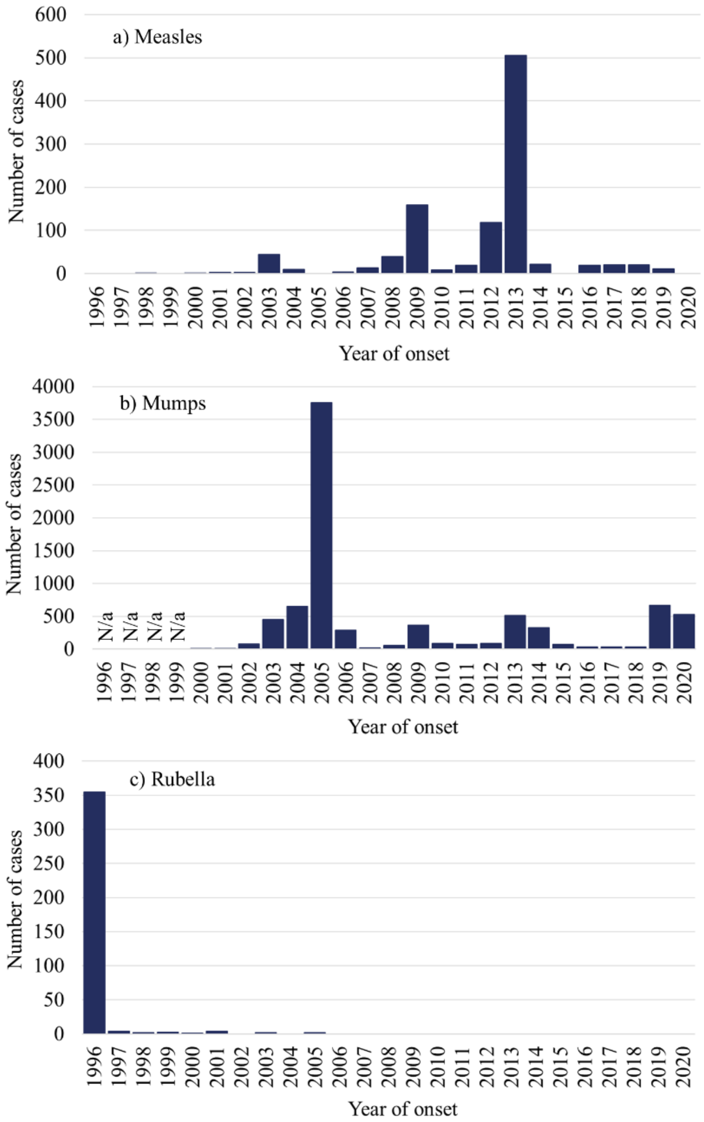


Figure 1.7. Number of measles (a), mumps (b) and rubella (c) laboratory confirmations 1996 – 2020, Wales, UK. Data sourced from Public Health Wales (82). Testing data for mumps available from 2000.

1.5 Data linkage and the Secure Anonymised Information Linkage (SAIL) Databank

National population registries have become an established and increasingly important tool to successfully evaluate vaccine programmes in many countries (84,85). Data linkage has often been used to evaluate effectiveness of vaccination programmes as it is possible to link vaccination registries to disease surveillance systems (86–95). Data linkage has also been used to look at vaccine equity in a small number of studies from the UK, Belgium, Norway, Sweden, Denmark and Israel (26,31,32,34,35,39), although as mentioned above, most published insight still comes from resource intensive surveys or ecological correlations.

Trusted Research Environments (TREs) have become increasingly useful as a research tool and provide a safe and ethical environment for public health researchers to link administrative datasets, including Electronic Health Records (EHRs) (96). The need for rapid information during the COVID-19 pandemic and enhanced collaboration between public health agencies and academic institutions expanded the use of TREs. The Administrative Data Research UK partnership of TREs have over 100 projects listed on their website, covering themes ranging from 'health and wellbeing' to 'crime and justice' (97).

In a climate of limited funding, demonstrating the impact of vaccination programmes through the use of routinely collected data can support decision making to achieve the best outcomes for the population. It can provide data to inform more detailed economic analysis and modelling with methods that are transferable to other vaccination programmes and health interventions. In terms of vaccine equity, linking a large number of individual level datasets has the benefit of including a number of independent variables which can be adjusted for in multivariable analysis. Any potential confounders can also be used to adjust for bias in observational VE studies.

There is the unique opportunity in Wales to perform robust vaccine programme evaluation and contribute to the global evidence base through use of the SAIL Databank. The SAIL Databank is a remote access TRE hosted by Swansea University that enables linkage of a number of anonymised datasets (98). Datasets are linked using a unique Anonymised Linkage Field (ALF) which is allocated to records on importation of data into the TRE (99). The ALF is assigned along with a status code which indicates the linkage confidence (Figure 1.8). Individuals registered with a GP in Wales (or elsewhere in the UK) will have a unique NHS number, although this number is not necessarily recorded in all datasets. For the purpose of this project any records with a status code of 35 (low confidence match) or 99 (no match) were excluded.

Many of the datasets within the SAIL Databank are national health and social care data that cover the whole population of Wales, enabling research to take place that would otherwise be resource intensive (100). A complete list of available datasets is listed on the SAIL website and researchers are able to apply to access those relevant to their research question (101). It is also possible to request project specific datasets to be imported and passed through the anonymisation process ready for linkage. All applications are reviewed by an Information Governance Review Panel (IGRP) for approval to ensure projects are appropriate and will benefit the health of the public (102).

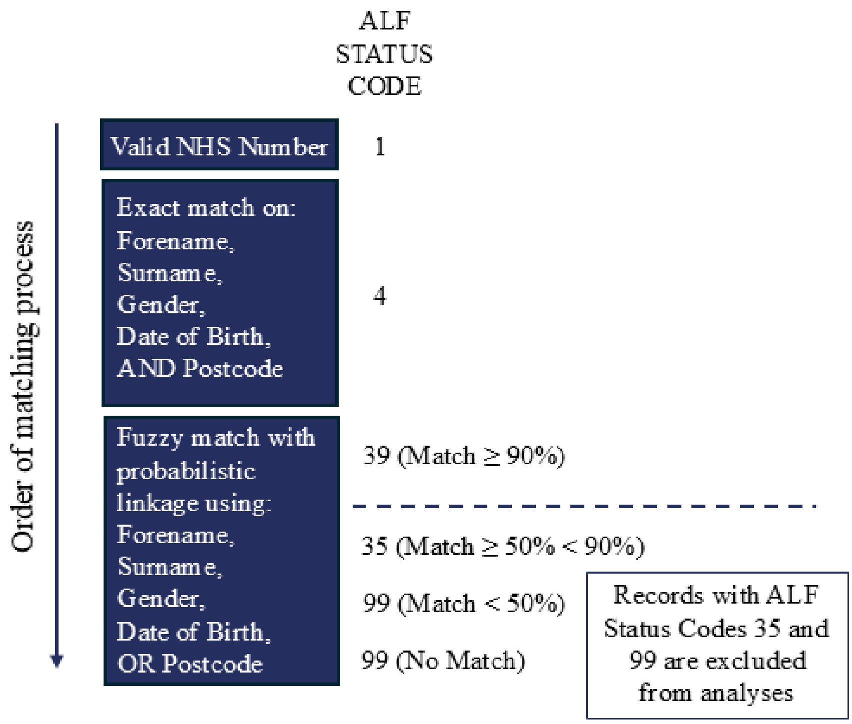


Figure 1.8. Diagram illustrating the process for assigning the Anonymised Linkage Field (ALF) status code within the Secure Anonymised Information Linkage (SAIL) Databank. (Original figure cc by Malorie Perry)

1.6 Data availability

When scoping this project, the full list of available SAIL Databank datasets was reviewed to identify those which could contribute to the aim of evaluating vaccination equity and/or effectiveness in Wales. Table 1.2 summarizes the datasets identified and provides the shortened naming convention that is used throughout this thesis. Specific methods are detailed in the chapters below and details of key variables can be found in Appendix 1.

Measles and mumps laboratory testing data are not available in SAIL Databank. Measles and mumps testing is primarily carried out by the UK Health Security Agency (UKHSA) reference laboratory on behalf of PHW. Results are reported directly to the

Wales Health Protection Team (HPT) for case management and are not entered into local laboratory data systems. Extracts of laboratory testing data are sent in an Excel file to PHW VPDP surveillance team on a quarterly basis using a Secure File Share Portal. Measles testing data back to 2008 were reconciled with local measles Polymerase Chain Reaction (PCR) test results, from the Wales Specialist Virology Centre in Cardiff. PCR testing for measles has been available in Wales since the 2013 outbreak. Following data cleansing and validation of details, measles and mumps test results, in addition to untested mumps notification records, between 2008 and 2020 were imported in to SAIL Databank as a project specific dataset. Records were deemed suitable for importation if they had one of; i) a valid NHS number, ii) Forename, Surname and Date of Birth, or iii) Forename, Surname and Postcode. Overall, 99.1% (940/949) of confirmed measles cases (Table 1.3.), 98.5% (2818/2862) of confirmed mumps cases (Table 1.4.) and 89.0% (5015/5637) notified but untested mumps cases (Table 1.5.) were imported.

Table 1.2. Datasets identified as suitable for analysis of vaccination equity and/or effectiveness within the Secure Anonymised Information Linkage (SAIL) Databank.

Reference	Dataset name	Coverage[a]	Description
ADBE	Annual District Birth Extract	100%	Office for National Statistics data for all registered births in Wales residents.
CDDS	COVID-19 Consolidated Deaths	100%	Details of deaths in Wales residents attributed to COVID-19. A consolidation of records from the Master Patient Index, the ONS Annual District Death Extract (ADDE) and the WDSD.
CENW	ONS 2011 Census Wales	100%	Responses for all residents who took part in the 2011 Census.
CVSP	Central register of COVID-19 Shielding Persons	100%	List of individuals advised to shield during the COVID-19 pandemic due to increased clinical risk.
CVVD	COVID-19 Vaccination Dataset	100%	Data from the Welsh Immunisation System, population vaccine register that was developed at the start of the pandemic. Contains details of COVID-19 vaccinations given to all Wales residents who are registered for NHS care.
EDUW	Education Wales Schools and Pupils Dataset	100%	Data on state funded learning centres and their pupils from the annual Census of schools in Wales.
NCCH	National Community Child Health Database	100%	Record of vaccinations given from birth up to 16 years of age in those who were/are resident in Wales, or resident outside Wales but treated in. Compiled from CYPrIS this dataset is also a source of maternal demographic information.
PATD	COVID-19 Test Results	100%	Details of all laboratory tests for SARS-CoV-2 carried out in Wales.
PEDW	Patient Episode Dataset for Wales	100%	National hospital admissions dataset for Wales.
WDSD	Welsh Demographic Service Dataset	100%	Address and GP registration history for all those who have been registered for NHS care in Wales since 1990.
WLGP	Welsh Longitudinal General Practice Dataset	84%	Event data extracted from GP systems across Wales. All consultation activity is recorded using Read Code Version 2.

[a] Geographical coverage. There may be 'hidden populations' who do not engage with health services. These individuals may not appear in any, or limited, administrative datasets.

Table 1.3. Count of records in the project specific dataset for importation into the Secure Anonymised Information Linkage (SAIL) Databank, with comparison to published figures; measles confirmations 2008-20, Wales, UK.[a]

Year of onset	Published figures (n)	Records in clean dataset (n)	Records with identifiers (n)
2008	39	43	42
2009	159	157	157
2010	8	4	4
2011	19	18	18
2012	118	122	114
2013	506	505	505
2014	22	18	18
2015	0	0	0
2016	19	22	22
2017	21	23	23
2018	20	23	23
2019	13	14	14
2020	0	0	0
Total	944	949	940

[a] Records with identifiers includes records with either i) a valid NHS number, ii) Forename, Surname and Date of Birth, or iii) Forename, Surname and Postcode.

Table 1.4. Count of records in the project specific dataset for importation into the Secure Anonymised Information Linkage (SAIL) Databank, with comparison to published figures; mumps confirmations 2008-20, Wales, UK.[a]

Year of onset	Published figures (n)	Records in clean dataset (n)	Records with identifiers (n)
2008	55	57	48
2009	363	359	342
2010	85	60	55
2011	75	76	74
2012	88	90	79
2013	513	484	484
2014	326	362	362
2015	71	79	79
2016	34	37	37
2017	34	36	36
2018	30	29	29
2019	665	665	665
2020	531	528	528
Total	2 870	2 862	2 818

[a] Records with identifiers includes records with either i) a valid NHS number, ii) Forename, Surname and Date of Birth, or iii) Forename, Surname and Postcode.

Table 1.5. Count of records in the project specific dataset for importation into the Secure Anonymised Information Linkage (SAIL) Databank, with comparison to published figures; mumps notifications (cases notified but not tested) 2008-20, Wales, UK.[a]

Year of onset	Records in clean dataset (n)	Records with identifiers (n)
2008	143	70
2009	613	355
2010	358	235
2011	333	245
2012	311	231
2013	343	343
2014	507	507
2015	202	202
2016	173	173
2017	221	221
2018	205	205
2019	1 364	1 364
2020	864	864
Total	5 637	5 015

[a] Records with identifiers includes records with either i) a valid NHS number, ii) Forename, Surname and Date of Birth, or iii) Forename, Surname and Postcode.

1.5 Ethics

All analyses were conducted within the SAIL Databank secure research environment as part of IGRP approved project numbers 1549 and 0899 (101,102). Accredited Researcher Status was provided by ONS (Accredited Researcher number 33928) (103). Importation of the project specific measles and mumps dataset followed a Data Protection Impact Assessment (DPIA) and signing of the SAIL Tripartite Agreement for dataset importation.

1.6 Aim

Through linkage of routine administrative data, this research project aims to develop methods for two areas of vaccine programme evaluation that are not currently established in Wales.

i) Identification of factors associated with low or inequitable vaccination coverage in both younger and older populations to assess vaccine equity and help guide discussions around tailoring of immunisation programmes.

ii) Development of national cohorts for both younger and older individuals to enable production of robust VE estimates for measles, mumps and COVID-19.

Through four distinct investigations, this project aims to contribute valuable information to the scientific evidence base. Through my role as Senior Epidemiologist within the VPDP at PHW, there is the opportunity to feed information directly back to the NHS, national expert groups and wider stakeholders to help guide interventions to improve vaccination uptake.

The remainder of this thesis is as follows:

Chapter 2 describes the development of a cohort of adults eligible for COVID-19 vaccination in the first four months of the vaccination campaign, which began in December 2020. Due to the need to produce rapid evidence for this new, emergency vaccination programme, this early analysis showed how coverage varied by a limited number of key characteristics; sex, LHB of residence, rural/urban classification, deprivation quintile and ethnic group. Using multivariable logistic regression, this element of vaccine programme evaluation aimed to highlight the areas of improvement needed to reduce vaccine inequity and was the first known use of Census data for such analysis.

Using this same cohort of individuals, Chapter 3 provides early estimates of VE for the BNT162b2 and ChAdOx1 COVID-19 vaccines through the use of Cox regression models.

Chapter 4 describes the development of a cohort of four to 25 year olds, to assess factors associated with uptake of measles-containing vaccines. Expanding on the rapid analysis for COVID-19, a larger number of determinants applicable to childhood vaccinations were explored, including a separate analysis for recorded vaccine refusal.

Chapter 5 applies methodology developed in Chapter 3 to the cohort of children and young adults to evaluate long-term VE for measles and mumps-containing vaccines. Figure 1.9 illustrates how Chapters 2 to 5 are inter-linked.

Finally, in Chapter 6 the findings are brought together. A brief update of COVID-19 literature is provided, given the time elapsed since peer-reviewed publication of the work presented in Chapter 2 and Chapter 3 of this thesis. The strengths and limitations of data linkage for evaluating vaccine programmes are summarised alongside the potential public health impact of this project and a number of recommendations to be considered by organisations looking to expand their expertise in this field.

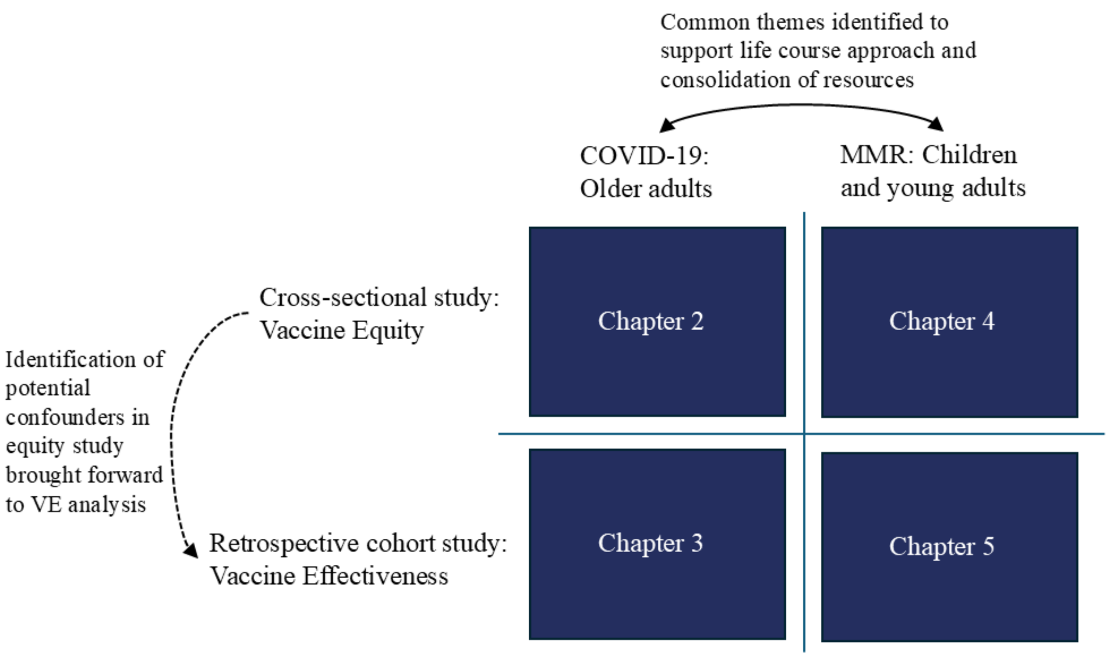


Figure 1.9. Diagram illustrating how chapters of the thesis are inter-linked. (Original figure cc by Malorie Perry)

Chapter 2 - Inequalities in coverage of COVID-19 vaccination: A population register based cross-sectional study in Wales, UK

The material in this chapter formed the basis for the following publication, with additional information provided here for clarity, and to allow for additional results to be included:

Perry M, Akbari A, Cottrell S, Gravenor MB, Roberts R, Lyons RA, Bedston S, Torabi F, Griffiths L. Inequalities in coverage of COVID-19 vaccination: A population register based cross-sectional study in Wales, UK. Vaccine. 2021;39(42):6256-6261. doi: 10.1016/j.vaccine.2021.09.019.

2.0 Abstract

The COVID-19 pandemic has highlighted existing health inequalities for ethnic minority groups and those living in more socioeconomically deprived areas in the UK. With higher levels of severe outcomes in these groups, equitable vaccination coverage should be prioritised. The aim of this study was to identify inequalities in coverage of COVID-19 vaccination in Wales, UK and to highlight areas which may benefit from routine enhanced surveillance and targeted interventions. Records within the WIS population register were linked to the Welsh Demographic Service Dataset (WDSD) and central list of shielding patients, held within the SAIL Databank. Ethnic group was derived from the ONS 2011 Census (CENW) and over 20 administrative EHR data sources. Uptake of first dose of any COVID-19 vaccine was analysed over time, with the odds of being vaccinated as at 25th April 2021 by sex, LHB of residence, rural/urban classification, deprivation quintile and ethnic group presented. Using logistic regression models, analyses were adjusted for age group, care home resident status, health and social care worker status and shielding status. This study included 1 256 412 individuals aged 50 years and over. Vaccine coverage increased steadily from 8th December 2020 until mid-April 2021. Overall uptake of the first dose of COVID-19 vaccine in this group was 92.1%. After adjustment the odds of being vaccinated were lower for individuals who were male, resident in the most deprived areas, resident in an urban area and an ethnic group other than White. The largest inequality was seen between ethnic groups, with the odds of being vaccinated 0.22 (95 %CI 0.21–0.24) if in any Black ethnic group compared to any White ethnic group. Ongoing monitoring of inequity in uptake of vaccinations is required, with better targeted interventions and engagement with deprived and ethnic communities to improve vaccination uptake.

2.1 Introduction

As at 14th May 2021 the COVID-19 pandemic has led to 3 339 002 deaths worldwide with a total of 160 813 869 confirmed cases and an unmeasurable impact on people's wellbeing (104). A number of licenced vaccines are providing hope for all that the pandemic may come to an end, and livelihoods can return to a sense of normality. The WHO Europe Health 2020 policy framework highlighted reducing health inequity both between and within countries, including equitable access to vaccinations, as a priority (105). Equitable access to vaccination is of particular importance given more severe outcomes from COVID-19 disease has been seen in Black and Asian ethnic groups and individual's resident in more deprived areas (106–108).

Wales is a nation of the UK with a population of approximately 3.1 million and devolved responsibility for the NHS, which provides free health care to the population. As at 6th May 2021 there had been a total of 211 827 confirmed COVID-19 cases and 5 552 related deaths in Wales (74). The COVID-19 vaccination programme in Wales started on 8th December 2020 and followed the JCVI guidance on groups to prioritise (109). Those at highest risk of severe outcomes or at occupational risk were vaccinated first, this included older adults in care homes, front-line health and social care staff, adults aged 80 years and older, and those at increased clinical risk. Vaccinations were then rolled out to the adult general population in decreasing age order. NHS services in Wales, including access to vaccinations, are provided by seven LHBs, which cover different geographical regions. Each LHB led its own roll-out of the COVID-19 mass vaccination programme, with central provision of vaccines and oversight from a multi-organisation COVID-19 Vaccination Board (CVB) chaired by Welsh Government. A national, patient level vaccination register, the WIS, was developed by Digital Health Care Wales (DHCW) working alongside delivery and surveillance stakeholders. The WIS vaccination register was built on experiences and infrastructure of the pre-existing CYPrIS system. WIS primary functions include: scheduling vaccination clinics, providing patient invitations by written letter and SMS text, recall of patients to missed appointments, and providing a national repository of timely vaccination data. The denominator spine of WIS is a national list of those registered for NHS care in Wales (WDSD). Within WIS there is the ability to manually add those not previously registered for NHS care. To identify those who were a priority for vaccination due to clinical or occupational risks, WIS denominator data were supplemented with additional information from general practices, the national shielded patient list and health and social care employers. Invitation letters generated using WIS were posted to individuals with the date and time of their appointment at a local MVC, general practice or community pharmacy. Individuals were encouraged to contact a telephone helpline to rearrange their appointment if they could not attend. Appointments for the second dose were scheduled at the nationally recommended interval after administration of the first dose.

Pfizer-BioNTech BNT162b2 vaccine was the first to be offered. Due to the logistics of handling the refrigeration requirements for this vaccine, the main method of delivery for the early part of the programme was via MVCs with many front-line health and social care workers amongst the first to be vaccinated. Vaccination coverage in care home residents and older adults increased rapidly throughout January as the Oxford- AstraZeneca ChAdOx1 vaccine became available, which due to better stability at 2–8°C was more suited to smaller vaccination clinics in a wider number of settings. Moderna mRNA-1273 COVID-19 vaccine was supplied for use in Wales from 7th April 2021 in one LHB. As at 15th April 2021 a first dose of COVID-19 vaccination had been offered to all individuals aged 50 years and older.

The PHW VPDP provide daily updates on vaccination uptake through the PHW rapid COVID-19 surveillance dashboard (74). This includes a monthly report, showing breakdown of uptake by sex, social deprivation quintile and ethnic group, with data suggesting inequity in vaccine uptake exists within the country. However, the interaction between these factors has not been explored. There are a number of published studies looking at factors associated with low vaccination uptake in both children and adults (12,15,41,46,48). However, large studies covering whole populations are limited (34,110,111). The majority of studies in adults focus on influenza vaccination, with low uptake associated with socioeconomic status, ethnicity, sex, rural/urban residence, income, educational status, household size, living alone, co-morbidities, alcohol consumption and smoking status (15,41,46,48).

Reasons for not being vaccinated can be numerous and complex, related to access barriers and challenges in attending appointments, awareness of reliable information and health literacy, vaccine hesitancy or anti-vaccine views (112). Prior to the COVID-19 vaccine roll-out, hesitancy had been identified as a potential challenge amongst Black and Pakistani ethnic groups, and also in those with lower levels of education attainment in the UK (113). In the US, acceptance was lower in females, younger adults, Black/African Americans and those without a college degree (114). It is important to recognise that equitable access acknowledges that some population groups will need special consideration, such as tailored method of invitation and access to suitable vaccination venues.

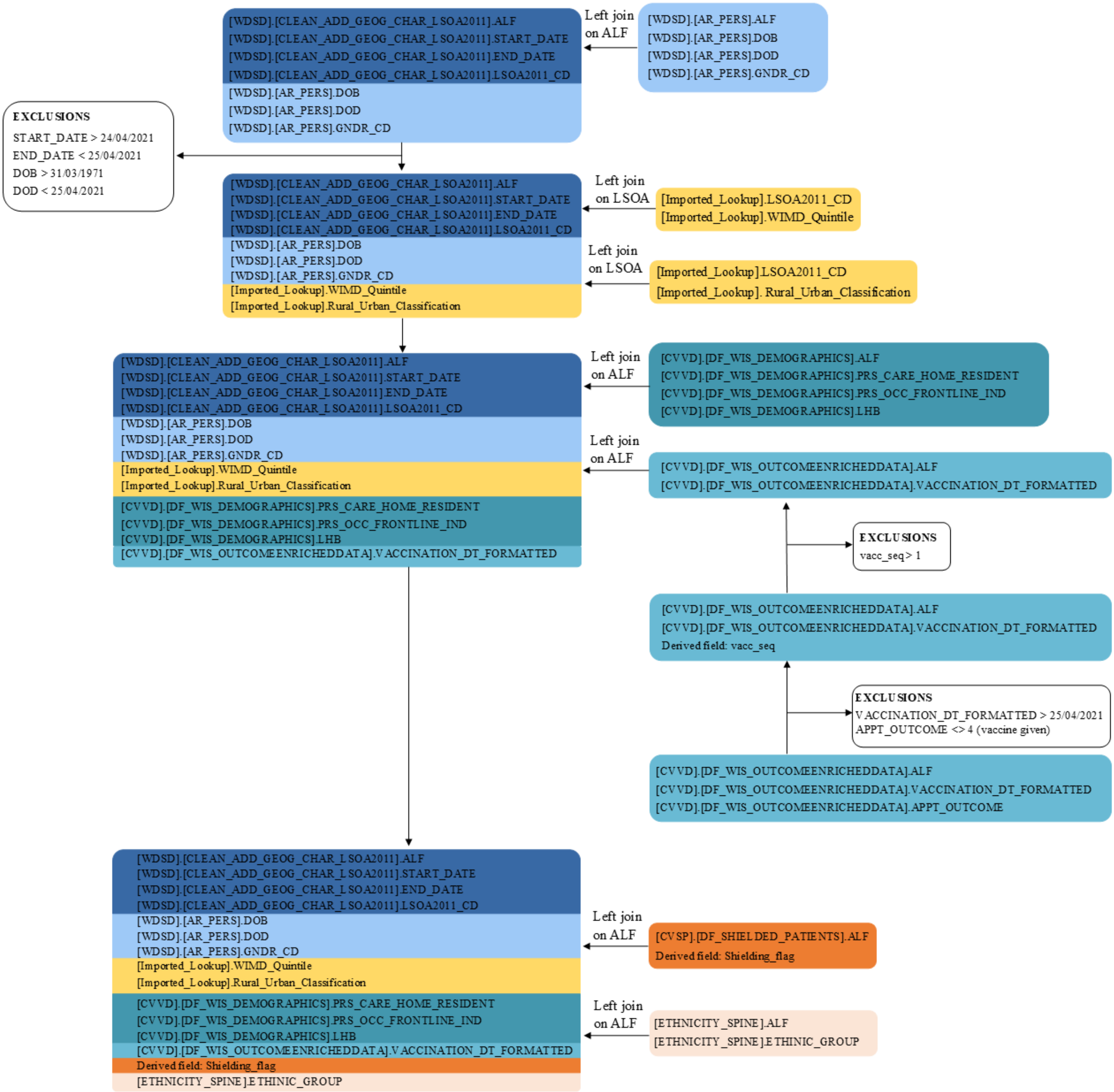
The aim of this study was to look at the equality of coverage of COVID-19 vaccination in Wales over the first five months of the mass vaccination programme, and to highlight inequalities which may benefit from routine enhanced surveillance and targeted interventions.

2.2 Methods

All analyses were completed via the SAIL Databank, hosted by Swansea University, as part of the Con-COV project (115). All individuals aged 50 years and over as at 31st March 2021 alive, resident and registered for NHS care in Wales as at 25th April 2021 were included. Uptake of first dose of (any) COVID-19 vaccine type was analysed and is presented by sex, LHB of residence, rural/urban classification, deprivation quintile and ethnic group. Additional characteristics including: age group, care home resident status, health and social care worker status and shielding status were added as covariates to allow adjustment for differing characteristics of those prioritised in the vaccine roll-out. Odds of being vaccinated with at least one dose of COVID-19 vaccine as at 25th April 2021 was estimated using univariable and multivariable logistic regression.

Sex and LSOA of residence were obtained from the WDSD (which is based on individuals registered for NHS care in Wales) and includes address history, date of birth and date of death. Date of vaccination, LHB of residence, care home resident status and health and social care worker status were taken from the WIS data, as at 25th April 2021. WIS contains information on vaccination status, vaccination dates, vaccination priority/risk group information and limited demographic information based on all WDSD registered individuals. The use of WIS, the national person level vaccine registry, ensures that analyses are representative of the population of Wales. There will be small numbers of Welsh residents who are not registered with the NHS, including unregistered recent migrants, those whose residency status changes frequently, and those experiencing homelessness. However, outreach services are actively offering vaccination services to groups where possible, including manually registering unregistered individual with WIS and the wider NHS.

Figure 2.1. Diagram illustrating linkage of SAIL datasets as described in Chapter 2: Inequalities in coverage of COVID-19 vaccination.



LSOA of residence for an individual's most recent recorded address was linked to the Welsh Index of Multiple Deprivation (WIMD) 2019 estimated deprivation scores (116). Deprivation scores at ecological (LSOA) level were then ranked and divided into quintiles to categorise the most (group 1) and least deprived (group 5) LSOA areas. Rural/urban location of residence was assigned by joining LSOA to the 2011 Census rural/urban classification data provided by the Office for National Statistics (ONS) (117). Shielding status, was sourced from the national list of individuals for whom additional social restrictions were recommended at the start of the COVID-19 pandemic due to high clinical risk, based on clinician assessment and general practice records, a copy of which is held in SAIL (CVSP). A standardised set of ethnicity groups were used based on harmonised ethnicity data from 20 EHR data sources across primary and secondary care, as well as administrative and specialist services data sources available in the SAIL Databank, and CENW into a standard set of categories (118). The process for linking the different datasets in this analysis is shown in Figure 2.1. Analyses were carried out using R version 4.0.4.

2.3 Results

The study population included 1 256 412 individuals aged 50 years and over. Overall uptake of the first dose of COVID-19 vaccine was 92.1% as at 25th April 2021. Coverage in this age group increased steadily across age deciles until around the 10th April 2021 when it began to plateau (Figure 2.2). As at 25th April 2021 the largest inequality in coverage was seen by ethnic group, with a gap of 20.2 percentage points between those in any White ethnic group and those in any Black ethnic group, a gap of 9.1 percentage points between those in any White ethnic group and those in any Asian ethnic group, and gap of 11.6 percentage points between those in any White ethnic group and those with a Mixed ethnic background (Table 2.1). Significant differences were seen across all characteristics, with gaps of 4.3, 4.3, 2.7 and 0.6 percentage points when comparing the most and least deprived quintile, LHB of residence with highest and lowest coverage, sex and rural/urban classification respectively.

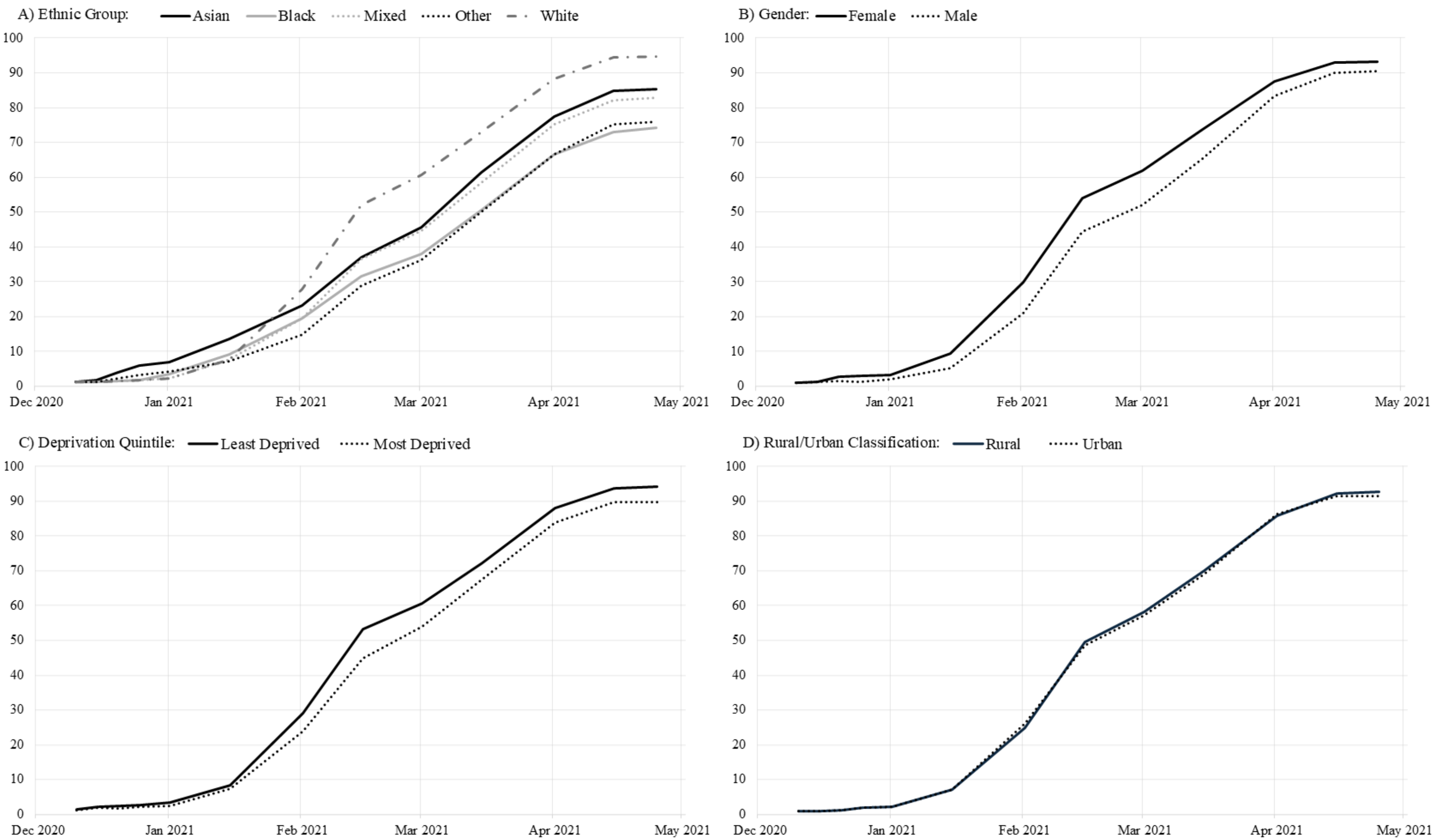


Figure 2.2. Cumulative uptake of one dose of COVID-19 vaccine (any type) by ethnic group, sex, rural/urban residence classification and social quintile of deprivation 2020–21, Wales, UK. Data sourced from the all Wales Immunisation System (WIS) in SAIL within the COVID Vaccination Data (CVVD) as at 25th April 2021. To define the most and least deprived areas of Wales small area geography Lower Super Output Area (LSOA) of residence were ranked by Welsh Index of Multiple Deprivation (WIMD) score and the populations divided into quintiles.

Table 2.1. Uptake of one dose of COVID-19 vaccine (any type) and odds of being vaccinated, Wales, UK; 25th April 2021.[a, b, c]

Characteristic	Category	Population (n)	Uptake (%)	Univariable			Multivariable		
				OR	95% CI	P-value	aOR	95% CI	P-value
Ethnicity	White	1 134 610	94.1						
	Black	3 954	73.9	0.18	(0.17-0.19)	<0.01	0.22	(0.21-0.24)	<0.01
	Asian	14 001	85.0	0.36	(0.34-0.37)	<0.01	0.41	(0.39-0.43)	<0.01
	Mixed	7 657	82.5	0.30	(0.28-0.32)	<0.01	0.36	(0.34-0.38)	<0.01
	Other	2 815	75.6	0.20	(0.18-0.21)	<0.01	0.24	(0.22-0.27)	<0.01
	Unknown	93 348	72.0	0.16	(0.16-0.17)	<0.01	0.20	(0.19-0.20)	<0.01
Health Board	HB 1	236 013	93.1						
	HB 2	291 589	91.1	0.75	(0.74-0.77)	<0.01	0.66	(0.65-0.68)	<0.01
	HB 3	170 399	91.0	0.75	(0.73-0.77)	<0.01	0.81	(0.79-0.83)	<0.01
	HB 4	176 381	93.5	1.06	(1.04-1.09)	<0.01	1.03	(1.01-1.06)	0.01
	HB 5	167 622	92.7	0.93	(0.91-0.96)	<0.01	0.80	(0.78-0.82)	<0.01
	HB 6	59 962	89.3	0.61	(0.59-0.63)	<0.01	0.52	(0.50-0.54)	<0.01
	HB 7	154 419	92.7	0.94	(0.92-0.96)	<0.01	0.86	(0.84-0.88)	<0.01
Sex	Male	605 751	90.8						
	Female	650 632	93.4	1.45	(1.43-1.47)	<0.01	1.18	(1.16-1.19)	<0.01
Location Classification	Rural	434 525	92.5						
	Urban	821 860	91.9	0.92	(0.90-0.93)	<0.01	0.86	(0.84-0.87)	<0.01
Deprivation Quintile	Least deprived	276 237	94.0						
	4	273 049	92.5	0.78	(0.76-0.80)	<0.01	0.81	(0.79-0.83)	<0.01
	3	257 936	92.1	0.74	(0.72-0.75)	<0.01	0.78	(0.76-0.79)	<0.01
	2	239 753	91.8	0.72	(0.70-0.73)	<0.01	0.71	(0.70-0.73)	<0.01
	Most deprived	209 410	89.7	0.55	(0.54-0.56)	<0.01	0.59	(0.57-0.60)	<0.01

[a] Data sourced from the all Wales Immunisation System (WIS) as at 25th April 2021.
[b] Multivariable regression model estimates adjusted for ethnic group, health board, sex, rural/urban classification, deprivation quintile of residence, age group, health and social care worker status, care home resident status, shielding status.
[c] To assign deprivation quintile, small area geography Lower Super Output Area (LSOA) of residence were ranked by Welsh Index of Multiple Deprivation (WIMD) score and the populations divided in to quintiles.

The gap in coverage observed between ethnic groups widened over the first five months of the programme as additional priority groups became eligible (Figure 2.2). However, the sex gap has narrowed compared to 12.2 percentage points as at 5th February 2021.

After adjusting for age group, health and social care worker status, care home resident status and shielding status the odds of being vaccinated were lower if from a Black (0.22 95% CI 0.21–0.24), Asian (0.41 95% CI 0.39–0.43), Mixed ethnic background (0.36 95% CI 0.34–0.38) or Other (0.24 95% CI 0.22–0.27) ethnic group compared to the aggregated White ethnic group and also, if resident in the most deprived quintile compared to the least deprived quintile (0.59 95% CI 0.57–0.60) (Table 2.1). The odds of being vaccinated also varied by LHB of residence. The odds of being vaccinated were lower if resident in an urban area compared to a rural area (0.86 95% CI 0.84–0.87).

2.4 Discussion

Coverage of the first dose in the population aged 50 years and older is high and suggests that at a population level, new vaccinations against COVID-19 have been positively received. However, as with other vaccinations focused at older adults, a number of significant social inequities in coverage are evident. Despite adjusting for age, care home resident status, occupation and shielding status, adults (over 50 years) in Wales are, so far, less likely to be vaccinated if they live in a more deprived area or belong to an ethnic group other than White. Given the media attention, levels of disease and mortality in older adult age-groups, and the disruption the COVID-19 pandemic has caused to livelihoods, the overall high uptake in the population may be unsurprising. This study shows that, on the whole, for those aged 50 years and over, gaps in coverage do not appear to be reducing with time, with a risk of increasing the disproportionate impact of the pandemic on these populations during future waves (119). Many administrative health datasets have large amounts of missing data on ethnicity, with coding completeness in primary care records <50% in England (118,120). To our knowledge this is the first study to include Census linkage to look at vaccine coverage, enabling a population-scale analysis of inequalities.

It cannot be assumed that these results are generalizable to other nations, but they highlight the importance of ensuring surveillance is in place to make sure no one is left behind in terms of access to health care and being able to make accurately informed decisions. Limitations of this study mainly relate to misclassification of data. Information may be entered incorrectly into WIS and appearing on the shielding list relies on the accurate recording of clinical risk factors in general practice records. Data completeness was generally good, although small numbers of individuals did not have sex information available (n<5) and, although it was possible to attain ethnic group information for the majority of the study population, it was unknown for 7.4% of individuals. Vaccination uptake in the population with unknown ethnic group is low and this is a group that needs further investigation. Sociodemographic data in this study are at an ecological level rather than individual level, while this demonstrates inequality according to the overall status of a small area of residence (mean LSOA population size of 1 500), it may be prone to ecological fallacy at individual level. Ethnic grouping used in this study is broad and further work is needed to look into minority groups where coverage could be comparatively low, but it is not apparent when looking at the data aggregated in this way.

Existing interventions to minimise inequalities include active invitation by letter, phone or text for all those on the WIS database, and engagement with underserved communities. Due to the stepwise roll-out of the vaccination programme to incremental risk groups, it will be important to track the gap in coverage for specific age and risk groups, which may show a differed pattern of widening or narrowing inequality over time.

This study identifies inequality in coverage and further targeted work is required to ascertain whether the root-causes may be inequities in service provision or other factors. Geographical clustering of risk groups are potential hotspots for virus transmission and can be identified in linked databases and prioritised in targeted intervention. It is important not to assume that inequalities in coverage are due to differing levels of vaccine hesitancy and further analysis of opt out/decliner information would help determine whether this is the case in Wales, as has been shown elsewhere (113,114,121,122).

Additional factors such as access to vaccination clinics for the elderly who live alone need to be explored (15). The use of a population register alongside data linkage enables representative analysis of vaccination inequalities in the population who have registered for health care. Consideration also needs to be taken to identify minority groups such as asylum seekers, refugees, the homeless and travelling population who may face barriers in accessing health care or registering with services which would ensure they are invited for vaccination (123–125).

This analysis highlights the need for ongoing monitoring of inequity in uptake of vaccinations. In addition to existing interventions to mitigate inequalities, further engagement should be undertaken with those in ethnic minority groups and in more socially deprived areas, including the development of tailored vaccination approaches to minimise observed inequities in vaccination coverage to prevent severe outcomes from COVID-19, utilising available resources (126). Closing the vaccination equity gap before further waves of infection occur should be a priority.

Chapter 3 - COVID-19 vaccine uptake and effectiveness in adults aged 50 years and older in Wales UK: a 1.2m population data linkage cohort approach

The material in this chapter formed the basis for the following publication, with additional information provided here for clarity, and to allow for additional results to be included:

Perry M, Gravenor MB, Cottrell S, Bedston S, Roberts R, Williams C, Salmon J, Lyons J, Akbari A, Lyons RA, Torabi F, Griffiths LJ. COVID-19 vaccine uptake and effectiveness in adults aged 50 years and older in Wales UK: a 1.2m population data linkage cohort approach. Hum Vaccin Immunother. 2022;18(1):2031774. doi: 10.1080/21645515.2022.2031774.

3.0 Abstract

Vaccination programs against COVID-19 vary globally with estimates of VE affected by vaccine type, schedule, strain, outcome, and recipient characteristics. This study assessed VE of BNT162b2 and ChAdOx1 vaccines against PCR positive SARS-CoV-2 infection, hospital admission, and death among adults aged 50 years and older in Wales, UK during the period 7th December 2020 to 18th July 2021, when Alpha, followed by Delta, were the predominant variants. Individual level linked routinely collected data within the SAIL Databank was used. Data were available for 1 262 689 adults aged 50 years and over; coverage of one dose of any COVID-19 vaccine in this population was 92.6%, with coverage of two doses 90.4%. VE against PCR positive infection at 28 days or more post first dose of any COVID-19 vaccine was 16.0% (95% CI 9.6–22.0), and 42.0% (95% CI 36.5– 47.1) seven or more days after a second dose. VE against hospital admission was higher at 72.9% (95% CI 63.6–79.8) 28 days or more post vaccination with one dose of any vaccine type, and 84.9% (95% CI 78.2–89.5) at seven or more days post two doses. VE for one dose against death was estimated to be 80.9% (95% CI 72.1–86.9). VE against PCR positive infection and hospital admission was higher for BNT162b2 compared to ChAdOx1. In conclusion, vaccine uptake has been high among adults in Wales and VE estimates are encouraging, with two doses providing considerable protection against severe outcomes. Continued roll-out of the vaccination programme within Wales, and globally, is crucial in our fight against COVID-19.

3.1 Introduction

As of July 2021, almost every country has introduced a vaccination programme against COVID-19, with variations in coverage (104). There are a number of authorized vaccines available with further candidates in development, with consideration for changing SARS-CoV-2 variants and potential booster doses required (127). Early data suggest good effectiveness of the available vaccines against the current circulating variants (128–136). The COVID-19 vaccination program in Wales began on 8th December 2020, at a time when the second wave of the pandemic was reaching its peak locally. Individuals were invited for vaccination through the NHS Wales electronic vaccination register (WIS), in a phased approach according to the priority groups advised by the JCVI (109). The Pfizer-BioNTech (BNT162b2) vaccination was available first and was the sole vaccine used throughout December 2020, being mainly distributed through MVCs, due to the cold-chain and handling requirements of the vaccine at the time, and the limitations these posed for remote vaccination. The Oxford- AstraZeneca (ChAdOx1) vaccine was used from 4th January 2021 in a variety of settings, including care homes, general practices and (later) community pharmacies, which contributed to rapid increases in coverage among the elderly population including care home residents. The Moderna mRNA-1273 vaccine has been used in a limited way, mainly in one of seven LHB areas, since 7th April 2021. All three of these vaccinations follow a two dose schedule, which from January 2021 used a dose interval of 8 to 12 weeks.

The COVID-19 vaccination program has received high levels of acceptance in the Welsh population. As of 18th July 2021, routine surveillance reported that 85.6% of the population aged 18 years and older had received one dose of any COVID-19 vaccine and 72.8% had received two doses (74). Coverage in those aged 50 years of age and older was 93.6% and 91.6% for one and two doses, respectively. As of 18th July 2021, there had been cumulatively 232 672 PCR confirmed episodes in Wales with 5 589 associated deaths. The Alpha variant of SARS-CoV-2 was dominant in Wales from December 2020 to end of May 2021, accounting for over 98% of all genomically confirmed and probable cases (n = 12 848) (74). Onset of circulation of the Delta variant of SARS-CoV-2 in Wales was first detected in late April 2021 and became the dominant virus type by the beginning of June.

Independently reviewed estimates of VE have been published from a relatively small number of large post-implementation studies in Israel, Qatar, Canada, England, and Scotland, assessing effectiveness of different vaccines against a range of outcomes and taking different approaches to analysis (128,130–133). Large population based studies are important in strengthening the evidence for ongoing vaccination programmes and building capacity for ongoing monitoring of ‘real-world’ COVID-19 VE in different populations. The aim of this study was to provide estimates of VE of BNT162b2 and ChAdOx1 against PCR positive SARS-CoV-2 infection, hospital admission due to SARS-CoV-2 infection and death amongst adults aged 50 years and older in Wales.

3.2 Methods

Analyses were carried out using individual level linked routinely collected national-scale data available in the SAIL Databank, hosted by Swansea University (98–100). The study population was all individuals aged 50 years and over, alive and resident in Wales as at 7th December 2020 and part of the SAIL Databank Con-COV e-cohort (115). The population was identified on the basis of those registered for NHS care in Wales on the WDSD within SAIL, which includes information on LSOA small geography of residence, date of birth, and sex. As care homes are prone to outbreaks and residents are subject to ongoing frequent virology testing in Wales, those identified as living at a residential care home address were excluded from this analysis to limit bias. Healthcare workers were included in the study population, but occupational status was controlled for. Although this population may be at increased risk of COVID-19 due to increased exposure, they are a fairly large cohort to exclude (n = 75 324), and level of risk may differ within this group and be challenging to define. Other occupational groups may be at comparable risk of infection to healthcare workers and may also be subject to increased testing (137). Vaccination date and vaccine type were recorded in the COVID-19 Vaccination Data (CVVD) data, which originates from the WIS population vaccination register for COVID-19. A second dose was considered valid when given at least 21 days after the first, doses with shorter time intervals were discarded and there was no upper exclusion limit to this interval.

The study population was described, and the odds of being vaccinated based on a number of characteristics, as at 18th July 2021 was calculated using univariable logistic regression. Using a retrospective cohort study design, HRs were calculated using an extended Cox regression model with vaccination status introduced as a time varying covariate. VE was calculated based on the HR, with VE = 1-HR. The baseline for all estimates is the unvaccinated population. Individuals entered the study at time zero (7th December 2020) and moved through categories based on the time since vaccination in 7-day intervals. In this design, individuals contribute unvaccinated time until the end of the observation period or point they are vaccinated. Individuals were censored if they moved out of Wales, died, reached the end of follow-up (18th July 2021) or had the outcome of interest. VE was assessed against three outcomes: i) PCR positive infection, defined as any PCR positive SARS-CoV-2 test recorded in the Pathology COVID-19 Daily data (PATD) allowing for 90 days between episodes for those with potential repeat infection ii) Hospital admission due to SARS-CoV-2 infection, defined as any hospital admission recorded in the Patient Episode Dataset for Wales (PEDW) where the individual had a PCR positive test in the 28 days prior to admission, on the day of admission or the day after admission and COVID-19 was listed as the primary cause for admission, and iii) Death with COVID-19 recorded as an underlying cause on the death certificate, where the individual had a PCR positive SARS-CoV-2 test in the 28 days prior.

The unadjusted Cox regression models included vaccination status and variables associated with priority status, and therefore when someone would have had the opportunity to be vaccinated: age as at 31st March 2021 as a restricted cubic spline, individual identified as clinically extremely vulnerable (CEV) based on shielding list status and health and care worker status (138). In the fully adjusted model, a number of additional variables were included: any previous PCR positive SARS-CoV-2 test prior to the cohort start date, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, LHB of residence, sex, ethnic group, deprivation quintile (a measure for deprivation for small areas in Wales), and rural/urban location of residence (139). Adjustment was also made for previous vaccination against shingles, previous vaccination against pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales. As part of a sensitivity analysis, VE was also calculated with models that included inverse propensity score weighting (IPW) (140). All variables included in the adjusted model were included in the calculation of propensity score to be vaccinated with at least one dose of COVID-19 vaccine.

LHB of residence, identification of care home residents (based on address) and health and care worker status (based on provision of occupational records from employing organizations) were as recorded in the CVVD. Level of deprivation was assigned at ecological level by linking LSOA of residence to the WIMD 2019, LSOA's were then ranked according to overall WIMD score and divided into quintiles (116). Rural/urban location was assigned by linking LSOA of residence to the 2011 Census rural/urban classification data provided by the ONS (117). Shielding status for individuals was sourced from CVSP who were advised to isolate due to high clinical risk. Adjustment for important comorbidities was done using the QCOVID algorithm, which predicts the risk of being admitted to hospital or dying from COVID-19 in adults (139,141). Ethnicity data were sourced from 20 EHR and administrative data sources, including CENW, and collated into the five minority ethnic categories (White, Asian, Black, Mixed, and Other) (142).

Previous vaccination history, for pneumococcal disease, shingles, and influenza vaccination was assessed using Read coded primary care events data as part of the Wales Longitudinal General Practice (WLGP) dataset and included in the model as separate binary variables (Appendix 2). WLGP includes data from ~80% of practices in Wales and was also used to determine the number of days with a GP consultation recorded in the year prior to the pandemic as a proxy for GP visits. These adjustments were made to account for differences in healthcare seeking behaviour between the vaccinated and unvaccinated individuals. Where data were missing an unknown category was assigned.

SARS-CoV-2 PCR test data were taken from PATD which were obtained from PHW Datastore and include all test data from NHS hospital laboratories (mainly hospital samples, with some community and other settings) and COVID-19 Lighthouse Laboratories (mainly community samples, with some other non-hospital settings). Hospital admissions were identified using PEDW where the primary cause for admission was recorded as COVID-19 (coded as ICD-10 U07.1 or U07.2) and linked to PATD to identify individuals who had a positive PCR test within the defined time period. The earliest of hospital admission date and positive PCR test sample date was used as the end point for follow-up as this will be the closest to when the individual was first infected. COVID-19 related deaths were identified using the Consolidated Death Data Source (CDDS) held in SAIL (a consolidation of records from the Master Patient Index, the ONS Annual District Death Extract (ADDE) and the WDSD sources of all mortality records), linked to PATD.

Due to small numbers, estimates against death are presented for effectiveness of any COVID-19 vaccine type, whilst VE of one and two doses of vaccine against PCR confirmed infection and admission due to SARS-CoV-2 infection is additionally stratified by vaccine type. All analysis were carried out using R version 4.0.4.

3.3 Results

There were 1 262 689 adults aged 50 years and over eligible for inclusion in the study, after excluding care home residents (n = 16 062) and individuals who had a vaccination other than BNT162b2 or ChAdOx1 (n = 5 406) or a mixed vaccine course (n = 551). As at 18th July 2021, coverage of one dose of any COVID-19 vaccine in the study population was 92.6%, with coverage of two doses 90.4%. Over the course of the follow-up period 29.0% (n = 331 064) of those who received two doses, had received BNT162b2 and 71.0% (n = 810 771) had received ChAdOx1. In total, 36.8% (n = 464 455) were aged 70 years or over (Table 3.1). Over half (51.5%, n = 650 835) were female, with the odds of being vaccinated with a full two dose course 1.40 (95% CI 1.38–1.42) times higher compared to males (Table 3.1). Coverage varied by LHB of residence, and coverage of a full two dose course was lowest in the most deprived areas (87.2%) compared to the least deprived areas (92.9%) and urban areas (92.4%) compared to rural areas (93.0%) (Table 3.1). The odds of being vaccinated with a complete two dose course for a person in a Black ethnic group was 0.21 (95% CI 0.20–0.23) compared to those in a White ethnic group (Table 3.1).

Health and care workers (n = 75 324), and those on the list of individuals advised to shield due to increased clinical risk from COVID-19 (n = 94 531), were also more likely to be vaccinated (Table 3.1).

Table 3.1. Summary of the study population used in the estimation of BNT162b2 and ChAdOx1 vaccine effectiveness and odds of being vaccinated based on select characteristics, Wales, UK.

Characteristic	Category	Population (n)	Dose 1			Dose 2		
			Uptake (%)	OR	(95% CI)	Uptake (%)	OR	(95% CI)
Age group as at 31st March 2021	50-54	211 469	88.7			85.4		
	55-59	220 582	90.9	1.26	(1.24 - 1.29)	88.4	1.30	(1.28 - 1.32)
	60-64	194 705	92.5	1.58	(1.55 - 1.62)	90.6	1.64	(1.61 - 1.67)
	65-69	171 478	94.1	2.04	(1.99 - 2.09)	92.6	2.12	(2.08 - 2.17)
	70-74	175 223	95.3	2.60	(2.54 - 2.67)	94.1	2.73	(2.67 - 2.80)
	75-79	126 797	95.6	2.75	(2.67 - 2.83)	94.0	2.66	(2.59 - 2.73)
	80+	162 435	93.5	1.84	(1.80 - 1.89)	90.5	1.63	(1.60 - 1.67)
Gender	Male	611 854	91.2			88.9		
	Female	650 835	94.0	1.51	(1.49 - 1.53)	91.8	1.40	(1.38 - 1.42)
Ethnic group	White	1 139 248	94.5			92.3		
	Mixed	7 719	84.1	0.31	(0.29 - 0.33)	79.9	0.33	(0.31 - 0.35)
	Asian	14 253	87.3	0.40	(0.38 - 0.42)	83.4	0.42	(0.40 - 0.44)
	Black	4 027	76.8	0.19	(0.18 - 0.21)	72.1	0.21	(0.20 - 0.23)
	Other	2 893	77.4	0.20	(0.18 - 0.22)	73.3	0.23	(0.21 - 0.25)
	Unknown	94 549	73.2	0.16	(0.16 - 0.16)	70.5	0.20	(0.20 - 0.20)
Health Board of residence	HB 1	237 535	93.6			91.7		
	HB 2	293 949	92.4	0.83	(0.82 - 0.85)	90.0	0.82	(0.80 - 0.83)
	HB 3	172 261	91.3	0.72	(0.70 - 0.73)	89.2	0.75	(0.73 - 0.77)
	HB 4	178 376	93.8	1.05	(1.02 - 1.07)	91.4	0.97	(0.95 - 0.99)
	HB 5	164 316	92.7	0.88	(0.86 - 0.90)	90.4	0.85	(0.83 - 0.87)
	HB 6	60 640	90.1	0.63	(0.61 - 0.65)	88.5	0.70	(0.68 - 0.72)
	HB 7	155 612	92.8	0.88	(0.86 - 0.90)	90.4	0.85	(0.84 - 0.87)

Table 3.1. continued. Summary of the study population used in the estimation of BNT162b2 and ChAdOx1 vaccine effectiveness and odds of being vaccinated based on select characteristics, Wales, UK.

Characteristic	Category	Population (n)	Dose 1			Dose 2		
			Uptake (%)	OR	(95% CI)	Uptake (%)	OR	(95% CI)
Deprivation quintile	Most deprived	210 774						
	Quintile 2	240 295	92.3	1.28	(1.25 - 1.31)	89.7	1.28	(1.26 - 1.30)
	Quintile 3	258 405	92.5	1.33	(1.30 - 1.35)	90.4	1.38	(1.35 - 1.40)
	Quintile 4	274 767	93.0	1.43	(1.40 - 1.46)	91.1	1.51	(1.48 - 1.54)
	Least deprived	278 448	94.5	1.85	(1.81 - 1.89)	92.9	1.92	(1.89 - 1.96)
Residence classification	Rural	436 106	93.0			91.0		
	Urban	826 583	92.4	0.91	(0.90 - 0.93)	90.1	0.90	(0.89 - 0.91)
Health or care worker	No	1 187 365	92.3			90.0		
	Yes	75 324	98.5	5.41	(5.11 - 5.74)	97.3	3.98	(3.81 - 4.16)
Advised to shield due to high clinical risk	No	1168158	92.4			90.2		
	Yes	94531	96.0	1.99	(1.93 - 2.06)	92.9	1.42	(1.39 - 1.46)
Q-COVID co-morbidity score	0	453 060	90.7			88.8		
	1	413 964	92.8	1.31	(1.29 - 1.33)	90.7	1.23	(1.21 - 1.25)
	2	205 667	94.7	1.82	(1.78 - 1.86)	92.2	1.50	(1.47 - 1.52)
	3	102 322	95.1	1.98	(1.92 - 2.04)	92.4	1.54	(1.50 - 1.58)
	4	48 780	95.0	1.96	(1.88 - 2.04)	92.1	1.46	(1.41 - 1.51)
	5+	38 896	94.1	1.63	(1.56 - 1.70)	90.0	1.13	(1.09 - 1.17)
Record of herpes zoster vaccination	No	856 895	92.1			89.7		
	Yes	179 724	98.3	4.88	(4.70 - 5.06)	96.9	3.61	(3.51 - 3.71)
	Unknown	226 070	90.1	0.77	(0.76 - 0.79)	87.8	0.83	(0.81 - 0.84)
Record of pneumococcal vaccination as an adult	No	641 351	90.7			88.3		
	Yes	402 221	97.2	3.52	(3.45 - 3.59)	95.3	2.72	(2.67 - 2.76)
	Unknown	219 117	90.0	0.92	(0.90 - 0.93)	87.8	0.95	(0.94 - 0.97)

Table 3.1. continued. Summary of the study population used in the estimation of BNT162b2 and ChAdOx1 vaccine effectiveness and odds of being vaccinated based on select characteristics, Wales, UK.

Characteristic	Category	Population (n)	Dose 1			Dose 2		
			Uptake (%)	OR	(95% CI)	Uptake (%)	OR	(95% CI)
Record of influenza vaccination during the 2019-20 season	No	576 854	89.4			86.8		
	Yes	460 341	98.0	5.67	(5.54 - 5.79)	96.3	3.95	(3.88 - 4.01)
	Unknown	225 494	90.1	1.07	(1.06 - 1.09)	87.8	1.10	(1.09 - 1.12)
Number of COVID-19 PCR tests prior to cohort start	0	1 069 650	92.3			90.2		
	1	129 927	95.7	1.86	(1.81 - 1.91)	93.2	1.49	(1.45 - 1.52)
	2-4	43 397	92.9	1.10	(1.06 - 1.15)	89.0	0.88	(0.85 - 0.91)
	5-9	7 608	87.7	0.60	(0.56 - 0.64)	81.4	0.47	(0.45 - 0.50)
	10-14	4 297	92.6	1.05	(0.94 - 1.18)	89.2	0.90	(0.82 - 0.99)
	15-19	4 894	96.0	2.03	(1.76 - 2.34)	93.8	1.64	(1.46 - 1.84)
	20+	2 916	96.4	2.22	(1.83 - 2.70)	94.3	1.80	(1.54 - 2.11)
Positive COVID-19 PCR test prior to cohort start	No	1 235 911	92.6			90.4		
	Yes	26 778	94.5	1.37	(1.30 - 1.45)	91.7	1.18	(1.13 - 1.23)
Number of recorded days with a GP consultation 1st February 2019 to 31st January 2020	0	59 896	72.7			69.9		
	1	40 777	82.2	1.73	(1.68 - 1.79)	79.8	1.70	(1.65 - 1.75)
	2-4	83 928	89.2	3.10	(3.01 - 3.19)	86.9	2.87	(2.79 - 2.94)
	5-9	95 087	93.1	5.09	(4.93 - 5.25)	91.0	4.34	(4.22 - 4.47)
	10-19	228 908	95.2	7.39	(7.20 - 7.59)	93.2	5.91	(5.77 - 6.05)
	20-49	460 116	96.3	9.83	(9.60 - 10.06)	94.2	7.05	(6.90 - 7.20)
	50-99	72 583	94.9	6.95	(6.70 - 7.22)	91.4	4.56	(4.42 - 4.71)
	100-149	3 414	92.5	4.62	(4.06 - 5.26)	86.8	2.84	(2.57 - 3.15)
	150+	225	88.0	2.76	(1.84 - 4.13)	82.2	1.99	(1.41 - 2.81)
	Unknown	217 755	90.1	3.43	(3.35 - 3.51)	88.0	3.14	(3.08 - 3.21)

Additionally, those who had a record of receiving a herpes zoster, pneumococcal or seasonal influenza vaccine in the 2019-20 season were more likely to be fully vaccinated as at 18th July 2021 than those who did not, as were those with a higher QCOVID score (Table 3.1). Overall, those who consulted their GP more frequently in the year prior to the pandemic were more likely to be vaccinated compared to those who did not. Fifteen percent (n = 193 039) of the study cohort had at least one SARS-CoV-2 PCR test prior to the cohort start date on 7th December 2020 and overall, the more SARS-CoV-2 PCR tests individuals had the more likely they were vaccinated with two doses of vaccine (Table 3.1). Of these, 26 778 (2.1%) individuals had a positive result prior to the cohort start date. Those with previous PCR confirmed infection, were more likely to be fully vaccinated (OR 1.18, 95% CI 1.13–1.23) (Table 3.1).

Over the course of follow-up, 7th December 2020 to 18th July 2021, there were 38 163 individuals with SARS-CoV -2 PCR positive tests in the study population, 9 876 of which were in those aged 70 years and over (36.3 events per 1000 person years follow-up) and 28 287 in those aged 50 to 69 years (60.8 events per 1000 person years follow-up) (Table 3.2, Table 3.3). Adjusted estimates showed significant VE against SARS-CoV-2 PCR positive infection at 28 days or more post first dose of any COVID-19 vaccine to be 16.0% (95% CI 9.6–22.0) with effectiveness seven or more days after a second dose 42.0% (95% CI 36.5–47.1) (Table 3.2). VE was higher in those aged 70 years and over (66.0%, 95% CI 57.8–72.6) compared to those aged 50 to 69 years (38.4%, 95% CI 31.8–44.4) (Figure 3.1, Table 3.3). A difference was also seen by vaccine type with VE for those who received two doses of BNT162b2 higher than those who received ChAdOx1, 50.1% (95% CI 44.0–55.5) vs. 24.9% (95% CI 15.4–33.3) (Figure 3.1, Table 3.3).

VE against hospital admission was higher at 72.9% (95% CI 63.6–79.8) 28 days post vaccination with one dose of any vaccine type and 84.9% (95% CI 78.2–89.5) at seven or more days post two doses (Table 3.2). Estimates after two doses were lower in those aged 70 years and over (80.6% 95% CI 65.6–89.1) compared to those aged 50 to 69 years (88.4% 95% CI 80.9– 93.0) (Figure 3.2, Table 3.4). VE in those who received two doses of BNT162b2 (88.2% 95% CI 80.6–92.8) was higher compared to ChAdOx1 (81.4% 95% CI 71.5–87.9) (Figure 3.2, Table 3.4). Neither difference was statistically significant.

Table 3.2. Cox regression estimates of outcomes from COVID-19 infection following vaccination with BNT162b2 or ChAdOx1 in those aged 50 years and over, Wales, UK.[a, b]

Outcome	Category	Individuals (n)	Person years	Events	Events per 1000 Person Years	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)
PCR positive infection	Unvaccinated	1 253 665	284 477.9	32 192	113.2	-	-
	0-6 days post dose 1	1 130 966	18 571.2	596	32.1	0.80 (0.74 - 0.87)	0.75 (0.69 - 0.81)
	7-13 days post dose 1	1 129 786	21 639.2	811	37.5	1.15 (1.07 - 1.24)	1.07 (0.99 - 1.15)
	14-20 days post dose 1	1 128 169	21 610.3	530	24.5	0.96 (0.88 - 1.06)	0.88 (0.81 - 0.97)
	21-27 days post dose 1	1 126 833	21 571.2	326	15.1	0.76 (0.67 - 0.85)	0.69 (0.61 - 0.77)
	>27 days post dose 1	1 123 892	128 657.6	1 135	8.8	0.95 (0.88 - 1.02)	0.84 (0.78 - 0.90)
	0-6 days post dose 2	1 100 268	18 056.3	144	8.0	0.90 (0.76 - 1.07)	0.81 (0.68 - 0.96)
	>6 days post dose 2	1 097 663	222 928.2	2 429	10.9	0.68 (0.62 - 0.75)	0.58 (0.53 - 0.64)
Hospital admission with PCR positive infection	Unvaccinated	1 253 665	289 765.6	3 213	11.1	-	-
	0-6 days post dose 1	1 157 469	19 009.6	54	2.8	0.47 (0.36-0.63)	0.45 (0.34-0.59)
	7-13 days post dose 1	1 156 803	22 163.1	71	3.2	0.64 (0.50-0.82)	0.60 (0.46-0.77)
	14-20 days post dose 1	1 155 880	22 145.2	46	2.1	0.50 (0.37-0.68)	0.46 (0.34-0.63)
	21-27 days post dose 1	1 154 968	22 112.0	25	1.1	0.33 (0.22-0.50)	0.30 (0.20-0.45)
	>27 days post dose 1	1 152 177	132 097.5	68	0.5	0.32 (0.24 -0.42)	0.27 (0.20-0.36)
	0-6 days post dose 2	1 128 482	18 519.5	<10	-	-	-
	>6 days post dose 2	1 125 839	228 080.4	99	0.4	0.19 (0.13-0.27)	0.15 (0.10-0.22)
Deaths	Unvaccinated	1 253 438	290 130.7	1906	6.6	-	-
	0-6 days post dose 1	1 159 532	19 043.6	31	1.6	0.23 (0.16 - 0.33)	0.23 (0.16 - 0.33)
	7-13 days post dose 1	1 158 888	22 203.5	41	1.8	0.29 (0.21 - 0.40)	0.29 (0.21 - 0.40)
	14-20 days post dose 1	1 158 003	22 186.1	38	1.7	0.29 (0.20 - 0.41)	0.29 (0.20 - 0.41)
	21-27 days post dose 1	1 157 105	22 153.0	17	0.8	0.16 (0.10 - 0.26)	0.16 (0.09 - 0.26)
	>27 days post dose 1	1 154 321	132 371.1	48	0.4	0.21 (0.14 - 0.30)	0.19 (0.13 - 0.28)
	0-6 days post dose 2	1 130 563	18 553.5	<10	-	-	-
	>6 days post dose 2	1 127 897	228 453.3	<10	-	-	-

[a] Unadjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status.

[b] Adjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

Table 3.3a. Cox regression estimates of PCR positive SARS-CoV-2 infection following vaccination with BNT162b2 or ChAdOx1 in those aged 50 years and over, Wales, UK. Estimates by broad age group.[a, b, c]

Study population	Category	Individuals (n)	Person years	Events	Events per 1000 Person Years	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)	Adjusted model with IPW Hazard Ratio (95% CI)
Aged 70 years and over	Unvaccinated	462 091	76 924.0	8 196	106.5	-	-	-
	0-6 days post dose 1	431 261	7 082.0	151	21.3	0.33 (0.28 - 0.39)	0.32 (0.27 - 0.38)	0.05 (0.04 - 0.06)
	7-13 days post dose 1	430 902	8 253.9	212	25.7	0.41 (0.35 - 0.49)	0.39 (0.34 - 0.46)	0.07 (0.06 - 0.09)
	14-20 days post dose 1	430 342	8 243.3	188	22.8	0.41 (0.35 - 0.49)	0.39 (0.32 - 0.46)	0.08 (0.07 - 0.11)
	21-27 days post dose 1	429 823	8 230.5	114	13.9	0.32 (0.26 - 0.40)	0.29 (0.24 - 0.36)	0.07 (0.05 - 0.10)
	>27 days post dose 1	428 990	44 084.3	392	8.9	0.51 (0.43 - 0.61)	0.44 (0.37 - 0.53)	0.20 (0.15 - 0.28)
	0-6 days post dose 2	421 592	6 923.1	24	3.5	0.33 (0.22 - 0.51)	0.29 (0.19 - 0.45)	0.34 (0.20 - 0.57)
	>6 days post dose 2	421 197	112 286.3	599	5.3	0.40 (0.32 - 0.49)	0.34 (0.27 - 0.42)	0.45 (0.26 - 0.78)
Aged 50-69 years	Unvaccinated	791 574	207 553.9	23 996	115.6	-	-	-
	0-6 days post dose 1	699 705	11 489.2	445	38.7	0.99 (0.90 - 1.09)	0.91 (0.83 - 1.00)	0.67 (0.58 - 0.77)
	7-13 days post dose 1	698 884	13 385.3	599	44.8	1.41 (1.30 - 1.54)	1.29 (1.19 - 1.41)	0.93 (0.81 - 1.06)
	14-20 days post dose 1	697 827	13 367.0	342	25.6	1.05 (0.94 - 1.17)	0.95 (0.85 - 1.06)	0.66 (0.57 - 0.78)
	21-27 days post dose 1	697 010	13 340.7	212	15.9	0.84 (0.73 - 0.96)	0.76 (0.66 - 0.87)	0.52 (0.44 - 0.63)
	>27 days post dose 1	694 902	84 573.3	743	8.8	1.07 (0.98 - 1.16)	0.94 (0.86 - 1.02)	0.73 (0.63 - 0.85)
	0-6 days post dose 2	678 676	11 133.2	120	10.8	1.04 (0.86 - 1.26)	0.93 (0.77 - 1.12)	0.88 (0.70 - 1.10)
	>6 days post dose 2	676 466	110 642.0	1 830	16.5	0.73 (0.66 - 0.81)	0.62 (0.56 - 0.68)	0.64 (0.53 - 0.77)

[a] Unadjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status.

[b] Adjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

[c] IPW - Inverse propensity weighting.

Table 3.3b. Cox regression estimates of PCR positive SARS-CoV-2 infection following vaccination with BNT162b2 or ChAdOx1 in those aged 50 years and over, Wales, UK. Estimates by vaccine type.[a, b, c]

Study population	Category	Individuals (n)	Person years	Events	Events per 1000 Person Years	Unadjusted model	Adjusted model	Adjusted model with IPW
						HR (95% CI)	aHR (95% CI)	Hazard Ratio (95% CI)
BNT162b2	Unvaccinated	1 253 665	284 477.9	32 192	113.2	-	-	-
	0-6 days post dose 1	326 679	5 363.2	367	68.4	0.86 (0.77 - 0.95)	0.82 (0.73 - 0.91)	0.30 (0.26 - 0.35)
	7-13 days post dose 1	326 153	6 244.4	491	78.6	1.19 (1.09 - 1.31)	1.12 (1.02 - 1.23)	0.41 (0.35 - 0.47)
	14-20 days post dose 1	325 429	6 232.9	280	44.9	0.87 (0.77 - 0.98)	0.81 (0.72 - 0.91)	0.29 (0.24 - 0.34)
	21-27 days post dose 1	324 983	6 213.0	173	27.8	0.70 (0.60 - 0.82)	0.65 (0.56 - 0.76)	0.23 (0.19 - 0.29)
	>27 days post dose 1	323 278	19 282.6	458	23.8	0.93 (0.84 - 1.02)	0.84 (0.76 - 0.92)	0.35 (0.30 - 0.42)
	0-6 days post dose 2	320 319	5 257.5	58	11.0	0.68 (0.53 - 0.89)	0.62 (0.48 - 0.81)	0.37 (0.27 - 0.51)
	>6 days post dose 2	319 666	96 388.4	765	7.9	0.59 (0.52 - 0.66)	0.50 (0.45 - 0.56)	0.46 (0.38 - 0.57)
ChAdOx1	Unvaccinated	1 253 665	284 477.9	32 192	113.2	-	-	-
	0-6 days post dose 1	804 287	13 208.0	229	17.3	2.47 (2.25 - 2.70)	0.63 (0.55 - 0.72)	0.13 (0.11 - 0.15)
	7-13 days post dose 1	803 633	15 394.7	320	20.8	1.96 (1.78 - 2.17)	0.94 (0.84 - 1.06)	0.20 (0.17 - 0.23)
	14-20 days post dose 1	802 740	15 377.3	250	16.3	1.78 (1.60 - 1.98)	0.93 (0.81 - 1.05)	0.20 (0.17 - 0.24)
	21-27 days post dose 1	801 850	15 358.2	153	10.0	1.61 (1.43 - 1.82)	0.70 (0.59 - 0.82)	0.17 (0.13 - 0.21)
	>27 days post dose 1	800 614	109 374.9	677	6.2	0.32 (0.28 - 0.36)	0.83 (0.75 - 0.91)	0.35 (0.29 - 0.41)
	0-6 days post dose 2	779 949	12 798.8	86	6.7	1.65 (1.34 - 2.03)	1.10 (0.87 - 1.38)	1.00 (0.74 - 1.34)
	>6 days post dose 2	777 997	126 539.8	1 664	13.2	0.16 (0.12 - 0.20)	0.75 (0.67 - 0.85)	0.61 (0.50 - 0.76)

[a] Unadjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status.

[b] Adjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

[c] IPW - Inverse propensity weighting.

Table 3.4a. Cox regression estimates of hospital admission with PCR positive SARS-CoV-2 infection following vaccination with BNT162b2 or ChAdOx1 in those aged 50 years and over, Wales, UK. Estimates by broad age group.[a, b, c]

Study population	Category	Individuals (n)	Person years	Events	Events per 1000 Person Years	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)	Adjusted model with IPW Hazard Ratio (95% CI)
Aged 70 years and over	Unvaccinated	462 091	77 695.7	1 767	22.7	-	-	-
	0-6 days post dose 1	436 573	7 170.0	32	4.5	0.32 (0.22 - 0.46)	0.31 (0.22 - 0.45)	0.04 (0.03 - 0.06)
	7-13 days post dose 1	436 321	8 358.8	48	5.7	0.45 (0.32 - 0.63)	0.44 (0.32 - 0.61)	0.07 (0.05 - 0.11)
	14-20 days post dose 1	435 889	8 350.6	33	4.0	0.34 (0.23 - 0.52)	0.33 (0.22 - 0.50)	0.07 (0.04 - 0.12)
	21-27 days post dose 1	435 492	8 339.3	19	2.3	0.24 (0.14 - 0.40)	0.23 (0.13 - 0.38)	0.06 (0.03 - 0.11)
	>27 days post dose 1	434 685	44 738.7	51	1.1	0.26 (0.17 - 0.40)	0.23 (0.15 - 0.35)	0.12 (0.06 - 0.23)
	0-6 days post dose 2	427 274	7 016.3	<10	-	-	-	-
	>6 days post dose 2	426 872	113 684.9	62	0.5	0.23 (0.13 - 0.41)	0.19 (0.11 - 0.34)	0.08 (0.03 - 0.22)
Aged 50-69 years	Unvaccinated	791 574	212 069.9	1 446	6.8	-	-	-
	0-6 days post dose 1	720 896	11 839.6	22	1.9	0.75 (0.48 - 1.15)	0.66 (0.43 - 1.02)	0.22 (0.13 - 0.37)
	7-13 days post dose 1	720 482	13 804.3	23	1.7	0.83 (0.54 - 1.27)	0.72 (0.46 - 1.10)	0.24 (0.14 - 0.41)
	14-20 days post dose 1	719 991	13 794.6	13	0.9	0.60 (0.34 - 1.05)	0.51 (0.29 - 0.89)	0.17 (0.08 - 0.33)
	21-27 days post dose 1	719 476	13 772.6	<10	-	-	-	-
	>27 days post dose 1	717 492	87 358.8	17	0.2	0.31 (0.18 - 0.53)	0.25 (0.15 - 0.43)	0.1 (0.05 - 0.23)
	0-6 days post dose 2	701 208	11 503.2	<10	-	-	-	-
	>6 days post dose 2	698 967	114 395.5	37	0.3	0.15 (0.09 - 0.25)	0.12 (0.07 - 0.19)	0.09 (0.05 - 0.16)

[a] Unadjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status.

[b] Adjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

[c] IPW - Inverse propensity weighting.

Table 3.4b. Cox regression estimates of hospital admission with PCR positive SARS-CoV-2 infection following vaccination with BNT162b2 or ChAdOx1 in those aged 50 years and over, Wales, UK. Estimates by vaccine type.[a, b, c]

Study population	Category	Individuals (n)	Person years	Events	Events per 1000 Person Years	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)	Adjusted model with IPW Hazard Ratio (95% CI)
BNT162b2	Unvaccinated	1 253 665	289 765.6	3 213	11.1	-	-	-
	0-6 days post dose 1	333 018	5 469.3	18	3.3	0.45 (0.28 - 0.72)	0.46 (0.29 - 0.73)	0.06 (0.03 - 0.10)
	7-13 days post dose 1	332 832	6 376.6	18	2.8	0.44 (0.27 - 0.71)	0.44 (0.27 - 0.71)	0.06 (0.04 - 0.11)
	14-20 days post dose 1	332 575	6 372.4	11	1.7	0.31 (0.17 - 0.57)	0.31 (0.17 - 0.57)	0.05 (0.03 - 0.11)
	21-27 days post dose 1	332 392	6 356.1	<10	-	-	-	-
	>27 days post dose 1	330 786	19 848.2	14	0.7	0.27 (0.16 - 0.47)	0.25 (0.15 - 0.44)	0.07 (0.03 - 0.13)
	0-6 days post dose 2	328 110	5 385.6	<10	-	-	-	-
	>6 days post dose 2	327 471	98 656.0	26	0.3	0.15 (0.09 - 0.24)	0.12 (0.07 - 0.19)	0.06 (0.03 - 0.12)
ChAdOx1	Unvaccinated	1 253 665	289 765.6	3 213	11.1	-	-	-
	0-6 days post dose 1	824 451	13 540.3	36	2.7	0.48 (0.34 - 0.67)	0.43 (0.31 - 0.61)	0.06 (0.04 - 0.09)
	7-13 days post dose 1	823 971	15 786.5	53	3.4	0.73 (0.55 - 0.97)	0.66 (0.49 - 0.87)	0.11 (0.07 - 0.15)
	14-20 days post dose 1	823 305	15 772.9	35	2.2	0.58 (0.41 - 0.83)	0.52 (0.36 - 0.74)	0.10 (0.06 - 0.15)
	21-27 days post dose 1	822 576	15 755.9	20	1.3	0.40 (0.26 - 0.64)	0.36 (0.22 - 0.56)	0.08 (0.04 - 0.14)
	>27 days post dose 1	821 391	112 249.3	54	0.5	0.33 (0.24 - 0.46)	0.28 (0.20 - 0.38)	0.10 (0.06 - 0.16)
	0-6 days post dose 2	800 372	13 133.9	<10	-	-	-	-
	>6 days post dose 2	798 368	129 424.4	73	0.6	0.24 (0.16 - 0.37)	0.19 (0.12 - 0.29)	0.10 (0.05 - 0.20)

[a] Unadjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status.

[b] Adjusted model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

[c] IPW - Inverse propensity weighting.

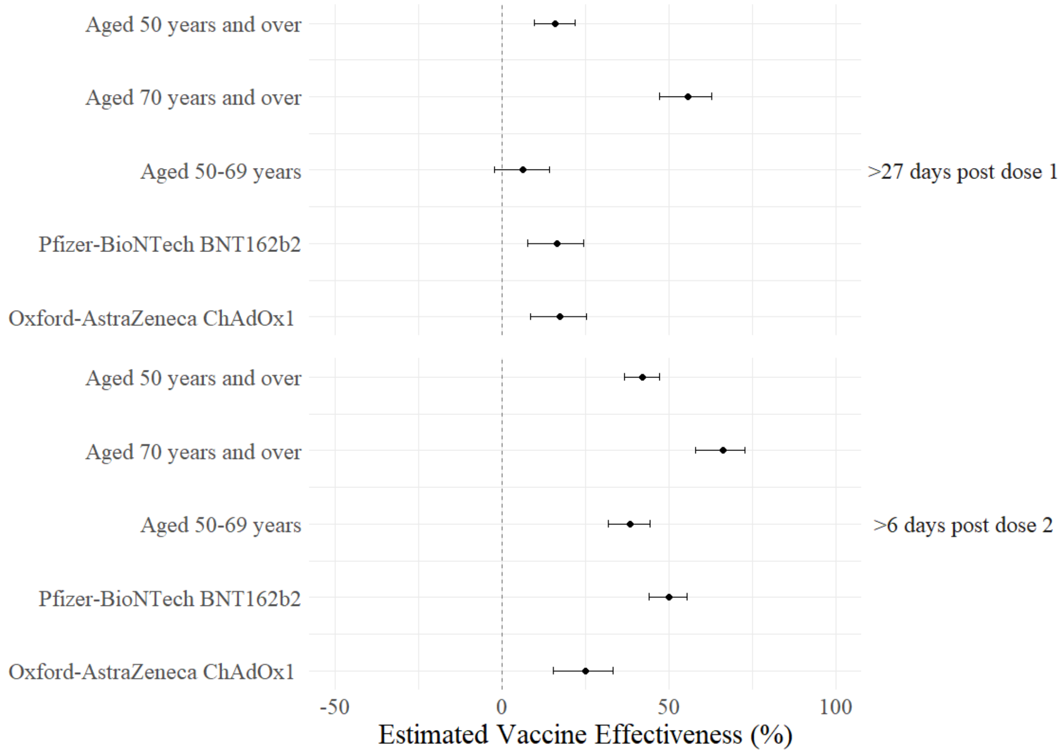


Figure 3.1. Vaccine effectiveness estimates of COVID-19 vaccination with BNT162b2 or ChAdOx1 against PCR positive SARS-CoV-2 infection in those aged 50 years and over, Wales, UK. Cox regression model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

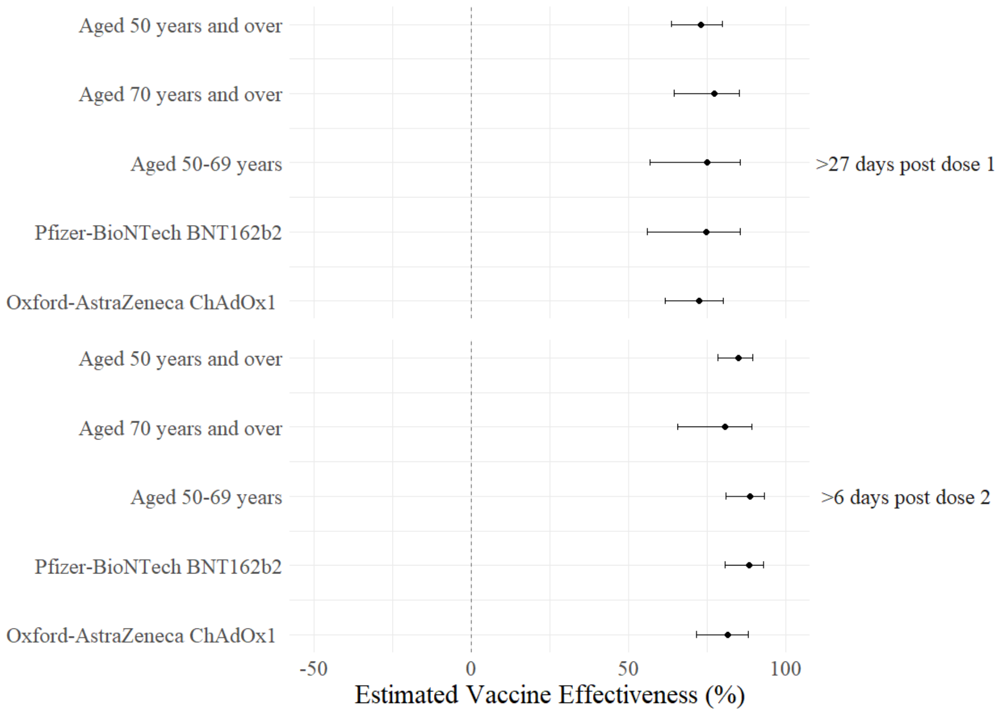


Figure 3.2. Vaccine effectiveness estimates of COVID-19 vaccination with BNT162b2 or ChAdOx1 against hospitalization due to SARS-CoV-2 infection in those aged 50 years and over, Wales, UK. Cox regression model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

Table 3.5. Comparison of adjusted hazard ratios for vaccination, against PCR positive SARS-CoV-2 infection, using different modelling approaches. Individuals aged 50 years and over, Wales, UK.[a, b]

Category	Admission events	Rate Per 1 000 Person Years	Poisson split by calendar time	Poisson not split by calendar time	Cox regression
			aHR (95% CI)	aHR (95% CI)	aHR (95% CI)
Unvaccinated	32069	114.4	-	-	-
0-6 days post dose 1	593	32.0	0.71 (0.65-0.77)	0.24 (0.22-0.26)	0.73 (0.67-0.79)
7-13 days post dose 1	809	37.4	1.03 (0.95-1.10)	0.29 (0.27-0.31)	1.04 (0.97-1.12)
14-20 days post dose 1	529	24.5	0.84 (0.77-0.92)	0.19 (0.17-0.20)	0.86 (0.78-0.94)
21-27 days post dose 1	324	15.0	0.65 (0.58-0.73)	0.11 (0.10-0.13)	0.66 (0.59-0.75)
>27 days post dose 1	1068	8.4	0.77 (0.71-0.83)	0.07 (0.06-0.07)	0.79 (0.73-0.85)
0-6 days post dose 2	120	6.8	0.66 (0.55-0.80)	0.05 (0.04-0.06)	0.68 (0.56-0.83)
>6 days post dose 2	769	4.7	0.49 (0.44-0.55)	0.03 (0.03-0.03)	0.50 (0.45-0.57)

[a] Individuals followed up from 7th December 2020 to 27th June 2021. Poisson model including calendar time split at 7 day intervals.

[b] Model adjusted for age as at 31st March 2021, shielding list status and health and care worker status, any previous PCR positive SARS-CoV-2 test, number of SARS-CoV-2 PCR tests prior to the cohort start, QCOVID score, Health Board of residence, sex, ethnic group, socio economic quintile of deprivation, rural/urban location of residence, previous vaccination against shingles or pneumococcal disease, vaccination against influenza between 1st October 2020 and 31st March 2021 and number of days with a GP consultation recorded in the year prior to 1st February 2020, prior to the pandemic reaching Wales.

Estimates from models including IPW were higher at all-time points post vaccination, although estimates for seven or more days after dose two were similar (Table 3.3, Table 3.4).

VE for one dose of any vaccine type against death with COVID-19, where COVID-19 was mentioned as a cause or contributing factor, was estimated to be 80.9% (95% CI 72.1–86.9).

Fewer than 10 individuals who had two doses of COVID-19 vaccine died between 7th December 2020 and 18th July 2021; therefore, VE estimates for two doses could not be produced due to potential disclosure of identity.

In scoping the methodology for VE in this study, a Poisson model controlling for calendar time was explored (143). Whilst controlling for suitably small time points, this model produced similar estimates for COVID-19 VE as the Cox regression models (Table 3.5).

3.4 Discussion

The overall VE estimate seven or more days post dose two of any vaccine type against SARS-CoV-2 PCR positive infection, in this large cohort study of the Welsh population was 42%. This estimate is lower compared to other published studies, which mainly include estimates for BNT162b2, whilst two thirds of this study population had received ChAdOx1 (128,129,136). Estimates against SARS-CoV-2 PCR positive infection were lower for ChAdOx1 compared to BNT162b2, as has been seen elsewhere (134,135).

However, estimates of 85% against hospital admission due to SARS-CoV-2 PCR infection seven or more days post dose two are encouraging, and in line with estimates from other studies. Haas EJ *et al.* (128) reported 97.2% (96.8–97.5) effectiveness of two doses of Pfizer-BioNTech BNT162b2 vaccine against COVID-19 related hospitalization seven days after the second dose, and data from Qatar showed 97.4% (95% CI 92.2–99.5) VE for BNT162b2 against severe, critical or fatal disease 14 days after the second dose (131). Interim data from a large population cohort in Scotland estimated 91% (95% CI 85–94) effectiveness of one dose of BNT162b2 against hospitalization at 28 to 34 days post vaccination and 88% (95% CI 75–94) effectiveness of ChAdOx1 against the same outcome (130).

Due to small numbers of COVID-19 related deaths in the study population, it was not possible to obtain estimates of VE against a complete two dose course at this time; however, one vaccine dose was estimated to reduce deaths by 81%.

Follow-up in this cohort started on 7th December 2020 when the vaccination program began in Wales. At this time Wales was reaching the peak in a second outbreak wave where the dominant variant was Alpha (74). This adds complexities in interpreting the impact of the vaccine compared to other factors that changed over time, including changes in infection prevalence and restrictions that were implemented to control the second wave (72). By the end of March 2021, cases returned to low levels and remained low until the beginning of June 2021 when cases started to increase, and Delta became the dominant variant.

The estimates in this study can be considered to be mainly against the Alpha variant and provide a baseline for how the vaccination is working overtime and can be useful in comparing VE in the face of new variants of SARS-CoV-2 arising. A systematic long-term approach to surveillance of VE is important due to changing variants, the large number of vaccine candidates and proposed schedules and booster doses. At the time of writing, evidence is still emerging, but recent studies from England and Scotland suggest effectiveness against sequenced symptomatic cases is slightly reduced for Delta compared to Alpha after two doses of BNT162b2 or ChAdOx1 (134,135). Early data from Canada suggest similar VE following two doses of BNT162b2 when comparing Delta and Alpha, and similar VE for one dose against hospitalization or death(133). It is too early to produce robust variant-specific estimates for Wales but the Delta dominant third wave does not appear to have resulted in a large increase in hospital admissions, as with waves 1 and 2 and mortality due to COVID-19 infection also appears lower than the previous two waves (74). Currently, confirmed case incidence is consistently lower in the most highly vaccinated age-groups. Early evidence suggests VE against confirmed COVID-19 for BNT162b2 vaccination may decrease by more than ten percentage points four months post second dose (144).

Comparing estimates from different studies using different definitions and statistical methods should be done with caution due to differences in surveillance systems and study populations, vaccine schedule, circulating strain, outcome, and recipient characteristics. Whist direct comparison of our VE estimates against those reported from other studies is difficult due to differences in approach and the samples used, in general our VE estimates against positive PCR were lower but our estimates against hospitalization were similar.

VE against hospital admission was seen 0 to 6 days post dose 1. This apparent immediate effectiveness post vaccination may be explained by bias in those who are unwell or having received a positive test, not being vaccinated in line with policy for attending appointments. These individuals would then be more likely to be admitted to hospital due to a COVID-19 related illness than people who were well enough to be vaccinated.

Symptom information was unavailable for this study, and when looking at the outcome of SARS-CoV-2 PCR positive infection, data may include those with asymptomatic infection identified through community screening activities, and enhanced case finding in other closed settings, outbreaks and incidents. This is likely to lead to underestimates of COVID-19 VE against symptomatic disease. In this study, estimates for hospital admission with COVID-19 may also be underestimated, given the age of the cohort, although COVD-19 may have been listed as the primary cause for admission, reasons for admission can be complex and co-morbidities are likely. The addition of misclassified outcomes (hospital admissions due to reasons other than testing positive for COVID-19) to both vaccinated and unvaccinated groups will tend to lead to an underestimation of VE. Conversely, 47% of all admissions that could be linked to a SARS-CoV-2 PCR positive test were not included in this analysis, as COVID-19 was not listed as the primary reason for admission, these too could be miscoded.

Due to the rapid roll-out of the vaccine program and high coverage, the individuals who remain unvaccinated are likely to have different characteristics or be less engaged with healthcare services compared to those who have received the vaccine, and if there is lower access to health care in the unvaccinated, case ascertainment is also likely to be lower, resulting in underestimation of VE. The impact of healthcare access bias was reduced by adjusting for number of GP consultations and previous vaccination history for this population. However, there is currently disruption in healthcare-seeking patterns, it is not known whether propensity to consult with a GP will be as good at predicting likelihood of accessing health care in the current context.

Propensity scores are commonly used in observational studies where ‘gold standard’ randomisation of exposed and unexposed individuals is not possible (145). Assigning propensity weights based on odds of being vaccinated with one dose as at 17th June 2021, when coverage was high produced large weights, which can cause estimation problems (146). To account for this, weights can be trimmed to remove extreme values, however, this method lacks a clear framework and can be variably applied (147). A sensitivity analysis in this study produced a range of estimates (data not shown), when applying different IPW trimming methods; therefore, these extreme estimates produced from the IPW model are potentially over adjusting and should be interpreted with caution. Acknowledging this, the adjusted model without propensity weighting is potentially underestimating VE.

The main limitation to this study was being unable to obtain further information on severity of illness. Having symptom information available to determine VE against asymptomatic and symptomatic infection would be beneficial. The proportion of missing data for the GP-derived variables used to control for propensity to consult (approximately 20%) may affect VE estimates, although sensitivity analysis shows this is minimal. Due to small population sizes, broad ethnic grouping was used in this analysis. As ethnicity is strongly associated with vaccination uptake, being able to use more refined categories to identify intra-group variation may have been beneficial.

These analyses included a diverse population and therefore further analysis for sub-groups, such as healthcare workers who have higher exposure or care home residents who may have higher transmission rates, is under way. In this study, the exclusion of care home residents may cause a bias to lower death rate in older age groups who are infected.

Vaccine uptake has been high amongst adults in Wales and VE estimates are encouraging, with two doses providing considerable protection against severe infection. Continued roll-out of the vaccination program within Wales and more globally, and ensuring people complete the two dose course, is crucial in our fight against COVID-19. Continued evaluation of effectiveness is important to assess issues such as waning and the impact of new COVID-19 variants.

Chapter 4 - Determinants of equity in coverage of measles-containing vaccines in Wales, UK, during the elimination era

The material in this chapter formed the basis for the following publication, with additional information provided here for clarity, and to allow for additional results to be included:

Perry M, Cottrell S, Gravenor MB, Griffiths L. Determinants of equity in coverage of measles-containing vaccines in Wales, UK, during the elimination era. Vaccines (Basel). 2023;11(3):680. doi: 10.3390/vaccines11030680.

4.0 Abstract

In the context of the WHO's measles and rubella elimination targets and European Immunization Agenda 2030, this large cross-sectional study aimed to identify inequalities in measles vaccination coverage in Wales, UK. The vaccination status of individuals aged two to 25 years of age, alive and resident in Wales as of 31st August 2021, was ascertained through linkage of the NCCHD and primary care data. A series of predictor variables were derived from five national datasets and all analysis was carried out in the SAIL Databank at Swansea University. In these 648 895 individuals, coverage of the first dose of measles-containing vaccine (due at 12 to 13 months of age) was 97.1%, and coverage of the second dose (due at three years and four months) in four to 25-year-olds was 93.8%. In multivariable analysis, excluding 0.7% with known vaccine refusal, the strongest association with being unvaccinated was birth order (families with six or more children) and being born outside of the UK. Living in a deprived area, being eligible for free school meals, a lower level of maternal education, and having a recorded language other than English or Welsh were also associated with lower coverage. Some of these factors may also be associated with refusal. This knowledge can be used to target future interventions and prioritise areas for catch-up in a time of limited resource.

4.1 Introduction

The 2012 the WHO Global Measles and Rubella Strategic Plan outlined the aim to achieve elimination of measles and rubella in at least five of the six WHO regions by the end of 2020 (75). In 2018, the UK lost its measles elimination status, and as at 2020 endemic transmission remained re-established (83). Although there has not been a confirmed case of rubella in Wales since 2005, there have been regular and sometimes large outbreaks of measles (78,80,81). A milestone achievement in the 2012 strategy was to ensure countries have at least a 95% uptake of two routine doses of measles- and rubella-containing vaccine by 2020. In line with these aims, the Wales Measles Elimination Task Group Action Plan 2019–2021 specifically highlighted the importance of increasing MMR vaccination coverage in young people (148).

PHW has produced COVER reports for over 30 years (6). These reports present uptake of all routine childhood immunisations up to 16 years of age. These figures are fed back to vaccination providers to guide service improvements and requirements for catch-up. Data for these reports come from the NCCHD, which is a population register of all children in Wales registered with the NHS. Primary care doctors and nurses, school nurses and immunisation teams administering vaccines send completed vaccination forms to their LHB child health office, detailing vaccinations that have been given. This information is then entered into the LHB child health database, with the records extracted on a monthly basis and combined to form the NCCHD. At the time of writing, the first dose of MMR is due at 12 to 13 months of age with a second routine dose at 3 years and 4 months, before school entry. Vaccination status checks are encouraged at routine primary care appointments, on entry to primary and secondary school, and alongside administration of teenage immunisations.

Routine reporting in Wales has shown that national coverage of one dose of MMR reported at 2 years of age has ranged between 86% and 98% over the last 20 years, whilst coverage of two doses at 5 years of age has varied between 71% and 94% (6). Currently coverage is generally high; however, coverage in teenagers is lower and varies by region. Coverage in those aged older than 16 years is not routinely reported due to archiving of NCCHD data around this age. At an ecological level, it is known that there is lower vaccine uptake in more deprived areas compared to less deprived areas across all age groups (10). Equitable access and coverage of vaccinations has been highlighted in the WHO European Immunization Agenda 2030 (149). Socioeconomic factors are often associated with vaccination coverage for routine childhood immunisations. In developed countries, areas experiencing poverty, families that have a lower income, parents with a lower level of education and those experiencing unemployment are generally associated with lower vaccine uptake (12,19). In contrast, higher education status (45) and higher income (47) have also been shown to be associated with lower uptake of vaccines in some populations. The association between poverty and low vaccine coverage is also seen in many Low and Middle Income Countries (LMICs) (150). Vaccination coverage also appears to be lower in children resident in large or single parent households (19,151,152). Demographic factors such as ethnicity, age of mother, COB, religion and gender have also been shown to be predictors of vaccination status (42,150,153–155).

Large ecological studies looking at routine childhood immunisations are still rare, and specific reasons for low uptake in Wales have not been previously explored. In this study data linkage of national datasets was used to identify factors associated with lower coverage of measles-containing vaccine, with the aim that this knowledge can be used to investigate what the barriers are for uptake of vaccination, develop interventions and prioritise areas for catch-up in a time of limited resources.

4.2 Methods

Analyses were completed within the SAIL Databank held at Swansea University (100). A cohort of individuals aged 2 to 25 years of age, alive and resident in Wales as of 31st August 2021, was created using the WDSD. Individuals who do not have a record in the NCCHD or were registered to a GP that does not submit data to SAIL were excluded. Approximately 80% of GP practices in Wales submit data to SAIL (156).

Measles vaccination status was assigned using an extract from the NCCHD, supplemented by Read coded vaccination status data from primary care GPs (Appendix 3, Appendix 4). MMR, measles and rubella (MR) and single antigen measles vaccination were all considered valid vaccinations in this analysis. In line with UK guidance, the first dose of vaccine had to have been given at 12 months of age or later with the second dose given at least one month after the first at 15 months of age or later (77).

A series of independent variables were identified to test for association with vaccination coverage. Gender, age as of 31st August 2021, month of birth, mothers' age at birth, LHB of residence, and age first moved to Wales were taken from the WDSD. Rural/urban classification of residence and deprivation quintile of residence were derived as described previously (157). Broad ethnic group was derived from CENW, with information taken from the Education Wales Schools and Pupils Dataset (EDUW) or primary care GP record, if CENW data were unavailable. Total number of primary care visits in the 1st September 2020 to 31st August 2021 year and age first registered with a primary care GP in Wales were calculated using data from primary care GPs, and flags were derived for learning disability, diagnosed sight loss and hearing loss based on published primary care Read code sets (158,159). Mothers' unique SAIL identifier, birth order, maternal smoker flag and premature status (born before 37 weeks' gestation) were taken from the NCCHD. A flag for ever being eligible for free school meals, attendance at a special school or ever being excluded from school was taken from the EDUW. Information on mothers' highest qualification was taken from CENW. Religion was as recorded in Census data, otherwise as recorded in data from primary care GPs. Where there were contradicting values, the most recent record was kept. Mothers' religion was used as default; otherwise, where this was missing, the child's recorded religion was used. COB was derived from the ONS Annual District Birth Extract (ADBE). If a child was born in Wales they appear in this data; otherwise, this information was taken from the 2011 Census or data from primary care GPs. Where a child's COB was unknown, mother's COB was used. Mother and child's recorded language was taken from Census data, and where this was unavailable, language data from primary care GPs was used. If this information was not recorded in either dataset but they were born in Wales, it was assumed English/Welsh was a primary language. A Charlson Comorbidity Index score was created using data from primary care GPs based on published Read code sets (160). Previous childhood vaccinations (three doses of pertussis-containing vaccine, one dose of pneumococcal vaccine and two doses of rotavirus vaccine) as outlined in the UK schedule were derived using the same methods used for measles-containing vaccine (Appendix 3, Appendix 4).

The odds of being vaccinated with one and two doses of measles-containing vaccine were calculated, with independent variables considered significant at the 0.05 level. In a multivariable analysis of those aged four to 25 years, records with missing information were dropped. The maternal smoker flag was dropped due to a high proportion of missing data. Mothers' recorded language and age first moved to Wales were excluded from the multivariable model due to co-linearity with child's recorded language and age first registered with a Wales GP, respectively. The final model was constructed stepwise in order of strength of association as indicated by the univariable analysis; variables which did not improve the Akaike Information Criterion score were dropped.

Unvaccinated individuals with a vaccine refusal Read code (68NY., 68NB., 68NP., 68NR., 68Nb., 68Na., 8I3x., 68N6., 68NM.) on their GP record were excluded from the equality analysis and described separately.

4.3 Results

There were 795 734 individuals aged two to 25 years of age, alive and resident in Wales as of 31st August 2021. Of these, 35 254 did not have a record in the NCCHD and a further 111 585 were not registered with a GP who submits data to the SAIL Databank. Using NCCHD data only, coverage of one dose of measles-containing vaccine in these 648 895 remaining individuals was 96.2% and coverage of two doses in those aged four to 25 years of age was 92.0%. After reconciling with GP data, coverage increased to 97.1% for one dose and 93.8% for two doses (Figure 4.1). Of those who were vaccinated, 1 620 had received measles-containing vaccines other than MMR for their first dose and 2 781 had received measles-containing vaccines other than MMR for their second dose. The majority of non-MMR measles vaccines were given to those aged 15 to 21 years (with the highest proportion received by 20-year-olds, 1.3%). The proportion of all measles vaccines received that were non-MMR was under 0.5% in all other age groups.

After exclusion of 4 688 individuals with vaccine refusal codes, there were 644 207 individuals aged two to 25 years in the equity study population. In a univariable analyses, month of birth was the only variable that was not significantly associated with vaccination uptake of either dose. Having had previous vaccinations was strongly associated with having had at least one dose of measles-containing vaccine; OR 177.45 (95% CI 162.99–193.60) for pneumococcal vaccine, OR 100.25 (95% CI 96.52–104.14) for three doses of pertussis vaccine and OR 27.60 (95% CI 25.82–29.50) for two doses of rotavirus vaccine.

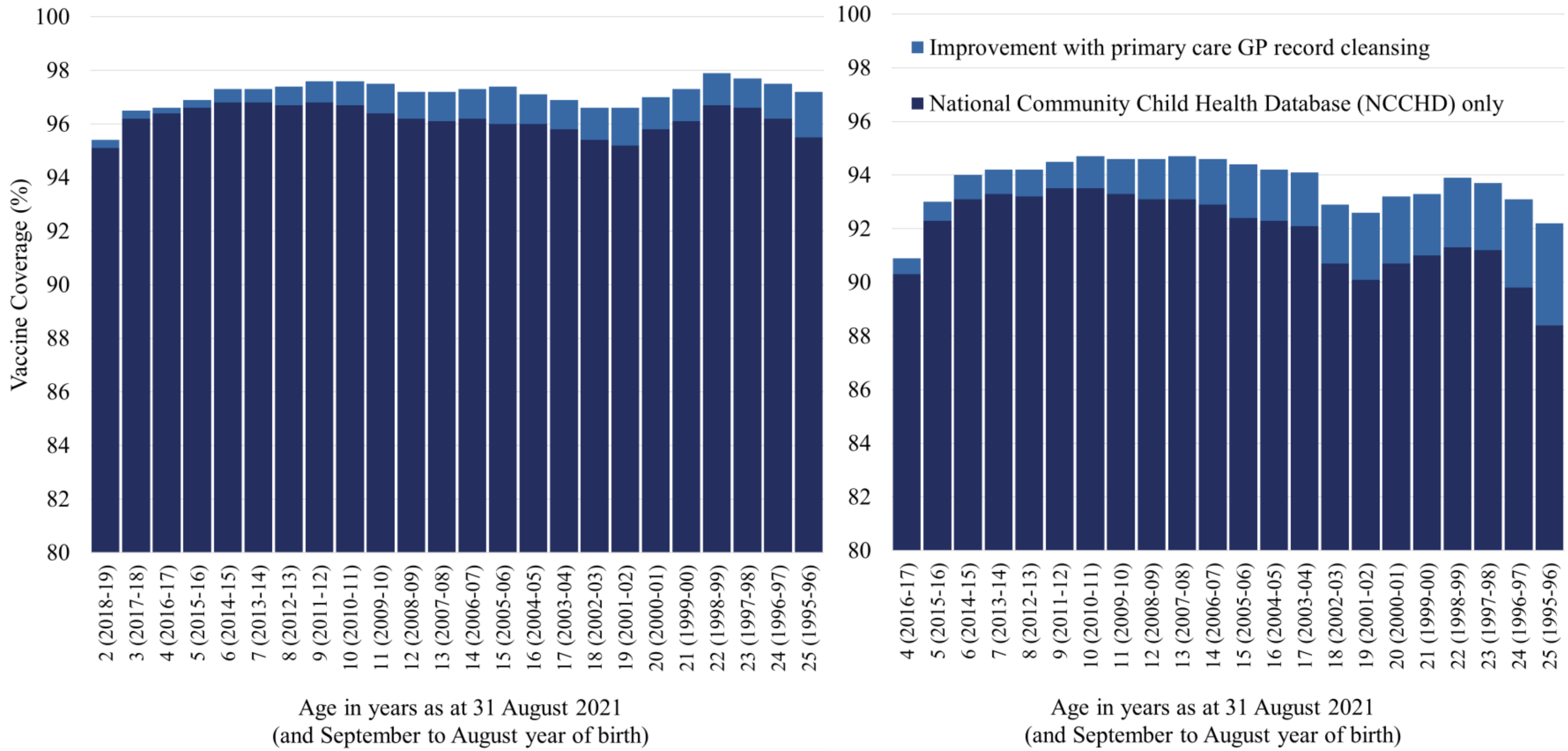


Figure 4.1. Coverage of one (a) and two (b) doses of measles-containing vaccine in those aged two to 25 years of age, alive and resident in Wales, UK as at 31st August 2021. The improvement in coverage from reconciling the National Community Child Health Database and primary care GP data is also shown.

Age first registered with a primary care GP in Wales was most strongly associated with vaccine coverage, with those first registering at secondary school age (12 to 16 years of age) least likely to be recorded as vaccinated, compared to those born in Wales. Those born outside of the UK were less likely to be vaccinated, OR 0.07 (95% CI 0.06–0.07) for one dose. For groups with at least 100 persons, coverage of one dose was under 80% in those born in Romania, Bulgaria, Syria, Lithuania, Turkey, Slovakia, Czech Republic, Nigeria, Zimbabwe, Iraq, South Africa and Asia (country not otherwise specified). Coverage was also higher in those who had English or Welsh recorded as a language, OR 8.45 (95% CI 7.88–9.06) for one dose. For groups with at least 100 persons, coverage of one dose was under 80% in those recorded as speaking Bulgarian, Romanian, Lithuanian, Russian, Hungarian, Slovak, Italian and Spanish. There was also association with ethnicity and coverage, with those who were in a combined Black, Asian, Mixed or other ethnic group having lower coverage than those in the combined White ethnic group. In the univariable analysis those with a recorded religion of Buddhism, Islam, Pagan or other religions were less likely to be vaccinated than those who stated they had no religion.

Females were more likely to be vaccinated than males, OR 1.09 (95% CI 1.05-1.12) for one dose. Mothers who were older (36 years and over) and younger (under 17) when giving birth were less likely to have children who were vaccinated, as well as those born into families with more children (OR 0.16 95% CI 0.14–0.18 if sixth or greater compared to first born). There was variation by LHB and deprivation quintile of residence, with vaccination less likely in more deprived areas. Coverage was also lower in urban areas, compared to rural areas, OR 0.74 (95% CI 0.71–0.77) for one dose. Those who have ever been eligible for free school meals were less likely to be vaccinated, OR 0.86 (95% CI 0.82–0.89) as well as those who were born to mothers who smoked during pregnancy (OR 0.76 95% CI 0.69–0.84) and mothers who had no qualifications compared to those with at least GCSE qualifications. People were less likely to be vaccinated with two doses if they had a school exclusion record (OR 0.76 95% CI 0.72–0.80), although this association was not seen with one dose. This association was stronger for those with a permanent school exclusion record compared to a temporary school exclusion record.

Table 4.1. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as at 31st August 2021, without a vaccine refusal code, by individual characteristics. Univariable Odds Ratios and 95% Confidence Intervals are also presented. Groups with uptake under 95% are indicated with bold text. Analysis is presented for the whole study cohort.

Characteristic	Category	One dose of measles-containing vaccine (2-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
		Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)	Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)
Gender	Male	322 953	331 333	97.5	Baseline	288 712	306 527	**94.2**	Baseline
	Female	305 572	312 874	97.7	1.09 (1.05-1.12)	273 985	289 294	**94.7**	1.10 (1.08-1.13)
Age cohort	Young child (2-3)	46 734	48 386	96.6	0.64 (0.61 - 0.68)	N/a	N/a		
	Primary school (4-11)	220 869	225 882	97.8	Baseline	213 543	225 882	**94.5**	Baseline
	Secondary school (12-16)	141 487	144 962	97.6	0.92 (0.88 - 0.97)	137 865	144 962	95.1	1.22 (1.09 - 1.16)
	College (17-18)	51 925	53 411	97.2	0.79 (0.75 - 0.84)	50 353	53 411	**94.3**	0.95 (0.91 - 0.99)
	University (19-21)	69 204	71 067	97.4	0.84 (0.80 - 0.89)	66 689	71 067	**93.8**	0.88 (0.85 - 0.91)
	Young adults (22-25)	98 306	100 499	97.8	1.02 (0.97 - 1.07)	94 247	100 499	**93.8**	0.87 (0.84 - 0.90)
Health board of residence	HB1	126 605	129 008	98.1	Baseline	114 841	119 559	96.1	Baseline
	HB2	86 092	88 675	97.1	0.63 (0.60-0.67)	76 489	81 930	**93.4**	0.58 (0.55-0.60)
	HB3	66 005	68 067	97.0	0.61 (0.57-0.64)	59 104	63 174	**93.6**	0.60 (0.57-0.62)
	HB4	10 867	11 157	97.4	0.71 (0.63-0.81)	9 776	10 365	**94.3**	0.68 (0.62-0.75)
	HB5	112 457	114 820	97.9	0.90 (0.85-0.96)	100 300	106 022	**94.6**	0.72 (0.69-0.75)
	HB6	118 608	121 427	97.7	0.80 (0.76-0.84)	106 272	112 274	**94.7**	0.73 (0.70-0.76)
	HB7	107 891	111 053	97.2	0.65 (0.61-0.68)	95 915	102 497	**93.6**	0.60 (0.58-0.62)
Rural/urban residence	Rural	167 637	170 966	98.1	Baseline	151 717	158 769	95.6	Baseline
	Urban	460 888	473 241	97.4	0.74 (0.71-0.77)	410 980	437 052	**94.0**	0.73 (0.71-0.75)
Deprivation quintile of residence	Most deprived	156 244	161 365	96.8	Baseline	137 637	148 583	**92.6**	Baseline
	2	132 238	135 455	97.6	1.35 (1.29-1.41)	118 200	125 111	**94.5**	1.36 (1.32-1.40)
	3	114 339	117 179	97.6	1.32 (1.26-1.38)	102 476	108 317	**94.6**	1.40 (1.35-1.44)
	4	107 384	109 686	97.9	1.53 (1.45-1.61)	96 969	101 701	95.3	1.63 (1.57-1.69)
	Least deprived	118 320	120 522	98.2	1.76 (1.67-1.85)	107 415	112 109	95.8	1.82 (1.76-1.89)

Table 4.1. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as at 31st August 2021, without a vaccine refusal code, by individual characteristics. Univariable Odds Ratios and 95% Confidence Intervals are also presented. Groups with uptake under 95% are indicated with bold text. Analysis is presented for the whole study cohort.

Characteristic	Category	One dose of measles-containing vaccine (2-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
		Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)	Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)
Premature birth	No	532 270	539 189	98.7	Baseline	478 081	496 521	96.3	Baseline
	Yes	42 682	43 235	98.7	1.00 (0.92-1.10)	37 967	39 558	96.0	0.92 (0.87-0.97)
	Unknown	53 573	61 783	86.7	-	46 649	59 742	**78.1**	-
Maternal smoker	No	151 121	152 720	99.0	Baseline	135 418	139 150	97.3	Baseline
	Yes	40 463	41 027	98.6	0.76 (0.69-0.84)	36 409	38 115	95.5	0.59 (0.55-0.62)
	Unknown	436 941	450 460	97.0	-	390 870	418 556	**93.4**	-
Ethnic group	White	512 072	520 137	98.4	Baseline	494 533	516 375	95.8	Baseline
	Other	5 338	6 283	85.0	0.09 (0.08-0.10)	4 575	6 061	**75.5**	0.14 (0.13-0.14)
	Asian	16 381	17 133	95.6	0.34 (0.32-0.37)	15 348	16 820	**91.2**	0.46 (0.44-0.49)
	Mixed	15 528	16 169	96.0	0.38 (0.35-0.41)	14 606	15 953	**91.6**	0.48 (0.45-0.51)
	Unknown	75 026	79 870	93.9	-	29 911	36 089	**82.9**	-
	Black	4 180	4 615	90.6	0.15 (0.14-0.17)	3 724	4 523	**82.3**	0.21 (0.19-0.22)
Learning disability	No	625 181	640 778	97.6	Baseline	559 620	592 455	**94.5**	Baseline
	Yes	3 344	3 429	97.5	0.98 (0.80-1.23)	3 077	3 366	**91.4**	0.62 (0.55-0.71)
Sight-loss	No	626 900	642 556	97.6	Baseline	561 160	594 208	**94.4**	Baseline
	Yes	1 625	1 651	98.4	1.56 (1.08-2.36)	1 537	1 613	95.3	1.19 (0.95-1.51)
Hearing-loss	No	587 209	602 418	97.5	Baseline	522 834	554 578	**94.3**	Baseline
	Yes	41 316	41 789	98.9	2.26 (2.07-2.48)	39 863	41 243	96.7	1.75 (1.66-1.85)
Co-morbidity score	0	512 258	526 379	97.3	Baseline	451 772	480 263	**94.1**	Baseline
	1	106 178	107 558	98.7	2.12 (2.01-2.24)	101 423	105 545	96.1	1.55 (1.50-1.60)
	2	7 302	7 425	98.3	1.64 (1.38-1.97)	6 857	7 215	95.0	1.21 (1.09-1.35)
	3+	2 787	2 845	98.0	1.32 (1.03-1.74)	2 645	2 798	**94.5**	1.09 (0.93-1.29)
UK Born	Yes	585 022	592 771	98.7	Baseline	525 993	546 671	96.2	Baseline
	No	8 044	9 611	**83.7**	0.07 (0.06-0.07)	6 679	9 434	**70.8**	0.10 (0.09-0.10)
	Unknown	35 459	41 825	**84.8**	-	30 025	39 716	**75.6**	-

Table 4.1. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as at 31st August 2021, without a vaccine refusal code, by individual characteristics. Univariable Odds Ratios and 95% Confidence Intervals are also presented. Groups with uptake under 95% are indicated with bold text. Analysis is presented for the whole study cohort.

Characteristic	Category	One dose of measles-containing vaccine (2-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
		Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)	Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)
Age first registered with Primary Care GP in Wales	At birth	511 628	517 554	98.9	Baseline	457 432	473 459	96.6	Baseline
	Young child (1-3)	59 968	61 637	97.3	0.42 (0.39 - 0.44)	53 622	57 346	**93.5**	0.50 (0.49 - 0.52)
	Primary school (4-11)	34 937	39 861	**87.6**	0.08 (0.08 - 0.09)	31 401	39 861	**78.8**	0.13 (0.13 - 0.13)
	Secondary school (12-16)	7 760	10 172	**76.3**	0.04 (0.04 - 0.04)	6 714	10 172	**66.0**	0.07 (0.07 - 0.07)
	College (17-18)	1 712	2 112	**81.1**	0.05 (0.04 - 0.06)	1 539	2 112	**72.9**	0.09 (0.09 - 0.10)
	University (19-21)	6 903	7 130	96.8	0.35 (0.31 - 0.40)	6 598	7 130	**92.5**	0.43 (0.40 - 0.48)
	Young adults (22-25)	5 617	5 741	97.8	0.52 (0.44 - 0.63)	5 391	5 741	**93.9**	0.54 (0.48 - 0.60)
Mothers age at delivery	Under 17	5 122	5 241	97.7	0.82 (0.68-0.99)	4 815	5 114	**94.2**	0.79 (0.70-0.89)
	17-18	22 763	23 184	98.2	1.03 (0.93-1.14)	21 227	22 353	95.0	0.92 (0.86-0.98)
	19-20	40 786	41 503	98.3	1.08 (1.00-1.17)	37 654	39 425	95.5	1.04 (0.99-1.10)
	21-25	140 031	142 749	98.1	0.98 (0.93-1.03)	126 325	133 093	**94.9**	0.91 (0.88-0.94)
	26-30	179 326	182 735	98.1	Baseline	159 845	167 660	95.3	Baseline
	31-35	145 484	148 332	98.1	0.97 (0.92-1.02)	129 221	135 264	95.5	1.05 (1.01-1.08)
	36-40	60 235	61 641	97.7	0.81 (0.77-0.87)	53 192	55 981	95.0	0.93 (0.89-0.97)
	Over 40	34 778	38 822	**89.6**	0.16 (0.16-0.17)	30 418	36 931	**82.4**	0.23 (0.22-0.24)
Birth order	First born	227 676	229 767	99.1	Baseline	207 864	213 812	97.2	Baseline
	Second born	168 229	170 200	98.8	0.78 (0.74-0.83)	150 965	156 332	96.6	0.80 (0.78-0.84)
	Third born	68 252	69 437	98.3	0.53 (0.49-0.57)	60 870	64 162	**94.9**	0.53 (0.51-0.55)
	Forth born	24 167	24 831	97.3	0.33 (0.31-0.37)	21 154	22 873	**92.5**	0.35 (0.33-0.37)
	Fifth born	8 518	8 851	96.2	0.23 (0.21-0.26)	7 357	8 132	**90.5**	0.27 (0.25-0.29)
	Sixth or more	5 487	5 804	**94.5**	0.16 (0.14-0.18)	4 640	5 270	**88.0**	0.21 (0.19-0.23)
	Unknown	126 196	135 317	**93.3**	-	109 847	125 240	**87.7**	-
Recorded language English/Welsh	No	8 173	9 147	**89.4**	Baseline	7 271	8 961	**81.1**	Baseline
	Yes	582 599	590 815	98.6	8.45 (7.88-9.06)	523 439	544 991	96.0	5.65 (5.34-5.96)
	Unknown	37 753	44 245	**85.3**	-	31 987	41 869	**76.4**	-

Table 4.1. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as at 31st August 2021, without a vaccine refusal code, by individual characteristics. Univariable Odds Ratios and 95% Confidence Intervals are also presented. Groups with uptake under 95% are indicated with bold text. Analysis is presented for the whole study cohort.

Characteristic	Category	One dose of measles-containing vaccine (2-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
		Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)	Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)
Total primary care GP visits 1st September 2020 to 31st August 2021	None	59 987	63 848	94.0	Baseline	53 951	61 281	**88.0**	Baseline
	1-2	164 529	168 730	97.5	2.52 (2.41-2.64)	152 549	160 991	**94.8**	2.46 (2.38-2.54)
	3-4	111 531	114 098	97.8	2.80 (2.66-2.94)	99 485	104 731	95.0	2.58 (2.48-2.67)
	5-9	144 593	147 332	98.1	3.40 (3.23-3.57)	124 742	130 716	95.4	2.84 (2.74-2.94)
	10-14	62 750	63 755	98.4	4.02 (3.75-4.31)	54 474	56 957	95.6	2.98 (2.84-3.12)
	15-19	34 843	35 345	98.6	4.47 (4.07-4.91)	31 167	32 544	95.8	3.08 (2.90-3.26)
	20-24	19 818	20 119	98.5	4.24 (3.77-4.78)	18 062	18 897	95.6	2.94 (2.73-3.17)
	25-49	27 023	27 458	98.4	4.00 (3.62-4.43)	25 036	26 294	95.2	2.70 (2.54-2.88)
	50+	3 451	3 522	98.0	3.13 (2.49-4.00)	3 231	3 410	**94.8**	2.45 (2.11-2.87)
Recorded religion	No religion	223 619	226 128	98.9	Baseline	203 422	210 887	96.5	Baseline
	Christianity	253 174	255 982	98.9	1.01 (0.96-1.07)	232 740	240 517	96.8	1.10 (1.06-1.13)
	Buddhism	1 320	1 396	**94.6**	0.19 (0.16-0.25)	1 193	1 340	**89.0**	0.30 (0.25-0.36)
	Unknown	134 301	144 207	**93.1**	-	110 499	127 322	**86.8**	-
	Islam	11 280	11 520	97.9	0.53 (0.46-0.60)	10 441	11 019	**94.8**	0.66 (0.61-0.72)
	Other religions	2 842	2 933	96.9	0.35 (0.29-0.44)	2 575	2 781	**92.6**	0.46 (0.40-0.53)
	Paganism	869	910	95.5	0.24 (0.18-0.33)	779	860	**90.6**	0.35 (0.28-0.45)
	Hinduism	1 120	1 131	99.0	1.14 (0.66-2.21)	1 048	1 095	95.7	0.82 (0.62-1.11)
Mothers highest qualification	None	67 273	68 404	98.3	Baseline	62 218	65 702	**94.7**	Baseline
	A-levels	74 917	75 607	99.1	1.83 (1.66-2.01)	68 504	70 398	97.3	2.03 (1.91-2.14)
	GCSE/O-Level high	99 175	100 106	99.1	1.79 (1.64-1.95)	91 236	93 988	97.1	1.86 (1.76-1.95)
	GCSE/O-Level any	86 051	87 030	98.9	1.48 (1.36-1.61)	79 594	82 565	96.4	1.50 (1.43-1.58)
	Unknown	144 762	154 892	**93.5**	-	116 405	133 744	**87.0**	-
	Degree	141 845	143 273	99.0	1.67 (1.54-1.81)	131 434	135 228	97.2	1.94 (1.85-2.03)
	Apprenticeship	3 601	3 647	98.7	1.32 (0.99-1.80)	3 254	3 367	96.6	1.61 (1.34-1.96)
	Other	10 901	11 248	96.9	0.53 (0.47-0.60)	10 052	10 829	**92.8**	0.72 (0.67-0.79)

Table 4.1. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as at 31st August 2021, without a vaccine refusal code, by individual characteristics. Univariable Odds Ratios and 95% Confidence Intervals are also presented. Groups with uptake under 95% are indicated with bold text. Analysis is presented for the whole study cohort.

Characteristic	Category	One dose of measles-containing vaccine (2-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
		Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)	Vaccinated (n)	Population (n)	Uptake (%)	OR (95% CI)
Ever eligible for free school meals	No	375 348	381 941	98.3	Baseline	366499	381 941	96.0	Baseline
	Yes	168 934	172 397	98.0	0.86 (0.82-0.89)	162129	172 397	**94.0**	0.67 (0.65-0.68)
	Too young	46 734	48 386	96.6	-	N/a	N/a	N/a	-
	Unknown	37 509	41 483	**90.4**	-	34069	41 483	**82.1**	-
Ever attended a special school	No	537 716	547 626	98.2	Baseline	522515	547 626	95.4	Baseline
	Yes	6 566	6 712	97.8	0.83 (0.71-0.98)	6113	6 712	**91.1**	0.49 (0.45-0.53)
	Too young	46 734	48 386	96.6	-	N/a	N/a	N/a	-
	Unknown	37 509	41 483	**90.4**	-	34069	41 483	**82.1**	-
Ever excluded from school	No	514 916	524 387	98.2	Baseline	500456	524 387	95.4	Baseline
	Yes	29 365	29 950	98.0	0.92 (0.85-1.01)	28171	29 950	**94.1**	0.76 (0.72-0.80)
	Too young	46 734	48 386	96.6	-	N/a	N/a	N/a	-
	Unknown	37 510	41 484	**90.4**	-	34070	41 484	**82.1**	-
Pneumococcal vaccine	No	31 227	40 106	**77.9**	Baseline	26668	37 696	**70.7**	Baseline
	Yes	350 740	351 302	99.8	177.45 (162.99-193.60)	298337	305 326	97.7	17.65 (17.09-18.24)
	Too young	246 558	252 799	97.5	-	237692	252 799	**94.0**	-
Three doses of pertussis vaccine	No	14 561	25 600	**56.9**	Baseline	9566	23 385	**40.9**	Baseline
	Yes	613 964	618 607	99.2	100.25 (96.52-104.14)	553131	572 436	96.6	41.39 (40.18-42.64)
Two doses of rotavirus vaccine	No	9 277	11 960	**77.6**	Baseline	5973	8 584	**69.6**	Baseline
	Yes	142 752	144 248	99.0	27.60 (25.82-29.50)	95261	99 238	96.0	10.47 (9.90-11.07)
	Too young	476 496	487 999	97.6	-	461463	487 999	**94.6**	-

There was no association with vaccination and premature birth for dose one but coverage of two doses was significantly lower if born premature, OR 0.92 (95% CI 0.87–0.97). Those who consulted with their GP at least once between 1st September 2020 and 31st August 2021 were more likely to be vaccinated, and coverage was significantly higher in those with recorded comorbidities. Those with chronic pulmonary disease, renal disease and uncomplicated diabetes were significantly more likely to be vaccinated, and those with liver disease, peptic ulcer and rheumatic disease were significantly less likely to be vaccinated. Coverage of at least one dose in those with hearing loss or sight loss was higher than the rest of the study population; coverage of two doses in those with sight loss was not significantly different. Coverage of two doses in those with a learning disability was lower than the general population, OR 0.62 (95% CI 0.55–0.71), although there was no difference for one dose. Those who attend, or have attended, a special school had lower coverage of one and two doses. The univariable analyses including the full cohort can be found in Table 4.1.

The variables included in the final model are presented in Table 4.2. The cohort was restricted to those aged four to 25 years without missing information across all variables, producing a study population of 419 405. This restricted cohort had higher vaccine coverage overall and led to some notably different estimates in the univariable analyses. Although having a comorbidity score of one was associated with higher vaccination coverage compared to those with no comorbidities, those with a score of three or more were less likely to be vaccinated in the restricted cohort. Also, younger mothers (aged under 17) in the restricted cohort were more likely to have vaccinated children compared to the univariable analysis in the full cohort, which showed they were less likely.

In the multivariable analysis, after controlling for other factors, the strongest association with vaccination uptake was birth order (OR 0.21 95% CI 0.17–0.26 for one dose if sixth or greater compared to first born) and being born outside of the UK (OR 0.21 95% CI 0.18–0.25 for one dose). Living in a more deprived area of residence was still associated with lower coverage but the association was not as strong. The association with recorded language, free school meal eligibility and mothers' highest qualification was also slightly reduced. Having a comorbidity score of 3 or more was no longer significant.

Table 4.2. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as of 31st August 2021, without a vaccine refusal code, by individual characteristics. Odds Ratios and 95% Confidence Intervals are also presented. Analysis restricted to those with complete information across all variables.

Characteristic	Category	Population (n)	One dose of measles-containing vaccine (4-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
			Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)	Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)
Gender	Male	213 518	215 626	99.0	Baseline	Baseline	208 567	96.7	Baseline	Baseline
	Female	202 068	203 779	99.2	1.17 (1.09-1.24)	1.11 (1.03-1.18)	197 973	97.2	1.15 (1.11-1.20)	1.11 (1.07-1.15)
Age cohort	Primary school (4-11)	132 916	133 857	99.3	Baseline	Baseline	130 258	97.3	Baseline	Baseline
	Secondary school (12-16)	109 335	110 028	99.4	1.12 (1.01-1.23)	1.38 (1.24-1.52)	107 809	98.0	1.34 (1.27-1.42)	1.60 (1.51-1.69)
	College (17-18)	40 779	41 175	99.0	0.73 (0.65-0.82)	0.90 (0.80-1.02)	39 946	97.0	0.90 (0.84-0.96)	1.08 (1.01-1.16)
	University (19-21)	54 384	55 079	98.7	0.55 (0.50-0.61)	0.70 (0.63-0.78)	52 902	96.0	0.67 (0.64-0.71)	0.83 (0.78-0.88)
	Young adults (22-25)	78 172	79 266	98.6	0.51 (0.46-0.55)	0.66 (0.60-0.73)	75 625	95.4	0.57 (0.55-0.60)	0.73 (0.69-0.77)
Health board of residence	HB1	81 805	82 299	99.4	Baseline	Baseline	80 763	98.1	Baseline	Baseline
	HB2	57 912	58 599	98.8	0.51 (0.45-0.57)	0.51 (0.45-0.57)	56 282	96.0	0.46 (0.43-0.49)	0.46 (0.43-0.49)
	HB3	43 403	44 002	98.6	0.44 (0.39-0.49)	0.44 (0.39-0.49)	42 355	96.3	0.49 (0.46-0.52)	0.47 (0.44-0.50)
	HB4	6 801	6 902	98.5	0.41 (0.33-0.51)	0.38 (0.31-0.48)	6 636	96.1	0.47 (0.42-0.54)	0.45 (0.39-0.51)
	HB5	76 485	77 197	99.1	0.65 (0.58-0.73)	0.62 (0.55-0.69)	74 573	96.6	0.54 (0.51-0.58)	0.54 (0.51-0.58)
	HB6	79 422	80 048	99.2	0.77 (0.68-0.86)	0.76 (0.68-0.86)	77 768	97.2	0.65 (0.61-0.69)	0.66 (0.62-0.71)
	HB7	69 758	70 358	99.1	0.70 (0.62-0.79)	0.80 (0.71-0.91)	68 163	96.9	0.59 (0.55-0.63)	0.64 (0.60-0.68)
Deprivation quintile of residence	Most deprived	97 159	98 266	98.9	Baseline	Baseline	94 183	95.8	Baseline	Baseline
	2	87 377	88 209	99.1	1.20 (1.09-1.31)	1.06 (0.97-1.17)	85 432	96.9	1.33 (1.27-1.40)	1.15 (1.09-1.21)
	3	75 674	76 343	99.1	1.29 (1.17-1.42)	1.10 (1.00-1.23)	74 185	97.2	1.49 (1.41-1.57)	1.16 (1.10-1.23)
	4	72 632	73 239	99.2	1.36 (1.23-1.51)	1.11 (0.99-1.23)	71 339	97.4	1.63 (1.54-1.72)	1.18 (1.11-1.26)
	Least deprived	82 744	83 348	99.3	1.56 (1.41-1.73)	1.13 (1.01-1.26)	81 401	97.7	1.81 (1.72-1.91)	1.22 (1.15-1.30)
Recorded language English/Welsh	No	5 525	5 863	**94.2**	Baseline	Baseline	5 170	**88.2**	Baseline	Baseline
	Yes	410 061	413 542	99.2	7.21 (6.41-8.07)	1.71 (1.44-2.03)	401 370	97.1	4.42 (4.07-4.79)	1.33 (1.18-1.49)

Table 4.2. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as of 31st August 2021, without a vaccine refusal code, by individual characteristics. Odds Ratios and 95% Confidence Intervals are also presented. Analysis restricted to those with complete information across all variables.

Characteristic	Category	Population (n)	One dose of measles-containing vaccine (4-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
			Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)	Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)
Ethnic group	White	392 908	396 329	99.1	Baseline	Baseline	384 621	97.0	Baseline	Baseline
	Other	1 817	1 868	97.3	0.31 (0.24-0.42)	1.08 (0.77-1.54)	1 745	**93.4**	0.43 (0.36-0.52)	1.08 (0.86-1.36)
	Asian	9 762	9 900	98.6	0.62 (0.52-0.73)	1.58 (1.27-1.97)	9 473	95.7	0.68 (0.61-0.75)	1.31 (1.14-1.50)
	Mixed	9 201	9 338	98.5	0.58 (0.49-0.70)	0.76 (0.64-0.92)	8 920	95.5	0.65 (0.59-0.72)	0.78 (0.71-0.87)
	Black	1 898	1 970	96.3	0.23 (0.18-0.29)	0.99 (0.75-1.33)	1 781	**90.4**	0.29 (0.25-0.33)	0.92 (0.77-1.11)
Age first registered with primary care GP in Wales	At birth	358 121	360 620	99.3	Baseline	Baseline	351 458	97.5	Baseline	Baseline
	Young child (2-3)	33 881	34 335	98.7	0.52 (0.47-0.58)	0.70 (0.63-0.78)	32 798	95.5	0.56 (0.53-0.59)	0.69 (0.65-0.73)
	Primary school (4-11)	11 535	12 120	95.2	0.14 (0.13-0.15)	0.31 (0.27-0.35)	10 663	**88.0**	0.19 (0.18-0.20)	0.36 (0.33-0.39)
	Secondary school (12-16)	1 609	1 761	**91.4**	0.07 (0.06-0.09)	0.16 (0.13-0.20)	1 472	**83.6**	0.13 (0.12-0.15)	0.25 (0.22-0.29)
	College (17-18)	672	691	97.3	0.25 (0.16-0.40)	0.37 (0.24-0.61)	645	**93.3**	0.37 (0.27-0.50)	0.53 (0.39-0.73)
	University (19-21)	5 266	5 330	98.8	0.57 (0.45-0.74)	0.70 (0.54-0.91)	5 133	96.3	0.68 (0.59-0.79)	0.78 (0.68-0.91)
	Young adults (22-25)	4 502	4 548	99.0	0.68 (0.52-0.93)	0.84 (0.63-1.15)	4 371	96.1	0.64 (0.55-0.75)	0.77 (0.66-0.90)
Mothers age at delivery	Under 17	2 987	3 002	99.5	1.69 (1.05-2.95)	1.91 (1.18-3.37)	2 905	96.8	0.90 (0.74-1.11)	0.97 (0.79-1.20)
	17-18	14 508	14 610	99.3	1.21 (0.99-1.49)	1.30 (1.05-1.62)	14 143	96.8	0.91 (0.83-1.01)	0.92 (0.83-1.02)
	19-20	26 875	27 051	99.3	1.30 (1.11-1.53)	1.33 (1.13-1.58)	26 293	97.2	1.04 (0.97-1.13)	1.03 (0.95-1.13)
	21-25	95 435	96 284	99.1	0.95 (0.87-1.05)	1.02 (0.93-1.12)	93 125	96.7	0.89 (0.85-0.93)	0.92 (0.88-0.97)
	26-30	125 482	126 548	99.2	Baseline	Baseline	122 849	97.1	Baseline	Baseline
	31-35	102 444	103 414	99.1	0.90 (0.82-0.98)	0.88 (0.80-0.96)	100 419	97.1	1.01 (0.96-1.06)	0.99 (0.94-1.04)
	36-40	41 039	41 555	98.8	0.68 (0.61-0.75)	0.70 (0.63-0.78)	40 176	96.7	0.88 (0.82-0.93)	0.91 (0.85-0.97)
	Over 40	6 816	6 941	98.2	0.46 (0.39-0.56)	0.60 (0.49-0.73)	6 630	95.5	0.64 (0.57-0.72)	0.79 (0.70-0.90)

Table 4.2. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as of 31st August 2021, without a vaccine refusal code, by individual characteristics. Odds Ratios and 95% Confidence Intervals are also presented. Analysis restricted to those with complete information across all variables.

Characteristic	Category	Population (n)	One dose of measles-containing vaccine (4-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
			Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)	Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)
Co-morbidity score	0	328 434	331 538	99.1	Baseline	Baseline	321 268	96.9	Baseline	Baseline
	1	79 664	80 288	99.2	1.21 (1.11-1.32)	1.17 (1.07-1.28)	77 985	97.1	1.08 (1.03-1.13)	1.10 (1.05-1.16)
	2	5 353	5 404	99.1	0.99 (0.76-1.33)	1.03 (0.78-1.39)	5 209	96.4	0.85 (0.74-0.99)	0.95 (0.82-1.10)
	3+	2 135	2 175	98.2	0.50 (0.37-0.70)	0.58 (0.42-0.81)	2 078	95.5	0.68 (0.56-0.85)	0.87 (0.71-1.09)
Birth order	First born	160 101	160 931	99.5	Baseline	Baseline	157 847	98.1	Baseline	Baseline
	Second born	182 014	183 880	99.0	0.51 (0.47-0.55)	0.74 (0.68-0.81)	177 856	96.7	0.58 (0.55-0.60)	0.70 (0.66-0.73)
	Third born	48 304	48 845	98.9	0.46 (0.42-0.52)	0.54 (0.49-0.61)	46 895	96.0	0.47 (0.44-0.50)	0.50 (0.47-0.53)
	Forth born	16 425	16 726	98.2	0.28 (0.25-0.32)	0.37 (0.32-0.43)	15 713	**93.9**	0.30 (0.28-0.33)	0.35 (0.33-0.38)
	Fifth born	5 506	5 658	97.3	0.19 (0.16-0.22)	0.27 (0.23-0.33)	5 209	**92.1**	0.23 (0.20-0.25)	0.29 (0.26-0.32)
	Sixth or more	3 236	3 365	96.2	0.13 (0.11-0.16)	0.21 (0.17-0.26)	3 020	**89.7**	0.17 (0.15-0.19)	0.23 (0.20-0.26)
Total primary care GP visits 1st September 2020 to 31st August 2021	None	38 114	38 843	98.1	Baseline	Baseline	36 931	95.1	Baseline	Baseline
	1-2	114 209	115 168	99.2	2.28 (2.07-2.51)	2.18 (1.97-2.41)	111 863	97.1	1.75 (1.65-1.86)	1.72 (1.62-1.83)
	3-4	72 737	73 290	99.2	2.52 (2.25-2.81)	2.53 (2.25-2.84)	71 298	97.3	1.85 (1.74-1.98)	1.92 (1.80-2.05)
	5-9	90 044	90 745	99.2	2.46 (2.21-2.73)	2.52 (2.26-2.81)	88 290	97.3	1.86 (1.75-1.98)	1.98 (1.86-2.11)
	10-14	40 422	40 743	99.2	2.41 (2.11-2.75)	2.64 (2.30-3.04)	39 565	97.1	1.74 (1.62-1.87)	1.97 (1.82-2.13)
	15-19	23 819	23 992	99.3	2.63 (2.24-3.12)	3.06 (2.57-3.65)	23 298	97.1	1.74 (1.59-1.90)	2.09 (1.91-2.30)
	20-24	13 989	14 122	99.1	2.01 (1.68-2.43)	2.43 (2.01-2.97)	13 632	96.5	1.44 (1.30-1.60)	1.82 (1.64-2.03)
	25-49	19 737	19 952	98.9	1.76 (1.51-2.05)	2.31 (1.96-2.74)	19 222	96.3	1.36 (1.25-1.49)	1.88 (1.71-2.07)
	50+	2 515	2 550	98.6	1.37 (0.99-1.97)	2.12 (1.51-3.09)	2 441	95.7	1.16 (0.96-1.42)	1.90 (1.55-2.35)
Ever eligible for free school meals	No	296 942	299 262	99.2	Baseline	Baseline	291 750	97.5	Baseline	Baseline
	Yes	118 644	120 143	98.8	0.62 (0.58-0.66)	0.73 (0.68-0.79)	114 790	95.5	0.55 (0.53-0.57)	0.73 (0.70-0.76)
Ever attended a special school	No	410 837	414 573	99.1	Baseline	Baseline	402 105	97.0	Baseline	Baseline
	Yes	4 749	4 832	98.3	0.52 (0.42-0.65)	0.67 (0.53-0.85)	4 435	91.8	0.35 (0.31-0.38)	0.43 (0.39-0.48)

Table 4.2. continued. Uptake of one or two doses of measles-containing vaccine in those aged four to 25 years alive and resident in Wales, UK as of 31st August 2021, without a vaccine refusal code, by individual characteristics. Odds Ratios and 95% Confidence Intervals are also presented. Analysis restricted to those with complete information across all variables.[a]

Characteristic	Category	Population (n)	One dose of measles-containing vaccine (4-25 year olds)				Two doses of measles-containing vaccine (4-25 year olds)			
			Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)	Vaccinated (n)	Uptake (%)	OR (95% CI)	aOR (95% CI)
Mothers highest qualification	None	59 223	60 034	98.6	Baseline	Baseline	57 107	95.1	Baseline	Baseline
	A-levels	63 435	63 907	99.3	1.84 (1.64-2.06)	1.12 (0.99-1.27)	62 375	97.6	2.09 (1.96-2.22)	1.25 (1.17-1.34)
	GCSE/O-Level high grades	85 168	85 779	99.3	1.91 (1.72-2.12)	1.25 (1.12-1.40)	83 527	97.4	1.90 (1.80-2.01)	1.25 (1.17-1.32)
	GCSE/O-Level any grades	74 792	75 459	99.1	1.54 (1.39-1.70)	1.10 (0.99-1.22)	72 997	96.7	1.52 (1.44-1.61)	1.11 (1.04-1.17)
	Degree	120 598	121 585	99.2	1.67 (1.52-1.84)	1.10 (0.98-1.23)	118 564	97.5	2.01 (1.91-2.12)	1.18 (1.11-1.26)
	Apprenticeship	2 965	2 999	98.9	1.19 (0.86-1.72)	0.83 (0.59-1.20)	2 910	97.0	1.68 (1.36-2.09)	1.12 (0.91-1.40)
	Other	9 405	9 642	97.5	0.54 (0.47-0.63)	0.97 (0.82-1.16)	9 060	94.0	0.80 (0.73-0.88)	1.06 (0.95-1.17)
Recorded religion	No religion	187 177	188 816	99.1	Baseline	Baseline	182 806	96.8	Baseline	Baseline
	Christianity	214 191	216 089	99.1	0.99 (0.92-1.06)	1.11 (1.03-1.19)	209 973	97.2	1.13 (1.09-1.17)	1.09 (1.05-1.13)
	Buddhism	1 093	1 146	95.4	0.18 (0.14-0.24)	0.40 (0.29-0.56)	1 044	91.1	0.34 (0.28-0.42)	0.56 (0.45-0.71)
	Islam	9 219	9 342	98.7	0.66 (0.55-0.79)	1.45 (1.13-1.87)	8 961	95.9	0.77 (0.70-0.86)	1.42 (1.23-1.66)
	Other religions	2 344	2 412	97.2	0.30 (0.24-0.39)	0.38 (0.30-0.50)	2 251	93.3	0.46 (0.39-0.54)	0.51 (0.43-0.60)
	Paganism	*	*	*	0.22 (0.15-0.32)	0.32 (0.22-0.48)	729	91.5	0.35 (0.28-0.46)	0.43 (0.33-0.56)
	Hinduism	*	*	*	1.00 (0.51-2.33)	1.70 (0.83-4.08)	776	96.6	0.94 (0.66-1.42)	1.34 (0.90-2.07)
UK Born	Yes	410 890	414 182	99.2	Baseline	Baseline	402 474	97.2	Baseline	Baseline
	No	4 696	5 223	**89.9**	0.07 (0.06-0.08)	0.21 (0.18-0.25)	4 066	77.8	0.10 (0.10-0.11)	0.23 (0.21-0.26)

[a] Data suppressed to comply with statistical disclosure policy.

However, the biggest difference was seen in ethnicity, where those in the combined Asian ethnic group were more likely to be vaccinated with at least one and two doses after controlling for other factors (OR 1.58 (95% CI 1.27–1.97) for at least one dose), and those in the combined Black ethnic group were no longer significantly less likely to be vaccinated. Differences were also seen in those who had recorded religion of Islam, who were more likely to be vaccinated with one and two doses after controlling for other factors (OR 1.45 (95% CI 1.13–1.87) for at least one dose).

A total of 4 688 individuals aged two to 25 years had a vaccine refusal code on their GP record (0.7% of the full study population). Of these, 1 814 had received one dose of measles-containing vaccine but not two. The proportion of recorded refusals were highest in those aged two and three years (over 1.0%).

In a univariable analysis comparing individuals who had received one dose of measles-containing vaccine, with those who had a vaccine refusal code; those resident in urban areas were more likely to be vaccinated than have a refusal code compared to those resident in rural areas (OR 1.51 95% CI 1.40–1.63). Additionally, those with a recorded language of English or Welsh were more likely to be vaccinated (OR 1.53 95% CI 1.27–1.81), as well as those in less deprived areas compared to more deprived areas (OR 1.19 95% CI 1.06–1.35). Children born to mothers who were over 30 years of age were less likely to be vaccinated than have a refusal code, compared to those aged 26 to 30 years (OR 0.54 95%, CI 0.46–0.62 for mothers aged over 40), as well as those with more siblings (OR 0.31 95% CI 0.24–0.40 if sixth or greater compared to first born) and those eligible for free school meals (OR 0.83 95% CI 0.76–0.91). Having a recorded religion of Buddhism (OR 0.27 95% CI 0.17–0.44) or Paganism (OR suppressed due to small numbers) was associated with being less likely to be vaccinated than have a refusal code, compared to those with no religion, whereas having a recorded religion of Christian was associated with being more likely to be vaccinated (OR 1.22 95% CI 1.11–1.34). Those in the combined Asian ethnic group were more likely to be vaccinated compared to those in the combined White ethnic group (OR 2.21 95% CI 1.57–3.24), whereas those in the combined Black ethnic group (OR 0.65 95% CI 0.45–0.98) or combined Mixed ethnic group (OR 0.70 95% CI 0.57–0.87) were less likely to be vaccinated than have a refusal code.

4.4 Discussion

Measles vaccination uptake in this cohort of children and young adults in Wales is reassuringly high, with coverage of one dose over 95% in all NHS-registered children and young adults aged two to 25 years. However, potential remains for outbreaks of measles where unvaccinated individuals are clustered. All routine childhood vaccinations in Wales should be recorded in the child health system until 16 years of age to manage appointment call and recall and enable accurate reporting. However, it was shown that administrative records are not always correct, and reconciling multiple data systems may help improve accuracy. Despite high coverage, minor improvements in some age groups may be the difference between reaching the 95% coverage target or not. Although the oldest individuals in this analysis would have been scheduled for vaccination in the latter years of the decline in MMR uptake seen following the Wakefield scandal, coverage appears high. However, the young adults who were young children at the time of the negative publicity might explain some of the significantly reduced odds of vaccination in those aged 19 years and older. This analysis may also exclude a number of individuals who are not registered with the NHS, and therefore not included in the datasets used to produce these figures.

MMR coverage is frequently reported as a measure of the proportion of the population protected from measles infection. These analyses have identified that over 4 000 single (or duel MR) antigen measles doses had been received by those in the study cohort. However, the receipt of non-MMR vaccines has decreased in younger age groups. Some of these records may be miscoded and validation of the type of vaccination received would be necessary to have accurate records of which viruses individuals are protected against.

A small proportion of the study population (0.7%) had a GP Read code indicating measles vaccine refusal. A higher proportion of those in younger age groups had a refusal code, which could be an indication of a recent increase in vaccine hesitancy. However, this trend could also be due to improvement in coding over time. Although this study tries to focus on factors associated with low coverage in those who have not actively refused vaccination, there is suggestion of variation in refusal by different characteristics, some of which, such as residing in rural areas, appear to be associated with refusal but not other reasons for being unvaccinated. Monitoring refusals would be beneficial to highlight any concerns or mistrust as early as possible

(161). The USA has seen a recent increase in exemptions for MMR vaccine due to religious, philosophical or personal reasons, which may be contributing to a resurgence in cases (162).

Excluding those with known refusal, it was shown that inequitable coverage is particularly prevalent in households with more children and for those born outside of the UK. Living in a deprived area, being eligible for free school meals, lower level of maternal education, and having a recorded language other than English or Welsh were also associated with lower coverage. These factors are similar to those mentioned in previously published literature (12,43,45,151). Lower coverage persists in deprived urban areas, and factors relating to deprivation are complex and hard to separate out.

Evidence from this study is useful to develop tailored interventions; for example, community health care visits (163), which in this case could be prioritised for large households with multiple unvaccinated children, or joint scheduling for siblings that require catch-up. Having had previous vaccines meant there was a higher chance of having had measles-containing vaccine, suggesting it may be efficient for catch-up campaigns to target more than one vaccine programme. Improving accessibility of resources and using tailored public health messaging may reduce inequities (164). In addition, using the WHO TIP approach can help us understand specific barriers in communities identified as having lower coverage (50,165).

A recent review has suggested migrants are half as likely to be vaccinated compared to non-migrants (166). Challenges specifically relating to migrants who have transited through a number of countries, and refugees, include lack of information on vaccination status at arrival, fear of registration with medical authorities and lack of coordination between public health authorities of neighbouring countries (167). It is likely that recording of immunisations in those who were on vaccination schedules different to the UK is difficult and parents often do not have evidence of their child's previous vaccinations, which makes entering dates into the system, and scheduling further doses, challenging. UK guidance indicates restarting a vaccine course if vaccination history is uncertain (168). Tailoring immunisation services to ensure there are no language barriers when carrying out vaccination status checks and ensuring flexible systems for recording immunisations from overseas could be beneficial. Low vaccination coverage in Eastern European communities has been linked to measles outbreaks in the UK, with language, literacy and trust of health care providers identified as potential barriers (169). Building trusting relationships with minority groups such as Gypsies, Travellers and Roma may also improve utilisation of health care services including uptake of vaccination (170).

There are limitations to this study. Some individuals will not be registered with NHS health services, and those who do not have a NCCHD record were excluded, which will affect those who first resided in Wales after 16 years of age. Additionally, some vaccinations recorded in primary care GP data, but not on the NCCHD record, for older ages may be due to catch-up immunisations given more recently. There is the possibility of 'ghost records' for those who have moved away and this not being recorded in the system. The multivariable analysis was restricted to those without missing information, which disproportionately affected some groups. This analysis would exclude those families who moved to Wales since 2011 when the Census took place, as variables such as mothers' highest education level were derived from Census data only. The higher vaccine coverage and reduction in effects that were seen in the multivariable analysis may therefore be due to this restricted cohort only including those who have been settled in Wales for a longer time period. It is challenging to draw conclusions around those factors, which showed different associations in the univariable analyses when using the full and restricted study population, including comorbidities and mothers' age. Additionally, some data may not reflect the current status of an individual as it may be out of date. This includes information taken from the 2011 Census and information on language, as even if a language other than English or Welsh is recorded, a person could be bilingual or have sufficient understanding of English or Welsh to access services and make an informed decision around vaccination. However, this analysis is still a useful indicator to highlight areas at risk of outbreaks and where coverage could be improved. This is a large population study that has been able to provide new evidence on a number of characteristics associated with measles vaccination coverage in Wales.

Reducing inequalities in vaccination coverage remains key for preventing measles outbreaks and reaching the WHO measles elimination targets (75). Disruption to routine vaccine schedules during the COVID-19 pandemic may have exacerbated the inequalities reported here, making the need for catch-up activities even more pressing

(171). Reported measles cases in Europe decreased from mid-2020 (172), but now that travel restrictions have been fully lifted, the likelihood of a resurgence in cases is high and identifying and reducing inequalities in vaccine coverage should remain a priority.

Chapter 5 - Estimates of vaccine effectiveness against measles and mumps; 14 years follow-up of a large cohort in Wales, UK

The material in this chapter formed the basis for the following publication which is currently under review, with additional information provided here for clarity, and to allow for additional results to be included:

Perry M, Gravenor MB, Cottrell S, Moore C, Griffiths L. Estimates of vaccine effectiveness against measles and mumps; 13 years follow-up of a large cohort in Wales, UK. (Under Review Int J Epi.).

5.0 Abstract

Uptake of MMR vaccine in Wales is high. However, sporadic measles cases still occur and there are large mumps outbreaks every few years. In this study, long-term VE of measles and mumps-containing vaccines is assessed. A retrospective cohort of 822 116 individuals aged one to 30 years were followed up between 1st January 2007 and 31st December 2020. WDSD was linked to vaccination status from NCCHD and WLGP. Outcomes were identified by linking to laboratory confirmations (measles and mumps) and notifications (mumps) data. Complications were sourced from PEDW and WLGP. Extended Cox regression was used to calculate HRs. Adjusted VE (aVE) against confirmed measles after two doses remained high after 15 years 99.7% (95% CI 99.2-99.9). aVE for confirmed mumps was lower, with decline over time; 93.6% (95% CI 90.2-95.8) for those receiving two doses less than five years previously, 49.9% (95% CI 34.4-61.8) after 15 years. A third dose of mumps vaccine temporarily increases protection (87.6%, 95% CI 71.7-94.6). aVE estimates for mumps were lower when based on clinical suspicion.VE was shown to be high against complications for both infections. High, sustained VE for measles strengthens evidence that elimination remains possible and high VE against mumps complications is encouraging. Evidence for waning of mumps immunity may be important when deciding to implement a third dose in outbreak settings. With increased use of data linkage, studies should be conducted to corroborate these findings.

5.1 Introduction

Vaccination against measles has been available in Wales since 1968 (77). However, uptake of the single antigen vaccine was low, and measles remained common until the introduction of the MMR vaccine in 1988. A two dose schedule has been in place since 1996, with doses given at 12-13 months and three years four months (173). An additional dose can be given prior to 12 months for protection during outbreaks (77). Vaccinations are free of charge through the NHS. Uptake ranged from 78% to 98% for one dose (at two years) and 71% to 94% for two doses (at five years) between 2000 and 2020 (6). High coverage is key to achieving the WHO measles and rubella elimination goals (174). Vaccinations for residents up to 16 years of age are recorded in the national register, CYPrIS, in addition to primary care GP records (175).

MMR vaccine has been highly effective against rubella with no confirmed cases in Wales since 2005. However, sporadic measles cases occur, with the last large outbreak in 2013 (82). Large outbreaks of mumps occur every few years (82). Suspected cases of measles and mumps are legally notifiable and recorded in the national case management system. As part of local processes, all suspected measles cases should be sent two test kits. An oral fluid sample is returned to the UKHSA reference laboratory for serology testing and one sample is sent for PCR testing at the Wales Specialist Virology Centre, for more rapid confirmation. Oral fluid testing for mumps is also performed by UKHSA, although the proportion of suspected mumps cases tested is low, especially during times of high incidence. Notifications are often used as an indicator of mumps activity.

Although VE of MMR against measles has been shown to be over 95%, most estimates are based on attack rates in outbreak settings (176–179). Larger studies are based on clinical diagnosis rather than confirmations, which leads to underestimates of effectiveness (93,180,181). VE for MMR against mumps infection is known to be lower than measles, with evidence of waning (182–185). However, there are no large studies of VE for two doses against confirmed infection. Studies with small sample sizes are often not adequately powered to provide precise results and detailed evidence of waning is unavailable (186,187). A summary of previously published VE studies for measles and mumps is found in Appendix 5 and Appendix 6, respectively. Large cohort studies are important in providing robust estimates for monitoring ongoing effectiveness of vaccinations, and country-specific data may help increase local vaccine confidence.

The aim of this study was to assess long-term VE of measles- and mumps-containing vaccines against i) confirmed measles infection and ii) notified/confirmed mumps infection. As a secondary aim, VE against complications was assessed.

5.2 Methods

Analyses were completed within the SAIL Databank, a repository of anonymised individual level national datasets (98,100). A retrospective cohort study of individuals aged one to 30 years at 31st December 2020 (born 1990-2019) and alive and resident in Wales between 1st January 2007 and 31st December 2020 was performed. A total of 1 327 297 eligible individuals were identified using the WDSD, a national demographic register of those registered for NHS care. Vaccination data were from the NCCHD, extracted from CYPrIS and supplemented with data from WLGP, as described previously (188). Confirmations for measles were from reconciled UKHSA and Wales Virology Centre test data, that are used for routine national surveillance. Notifications for mumps were linked to UKHSA serology results. Cases testing negative were discarded. Confirmed, equivocal or untested (notified only) cases were imported into SAIL. Where onset date was unavailable, the earliest of notification date or sample collection date was used.

Complications were sourced from PEDW and WLGP (Appendix 7). Complications were included if hospital admission date or GP consultation date occurred seven days before or 28 days after onset. In a sensitivity analysis, complications were looked for up to eight weeks post onset. There were less than ten additional coded GP complications 4 to 8 weeks post rash onset for both mumps and measles combined. In all of these instances generic codes were used, rather than codes directly associated with measles/mumps. There were no hospital admissions identified 4 to 8 weeks post rash onset. For this reason, four weeks (28 days) was used as the cut off for complications included in the VE estimates.

The following exclusions were applied to the cohort; those without a record in the NCCHD dataset (n=185 365, 14.0%), those not registered with a GP that submits data to SAIL (n=195 936, 14.8%), those with unknown vaccination dates (n=1 210, <0.1%), those with record of more than three measles- or mumps-containing vaccines (n=9 229, 0.7%), those where their first vaccination for measles or mumps was before the recommended age of 12 months (n=19 565, 1.5%) and those who were born overseas, for whom previous measles and mumps exposure is unknown and vaccination history can be less reliable (n=92 658, 7.0%). A further 529 (<0.1%) individuals were excluded because they had a measles or mumps related hospital admission or GP consultation but no notification or confirmation of disease. Additionally, 372 (<0.1%) possible (unconfirmed) measles/mumps cases and 689 (<0.1%) who had confirmed infection before their cohort entry date were excluded.

Individuals entered the study at the latest of; 1st January 2007, their first birthday, the date they first moved in to, or registered with a GP in Wales. Individuals were censored at the earliest of; onset date, date they moved out of Wales, date of death or

31st December 2020. An extended Cox regression model, as described by Zhang *et al.*(189) was used to calculate HRs, where VE=1-HR= 1-exp(γ).

$$h(t) = h_0(t) \times \exp(b_1x_1 + b_2x_2 \ldots b_nx_n + \gamma Xg(t))$$

Vaccination was introduced as a time varying covariate ($Xg(t)$), i.e. individuals vaccinated after study entry contributed an unvaccinated amount of person-time, prior to contributing vaccinated time. Vaccination dates were adjusted by 14 days, to account for time needed for immunity to develop. Adjusted analysis included categorical covariates (x_n) that were significant at the 0.2 level in univariable analysis (Table 5.1), the derivation of which has been described previously (188).

The baseline for estimates was the unvaccinated population. Individuals with confirmed (and notified, for mumps) infection but no recorded complication, were excluded from estimates against complications. This compared infected individuals with complications, to those with no record of infection. Data for missing adjusting variables (birth order (18.3%), broad ethnic group (8.4%), free school meals (4.4%)) were imputed using the Multivariable Imputation by Chained Equations (MICE) and the Nelson-Aalen estimator (190,191). Twenty iterations were performed using all model variables including the outcome, with no auxiliary variables (192). Polytomous logistic regression was used for birth order and free school meals, and logistic regression for imputing ethnic group. Analysis were carried out using R version 4.1.3.

5.3 Results

The final cohort included 822 116 individuals (Table 5.1). Of these, 96.8%, 85.5% and 6.1% had received one, two and three doses of measles-containing vaccine with lower coverage for mumps (96.8%, 84.8% and 4.9%, respectively). A small proportion (< 3%) had single antigen vaccines. Vaccination within six months of due date was, 93% for first dose and 63% for second dose.

Table 5.1. Descriptive summary of 822 116 one to 30 year olds in a retrospective cohort study of measles and mumps vaccine effectiveness, Wales, UK.

Characteristic	Category	Population (n)	%
Age cohort	1-4	199 189	24.2
	5-11	101 377	12.3
	12-16	144 403	17.6
	17-18	51 618	6.3
	19-21	76 166	9.3
	22-30	249 363	30.3
Gender	Male	421 046	51.2
	Female	401 070	48.8
Birth order	First born	300 579	36.6
	Second born	225 672	27.5
	Third born	92 874	11.3
	Forth born	33 286	4.0
	Fifth or more	19 190	2.3
	Unknown	150 515	18.3
Age first registered with Primary Care GP in Wales	Born in Wales	550 147	66.9
	Not born in Wales	271 969	33.1
Broad ethnic group	White	710 147	86.4
	Black/Asian/Mixed/Other	42 850	5.2
	Unknown	69 119	8.4
Health board of residence	HB1	171 326	20.8
	HB2	108 451	13.2
	HB3	88 202	10.7
	HB4	143 880	17.5
	HB5	138 441	16.8
	HB6	15 452	1.9
	HB7	156 364	19.0
Deprivation quintile of residence	Most deprived	197 933	24.1
	2	172 475	21.0
	3	152 105	18.5
	4	144 889	17.6
	Least deprived	154 714	18.8
Ever eligible for free school meals	No	489 021	59.5
	Yes	222 388	27.1
	Pre-school age	74 358	9.0
	Unknown	36 349	4.4
Total Primary Care GP visits 1st January 2020 to 31st December 2020	0	91 966	11.2
	1-4	193 847	23.6
	5-9	172 529	21.0
	10+	363 774	44.2
Rural/urban area of residence	Rural	225 863	27.5
	Urban	596 253	72.5

There were 568 confirmed measles cases, with 88 complications (15.5%, 95% CI 12.7-18.7). Age at onset ranged from one to 25 years (Table 5.2, Table 5.3).

Table 5.2. Descriptive summary of confirmed measles cases, as at date of onset, in a retrospective cohort study of vaccine effectiveness, Wales, UK. Data have been grouped/suppressed to avoid statistical disclosure.

Characteristic	Category	Population (n)
Age	1-4	132
	5-9	116
	10-14	198
	15-19	100
	20-30	22
Vaccine doses	0	390
	1	125
	2+	53
Health board of residence	HB1	44
	HB2	67
	HB3	14
	HB4	33
	HB5	76
	HB6	33
	HB7	301
Deprivation quintile of residence	Most deprived	142
	2	108
	3	142
	4	88
	Least deprived	88
Rural/urban area of residence	Rural	133
	Urban	435
Year of onset	2007	<10
	2008	<10
	2009	102
	2010	<10
	2011	10
	2012	74
	2013	316
	2014	<10
	2015	0
	2016	11
	2017	13
	2018	<10
	2019	<10
	2020	0

Table 5.3. Descriptive summary of confirmed measles cases with complications, as at date of onset, in a retrospective cohort study of vaccine effectiveness, Wales, UK. Data have been grouped/suppressed to avoid statistical disclosure.

Characteristic	Category	Population (n)
Age	1-4	33
	5-9	11
	10-14	31
	15+	13
Vaccine doses	0	55
	1+	33

aVE for one measles-containing vaccine, against confirmed infection was 94.7% (95% CI 93.1-96.0), increasing to 99.5% (95% CI 99.4-99.7) for two doses and similar estimates after three doses (99.6% (95% CI 98.7-99.9)) (Table 5.4). Against any complication, aVE was, 94.3% (95% CI 88.9-97.1), increasing to 99.7% (95% CI 99.2-99.9) for two doses (Table 5.4).

Over time, estimates for effectiveness of one dose of measles vaccine against confirmed infection decrease slightly, although CIs overlap at all time points (Figure 5.1). There was no evidence of waning following two doses, with aVE in those vaccinated less than five years ago 99.8% (95% CI 99.6-99.9) and in those vaccinated at least 15 years ago 99.7% (95% CI 99.2-99.9). There were too few outcomes to estimate waning after three doses.

There were 1 163 confirmed mumps cases, with an additional 2 340 notified but not tested, and 42 complications. Age at onset ranged from one to 30 years (Table 5.5, Table 5.6).

Table 5.4. Vaccine effectiveness estimates for measles-containing vaccination, against confirmed infection and complications, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK.[a, b]

Outcome	Category	Individuals (n)	Rate Per 100 000 Person Days	Unadjusted model	Adjusted model
				HR (95% CI)	aHR (95% CI)
Confirmed measles infection	Unvaccinated	399 410	0.209	-	-
	One dose	475 027	0.015	0.038 (0.029-0.050)	0.053 (0.040-0.069)
	Two doses	675 008	0.002	0.004 (0.003-0.005)	0.005 (0.003-0.006)
	Three doses	49 851	0.002	0.004 (0.001-0.011)	0.004 (0.001-0.013)
Complications with confirmed measles confirmation	Unvaccinated	389 930	0.034	-	-
	One dose	462 680	0.003	0.047 (0.025-0.091)	0.057 (0.029-0.111)
	Two doses	652 658	<0.001	0.002 (0.001-0.007)	0.003 (0.001-0.008)
	Three doses	N/a	N/a	N/a	N/a

[a] Hazard Ratios calculated using extended Cox regression models. Adjusted estimates adjusted for; Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad Ethnic Group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020, and residence in a rural/urban area.
[b] Estimates for vaccine effectiveness of three doses of measles-containing vaccine against complications with confirmed infection unavailable due to small numbers.

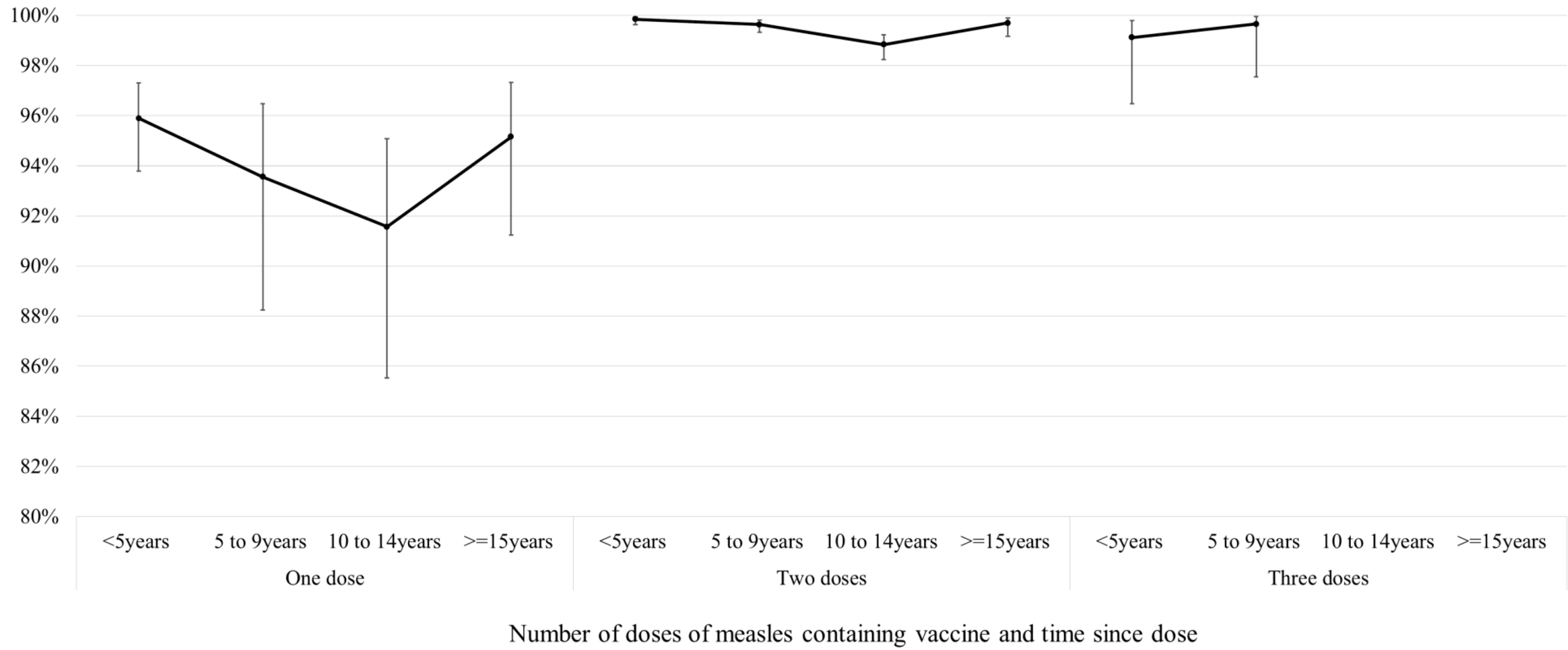


Figure 5.1. Estimated vaccine effectiveness for measles-containing vaccine against laboratory confirmed measles infection by time since dose, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK. Cox regression model adjusted for Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad ethnic group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020 (or year before they exited the study), and residence in a rural/urban area.

Table 5.5. Descriptive summary of confirmed mumps cases, as at date of onset, in a retrospective cohort study of vaccine effectiveness, Wales, UK. Data have been grouped/suppressed to avoid statistical disclosure.

Characteristic	Category	Population (n)
Age	1-4	21
	5-9	36
	10-14	119
	15-19	520
	20-24	387
	25-30	80
Vaccine doses	0	94
	1	92
	2	932
	3	45
Health board of residence	HB1	171
	HB2	163
	HB3	240
	HB4	199
	HB5	155
	HB6	18
	HB7	217
Deprivation quintile of residence	Most deprived	220
	2	204
	3	238
	4	205
	Least deprived	296
Rural/urban area of residence	Rural	331
	Urban	832
Year of onset	2007	<10
	2008	<10
	2009	82
	2010	<10
	2011	21
	2012	18
	2013	162
	2014	174
	2015	34
	2016	17
	2017	10
	2018	16
	2019	307
	2020	306

Table 5.6. Descriptive summary of confirmed mumps cases with complications, as at date of onset, in a retrospective cohort study of vaccine effectiveness, Wales, UK. Data have been grouped/suppressed to avoid statistical disclosure.

Characteristic	Category	Population (n)
Age	1-4	0
	5-19	26
	20+	16
Vaccine doses	0	10
	1+	32

aVE for one dose of mumps-containing vaccine against suspected (notified) or confirmed infection was 50.5% (95% CI 41.5-58.0), with estimates against two doses 63.5% (95% CI 58.0-68.3) and three doses 71.8% (95% CI 65.0-77.2). With only confirmed cases included, the aVE increased to 71.5% (95% CI 61.9-78.7), 76.0% (95% CI 70.1-80.7) and 84.5% (95% CI 77.8-89.2), respectively (Table 5.7). aVE against complications was higher at 80.6% (95% CI 40.2-93.7) for one dose, increasing to 94.4% (95% CI 86.4-97.7) for two doses and 93.5% (95% CI 62.0-98.9) for three doses (Table 5.7).

aVE against confirmed infection decreased with time since second dose of mumps-containing vaccine (Figure 5.2). Less than five years after receiving a second dose, aVE was estimated to be 93.6% (95% CI 90.2-95.8), declining to 86.3% (95% CI 81.7-89.7) at five to nine years and 49.9% (95% CI 34.4-61.8) after 15 years. Increases in aVE were seen after a third dose (87.6% (95% CI 71.7-94.6)), with aVE estimates remaining similar over time.

Analysis using a complete case approach showed similar estimates for VE (Table 5.8, Table 5.9).

Table 5.7. Vaccine effectiveness estimates for mumps-containing vaccination, against clinically notified cases, confirmed infection and complications, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK.[a]

Outcome	Category	Individuals (n)	Rate Per 100 000 Person Days	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)
Suspected and/or confirmed mumps infection	Unvaccinated	400 263	0.115	-	-
	One dose	479 658	0.094	0.484 (0.409-0.573)	0.495 (0.420-0.585)
	Two doses	677 764	0.122	0.402 (0.348-0.464)	0.365 (0.317-0.420)
	Three doses	40 571	0.108	0.332 (0.267-0.411)	0.282 (0.228-0.350)
Confirmed mumps infection	Unvaccinated	399 452	0.043	-	-
	One dose	478 673	0.020	0.271 (0.200-0.369)	0.285 (0.213-0.381)
	Two doses	675 961	0.043	0.314 (0.248-0.397)	0.240 (0.193-0.299)
	Three doses	40 472	0.034	0.230 (0.159-0.333)	0.155 (0.108-0.222)
Complications with confirmed mumps infection	Unvaccinated	399 290	0.005	-	-
	One dose	478 466	0.002	0.170 (0.062-0.468)	0.194 (0.063-0.598)
	Two doses	675 040	0.001	0.057 (0.026-0.124)	0.056 (0.023-0.136)
	Three doses	40 429	0.002	0.078 (0.017-0.362)	0.065 (0.011-0.380)

[a] Hazard Ratios calculated using extended Cox regression models. Adjusted estimates adjusted for; Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad Ethnic Group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020, and residence in a rural/urban area.

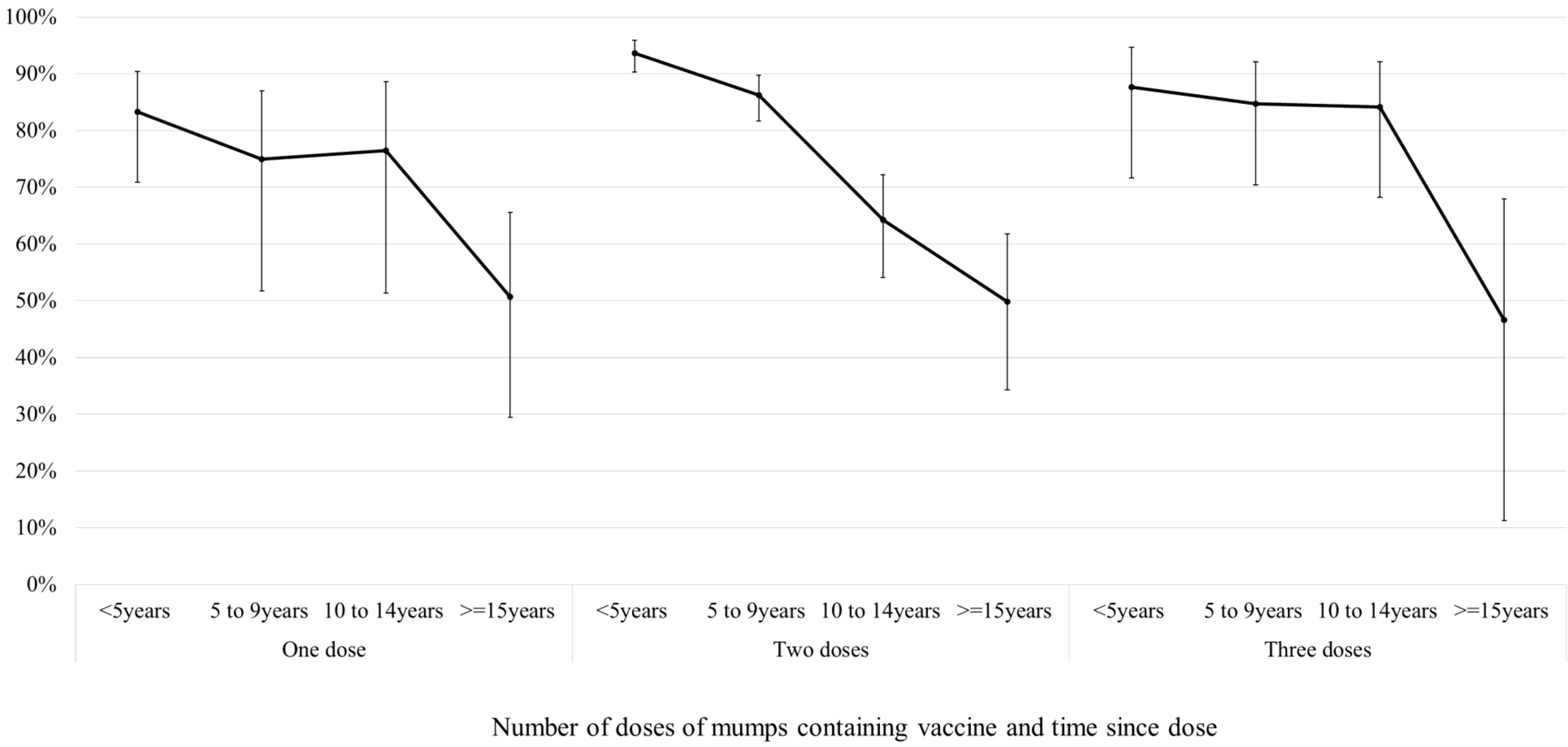


Figure 5.2. Estimated vaccine effectiveness for mumps-containing vaccine against laboratory confirmed mumps infection by time since dose, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK. Cox regression model adjusted for Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad ethnic group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020 (or year before they exited the study), and residence in a rural/urban area.

Table 5.8. Vaccine effectiveness estimates for measles-containing vaccination, against confirmed infection and complications, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK. Results from a complete case analysis approach (n=601 290). [a, b]

Outcome	Category	Individuals (n)	Rate Per 100 000 Person Days	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)
Confirmed measles infection	Unvaccinated	279 160	0.257	-	-
	One dose	344 579	0.015	0.032 (0.023-0.044)	0.047 (0.034-0.064)
	Two doses	538 077	0.002	0.003 (0.002-0.004)	0.004 (0.003-0.006)
	Three doses	36 344	0.002	0.003 (0.001-0.011)	0.004 (0.001-0.015)
Complications with confirmed measles confirmation	Unvaccinated	271 433	0.038	-	-
	One dose	334 736	0.003	0.047 (0.022-0.101)	0.057 (0.029-0.111)
	Two doses	520 965	<0.001	0.003 (0.001-0.008)	0.003 (0.001-0.008)
	Three doses	N/a	N/a	N/a	N/a

[a] Hazard Ratios calculated using extended Cox regression models. Adjusted estimates adjusted for; Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad Ethnic Group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020, and residence in a rural/urban area.

[b] Estimates for vaccine effectiveness of three doses of measles-containing vaccine against complications with confirmed infection unavailable due to small numbers.

Table 5.9. Vaccine effectiveness estimates for mumps-containing vaccination, against confirmed infection and complications, in a retrospective cohort of 822 116 one to 30 year olds, Wales, UK. Results from a complete case analysis approach (n=601 290). [a]

Outcome	Category	Individuals (n)	Rate Per 100 000 Person Days	Unadjusted model HR (95% CI)	Adjusted model aHR (95% CI)
Suspected and/or confirmed mumps infection	Unvaccinated	279 817	0.129	-	-
	One dose	347 664	0.093	0.431 (0.356-0.521)	0.454 (0.377-0.548)
	Two doses	540 098	0.121	0.343 (0.293-0.403)	0.324 (0.277-0.380)
	Three doses	29 905	0.106	0.277 (0.217-0.355)	0.250 (0.196-0.320)
Confirmed mumps infection	Unvaccinated	279 150	0.046	-	-
	One dose	346 886	0.021	0.266 (0.188-0.378)	0.294 (0.211-0.410)
	Two doses	538 673	0.042	0.276 (0.212-0.361)	0.222 (0.172-0.285)
	Three doses	29 833	0.033	0.194 (0.126-0.299)	0.140 (0.092-0.215)
Complications with confirmed mumps infection	Unvaccinated	279 017	0.004	-	-
	One dose	346 720	0.002	0.311 (0.096-1.012)	0.277 (0.087-0.882)
	Two doses	537 950	0.001	0.062 (0.024-0.164)	0.061 (0.024-0.159)
	Three doses	29 803	0.002	0.114 (0.022-0.581)	0.095 (0.019-0.484)

[a] Hazard Ratios calculated using extended Cox regression models. Adjusted estimates adjusted for; Age as at 31st December 2020, gender, birth order, age first registered with a Wales GP, broad Ethnic Group, Health Board of residence, deprivation quintile of residence, eligibility for free school meals, total GP visits in the year preceding 31st December 2020, and residence in a rural/urban area.

5.4 Discussion

This large study shows high VE against measles, with no strong evidence of waning 15 years after receiving a complete two dose course. VE for mumps-containing vaccines was lower, with decline five years after dose two, although a third dose appears to increase protection for several years. VE was lower when based on clinical suspicion, compared to confirmed cases only, as expected due to possible case misclassification. VE was high against complications for both infections. For those with confirmed measles, complication rates were high (over 15%), however, complications in the cohort as a whole were relatively rare.

Comparing estimates from other studies is challenging as vaccination schedules vary, different vaccines may be in use and the delivery settings can impact effectiveness. Underlying population immunity due to natural infection can also affect estimates. Many measles/mumps VE estimates are derived from small cohorts in outbreak settings, using attack rates, as described by Orenstein *et al*. or the screening method described by Farrington (66,70). Although these are rapid and convenient methods, estimates can vary and be imprecise. In line with estimates found here, a review of seventy published studies showed a median VE of 92.0% (IQR 86%-96%) for one dose of measles-containing vaccine when given at 12 months of age or later (176). Estimates for two dose VE against confirmed infection have been as low as 63.4% (95% CI -103.0-90.6) in some settings (193). However, estimates of over 99% are not uncommon (194–196). One dose VE in a previous Wales outbreak was estimated to be 99.3% (95% CI 90%-100%) (63).

The JCVI have advised that the second dose of MMR vaccine in the UK is moved to 18 months to improve coverage (197). This schedule has shown to confer good protection in other countries, with estimates of 99.7% (95% CI 99.2-99.9) for two doses against confirmed measles infection in an Australian study, and slightly lower estimates from Canada (179,198).

Waning protection from measles vaccine was not observed in this cohort. Previous studies in France and the UK using clinically diagnosed cases have observed slight waning, but estimates were imprecise (199,200). Other studies, where VE was estimated using Cox regression, considered one dose of measles-containing vaccine only, but gave similar results when using a confirmed case outcome (93,180,201).

Antibody concentration in vaccinated individuals is known to decline but this is not observed following natural infection (202,203). Those born prior to 1990 would have been more likely to have experienced natural measles infection and therefore life-long immunity (173). Identifying these individuals is challenging with lack of historical electronic records. Recent modelling suggests vaccination is highly protective for a number of decades, although there may be increases in breakthrough infections after 15 years (204). The maximum age of individuals in this cohort was 30 years, with the oldest case 25 years. Therefore, identification of longer-term waning to corroborate serological studies will need longer follow-up.

Vaccines containing the mumps Jeryl Lynn strain have shown to have high efficacy against mumps under clinical trial conditions, but lower VE in outbreak settings (182). Many studies use clinical diagnosis, rather than confirmed infection which may underestimate VE, as this study suggests. Estimates using clinical diagnosis as the outcome report VE for one dose of vaccine from 30% to over 90% (178,182,183,205–209). VE against clinically diagnosed infection for two doses have been as high as 93% (95% CI 85-97)(205), but have been commonly reported at 60-80% (183,206,208–210).

In the absence of PCR testing, confirming mumps infection in previously vaccinated individuals is challenging, which may lead to overestimates of VE (211). Estimates from studies using confirmed cases report VE as high as 94.6% (95% CI 92.9-95.9) for two doses (184,187,212). In contrast, Harling *et al*. compared clinical diagnosis with confirmed infection as an outcome, finding similar estimates for at least one dose (185). Using a more specific clinical case definition results in increased VE (213). Estimates here, using suspected or confirmed cases appear to be low compared to other studies using clinically diagnosed cases. It is possible in outbreak settings the positive predictive value is higher and the proportion of suspected cases that are true infections is higher, resulting in more accurate VE. Higher exposure in household studies may result in lower VE (205).

Orlíková *et al*. estimated VE of two doses of mumps vaccination against any complication at 68% (95% CI 61-75) similar to 76% (95% CI 61-86) reported by Sane *et al*. and 62.7% (95% CI 25.7-81.3) reported by Zamir *et al.* (214–216). For orchitis, Hahné *et al*. reported 74% (95% CI 49-87) (217). However, these studies look at individuals with mumps and estimate VE against developing a complication. Therefore here, the slightly higher estimate of 94.4% (95% CI 86.4-97.7) for two doses against mumps complications, where the comparison group are individuals who did not acquire any mumps infection, may be expected.

It has been estimated that vaccination against mumps wanes after approximately 27 years (95% CI 16-51), with the likelihood of complications increasing with time since second dose (183,214) However, in some outbreaks, notable decreases in VE over time since vaccination have not been seen (183). It was not possible to precisely measure waning following one dose of mumps vaccine, as people typically have a second dose within five years, reducing person-time after for analysis. Findings here may support the use of a third dose in some outbreak settings, unfortunately it was not possible to assess whether effectiveness against complications declines over time.

This study has a number of limitations. Although a national vaccination register was used, misclassification of vaccination status may exist. However, there is no reason this should differ between cases and non-cases. This study only includes people registered with a primary care GP in Wales. Those unregistered, may not have consulted for infection or been vaccinated, leading to an underestimate of VE. Additionally, only individuals registered to practices which submit data to SAIL are included, although these practices are considered to be representative of the total population registered for NHS care (218).

It is important to ensure equal exposure between vaccinated and unvaccinated groups. Recorded MMR vaccination coverage in Wales is lower in those born outside of the UK (188). Previous exposure and infection are also more uncertain for these individuals. If natural immunity is higher and vaccination coverage lower this will underestimate VE. To account for this, the population was restricted to individuals who were born in the UK where lifetime exposure would be relatively similar for this age group. However, within the UK there are larger urban areas which have higher prevalence. It is unknown if individuals had measles or mumps infection before 2008, or outside of Wales for those born elsewhere. Individuals may have been infected but did not seek health advice or get tested, under-ascertainment of cases will bias towards the null.

It is also important that case ascertainment is equal between exposure groups. Vaccinated cases may have milder attenuated infection which could be under-diagnosed, thus leading to overestimates of VE (219–222). A number of complications from infection were considered, although rarer complications such as oophoritis (mumps) and deafness (measles) were not considered. This is not expected to impact overall VE estimates. General practitioners ability to recognise and associate complications with a previous infection may be limited in a country where transmission is not endemic.

A strength of this study is that it was possible to adjust for a number of factors through data linkage. Missing data for a small number of independent variables were imputed to retain power. Data were assumed to be missing at random, although there may be reasons why these variables are less likely to be recorded for some individuals than others. More suitable methods for imputation may exist.

Different VE estimates may have been observed in populations excluded from this analysis. For example, the overall rate of measles infection was 38.9 per 100 000 population in the excluded non-UK born individuals over the study period, compared to 73.8 per 100 000 in the UK born study population. For mumps this was higher at 198.6 in the non-UK born and 426.2 in the UK born. It is known that vaccination coverage is lower in this population, but case ascertainment may also differ, particularly if infection is seen as common in childhood. Individuals may have had infection as a child and vaccinations may also have been given in less optimal settings which can reduce VE. Individuals vaccinated before 12 months of age were excluded, as maternal antibodies may interfere with seroconversion following vaccination. It is common for individuals to be vaccinated earlier in settings where the risk of infection is high. Individuals receiving an alternative schedule are likely to have some long-term protection (223). There is need to continuously review the timing of measles vaccine doses in the context of elimination, as schedules may need to be altered in areas where there is high susceptibility before the first dose is due (224).

This is the largest known VE study for both measles and mumps infection and associated complications. Precise estimates over time could be calculated using a national vaccination registry and confirmed infection as the outcome. The high, sustained VE for measles shown here, strengthens evidence that elimination remains possible. Longer periods of follow-up are required to estimate VE in older individuals, 15 years after vaccination.

High VE for mumps-containing vaccines against complications is encouraging. The evidence for waning immunity, even five years after dose two, may be useful when deciding whether to implement a third dose in outbreak settings. The need to fully understand waning of protection against mumps over time is important in understanding and planning for potential implications of changes in vaccination schedules. Although the majority of individuals received vaccination around the time it was due, further studies would be needed to assess the impact of late (or early) administration of the first or second dose of MMR vaccine.

This study highlights the importance of accurate classification of cases in VE studies. Although it may provide useful intelligence for acute management, it may not be useful to rely on VE estimates from outbreak settings. Depending on the age of the population, different levels of waning immunity are likely to be present, which will make results difficult to interpret. With the increasing availability of data linkage, further studies will be able to corroborate and expand upon the findings in this paper.

Chapter 6 – Discussion

6.0 Summary

Throughout the previous four chapters the successful development of methods for evaluating equity and effectiveness of vaccination programmes in Wales using data linkage have been presented. I have demonstrated the value of linking routine national datasets, through focusing on a well-embedded routine childhood vaccination, and an older adult programme with the unique opportunity to evaluate novel vaccines delivered in the midst of a global pandemic.

Evidence from public health surveillance reports showed that in the first few months of the COVID-19 pandemic vaccinations were delivered rapidly and uptake in older adults was high. Despite this, coverage was lower in more deprived areas and among ethnic minority groups and the equity gaps did not appear to be narrowing overtime. This was the first known study in the UK to use Census data linkage to provide high data coverage on ethnic group. Additionally, it was possible to provide encouraging VE estimates against severe COVID-19 infection using a robust cohort design, adding to the evidence base at a time when the COVID-19 vaccination was still being rolled out globally.

Through linkage of a wider number of administrative datasets, it was possible to look at the association of MMR uptake with a large number of social and demographic factors. At the time of publication, it was one of the most comprehensive data linkage studies assessing determinants of vaccine uptake. This study highlighted the importance of data cleansing to ensure official coverage figures are accurate, whilst identifying a number of under-vaccinated groups which may be vulnerable to future outbreaks of measles or mumps. Looking at data on vaccine refusal, it appears as though hesitancy is not the primary reason for being unvaccinated. Despite the approach to delivery of COVID-19 and MMR vaccinations being different, it has been shown that some inequities are consistent across programmes.

Lastly, through conducting the largest known contemporary field VE study for both measles and mumps infection and associated complications, it was possible for the first time to quantify vaccine waning. Demonstrating that 15 years after two doses of measles vaccine VE remains over 95%, provides strong evidence that the aim of global elimination remains deliverable. Showing that the effectiveness of mumps vaccine begins to decline after five years, provides useful evidence when deciding whether to implement a third dose of vaccine in outbreak settings. The importance of using specific outcome definitions for accuracy of estimates has been shown and it was concluded that VE estimates from field settings that do not account for time since vaccination are difficult to interpret.

6.1 Update on COVID-19 literature

Since the articles on COVID-19 vaccination presented in this thesis were published, the global evidence base has expanded rapidly. Further multi-dimensional COVID-19 vaccination studies have since been published by the UK (225–229), US (230), Israel (231–233), Norway (234), Canada (235–237) Italy (238), Australia (239), The Netherlands (240), Belgium (241,242), Germany (243), France (244), Sweden (245,246), Greece/Cyprus (247). However, many studies still focus on evidence from small surveys that do not include a large number of demographic and socioeconomic factors, specifically studies from LMICs (230,248). This is also the case for studies focusing on childhood immunisations (249).

In Wales, uptake of COVID-19 booster doses for those who are eligible has been consistently lower compared to uptake of the primary course. Lower uptake of COVID-19 vaccination among some ethnic groups has been a consistent trend across the UK, with those in the Black African or Black Caribbean groups having lower vaccination coverage compared to White British groups. These findings are the same across all age groups, for pregnant women or those with specific clinical risks (227–229,250,251). Uptake has also been shown to be consistently lower in more deprived areas (227,228,251). For uptake of the primary course, coverage was shown to be lower in those who identified as Muslim or Buddhist (227,228), those who did not have English recorded as their main language (228), those with a disability (227,228), fewer qualifications (228), or those who lived alone or in multigenerational homes (227). Differences by sex have been seen in younger age groups, but not older age groups (227,228). Many of the same factors were shown in Chapter 4 to be associated with lower measles vaccination coverage in children and young adults.

The WHO and International Vaccine Access Center have conducted a living systematic review on COVID-19 VE since 2021, providing a useful summary given the rapid evolution of the variant and vaccine landscape which includes the study published in Chapter 3 (252). As at August 2025 this included 686 studies from 54 countries. Chapter 3 assessed COVID-19 VE from the start of the vaccination campaign in December 2020 when Alpha was the dominant variant, up until mid-July 2021 when the dominant variant was Delta. Omicron was first detected in Wales at the end of 2021 and various sub-variants of this parent linage have been evolving and circulating since. The original COVID-19 programme in Wales used a combination Pfizer-BioNTech (BNT162b2) (Comirnaty), Oxford- AstraZeneca (ChAdOx1) and Moderna mRNA-1273 (Spikevax) vaccinations (109). The viral vector ChAdOx1 vaccine has since been withdrawn from use globally with modified versions of the Spikevax and Comirnaty mRNA vaccines, better matched to newly dominant variants, continuing to be used across the UK (109).

Updated VE studies have proven important for providing evidence for refining vaccine policy. The 2025-26 Autumn COVID-19 vaccine programme was reduced substantially, compared to the 2024-25 campaign which aligned with the wider influenza vaccine policy (253). This is in part due to higher levels of population immunity both from natural infection and vaccination, and a reduction in severity of disease for most individuals (109). Early data on the JN.1 variant Spikevax and Comirnaty mRNA vaccines in use during the 2025 spring booster programme appear to give moderate to good protection against hospitalisation, up to three or four months post vaccination, although further data are needed (254,255).

6.2 Strengths and limitations of data linkage for vaccine programme evaluation

The pandemic has shown that evidence for vaccination programmes can be expanded rapidly when resource allows. The ability to link large administrative datasets has improved the speed and detail in which vaccine programmes can be evaluated in terms of equity, effectiveness and safety (256). The ability to link administrative datasets enables high powered studies at fairly low cost. Through the use of TREs with robust information governance policies, high ethical research standards can be maintained. However, knowledge of the underlying data, context and systems is important - it can improve efficiency of analysis and help prevent false conclusions through overinterpretation of limited data.

However, for studies such as those described here to be commonplace, databases need to be of good quality. Data needs to be complete and accurate, otherwise information on groups with suboptimal vaccine coverage can be misleading, resulting in incorrect focus of time and resources. As described in Chapter 2, those with unknown ethnic group are a population that appear to have low vaccination coverage. This may be due to inefficient recording or could be a result of personal experiences resulting in individuals not wanting to divulge certain information in an official way. It was also observed that conflicting entries can be given for the same individual when looking at different datasets. How these issues are handled are an important consideration when designing studies that use routine administrative datasets. The SAIL Databank is a well-established TRE with robust methodology for assigning the ALF. However, data quality is essential in ensuring identifiers are complete and accurate, to limit miss-matches when linking datasets. Individuals need to engage with systems for their data to be recorded. Therefore, the most vulnerable people may be absent from routine datasets, and those who engage with services less frequently are likely to have data that are more out of date. Through data linkage it is possible to look at multiple systems at the same time, so findings may be more inclusive of the whole population.

In the studies presented in Chapter 2 and Chapter 4, I described vaccination uptake by a variety of key sociodemographic factors, for both adult and child immunisations but further factors may be identified through the use of more advanced statistical techniques (257). There are some factors which could not be reliably sourced from SAIL data at the time of analysis that were highlighted in the literature as potential correlates, for example, child's attendance at daycare, distance to GP or immigration status. In Chapter 4 it was highlighted how some socioeconomic or demographic information may be out of date, specifically that sourced from one off surveys. Now the 2021 Census data are available in the SAIL Databank some factors could be revisited. Other data linkages may also yield more insights, for example, linkage of primary care data with maternal records has been used to explore the impact of mothers mental health on uptake of childhood vaccinations in Scotland (258).

To ensure information governance procedures are adhered to, there are strict procedures for withdrawing results from the TRE. It was not possible to look at more specific ethnic groups due to small numbers, and small numbers also limited the level of data that could be exported for more localised research. The use of OR are not particularly useful for tracking improvements overtime but can help prioritise interventions (51). Consideration of the intended audience needs to be taken in to account when communicating these types of statistical findings, with insight from different communities included when disseminating results (259).

The value of systems for routinely assessing VE post vaccine implementation has been highlighted (256,260–264). However, observational studies are prone to bias which gold standard randomised controlled trials aim to eliminate. For studies linking routine administrative data, selection bias will be partly dependent on the data available, the source and population coverage. Although the datasets used in Chapters 2 through 5 should cover the whole of the population of Wales (with the exception of WLGP), there remains a gap for those who are the most vulnerable in society. Hidden populations or minorities who are not registered for NHS care are unlikely to be included, even when linking multiple datasets.

Unvaccinated individuals in a highly vaccinated population are likely to have very different characteristics to those who have been vaccinated. Adjustment variables were used to reduce confounding, and the use of propensity scores was also explored in Chapter 3, both common approaches for controlling for bias in observational cohort studies (265). The ability to control for a number of confounding factors, like those identified in the above equity studies, is a strength of data linkage.

There are other specific biases that should be considered when designing observational cohort studies (266). Confounding by indication occurs when those with more severe underlying chronic illnesses or multiple co-morbidities are more likely to be vaccinated. These individuals may have poor immune response relative to other individuals and this can lead to an underestimate of VE. Frailty bias occurs when those with more co-morbidities or general poor health may be less likely to be vaccinated due to access issues and may also be more likely to be infected or have serious outcomes, leading to overestimates in VE. In contrast, healthy vaccinee bias - where healthy people are more likely to be vaccinated but also less likely to have severe outcomes from disease, can also occur (267). The use of co-morbidity scores aimed to reduce these types of bias in the analysis above. In Chapter 3, VE was seen 0 to 6 days post COVID-19 vaccination, this was likely due to those being unwell not attending for their vaccination appointment and subsequently testing positive for SARS-CoV-2 or ending up in hospital.

It is also important to control for health care user bias. Individuals who attend for vaccination may be more likely to consult a physician when unwell, leading to an underestimate of VE. In contrast, those who are vaccinated may have attenuated disease and be less likely to attend primary or secondary care even though they are unwell, this will overestimate VE. Attempts were made to adjust for health care seeking behaviour in the above studies through measuring interaction with primary care. The development of a series of healthcare seeking indicators could be more beneficial and could be achieved through data linkage (268). Adjusting for individuals behaviour, such as compliance with wearing masks would be fairly unique to pandemic situations (269), although adjustment for risk behaviour may be important when looking at occupational vaccines or vaccines against sexually transmitted infections.

When constructing cohorts from administrative datasets and following up over a long time period, subjects may be susceptible to immortal time bias. For example, if they are registered as living here but have moved out of the country for a significant of time, any outcomes would not be recorded on local systems.

Misclassification of exposure or outcome can be difficult to avoid when using routinely collected data and can be a result of incorrect data linkage (270). Non-differential misclassification will always lead to an underestimate of VE, whilst differential misclassification can bias in either direction. Although vaccine registries are considered a gold standard for vaccination surveillance (84), they can be incomplete, as shown in Chapter 4. However, the use of linkage to supplement vaccine registries has also been demonstrated. Misclassification in exposure can be assumed to be non-differential and corrected for through statistical methods (271), however it may be that some individuals, such as those who were on alternative schedules in other countries or those who have no proof of prior vaccination are less likely to have accurate exposure status. Chapter 5 shows the importance of using robust definitions for outcomes where possible, although this can be influenced by specific test sensitivity and specificity (272). A clinicians decision to test could be influenced by the vaccination status of a patient.

There are a number of additional considerations that need to be taken in to account when measuring VE for common infections. It is important to control for prior infection where possible, although historical data may not be available (273). If individuals have previously been infected, they may be less likely to be vaccinated, leading to underestimation of VE as unvaccinated individuals have some level of immunity. In cohort studies, differential depletion of susceptibles can lead to artificial waning during periods of high incidence, as the proportion of individuals who are unvaccinated but are not susceptible to infection gets larger (274,275). Administrative databases may not capture mild or asymptomatic cases in large population cohort studies. In the case of COVID-19, as new vaccines and variants emerge, genomic characterisation of cases is particularly important to inform vaccine policy and development. The majority of the population are now likely to have ‘hybrid immunity’ where individuals have both been vaccinated and had natural infection at least once. The use of an unvaccinated comparison group is challenging when a high proportion of the population are vaccinated or have natural immunity (276). Smaller test negative case-control studies which have been the standard design for influenza VE studies for a number of years, may be more robust in this situation. Since the pandemic there has been a wider focus on strategies for estimating VE and several guidance documents have been published online by the WHO (277–279).

Although data linkage is becoming more common, without standardisation and guidance on recording it will be difficult to compare findings between countries. Suitable infrastructure and computer power may be costly making this type of research a particular challenge for LMICs.

6.3 Dissemination of research and public health impact

Through the University, as well as in my professional experience as a Senior Epidemiologist in PHW VPDP, I have had the opportunity to share my work through a number of channels. I was involved in discussions during the development of WIS in 2020, before the roll-out of the COVID-19 vaccination programme. As a lead within VPDP for setting up COVID-19 vaccination surveillance, I contributed to meetings to ensure the database was suitable for surveillance. I composed the documentation and metadata for the SAIL Databank CVVD dataset and worked with DHCW and LHB colleagues to improve completeness and quality of data. The COVID-19 vaccination campaign began in December 2020 and provisional results from Chapter 2 were available for presentation to the Welsh Government First Minister in February 2021 following concern around increased burden of disease in ethnic minority groups. Routine immunisation equity reports are now published by PHW VPDP, based on the methodology from Chapter 2, which are widely discussed with stakeholders across NHS immunisation services (82). Ongoing updates have been shared at the Vaccine Equity Committee (VEC) that was established during the pandemic as part of the Vaccination Equity Strategy for Wales (280). I also had the opportunity to present the published work at the 2021 PHW Science in Health Protection Seminar and at the UK Health Data Research (HDR) Alliance 'Diversity in Data - Ethnicity coding working group' in January 2022 (281). This work was featured as a HDR UK case study (282) and referenced in the 2024 COVID-19 public inquiry in the context of ensuring tailored messaging for those where uptake is suboptimal (283).

In March 2021 provisional results from Chapter 3 were presented at the UK COVID-19 VE working group for peer feedback from experts in conducting VE studies. I was also able to attend European Centre for Disease Prevention and Control webinars on 'Monitoring uptake and effectiveness of COVID-19 vaccine in the WHO European Region', discussing the preliminary results from the first COVID-19 VE studies conducted in Israel and Scotland which provided useful considerations for my analysis. The results from Chapter 3 were presented as a poster at the 2022 Swansea University Medical School Post Graduate Research Conference.

The findings from Chapter 4 have been timely in terms of providing supporting evidence for the PHW Measles and Rubella Elimination Task Group Action Plan which is currently under revision (148). The results were presented as an oral presentation at the 2023 Swansea University Medical School Post Graduate Research Conference. The findings were also shared at the UK 4 Nations Deep Dive into declining vaccination coverage in secondary school programmes in October 2024, as well as a Directors of Public Health Vaccination Inequalities update in June 2025. Although there are published studies highlighting inequalities in vaccination programmes internationally, disparities in uptake can be complex and context specific, and evidence is limited within Wales and the UK. This study provided important information appropriate to Welsh context and vital to inform service improvement.

I presented the work on measles and mumps VE as part of the Swansea University Medical School Lunch Time Seminar Series in February 2025 and have presented the mumps findings from Chapter 5 at the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2025.

Additionally, all aspects of the above have been disseminated to the wider VPDP clinical and engagement team through our monthly team meetings providing evidence to support practice. The VPDP engagement team was established during the pandemic to provide dedicated support to improving vaccination coverage in Wales and has a key role in trying to understand reasons for inequities that have been identified through studies such as those presented here.

The methods developed in this thesis have been used for further studies on vaccine equity where I have taken a supervisory role. A repository of useful code sets now exist and the code is available on GitHub: https://github.com/PerryM-epi/PhDThesis.git. I also have trained several of my team within PHW VPDP in performing multivariable analysis. A study on HPV vaccination is currently being written up for publication, making further use of the methodology developed here. I am also supervising a study on 'Evaluating equality in vaccine uptake during pregnancy: a quantitative data linkage study', supporting the development of methods to accurately report on uptake of maternal vaccines by a number of socioeconomic and demographic factors. This study is at the stage of having provisional results, ready to be shared with the PHW Maternal Vaccine Network which I currently chair.

During the COVID-19 pandemic, expanding on the work demonstrated in Chapter 2, my team were able to secure funding from Health and Care Research Wales Evidence Centre. This project looked at developing methods through SAIL Databank for estimating vaccination coverage in specific minority groups. As lead for this project that consisted of twenty professionals and lay members, I used skills developed through my PhD research to train a number of the team on data linkage and scoped datasets for identifying, homeless populations, people with physical and sensory disabilities, substance misuse history and asylum seeker and refugee populations amongst others (284). I was able to guide a colleague through successful submission and publication of their first, first author paper (225), in addition to publishing a joint first author article focusing on household composition (226). There is ongoing work to refine these methods and expand them for use outside of COVID-19 vaccination. I am currently leading a data linkage study entitled ‘Estimating the burden of severe acute respiratory infection (ARI) in those with lived experience of homelessness, creating evidence for vaccine policy’, with initial outputs from this study also presented at ESCAIDE 2025.

I have had the opportunity to contribute to other studies at Swansea University, including a study with my primary supervisor looking at vaccination coverage in looked after children (285), and providing advice on an MSc Dissertation looking at the long-term impact of measles infection. More formally through my role as a public health professional, I have supervised an MSc student at Cardiff University on developing methods for assessing effectiveness of HPV vaccine.

The size of the population of Wales can mean it takes time for enough outcomes to be accumulated for robust VE estimates to be produced through cohort studies. However, with the methodology now in place, we are in position to apply it to vaccination programmes as they are introduced and provide real life rapid evidence back to the scientific community. Methods developed within my programme of research are in the process of being applied to the Respiratory Syncytial Virus (RSV) programme which was introduced in September 2024 and can also be modified for the recent varicella vaccine roll-out.

6.4 Recommendations and further work

The use of a TRE to link national datasets that can be accessed by both public health organisations and academia to provide rapid, high quality vaccine programme evaluation should be encouraged. Countries such as Wales which are ahead in development of methods to use administrative data for this purpose can support other nations to do the same.

Ensuring vaccine equity should be considered a core part of any vaccination programme (286). Therefore, it should be an aim for vaccination coverage by certain characteristics such as ethnic group and language preference to be reported routinely, as has been recently introduced in Scotland (287). This should not be only considered for vaccination programmes but also uptake of other health services or outcomes (288).

New programmes or significant changes to existing programmes should be reviewed for their potential to exacerbate or relieve existing inequities or create new ones.

National guidance on collecting, recording and reporting such data would be beneficial, so that minimum data items can be standardised across national datasets and equity over time and regions can be compared (249). Enhanced collection of data on certain characteristics, potentially at the point of registration for primary care may improve coverage of data items that will enable tailoring of services to improve population health. Ensuring communities are consulted on how these data are gathered and the purpose of collecting such information is important. The National Immunisation Framework for Wales and NHS England Vaccination Strategy both aim for the provision of a national vaccination record for each individual (289,290). It should be ensured that experts in vaccine programme evaluation are included in discussions when specifications for development of these systems are made.

Similar inequities are shown to exist between countries so it would be beneficial to collaborate and learn from one another by sharing best practice (291). There is a general lack of evidence for interventions in minority communities and combining knowledge could accelerate improvements (292,293).

Data linkage has provided the tools for 'assessing the situation' and identifying groups with suboptimal vaccination coverage (50). This is an important component of the WHO TIP guidance (50,294). The next stages in this guidance should be followed to conduct research into the reasons for suboptimal coverage in the groups identified here; large families, those born outside of the UK or with specific language requirements. There are a number of frameworks that can be followed for conducting this kind of research (286). The evidence gathered in this thesis can provide useful background to support funding applications to conduct qualitative work, or trial interventions that may improve vaccine uptake. It may be beneficial to initially focus on reducing barriers to access and would be in line with recently published guidance for the UK (295).

It is clear from my experience working with LHBs that not all tested interventions to improve uptake are written up for peer-review publication. This should be encouraged and this end point considered at the design stage. This process could be supported by collaborating with academia. Wales is in the process of building a national repository so local initiatives which have not been published as peer-reviewed articles can be shared between LHBs to accelerate learning. Common issues can hopefully be identified, and collaborative working encouraged.

With an apparent, systematic lower vaccination uptake of both childhood and adult vaccinations by similar factors, despite differing delivery models, there should be more focus on generally embedding confidence in vaccination programmes across the life course. Some differences may be related to engagement with health services in general, therefore collaboration with other teams such as screening services may be more resourceful (296,297).

There is a need to identify ‘hidden populations’, if vaccination coverage data can be robustly used to assess the risk of future disease outbreaks. Identification of individuals missing from routine administrative datasets should be conducted in each country. Ensuring everyone has the same level of access to vaccinations and other preventative health care is challenging. Engagement with third sector organisations could be beneficial to ensure those with unstable living situations or those who have newly arrived in the UK are registered for NHS care. Bespoke methods for assessing coverage in these groups may be required (225,298).

Healthcare professionals should have enough knowledge to be confident in discussing vaccinations with individuals (299). Having robust local data on equity, effectiveness, impact and safety that individuals can relate to may help with these conversations and where possible should be included in training materials (300). This would support advice from a recent Royal College of Paediatrics and Child Health report, highlighting the need to strengthen health professionals’ confidence when having discussions about vaccinations with parents (295).

Although robustly conducted studies should be encouraged, it should be ensured that findings can be easily interpreted by lay individuals (301). Ensuring clear information and robust communications is a key component of the Public Vaccination Literacy Strategy for Wales (302). Easy read summaries and infographics may make scientific vaccine literature more accessible, with co-production of resources where possible.

A guidance document for conducting VE cohort studies through the use of routine administrative datasets in your chosen TRE, including how to control for different types of bias in observational studies, would speed up analysis and ensure teams are working to a set standard. Checks for residual confounding and holding simulated data to test methodology may be best practice (265,303–305). This should include a discussion on the appropriateness of cohort or case-control studies in different settings (306) and consideration of published guidance (277–279). The need for VE assessment in specific clinical groups would help refine policy and potentially improve uptake.

There has been a global decline in coverage of routine vaccinations which has not recovered since the COVID-19 pandemic (307). This has a substantial impact on elimination programmes, including measles and rubella (308,309). Outbreaks of measles in populations with low vaccination coverage are likely to become more frequent (308,309). Focused studies in elimination settings may help progress targets, not only for measles and rubella, but also polio, Hepatitis B and cervical cancer (HPV) (149).

Two elements of vaccine evaluation were not explored in this thesis: impact and safety. Impact studies which utilise methods such as regression discontinuity analysis, interrupted time series, or difference-in-differences are increasing (310,311). Results from these types of studies may be more intuitive to interpret and have the benefit of evaluating both direct and indirect protection afforded by vaccination (312). Large datasets provide the opportunity to look for rare side effects of vaccination and SAIL Databank has been used for this previously (313). The cohorts developed in this thesis may also provide a useful basis for taking forward some of this research.

6.5 Conclusions

Data linkage provides a valuable tool to produce rapid information to aid vaccine programme policy and delivery. Publication of the studies presented here have added to the global evidence base on vaccine equity and effectiveness. Although generally vaccine coverage is high, there are multiple disparities in uptake across Wales. Encouraging vaccine effectiveness estimates show that vaccination remains an important intervention for reducing morbidity and mortality from infectious disease globally. It is essential that with the wealth of evidence that can be produced, steps are taken to effectively communicate findings from large data linkage studies and ultimately implement improvements in vaccine programme policy and delivery.

6.6 Reflections

The initial idea for this project was to look at how data linkage could be used to evaluate childhood vaccination programmes. However, the timing of the COVID-19 pandemic meant the scope was expanded to include the new imminent vaccine programme. As a part-time student, there were substantial challenges producing rapid information alongside my professional role as an Epidemiologist during a pandemic. However, having the opportunity to estimate VE of novel vaccines in a mostly naive population is something many Epidemiologists would not get the chance to do in their career.

There were occasional practical challenges with using the TRE, including problems with timely data flows and lack of metadata for existing datasets. However, through connections within my professional role and communication with data providers, it was possible to negotiate many of these obstacles without too much delay.

Throughout the past five years I have become a more confident scientific writer, and as a consequence my articles have improved in quality. I have gained experience in the submission, review and the publishing process of four different journals.

Throughout the past five years, I have been compiling a database of published vaccine equity and effectiveness studies. It is evident, that there continues to be a bias of literature around COVID-19. As scientists we need to ensure the momentum within the scientific community gathered during the pandemic is maintained and this focus is now turned towards other vaccination programmes.

This project has afforded me the time to read more widely on the topic of the Epidemiology of Vaccine Preventable Disease and as a result I am more aware of gaps that exist in the literature and more confident in my contribution to discussions. Going forward I hope to progress some of the recommendations from this project and ensure research remains embedded as a part of my role, through work both locally and further afield.

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Authorship Declaration

The following people and institutions contributed to the publication of work undertaken as part of this thesis:

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Paper 1: Perry M, Akbari A, Cottrell S, Gravenor MB, Roberts R, Lyons RA, Bedston S, Torabi F, Griffiths L. Inequalities in coverage of COVID-19 vaccination: A population register based cross-sectional study in Wales, UK. Vaccine. 2021;39(42):6256-6261. doi: 10.1016/j.vaccine.2021.09.019.

Located in Chapter 2.

MP led the conception and design of this work with input from LJG and SC. MP performed the analysis with AA completing the linkage and analysis to derive the ethnic group variable. RAL and FT are members of the Con-COV group that created the linked data cohort that enabled these analyses to be undertaken. MP drafted the first iteration of the manuscript. All authors critically reviewed the manuscript, provided important intellectual input and approved the final version.

The candidate contributed over 80% of work to this study.

Paper 2: Perry M, Gravenor MB, Cottrell S, Bedston S, Roberts R, Williams C, Salmon J, Lyons J, Akbari A, Lyons RA, Torabi F, Griffiths LJ. COVID-19 vaccine uptake and effectiveness in adults aged 50 years and older in Wales UK: a 1.2m population data linkage cohort approach. Hum Vaccin Immunother. 2022;18(1):2031774. doi: 10.1080/21645515.2022.2031774.

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MP led the conception and design of this work with input from LJG, SC, MBG, SB, CW and JS. MP performed the analysis, JL created the underlying QCOVID dataset and SB provided the code for the imputation, AA completed the linkage and analysis to create the ethnic group variable. MP drafted the first iteration of the manuscript. All authors critically reviewed the manuscript, provided important intellectual input and approved the final version.

The candidate contributed over 80% of work to this study.

Paper 3: Perry M, Cottrell S, Gravenor MB, Griffiths L. Determinants of equity in coverage of measles-containing vaccines in Wales, UK, during the elimination era. Vaccines (Basel). 2023;11(3):680. doi: 10.3390/vaccines11030680.

Located in Chapter 4.

MP led the conception and design of this work with input from LJG, SC and MBG. Methodology, analysis and were data by MP. MP prepared the original article with all contributing to review and editing. SC, MBG and LJG supervised the study. All authors read and agreed to the published version of the manuscript.

The candidate contributed over 90% of work to this study.

We the undersigned agree with the above stated contributions for each of the above published peer-reviewed manuscripts contributing to this thesis:

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Personal Bibliography

This section lists additional papers and conference abstracts that I have been involved in during my candidature, related to the themes outlined in this thesis. Many of these studies have been possible due to work that was completed as part of this thesis, whilst for others, insights gathered as part of this work enabled me to make a meaningful contribution.

Jones G, **Perry M,** Song J, Johnson C, Cottrell S. (2022, November 23-25). Estimating COVID-19 and influenza vaccination coverage in homeless populations; Wales, UK. [Conference presentation]. European Scientific Conference on Applied Infectious Disease Epidemiology, Stockholm, Sweden. https://www.escaide.eu/en/publications-data/escaide-2022-abstract-book

Lench A, **Perry M,** McGowan A, Cottrell S. (2022, November 23-25). COVID-19 vaccine coverage in pregnant women and socioeconomic inequities, 2021-2022; Wales UK. [Conference presentation]. European Scientific Conference on Applied Infectious Disease Epidemiology, Stockholm, Sweden. https://www.escaide.eu/en/publications-data/escaide-2022-abstract-book

Lench A*, **Perry M***, Johnson RD, Fry R, Richardson G, Lyons RA, et al. Household Composition and Inequalities in COVID-19 Vaccination in Wales, UK. Vaccines (Basel). 2023;11(3):604. *Joint first authors.

Jones G, **Perry M**, Bailey R, Arumugam S, Edwards A, Lench A, et al. Dimensions of equality in uptake of COVID-19 vaccination in Wales, UK: A multivariable linked data population analysis. Vaccine. 2023;41(49):7333–41.

Bailey GA, Lee A, Bedford H, **Perry M**, Holland S, Walton S, et al. Immunisation status of children receiving care and support in Wales: a national data linkage study. Front Public Health. 2023;11:1231264.

Perry M, Gravenor MB, Cottrell S, Griffiths L. (2025, November 19-21). A large data linkage study to quantify waning of MMR vaccine against mumps, Wales, UK. [Conference presentation]. European Scientific Conference on Applied Infectious Disease Epidemiology, Warsaw, Poland. Link TBC

Perry M, Song J, Youlden H, Johnson C, Cottrell S. (2025, November 19-21). Hospital admissions for respiratory infections in those with lived experience of homelessness, evidence for vaccine policy from Wales; UK. [Conference presentation]. European Scientific Conference on Applied Infectious Disease Epidemiology, Warsaw, Poland. Link TBC

Jones R, Youlden H, McDermott C, **Perry M**, Norwood J. Understanding measles infection and how to improve uptake of the MMR vaccine. Nurs Child Young People. 2025. Online ahead of print.

Appendix 1. List of key variables used in analysis relating to vaccination equity and effectiveness.

Dataset	Table	Variable Name	Description
ADBE	BIRTHS	MOTHER_BIRTHCOUNTRY_CD	Country of birth for mothers of children born in Wales.
CDDS	DF_COVID_DEATHS_CONSOLIDATED	DEATH_DT	Date of death.
CENW	CENSUS_PER_HH_FAM_WALES_2011	ETHNICID	Ethnic group as recorded in the 2011 Census.
CENW	CENSUS_PER_HH_FAM_WALES_2011	MAINLANG	Main language as recorded in the 2011 Census.
CENW	CENSUS_PER_HH_FAM_WALES_2011	COB	Country of birth as recorded in the 2011 Census.
CENW	CENSUS_PER_HH_FAM_WALES_2011	RELIGION	Religion as recorded in the 2011 Census.
CENW	CENSUS_PER_HH_FAM_WALES_2011	HLQPUK11	Highest qualification as recorded in the 2011 Census.
CVVD	DF_WIS_DEMOGRAPHICS	PRS_PRIORITY_GRP	Highest COVID-19 vaccination priority group as defined by JCVI.
CVVD	DF_WIS_DEMOGRAPHICS	PRS_CARE_HOME_RESIDENT	Flag to indicate individual is a care home resident.
CVVD	DF_WIS_DEMOGRAPHICS	PRS_OCC_FRONTLINE_IND	Flag to indicate individual is a health or social care worker.
CVVD	DF_WIS_DEMOGRAPHICS	LHB	Individuals local health board of residence.
CVVD	DF_WIS_OUTCOMEENRICHEDDATA	APPT_OUTCOME	Outcome of COVID-19 vaccination appointment (APPT_OUTCOME=4 means vaccination was given).
CVVD	DF_WIS_OUTCOMEENRICHEDDATA	VACCINATION_DT_FORMATTED	COVID-19 vaccination date. Dates were also used to calculate vaccination dose.
CVVD	DF_WIS_OUTCOMEENRICHEDDATA	VACC_VACCINE_NAME	Type of COVID-19 vaccination given at appointment.
EDUW	EOTAS	ETHNICITY	Ethnic group as recorded in the education dataset for those educated otherwise than at school.
EDUW	EOTAS	FSMELIGIBLE	Flag indicating an individual is eligible for free school meals for those educated otherwise than at school.
EDUW	ESTAB_E_SCHSECTOR	SCHSECTOR	Type of school: Primary/Secondary/Independent/Special
EDUW	EXCLUSIONS_PERM_AND_FIXED	EXCLUSIONCATEGORY	Pupil exclusion category: Suspended/Permanent
EDUW	PUPIL	ETHNICITY	Ethnic group as recorded in the education dataset.
EDUW	PUPIL	FSM	Flag indicating an individual is eligible for free school meals.
NCCH	CHILD_TRUST	MAT_ALF_E	Mothers anonymised linkage field ID within SAIL Databank.
NCCH	CHILD_TRUST	GESTATION_AGE	Age of gestation at birth.

NCCH	CHILD_TRUST	PREV_LIVE_BIRTHS	Number of previous live births for mother.
NCCH	CHILD_TRUST	MAT_SMOKING_CD	Mothers smoking status during pregnancy.
NCCH	CHILD_BIRTHS	GEST_AGE_CAT	Age of gestation at birth (categorised).
NCCH	CHILD_BIRTHS	PREV_LIVE_BIRTHS	Number of previous live births for mother.
NCCH	CHILD_BIRTHS	MAT_SMOKING_CD	Mothers smoking status during pregnancy.
NCCH	IMM	COURSE_CD	Vaccination course code.
NCCH	IMM	COURSE_DT	Vaccination date.
PATD	DF_COVID_LIMS_TESTRESULTS	SPCM_COLLECTED_DT	Date COVID-19 specimen collected for testing.
PATD	DF_COVID_LIMS_TESTRESULTS	RESULTNAME	COVID-19 PCR test result.
PEDW	SPELL	ADMIS_DT	Date of hospital admission.
PEDW	EPISODE	EPI_NUM	Hospital admission episode number within a patient spell. Field used to identify the first episode.
PEDW	EPISODE	DIAG_CD_1234	Primary ICD-10 diagnosis code (primary reason for admission)
PEDW	DIAG	DIAG_CD	ICD-10 diagnosis code. Up to 14 codes are listed per hospital admission.
WDSD	AR_PERS	GNDR_CD	Individuals reported gender.
WDSD	AR_PERS	WOB	Monday of an individual's week of birth.
WDSD	AR_PERS	DOD	Date of death.
WDSD	CLEAN_ADD_GEOG_CHAR_LSOA2011	LSOA2011_CD	LSOA 2011 code of resident address. Used to identify Health Board, WIMD quintile and Rural/urban category of residence.
WDSD	CLEAN_ADD_GEOG_CHAR_LSOA2011	START_DATE	Address start date.
WDSD	CLEAN_ADD_GEOG_CHAR_LSOA2011	END_DATE	Address end date.
WLGP	CLEAN_GP_REG_BY_PRAC_INCLNONSAIL_MEDIAN	START_DATE	GP registration date.
WLGP	CLEAN_GP_REG_BY_PRAC_INCLNONSAIL_MEDIAN	END_DATE	End of GP registration if individual has signed up to a new practice.
WLGP	CLEAN_GP_REG_BY_PRAC_INCLNONSAIL_MEDIAN	GP_DATA_FLAG	Flag to indicate whether GP submits event data to SAIL databank.
WLGP	GP_EVENT_CLEANSED	EVENT_DT	Date of GP appointment.
WLGP	GP_EVENT_CLEANSED	EVENT_CD	Read V2 code assigned at GP appointment.

The Anonymised Linkage Field (ALF_E) was used to link individuals records between datasets.
A unique ID field was created by concatenating PROV_UNIT_ID and SPELL_NUM_E to link PEDW tables together.
A unique ID field was created by concatenating PROV_UNIT_CD and CLIENT_ID_E to link NCCH tables together

Appendix 2. Read Version 2 codes used to identify shingles, pneumococcal and influenza vaccinations within Primary Care GP data (WLGP).

Read Code	Description	Vaccination
65FY%	Herpes zoster vaccination	Shingles
n4v.%	VARICELLA-ZOSTER VACCINE	Shingles
657K%	Booster pneumococcal vaccination	Pneumococcal
657L%	First pneumococcal conjugated vaccination	Pneumococcal
657M%	Second pneumococcal conjugated vaccination	Pneumococcal
657N%	Third pneumococcal conjugated vaccination	Pneumococcal
657P%	Pneumococcal vaccination given by other healthcare provider	Pneumococcal
657R%	Supplemental pneumococcal conjugated vaccination	Pneumococcal
6572%	Pneumococcal vaccination	Pneumococcal
n4b%	PNEUMOCOCCAL VACCINE	Pneumococcal
n47%	INFLUENZA VACCINES	Influenza
65E%	Influenza vaccination	Influenza

Appendix 3. Codes used to identify childhood vaccinations within the NCCHD.

Course code	Course name	Vaccine simplified
23	Additional MMR	MMR
24	Additional MMR	MMR
25	M.M.R. 1	MMR
26	M.M.R. 2	MMR
55	Measles Rubella	Measles/Rubella
07	Measles	Measles
77	2nd Measles	Measles
37	Additional Mumps	Mumps
86	Mumps	Mumps
20	Rubella	Rubella
21	Rubella	Rubella
22	Rubella	Rubella
65	Pneumococcal	Pneumococcal
66	Pneumococcal Polysaccharide	Pneumococcal
3401	1st Prevener	Pneumococcal
3402	2nd Prevener	Pneumococcal
3403	3rd Prevener	Pneumococcal
65C1	1st 3-Dose Pneumococcal	Pneumococcal
65C2	2nd 3-Dose Pneumococcal	Pneumococcal
65C3	3rd 3-Dose Pneumococcal	Pneumococcal
65C4	1st 2-Dose Pneumococcal	Pneumococcal
65C5	2nd 2-Dose Pneumococcal	Pneumococcal
65P1	1st 3-Dose Pneumococcal	Pneumococcal
65P2	2nd 3-Dose Pneumococcal	Pneumococcal
65P3	3rd 3-Dose Pneumococcal	Pneumococcal
65P4	1st 2-Dose Pneumococcal	Pneumococcal
65P5	2nd 2-Dose Pneumococcal	Pneumococcal
65P6	1 Dose Pneumococcal	Pneumococcal
65P7	1st Pneumococcal	Pneumococcal
65P8	2nd Pneumococcal	Pneumococcal
65P9	Pneumococcal Booster	Pneumococcal
65PA	Additional Pneumococcal	Pneumococcal
9999	Rotavirus	Rotavirus
99R1	1st Rotavirus	Rotavirus
99R2	2nd Rotavirus	Rotavirus
99RA	Additional Rotavirus	Rotavirus
88B	Meningitis B	Meningitis B
88B1	1st Meningitis B	Meningitis B
88B2	2nd Meningitis B	Meningitis B
88B3	Meningitis B Booster	Meningitis B
88B4	1st Meningitis B Catchup	Meningitis B

88B5	2nd Meningitis B Catchup	Meningitis B
88B6	Meningitis B Catchup Booster	Meningitis B
36	Additional Hib	Hib
88C	Meningitis C	Meningitis C
88C1	1st Meningitis C	Meningitis C
88C2	2nd Meningitis C	Meningitis C
88C3	3rd Meningitis C	Meningitis C
88C4	Meningitis C - Catchup 1	Meningitis C
88C5	Meningitis C - Catchup 2	Meningitis C
88C6	Meningitis C - > 1yr	Meningitis C
88C7	1st Meningitis C	Meningitis C
88C8	2nd Meningitis C	Meningitis C
88CA	Additional Meningitis C	Meningitis C
88CR	Meningitis C Reinforcing	Meningitis C
88C9	HIB/Meningitis C Booster	Hib/Meningitis C
88CB	Additional Hib/Meningitis C	Hib/Meningitis C
04	1st Polio	Polio
05	2nd Polio	Polio
06	3rd Polio	Polio
11	School Entry Polio Booster	Polio
14	School Leaving Polio Booster	Polio
15	Additional Polio	Polio
40	Inactivated Polio - 1st Dose	Polio
41	Inactivated Polio - 2nd Dose	Polio
42	Inactivated Polio - 3rd Dose	Polio
43	Inactivated Polio - Booster	Polio
45	Additional Polio	Polio
46	Adult Polio	Polio
16	1st Additional tetanus	Tetanus
17	2nd Additional tetanus	Tetanus
18	3rd Additional tetanus	Tetanus
19	4th Additional tetanus	Tetanus
104	1st Tetanus	Tetanus
204	2nd Tetanus	Tetanus
304	3rd Tetanus	Tetanus
1004	School Entry Tetanus Booster	Tetanus
1304	School Leaving Tetanus Booster	Tetanus
3004	18 Month Tetanus Booster	Tetanus
4404	Additional Tetanus	Tetanus
101	1st Diphtheria	Diphtheria
201	2nd Diphtheria	Diphtheria
301	3rd Diphtheria	Diphtheria
1001	School Entry Diphtheria Booster	Diphtheria
1301	School Leaving Diphtheria Booster	Diphtheria
3001	18 Month Diphtheria Booster	Diphtheria
4401	Additional Diphtheria	Diphtheria

102	1st Pertussis	Pertussis
202	2nd Pertussis	Pertussis
302	3rd Pertussis	Pertussis
4402	Additional Pertussis	Pertussis
103	1st Diphtheria Pertussis	Diphtheria/Pertussis
203	2nd Diphtheria Pertussis	Diphtheria/Pertussis
303	3rd Diphtheria Pertussis	Diphtheria/Pertussis
4403	Additional Diphtheria Pertussis	Diphtheria/Pertussis
105	1st Diphtheria Tetanus	Diphtheria/Tetanus
205	2nd Diphtheria Tetanus	Diphtheria/Tetanus
305	3rd Diphtheria Tetanus	Diphtheria/Tetanus
1005	School Entry Diphtheria Tetanus Booster	Diphtheria/Tetanus
1305	School Leaving Diphtheria Tetanus Booster	Diphtheria/Tetanus
3005	18 Month Diphtheria Tetanus Booster	Diphtheria/Tetanus
4405	Additional Diphtheria Tetanus	Diphtheria/Tetanus
106	1st Pertussis Tetanus	Pertussis/Tetanus
206	2nd Pertussis Tetanus	Pertussis/Tetanus
306	3rd Pertussis Tetanus	Pertussis/Tetanus
4406	Additional Pertussis Tetanus	Pertussis/Tetanus
107	1st Diphtheria Pertussis Tetanus	Diphtheria/Pertussis/Tetanus
207	2nd Diphtheria Pertussis Tetanus	Diphtheria/Pertussis/Tetanus
307	3rd Diphtheria Pertussis Tetanus	Diphtheria/Pertussis/Tetanus
1007	School Entry Diphtheria Tetanus aPertussis Boost	Diphtheria/Pertussis/Tetanus
4407	Additional Diphtheria Pertussis Tetanus	Diphtheria/Pertussis/Tetanus
1313	Diphtheria Tetanus Polio Reinforcing	Polio/Diphtheria/Tetanus
4413	Add Diphtheria Tetanus Polio Reinforcing	Polio/Diphtheria/Tetanus
1015	Diphtheria Tetanus aPertussis Polio Booster	Polio/Diphtheria/Pertussis/Tetanus
4415	Add Diphtheria Tetanus aPertussis Polio Booster	Polio/Diphtheria/Pertussis/Tetanus
131	1st Diphtheria Tetanus aPertussis Polio Hib	Polio/Diphtheria/Pertussis/Tetanus/Hib
231	2nd Diphtheria Tetanus aPertussis Polio Hib	Polio/Diphtheria/Pertussis/Tetanus/Hib
331	3rd Diphtheria Tetanus aPertussis Polio Hib	Polio/Diphtheria/Pertussis/Tetanus/Hib
1031	Diphtheria Tetanus aPertussis Polio Hib Boost	Polio/Diphtheria/Pertussis/Tetanus/Hib
4431	Add Diphtheria Tetanus aPertussis Polio Hib	Polio/Diphtheria/Pertussis/Tetanus/Hib
161	1st Diphtheria Tetanus aPertussis Polio Hib Hepatitis B	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
261	2nd Diphtheria Tetanus aPertussis Polio Hib Hepatitis B	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
361	3rd Diphtheria Tetanus aPertussis Polio Hib Hepatitis B	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
68G1	1st HPV(Gardasil)	HPV
68G2	2nd HPV(Gardasil)	HPV
68G3	3rd HPV(Gardasil)	HPV
68G4	4th HPV(Gardasil)	HPV
68G5	5th HPV(Gardasil)	HPV
68GA	Additional HPV(Gardasil)	HPV
68H1	1st HPV	HPV
68H2	2nd HPV	HPV
68H3	3rd HPV	HPV
68H4	4th HPV	HPV

68H5	5th HPV	HPV
68HA	Addtional HPV	HPV
68X1	1st HPV(Cervarix)	HPV
68X2	2nd HPV(Cervarix)	HPV
68X3	3rd HPV(Cervarix)	HPV
68X4	4th HPV(Cervarix)	HPV
68X5	5th HPV(Cervarix)	HPV
68XA	Additional HPV(Cervarix)	HPV
35	ACWYVac	MenACWY
35C	Conjugate MenACWY	MenACWY
35P	Polysaccharide MenACWY	MenACWY
88WY	Meningitis ACWY	MenACWY
57	Seasonal Influenza	Influenza
58	Additional Seasonal Influenza	Influenza
76	Influenza Booster	Influenza
57A	Additional Flu	Influenza
57CO	Combined Seasonal Flu - Swine Flu	Influenza
57I	Initial Flu	Influenza
57R	Routine Flu	Influenza

Appendix 4. Read Version 2 codes used to identify childhood vaccinations within Primary Care GP data (WLGP).

Read Code	Description	Vaccination
65M1%	MMR vaccination	MMR
n4k%	MMR vaccine	MMR
65MA%	Measles mumps and rubella booster vaccination	MMR
65MB%	MMR pre-school booster vaccination	MMR
65MC%	MMR vaccination - 2nd dose	MMR
ZV064	[V]Measles-mumps-rubella (MMR) vaccination	MMR
65M2%	MR vaccination	Measles/Rubella
n4o%	*MEASLES+RUBELLA VACCINE	Measles/Rubella
65A%	Measles vaccination	Measles
n48%	*MEASLES VACCINE	Measles
ZV042	[V]Measles vaccination	Measles
65F5%	Mumps vaccination	Mumps
n49%	MUMPS VACCINE	Mumps
65B%	Rubella vaccination	Rubella
n4e%	Rubella vaccine	Rubella
ZV043	[V]Rubella vaccination	Rubella
657L%	First pneumococcal conjugated vaccination	Pneumococcal
657M%	Second pneumococcal conjugated vaccination	Pneumococcal
657N%	Third pneumococcal conjugated vaccination	Pneumococcal
6572%	Pneumococcal vaccination	Pneumococcal
657K%	Booster pneumococcal vaccination	Pneumococcal
657P%	Pneumococcal vaccination given by other healthcare provider	Pneumococcal
657R%	Supplemental pneumococcal conjugated vaccination	Pneumococcal
n4b%	PNEUMOCOCCAL VACCINE	Pneumococcal
65d0%	First rotavirus vaccination	Rotavirus

65d1%	Second rotavirus vaccination	Rotavirus
65d2%	Rotavirus vaccination given by other health care provider	Rotavirus
n4w%	ROTAVIRUS VACCINE	Rotavirus
65710%	First meningitis B vaccination	Meningitis B
65711%	Second meningitis B vaccination	Meningitis B
65712%	Third meningitis B vaccination	Meningitis B
65713%	Fourth meningitis B vaccination	Meningitis B
65714%	Meningitis B vaccination given by other healthcare provider	Meningitis B
65715%	First meningitis B vaccination given by other healthcare provider	Meningitis B
65716%	Second meningitis B vaccination given by other healthcare provider	Meningitis B
65717%	Third meningitis B vaccination given by other healthcare provider	Meningitis B
65718%	Fourth meningitis B vaccination given by other healthcare provider	Meningitis B
n4lC%	MENINGOCOCCAL GROUP B VACCINE suspension for injection pfs	Meningitis B
n4lB%	BEXSERO vaccine susp for injection prefilled syringe 0.5mL	Meningitis B
6571A%	Men B booster	Meningitis B
657A%	1st haemophilus B vaccination	Hib
657B%	2nd haemophilus B vaccination	Hib
657C%	3rd haemophilus B vaccination	Hib
657D%	Booster (single) haemophilus B vaccination	Hib
657E%	First meningitis C vaccination	Meningitis C
657F%	Second meningitis C vaccination	Meningitis C
657G%	Third meningitis C vaccination	Meningitis C
657I%	Single meningitis C vaccination	Meningitis C
657S%	Booster meningitis C vaccination	Meningitis C
n4l4%	*MENINGITEC VACCINE injection	Meningitis C
n4l5%	*MENJUGATE VACCINE injection	Meningitis C
n4l6%	NEISVAC-C VACCINE prefilled syringe	Meningitis C
n4l8%	MENINGITEC suspension for injection prefilled syringe 0.5mL	Meningitis C
n4lx%	MENINGOCOCCAL C CONJUGATE VACCINE prefilled syringe	Meningitis C
n4ly%	MENINGOCOCCAL C CONJUGATE VACCINE injection (pdr for recon)+solvent	Meningitis C

n4lz%	MENINGOCOCCAL C CONJUGATE VACCINE injection	Meningitis C
657H%	Meningitis A & C vaccination	Meningitis AC
n4l1%	MENINGITIS VACCINE AC injection 1 dose	Meningitis AC
n4l2%	*AC VAX injection 1 dose	Meningitis AC
n4l3%	MENGIVAC (A+C) injection 1 dose	Meningitis AC
n4x%	HAEMOPHILUS INFLUENZAE type b + MENINGITIS C VACCINE	Hib/Meningitis C
65b%	Haemophilus influenzae type B and meningitis C vaccination	Hib/Meningitis C
658%	Polio vaccination	Polio
ZV040%	[V]Poliomyelitis vaccination	Polio
n4c%	POLIOMYELITIS VACCINE	Polio
n4c1%	POLIO INACTIVATED VACCINE injection	Polio
654%	Diphtheria vaccination	Diphtheria
n4a%	PERTUSSIS VACCINE	Pertussis
655%	Pertussis vaccination	Pertussis
6554%	Pertussis booster vaccination	Pertussis
ZV036%	[V]Pertussis vaccination	Pertussis
656%	Tetanus vaccination	Tetanus
65L%	Tetanus + polio vaccination	Polio/Tetanus
65J%	Double - DT - vaccination	Diphtheria/Tetanus
65M3%	Tetanus/low dose diphtheria vaccination	Diphtheria/Tetanus
n45m%	DIPTHERIA / TETANUS / POLIOMYELITIS(inactivated) vaccine 0.5mL prefilled syringe	Polio/Diphtheria/Tetanus
65K%	DT (double)+polio vaccination	Polio/Diphtheria/Tetanus
ZV061%	[V]Diphtheria-tetanus-pertussis, combined (DTP) vaccination	Diphtheria/Pertussis/Tetanus
65H%	Triple - DTP - vaccination	Diphtheria/Pertussis/Tetanus
ZV063%	[V]Diphtheria-tetanus-pertussis with poliomyelitis (DTP + polio) vaccination	Polio/Diphtheria/Pertussis/Tetanus
n45u%	DIPTHERIA (HIGH DOSE) / TETANUS / PERTUSSIS / POLOIOMYELITIS(inactivated) vaccine 0.5mL prefilled syringe	Polio/Diphtheria/Pertussis/Tetanus
n45t%	DIPTHERIA (LOW DOSE) / TETANUS / PERTUSSIS / POLIOMYELITIS(inactivated) vaccine 0.5mL prefilled syringe	Polio/Diphtheria/Pertussis/Tetanus
65I%	DTP (triple)+polio vaccination	Polio/Diphtheria/Pertussis/Tetanus

n4p%	HAEMOPHILUS INFLUENZAE TYPE b (HIB)/DIPHTHERIA/TETANUS/PERTUSSIS VACCINE	Diphtheria/Pertussis/Tetanus/Hib
65M7%	First HiB and DTP vaccine given	Diphtheria/Pertussis/Tetanus/Hib
65M8%	Second HiB and DTP vaccine given	Diphtheria/Pertussis/Tetanus/Hib
65M9%	Third HiB and DTP vaccine given	Diphtheria/Pertussis/Tetanus/Hib
ZV062%	[V]Diphtheria-tetanus-pertussis with typhoid-paratyphoid (DTP + TAB) vaccination	Diphtheria/Pertussis/Tetanus/Typhoid
n45w%	DIPTHERIA/TETANUS/PERTUSSIS/POLIO(inact)/HIB inj 0.5mL pfs	Polio/Diphtheria/Pertussis/Tetanus/Hib
n4y%	HAEMOPHILUS INFLUENZAE type B/DIPHTHERIA/TETANUS/PERTUSSIS/POLIO V	Polio/Diphtheria/Pertussis/Tetanus/Hib
65a%	Diphtheria tetanus and five component acellular pertussis, haemophilus influenzae type b, inactivated polio vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MH%	First DTP polio and Hib vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MI%	Second DTP polio and Hib vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MJ%	Third DTP polio and Hib vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MK%	Fourth DTP polio and Hib vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MP%	Booster diphtheria, tetanus, acellular pertussis, haemophilus influenzae type b, inactivated polio vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MQ%	Booster diphtheria tetanus and three component acellular pertussis, haemophilus influenzae type b, inactivated polio vaccination	Polio/Diphtheria/Pertussis/Tetanus/Hib
65MZ1%	First DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
65MZ2%	Second DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
65MZ3%	Third DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
EMISNQFI26%	First DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
EMISNQSE78%	Second DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
EMISNQTH31%	Third DTaP, IPV, Hib, and hep B vaccination (also known as 6in1)	Polio/Diphtheria/Pertussis/Tetanus/Hib/HepB
65FS%	First human papillomavirus vaccination	HPV
65FT%	Second human papillomavirus vaccination	HPV
65FV%	Third human papillomavirus vaccination	HPV
65FW%	Quadrivalent human papillomavirus vaccination	HPV
65Fa%	Human papillomavirus vaccination given by other healthcare provider	HPV
n4l9%	MENVEO GROUP A+C+W135+Y conjugate vaccine injection	MenACWY

n4l8%	MENINGITEC suspension for injection prefilled syringe 0.5mL	MenACWY
n4l7%	*ACWY VAX injection	MenACWY
n4lA%	NIMENRIX powder and solvent for solution for injection	MenACWY
657J.	Meningitis ACW & Y vaccination	MenACWY
657J0	First meningitis ACW & Y vaccination	MenACWY
657J1	Second meningitis ACW & Y vaccination	MenACWY
657J2	Third meningitis ACW & Y vaccination	MenACWY
657J3	Fourth meningitis ACW & Y vaccination	MenACWY
657J4	Meningitis ACW & Y vaccination given by other healthcare provider	MenACWY
n47%	INFLUENZA VACCINES	Influenza
65E%	Influenza vaccination	Influenza

Appendix 5. Summary of measles vaccine effectiveness studies identified in published literature

Study	Study type	Analysis note	Country	Age group	Study size	Outcome	Dose	VE
Agócs MM (1992)	Cohort study	Attack rate	Hungary	14 to 18 years	906	Clinical	One dose	82 (59-92)
Agócs MM (1992)	Cohort study	Attack rate	Hungary	14 to 18 years	906	Clinical	One dose	57 (7-80)
Agócs MM (1992)	Cohort study	Attack rate	Hungary	6 to 14 years	341	Clinical	Two doses (relative VE)	90 (15-99)
Akramuzzaman SM (2002)	Matched CC	N/a	Bangladesh	0 to 9 years	981	Confirmed	One dose	80 (60-90)
Akramuzzaman SM (2002)	Matched CC	N/a	Bangladesh	0 to 9 years	455	Confirmed - severe	One dose	90 (70-94)
Akramuzzaman SM (2002)	Matched CC	N/a	Bangladesh	0 to 9 years	485	Confirmed	One dose	80 (60-90)
Akramuzzaman SM (2002)	Matched CC	N/a	Bangladesh	0 to 9 years	167	Confirmed - severe	One dose	80 (50-93)
Andrews DW (1974)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	One dose	96
Arenz S (2005)	screening method	N/a	Germany	5 to 18 years	N/a	Clinical	At least one dose	97.2 (95.7-98.3)
Arenz S (2005)	Cohort study	Attack Rate (HH)	Germany	0 to 18 years	43	Clinical	At least one dose	92 (48-98)
Arenz S (2005)	Cohort study	Attack Rate (HH)	Germany	0 to 18 years	43	Clinical	One dose	90 (35-97)
Barrabeig I (2011)	Cohort study	Attack Rate	Spain	15m to 6 years	1121	Confirmed or epi-linked	One dose	95.3 (86.9-98.3)
Barrabeig I (2011)	Cohort study	Attack Rate	Spain	15m to 6 years	1121	Confirmed or epi-linked	At least one dose	96.2 (89.4-98.6)
Biribawa C (2020)	Matched CC	N/a	Uganda	All	170	Clinical	At least one dose	95 (75-99)
Bitzegeio J (2019)	screening method	N/a	Germany	2 to 5 years	N/a	Confirmed	Two doses	> 99%
Bitzegeio J (2019)	screening method	N/a	Germany	6 to 15 years	N/a	Confirmed	Two doses	> 99%
Bitzegeio J (2019)	screening method	N/a	Germany	16 to 23 years	N/a	Confirmed	Two doses	> 99%
Bitzegeio J (2019)	screening method	N/a	Germany	24 to 30 years	N/a	Confirmed	Two doses	98.5 (97.0-99.5)
Bitzegeio J (2019)	screening method	N/a	Germany	31 to 42 years	N/a	Confirmed	Two doses	90.9 (74.1-97.6)
Borus PK (2003)	screening method	N/a	Kenya	0 to 5 years	N/a	Clinical - hospitalisation	One dose	84.1
Burström B (1992)	Unknown	Unknown	Kenya	Unknown	Unknown	Unknown	At least one dose	18
Burström B (1993)	Unknown	Unknown	Kenya	1 to 4 years	Unknown	Unknown	One dose	62

Chawla U (1990)	Cohort study	Attack Rate	India	Unknown	Unknown	Clinical	One dose	86.1 (75.1-97.1)
Chawla U (1990)	Cohort study	Attack Rate	India	Unknown	Unknown	Clinical	One dose	77
Chawla U (1990)	Cohort study	Attack Rate	India	Unknown	Unknown	Clinical	One dose	88
Chawla U (1990)	Cohort study	Attack Rate	India	Unknown	Unknown	Clinical	One dose	100
Chen RT (1994)	Cohort study	Unknown	Burundi	Unknown	Unknown	Clinical	One dose	73
Cheah D (1993)	Cohort study	Attack Rate	Australia	13 to 15 years	Unknown	Unknown	One dose	72 (45-86)
Choe YJ (2017)	Cohort study	Attack Rate	Korea	Unknown	14550	Clinical	Two doses	60.0 (38.2-74.1)
Coetzee N (1994)	Cohort study	Attack Rate	South Africa	Unknown	329	Unknown	At least one dose	79 (55-90)
Coetzee N (1994)	Cohort study	Attack Rate	South Africa	Unknown	329	Unknown	At least one dose	74
Coetzee N (1994)	Cohort study	Attack Rate	South Africa	Unknown	329	Unknown	At least one dose	100
Cortina Martínez I (1992)	Cohort study	Attack Rate	Spain	4 to 13 years	92	Clinical	At least one dose	82
Coulborn RM (2020)	Cohort study	Poisson regression	DRC	9 to 59 months	937	Clinical	At least one dose	53.9 (2.9-78.1)
Coulborn RM (2020)	Cohort study	Poisson regression	DRC	9 to 59 months	422	Clinical	One dose	66.6 (14.3-87.0)
Coulborn RM (2020)	Cohort study	Poisson regression	DRC	9 to 59 months	661	Clinical	At least one dose	78.5 (46.2-91.4)
Coulborn RM (2020)	Cohort study	Poisson regression	DRC	9 to 59 months	249	Clinical	At least one dose	95.6 (59.2-99.5)
Cutts FT (1990)	Cohort study	Attack Rate	Mozambique	12 to 35 months	1215	Clinical	One dose	40 (28-56)
Cutts FT (1990)	Cohort study	Attack Rate	Mozambique	12 to 35 months	810	Clinical	One dose	59 (37-72)
Davis RM (1987)	Cohort study	Attack rate	USA	5 to 18 years	1478	Clinical	One dose	96.9 (89.5-98.2)
De Serres G (2012)	Cohort study	Attack Rate	Canada	12 to 18 years	150	Confirmed or epi-linked	One dose	95.9 (87.4-98.7)
De Serres G (2012)	Cohort study	Attack Rate	Canada	12 to 18 years	1165	Confirmed or epi-linked	At least two doses	95.5 (93.8-96.7)
De Serres G (2012)	Cohort study	Attack Rate	Canada	12 to 18 years	1177	Confirmed or epi-linked	At least two doses	94.2 (92.9-95.6)
De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	36	Clinical	One dose	84 (65-92)
De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	128	Clinical	One dose	85 (78-90)
De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	73	Clinical	One dose	92 (82-96)
De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	55	Clinical	One dose	95 (84-98)

De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	80	Clinical	One dose	94 (85-97)
De Serres G (1995)	Cohort study	Attack Rate (HH)	Canada	1 to 19 years	69	Clinical	One dose	97 (89-99)
De Serres G (1996)	Cohort study	Unknown	Canada	6 to 11 months	79	Unknown	One dose	96% (72-99)
Desta T (2021)	screening method	N/a	Ethiopia	9 to 23 months	N/a	Clinical	One dose	75.3
Doshi RH (2015)	TNCC	N/a	DRC	12 to 59 months	2379	Confirmed	At least one dose	80 (74-85)
Doshi S (2009)	Cohort study	Attack Rate	Georgia	11 to 16 years	199	Clinical	At least one dose	86.4 (58.3-95.6)
Doshi S (2009)	Cohort study	Attack Rate	Georgia	11 to 16 years	148	Clinical	One dose	85.8 (54.1-95.6)
Doshi S (2009)	Cohort study	Attack Rate	Georgia	11 to 16 years	49	Clinical	Two doses	87.8 (36.8-97.6)
Franconeri L (2023)	screening method	N/a	France	2 to 5 years	N/a	Clinical	Two doses	99.6 (99.3-99.8)
Franconeri L (2023)	screening method	N/a	France	6 to 10 years	N/a	Clinical	Two doses	99.5 (99.2-99.7)
Franconeri L (2023)	screening method	N/a	France	11 to 15 years	N/a	Clinical	Two doses	99.3 (98.9-99.5)
Franconeri L (2023)	screening method	N/a	France	16 to 20 years	N/a	Clinical	Two doses	98.3 (97.3-98.9)
Franconeri L (2023)	screening method	N/a	France	21 to 25 years	N/a	Clinical	Two doses	98.1 (96.5-98.9)
Franconeri L (2023)	screening method	N/a	France	26 to 31 years	N/a	Clinical	Two doses	91.4 (85.1-95.0)
Gao J (1988)	Cohort study	Attack rate (HH)	Taiwan	0 to 15 years	61	Clinical	One dose	39.8 (x-67)
Geier DA (2019)	Cohort study	Cox regression	USA	1 to 10 years	76408	Clinical	One dose	80.7 (61.5-90.4)
Gidding HF (1999)	Cohort study	Attack Rate	Australia	2 to 15 years	23	Clinical	At least one dose	81.3 (17.0-98.8)
Gidding HF (1999)	Cohort study	Attack Rate	Australia	2 to 15 years	20	Clinical	At least one dose	84.6 (15.0-99.7)
Gillesberg Lassen S (2014)	Cohort study	Attack Rate	Germany	Unknown	55	Clinical	Two doses	97.1 (83.4-100.0)
Goodson JL (2010)	CC study	N/a	Tanzania	0 to 18 years	198	Confirmed or epi-linked	One dose	88 (40-98)
Goodson JL (2010)	CC study	N/a	Tanzania	0 to 18 years	198	Confirmed or epi-linked	Two doses	96 (75-99)
Guasparini R (1988)	Cohort study	Unknown	Canada	5 to 7 years	Unknown	Confirmed or epi-linked	One dose	92
Guasparini R (1988)	Cohort study	Unknown	Canada	8 to 12 years	Unknown	Confirmed or epi-linked	One dose	84

Guasparini R (1988)	Cohort study	Unknown	Canada	13 to 17 years	Unknown	Confirmed or epi-linked	One dose	39
Güriş D (1996)	Cohort study	Attack Rate (HH)	Palau	1 to 30 years	40	Confirmed or epi-linked	One dose	86 (60-95)
Hahné SJ (2016)	Cohort study	Attack Rate	Netherlands	24 to 43 years	83	Confirmed	Two doses	52 (-207-93)
Hales CM (2016)	Cohort study	Attack Rate (HH)	Micronesia	6m to 36 years	398	Confirmed or epi-linked	One dose (independent of campaign dose)	23.1 (-425-87.3)
Hales CM (2016)	Cohort study	Attack Rate (HH)	Micronesia	6m to 36 years	398	Confirmed or epi-linked	Two doses (independent of campaign dose)	63.4 (-103-90.6)
Hales CM (2016)	Cohort study	Attack Rate	Micronesia	6m to 36 years	398	Confirmed or epi-linked	Three doses (independent of campaign dose)	95.9 (45.0-100)
Hales CM (2016)	Cohort study	Attack Rate	Micronesia	6m to 36 years	398	Confirmed or epi-linked	One dose (with campaign dose)	78.7 (10.1-97.7)
Hales CM (2016)	Cohort study	Attack Rate (HH)	Micronesia	6m to 36 years	398	Confirmed or epi-linked	Two doses (with campaign dose)	83.6 (-93.5-98.6)
Hales CM (2016)	Cohort study	Attack Rate (HH)	Micronesia	6m to 36 years	398	Confirmed or epi-linked	Three doses (with campaign dose)	99.1 (70.9-100)
Hennessey KA (1999)	Cohort study	Attack Rate	Romania	6 to 15 years	2148	Clinical	One dose	89 (85-91)
Hennessey KA (1999)	Cohort study	Attack Rate	Romania	6 to 15 years	578	Clinical	Two doses	96 (92-98)
Hennessey KA (1999)	Matched CC	N/a	Romania	9m to 6 years	661	Clinical	One dose	94 (86-98)
Hennessey KA (1999)	Matched CC	N/a	Romania	9m to 6 years	145	Clinical	Two doses	99 (87-99)
Herceg A (1994)	Cohort study	Unknown	Australia	Unknown	384	Clinical	At least one dose	90 (75-96)
Herceg A (1994)	Cohort study	Unknown	Australia	Unknown	384	Clinical	At least one dose	87 (70-95)
Hersh BS (1991)	Cohort study	Attack Rate	USA	17 to 32 years	1216	Clinical	At least one dose	80 (51-92)
Hersh BS (1991)	Cohort study	Attack Rate	USA	17 to 32 years	1216	Clinical	At least one dose	94 (86-98)
Hull HF (1983)	Cohort study	Attack Rate	The Gambia	0 to 11 years	1073	Clinical	One dose	37
Hull HF (1983)	Cohort study	Attack Rate	The Gambia	0 to 11 years	1073	Clinical	One dose	89 (77-94)
Hull HF (1983)	Cohort study	Attack Rate	The Gambia	0 to 11 years	1073	Clinical	One dose	85 (52-94)
Hull HF (1983)	Cohort study	Attack Rate	The Gambia	0 to 11 years	1073	Clinical	One dose	90 (76-95)
Hutchins SS (2001)	CC study	N/a	USA	15 to 59 months	243	Confirmed or epi-linked	Two doses	99.5 (96.5-99.9)
Hutchins SS (2001)	CC study	N/a	USA	15 to 59 months	537	Confirmed or epi-linked	One dose	99.7 (98.6-100)
Hutchins SS (2001)	CC study	N/a	USA	15 to 59 months	107	Confirmed or epi-linked	One dose	97.6 (81.5-99.7)

Izadi S (2012)	CC study	N/a	Iran	0 to 18 years?	143	Confirmed	Two doses	74.2 (10.2-92.6)
Janaszek W (2003)	Cohort study	Attack rate	Poland	> 5 years	Unknown	Clinical	One dose	> 90
Janaszek W (2003)	Cohort study	Attack rate	Poland	> 5 years	Unknown	Clinical	Two doses	> 99
Jasem J (2012)	screening method	N/a	Iraq	8m to 12 years	N/a	Clinical	One dose	90.0
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	9 to 71 months	N/a	Clinical	One dose	98.4 (97.8-98.8)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	9 to 11 months	N/a	Clinical	One dose	87.3 (71.0-95.2)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	12 to 23 months	N/a	Clinical	One dose	96.2 (92.6-98.3)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	24 to 35 months	N/a	Clinical	One dose	97.3 (95.1-98.7)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	36 to 47 months	N/a	Clinical	One dose	98.6 (96.7-99.6)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	48 to 59 months	N/a	Clinical	One dose	89.2 (77.9-95.2)
Jean Baptiste AE (2021)	screening method	N/a	Nigeria	60 to 71 months	N/a	Clinical	One dose	99.5 (98.3-99.9)
Jedrychowski W (2005)	Unknown	N/a	Poland	11 years	1005	Unknown	One dose	58
Jedrychowski W (2005)	Unknown	N/a	Poland	11 years	1005	Unknown	Two doses	78
Jeremijenko AM (1996)	Cohort study	Attack Rate (HH)	Australia	9m to 21 years	48	Clinical	At least one dose	91 (74-97)
John S (2009)	Cohort study	Attack rate	India	0 to 18 years	1702	Clinical	One dose	43.2
John S (2009)	Cohort study	Attack rate	India	1 to 6 years	Unknown	Clinical	One dose	66
John S (2009)	Cohort study	Attack rate	India	7 to 15 years	Unknown	Clinical	One dose	48.8
John S (2009)	Cohort study	Attack rate	India	0 to 10 years	506	Clinical	One dose	21
John S (2009)	Cohort study	Attack rate	India	0 to 10 years	180	Clinical	One dose	62
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	9 to 11 months	6188	Clinical	One dose	82.8 (67.3-91.0)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	12 to 23 months	6188	Clinical	One dose	95.8 (93.7-97.2)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	24 to 35 months	6188	Clinical	One dose	95.8 (93.6-97.2)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	36 to 47 months	6188	Clinical	One dose	97.0 (95.3-98.1)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	48 to 59 months	6188	Clinical	One dose	87.6 (82.3-91.4)

Kaninda AV (1998)	Cohort study	Poisson regression	Niger	9 to 59 months	6188	Clinical	One dose	94.5 (93.4-95.4)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	48 to 59 months	6188	Clinical	Two doses	88.6 (75.4-94.7)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	12 to 59 months	6188	Clinical	Two doses	93.3 (85.9-96.8)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	6 to 8 months	6188	Clinical	One dose	19.8 (0.0-88.8)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	12 to 23 months	6188	Clinical	One dose	93.7 (83.1-97.7)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	24 to 35 months	6188	Clinical	One dose	92.0 (80.7-96.7)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	36 to 47 months	6188	Clinical	One dose	89.8 (76.9-95.4)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	48 to 59 months	6188	Clinical	One dose	74.7 (56.9-85.2)
Kaninda AV (1998)	Cohort study	Poisson regression	Niger	6 to 59 months	6188	Clinical	One dose	86.9 (81.3-90.7)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	1 to 14 years	144	Clinical	At least one dose	94 (45-99)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	1 to 14 years	146	Clinical	At least one dose	87 (37-97)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	1 to 14 years	140	Clinical	At least one dose	84 (41-96)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	15 to 30 years	148	Clinical	At least one dose	73 (11-92)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	15 to 30 years	136	Clinical	At least one dose	95 (70-100)
Kidd S (2012)	Matched CC	N/a	Burkina Faso	15 to 30 years	142	Clinical	At least one dose	86 (27-97)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	172	Clinical - severe	One dose	54 (36-67)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	155	Clinical - severe	One dose	51 (30-65)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	172	Clinical - severe	One dose	79 (68-86)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	66	Clinical - severe	One dose	78 (57-89)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	64	Clinical - severe	One dose	73 (54-84)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	59	Clinical - severe	One dose	72 (51-84)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	64	Clinical - severe	One dose	92 (84-96)
Killewo J (1991)	Matched CC	N/a	Tanzania	9m to 8 years	26	Clinical - severe	One dose	96 (83-99)

Kim SK (1995)	Cohort study	Attack Rate (HH)	Korea	1 to 5 years	134	Clinical	One dose	92.4 (83.6-96.4)
King GE (1991)	Cohort study	Attack Rate (HH)	USA	1 to 5 years	203	Clinical	One dose	95 (89-97)
Kotb MM (1999)	Matched CC	N/a	Egypt	Unknown	690	Clinical	One dose	53 (71-26)
La Torre G (2017)	Cohort study	Cox regression	Italy	3 to 5 years	11004	Clinical - severe	At least one dose	91 (68-99)
Landrigan PJ (1972)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	One dose	96
Lee MS (1992)	Cohort study	Attack rate	Taiwan	6 to 15 years	884	Confirmed	At least one dose	79.7 (65.0-88.5)
Lee MS (1992)	Cohort study	Attack rate	Taiwan	6 to 15 years	565	Confirmed	At least one dose	79.3 (0.0-97.0)
Lee MS (1992)	Cohort study	Attack rate	Taiwan	6 to 15 years	375	Confirmed	At least one dose	75.4 (1.0-93.7)
Lee MS (1992)	Cohort study	Attack rate	Taiwan	6 to 15 years	605	Confirmed	At least one dose	79.3 (62.0-88.5)
Lee MS (1999)	Cohort study	Attack Rate	Taiwan	3 to 6 years	174	Confirmed	One dose	79 (6-95)
Lee MS (1999)	Cohort study	Attack Rate	Taiwan	3 to 6 years	97	Confirmed	Two doses	88 (41-98)
Lerman SJ (1971)	Cohort study	Unknown	USA	Unknown	Unknown	Confirmed or epi-linked	One dose	99
Lertpiriyasuwat C (2002)	Cohort study	Unknown	Thailand	9 to 12 months	Unknown	Confirmed or epi-linked	One dose	91 (42-99)
Lowang D (2021)	Cohort study	Attack Rate	India	12 to 59 months	156	Clinical	One dose	80
Lowang D (2021)	Cohort study	Attack Rate	India	12 to 59 months	195	Clinical	Two doses	93
Luna Sánchez A (1997)	Cohort study	Attack Rate	Spain	Unknown	Unknown	Unknown	At least one dose	91.5
Luquero FJ (2011)	Matched CC	N/a	Cameroon	9m to 15 years	234	Clinical	At least one dose	96.4 (88.0-98.9)
Luquero FJ (2011)	Matched CC	N/a	Cameroon	9m to 15 years	1231	Clinical	At least one dose	97.7 (95.9-98.7)
Luquero FJ (2011)	Matched CC	N/a	Cameroon	9m to 15 years	312	Clinical	At least one dose	94.2 (86.7-97.4)
Lynn TV (2004)	Cohort study	Attack rate	USA	13 to 21 years	3679	Confirmed and epi-linked	Two doses (relative VE)	94.1 (55.9-99.2)
Lyons RA (1994)	CC study	N/a	UK	10 to 16 years	121	Clinical	One dose	99.3 (90-100)
Lyons RA (1994)	Cohort study	Attack rate	UK	10 to 16 years	338	Clinical	One dose	97.1 (90-100)
Mahomva AI (1997)	Cohort study	Attack Rate	Zimbabwe	9 to 34 months	294	Clinical	One dose	68
Majwala RK (2018)	Matched CC	N/a	Uganda	6 to 59 months	152	Clinical	One dose	75 (25-88)
Malfait P (1994)	CC study	Unknown	Niger	Unknown	Unknown	Clinical	One dose	92 (82-96)

Malfait P (1994)	Cohort study	Unknown	Niger	Unknown	Unknown	Clinical	One dose	26 (0-84)
Malfait P (1994)	Cohort study	Unknown	Niger	Unknown	Unknown	Clinical	One dose	94 (84-98)
Malfait P (1994)	Cohort study	Unknown	Niger	Unknown	Unknown	Clinical	One dose	88 (76-94)
Malfait P (1994)	Cohort study	Unknown	Niger	Unknown	Unknown	Clinical	One dose	89 (81-94)
Malfait P (1994)	screening method	N/a	Niger	Unknown	N/a	Clinical	One dose	87 (80-92)
Malfait P (1994)	screening method	N/a	Niger	Unknown	N/a	Clinical	One dose	90 (83-94)
Marks JS (1978)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	At least one dose	75
Marks JS (1978)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	At least one dose	90
Marks JS (1978)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	At least one dose	96
Marks JS (1978)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	At least one dose	97
Marks JS (1978)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	At least one dose	97
Marin M (2006)	Cohort study	Attack Rate (HH)	Marshall Islands	6m to 14 years	69	Clinical	One dose	92 (67-98)
Marin M (2006)	Cohort study	Attack Rate (HH)	Marshall Islands	6m to 14 years	127	Clinical	Two doses	95 (82-98)
Marufu T (1995)	screening method	N/a	Zimbabwe	10 to 23 months	N/a	Clinical	One dose	77 (75-79)
Mast EE (1990)	Cohort study	Unknown	USA	Unknown	Unknown	Confirmed or epi-linked	One dose	93 (81-98)
McDonnell LF (1995)	Matched CC	N/a	Australia	5 to 9 years	237	Unknown	One dose	94 (83-98)
McDonnell LF (1995)	Matched CC	N/a	Australia	5 to 9 years	237	Unknown	One dose	81 (46-93)
McDonnell LF (1995)	Matched CC	N/a	Australia	5 to 9 years	237	Unknown	One dose	96 (64-99)
McDonnell LF (1995)	Matched CC	N/a	Australia	5 to 9 years	237	Unknown	One dose	95 (81-99)
McDonnell LF (1995)	Matched CC	N/a	Australia	5 to 9 years	237	Unknown	One dose	93 (80-98)
McIntyre RC (1982)	Cohort study	Attack rate (HH)	Marshall Islands	1 to 9 years	258	Clinical	One dose	83.5 (74.0-89.1)
McMorrow ML (2009)	screening method	N/a	South Africa	12 to 59 months	N/a	Confirmed or epi-linked	At least one dose	85 (63-94)
McMorrow ML (2009)	screening method	N/a	South Africa	12 to 59 months	N/a	Confirmed or epi-linked	At least one dose	89 (77-95)
Minetti A (2013)	Cohort study	Binomial regression	Malawi	6m to 6 years	3305	Clinical	One dose	83.9 (70.8-90.8)
Minetti A (2013)	Cohort study	Binomial regression	Malawi	6m to 6 years	2570	Clinical	Two doses	90.5 (79.7-95.5)
Mori N (2008)	Cohort study	Unknown	Japan	Unknown	Unknown	Confirmed or epi-linked	One dose	77 (52-88)
Mori N (2008)	Cohort study	Unknown	Japan	Unknown	Unknown	Confirmed or epi-linked	One dose	99 (95-100)

Morse D (1994)	Cohort study	Attack rate	UK	11 to 18 years	924	Clinical	One dose	92.1
Mossong J (2000)	Cohort study	Attack rate	Luxembourg	4 to 11 years	563	Clinical	One dose	94.6 (90.4-97.0)
Mudzamiri WS (1996)	Cohort study	Attack Rate	Zimbabwe	12 to 23 months	500	Clinical	One dose	78.3 (54.1-89.8)
Mupere E (2006)	Cohort study	Attack Rate (HH)	Uganda	9 to 59 months	188	Confirmed or epi-linked	One dose	74 (64-81)
Murray M (2000)	Cohort study	Attack rate	Pakistan	9m to 13 years	455	Clinical	One dose	75.0 (57.5-85.3)
Murray M (2000)	Cohort study	Attack rate	Pakistan	9m to 13 years	455	Clinical	One dose	81.3 (68.8-88.8)
Murray M (2000)	Cohort study	Attack rate	Pakistan	9m to 13 years	347	Clinical	One dose	75.5 (47.5-88.6)
Murray M (2000)	Cohort study	Attack rate	Pakistan	9m to 13 years	347	Clinical	One dose	86.9 (65.9-94.9)
Murray M (2000)	Cohort study	Attack rate	Pakistan	9m to 13 years	347	Clinical	One dose	92.0 (75.4-97.4)
Musa S (2018)	Cohort study	Attack rate	Bosnia and Herzegovina	6 to 15 years	811	Clinical	One dose	91.9 (81.4-95.4)
Musa S (2018)	Cohort study	Attack rate	Bosnia and Herzegovina	6 to 15 years	811	Clinical	Two doses	97.3 (96.5-98.4)
Ndikuyeze A (1995)	Cohort study	Attack rate	Chad	12 to 60m olds	4975	Clinical	One dose	67 (60-73)
Ndikuyeze A (1995)	Cohort study	Attack rate	Chad	12 to 60m olds	3913	Clinical	One dose	71 (59-80)
Nkowane BM (1987)	Cohort study	Attack rate	USA	14 to 18 years	1000 approx.	Confirmed and epi-linked	One dose	94.4 (90.6-97.0)
Nieto Vera J (2010)	Unknown	Unknown	Spain	Unknown	Unknown	Clinical	At least one dose	>99%
None (1998)	CC study	N/a	Italy	15m to 7 years	301	Clinical	One dose	96 (93-98)
Nsubuga F (2018)	Matched CC	Mantel-Haenszel OR method	Uganda	9m to 52 years	250	Clinical	One dose	64 (17-85)
Nsubuga F (2018)	Matched CC	Mantel-Haenszel OR method	Uganda	9m to 5 years	152	Clinical	One dose	70 (24-88)
Nujum ZT (2015)	Cohort study	Attack rate	India	9 to 35 months	215	Clinical	At least one dose	76.6 (76.0-78.0)
Ong G (2007)	Cohort study	Attack rate	Singapore	7 to 13 years	184	Confirmed and epi-linked	One dose	97.8
Patel M (1998)	Cohort study	Attack rate	Australia	9m to 10 years	109	Confirmed or epi-linked	One dose	93.5 (86.7-96.8)
Pillsbury A (2015)	Matched CC	N/a	Australia	1 to 16 years	3969	Clinical	At least one dose	98.7 (97.9-99.2)

Pillsbury A (2015)	Matched CC	N/a	Australia	1 to 16 years	2022	Clinical	One dose	96.7 (94.5-98.0)
Pillsbury A (2015)	Matched CC	N/a	Australia	1 to 16 years	2544	Clinical	Two doses	99.7 (99.2-99.9)
Pillsbury A (2015)	Matched CC	N/a	Australia	0 to 5 years	1626	Clinical	One dose	97.9 (95.8-98.9)
Pillsbury A (2015)	Matched CC	N/a	Australia	6 to 10 years	214	Clinical	One dose	98.6 (91.8-99.8)
Pillsbury A (2015)	Matched CC	N/a	Australia	11 to 15 years	182	Clinical	One dose	82.7 (58.9-92.7)
Porter JD (1990)	Screening method	N/a	Mozambique	6m to 5 years	N/a	Clinical	At least one dose	92
Porter JD (1990)	Screening method	N/a	Mozambique	6m to 5 years	N/a	Clinical	At least one dose	97
Porter JD (1990)	Screening method	N/a	Mozambique	6m to 5 years	N/a	Clinical	At least one dose	96
Porter JD (1990)	Screening method	N/a	Mozambique	6m to 5 years	N/a	Clinical	At least one dose	92
Povey M (2021)	Matched CC	N/a	UK	1 to 13 years	1495	Clinical	At least one dose	78.0 (67.2-85.3)
Povey M (2021)	Matched CC	N/a	UK	1 to 13 years	105	Clinical - severe	At least one dose	91.6 (52.7-98.5)
Povey M (2021)	Matched CC	N/a	UK	4 to 13 years	185	Clinical	One dose	74.6 (-21.7-94.7)
Povey M (2021)	Matched CC	N/a	UK	4 to 13 years	185	Clinical	At least two doses	94.4 (79.7-98.5)
Puri A (2002)	Cohort study	Unknown	India	Unknown	Unknown	Clinical	One dose	62 (46-73)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	12 to 17 years	4468	Clinical	One dose	94 (88-97)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	18 to 22 years	4468	Clinical	One dose	72 (-34-94)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	23 to 27 years	4468	Clinical	One dose	87 (-43-99)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	12 to 27 years	4468	Clinical	One dose	92 (86-95)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	12 to 17 years	4912	Clinical	One dose	93 (87-96)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	18 to 22 years	4912	Clinical	One dose	19 (-244-81)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	23 to 27 years	4912	Clinical	One dose	88 (-36-99)
Ramsay ME (1994)	Cohort study	Poisson regression	UK	12 to 27 years	4912	Clinical	One dose	86 (78-92)
Rawls WE (1975)	Cohort study	Attack Rate	Canada	5 to 13 years	61	Clinical	One dose	-43.5
Rawls WE (1975)	Cohort study	Attack Rate	Canada	5 to 13 years	117	Clinical	One dose	57.6

Rawls WE (1975)	Cohort study	Attack Rate	Canada	5 to 13 years	116	Clinical	One dose	80.5
Reynolds G (2015)	screening method	N/a	New Zealand	15 to 24 years	N/a	Confirmed and epi-linked	At least one dose	92 (82-97)
Rivest P (1995)	Matched CC	Unknown	Canada	Unknown	Unknown	Confirmed or epi-linked	At least one dose	96.1 (32-100)
Rivest P (1995)	Matched CC	Unknown	Canada	Unknown	Unknown	Confirmed or epi-linked	At least one dose	92 (-54-100)
Rivest P (1995)	Matched CC	Unknown	Canada	Unknown	Unknown	Confirmed or epi-linked	At least one dose	96 (27-100)
Rivest P (1995)	Matched CC	Unknown	Canada	Unknown	Unknown	Confirmed or epi-linked	At least one dose	97 (43-100)
Rivest P (1995)	Matched CC	Unknown	Canada	Unknown	Unknown	Confirmed or epi-linked	At least one dose	98 (60-100)
Robertson SE (1992)	Cohort study	Attack Rate	USA	12 to 14 years	627	Clinical	One dose	70.2 (21.6-88.0)
Robertson SE (1992)	Cohort study	Attack Rate	USA	12 to 14 years	627	Clinical	One dose	91.6 (81.3-96.3)
Robertson SE (1992)	Cohort study	Attack Rate	USA	12 to 14 years	627	Clinical	One dose	84.0 (62.5-93.2)
Robertson SE (1992)	Cohort study	Attack Rate	USA	12 to 14 years	627	Clinical	One dose	95.1 (87.6-98.0)
Schmid D (2010)	Cohort study	Attack rate	Austria	5 to 20 years	240	Clinical	One dose	97.3 (80.8-99.6)
Sharma R (1998)	Cohort study	Unknown	India	Unknown	Unknown	Clinical	One dose	53 (35-71)
Sheppeard V (2009)	screening method	N/a	Australia	1 to 7 years	N/a	Confirmed or epi-linked	At least one dose	96 (78.1-99.3)
Simba DO (1995)	CC study	N/a	Tanzania	< 60 months	675	Confirmed or epi-linked	One dose (9-59m)	84 (61-93)
Simba DO (1995)	CC study	N/a	Tanzania	< 60 months	675	Confirmed or epi-linked	One dose (6-8m)	73 (11-92)
Simba DO (1995)	CC study	N/a	Tanzania	< 60 months	675	Confirmed or epi-linked	One dose (6-59m)	79 (55-90)
Simba DO (1995)	CC study	N/a	Tanzania	< 60 months	675	Confirmed or epi-linked	One dose (at rural HC)	89 (56-97)
Simba DO (1995)	CC study	N/a	Tanzania	< 60 months	675	Confirmed or epi-linked	One dose (at dispensary)	70 (22-88)
Singh J (1999)	Unknown	Unknown	India	Unknown	Unknown	Unknown	At least one dose	>90
Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	89 (78-95)
Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	86 (71-93)
Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	88 (77-94)
Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	91 (80-96)

Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	86 (69-94)
Srirajalingam M (1998)	Cohort study	Attack Rate	Australia	12 to 20 years	470	Clinical	At least one dose	91 (80-96)
So JS (2008)	CC study	Unknown	South Korea	Unknown	152	Confirmed	One dose	88.8
So JS (2008)	CC study	Unknown	South Korea	Unknown	152	Confirmed	Two doses	98.0
Sowe A (2021)	Cohort study	Attack rate	The Gambia	> 9months	404	Clinical	At least one dose	89.5
Stein-Zamir C (2023)	CC study	N/a	Israel	1 to 5 years	785	Confirmed - severe	One dose	79 (11-95)
Sugerman DE (2011)	screening method	N/a	Sierra Leone	12 to 59 months	N/a	Confirmed or epi-linked	At least one dose	74
Sutcliffe PA (1996)	Cohort study	Attack rate	Canada	14 to 21 years	966	Clinical	One dose	-200
Sutcliffe PA (1996)	Cohort study	Attack rate	Canada	14 to 21 years	135	Clinical	Two doses	67
Sutcliffe PA (1996)	Cohort study	Attack rate	Canada	14 to 21 years	1063	Clinical	Two doses vs one dose	89
Talley L (2003)	Cohort study	Attack Rate	Ethiopia	9 to 24m	160	Clinical	One dose	66.3 (23.1-90.5)
Talley L (2003)	Cohort study	Attack Rate	Ethiopia	9 to 36m	349	Clinical	One dose	66.9 (40.1-93.7)
Talley L (2003)	Cohort study	Attack Rate	Ethiopia	9 to 48m	563	Clinical	One dose	71.9 (55.1-88.7)
Tohani VK (1992)	Unknown	Unknown	Northern Ireland	Unknown	Unknown	Clinical	At least one dose	94 (91-96)
van Dam ASG (2020)	CC study	N/a	Netherlands	0 to 68 years	2563	Clinical - severe	At least one dose (relative VE)	28 (-50-50)
van Dam ASG (2020)	CC study	N/a	Netherlands	0 to 68 years	2563	Clinical - severe	One dose (relative VE)	13 (-43-49)
van Dam ASG (2020)	CC study	N/a	Netherlands	0 to 68 years	2563	Clinical - severe	Two doses (relative VE)	88 (11-100)
Velicko I (2008)	Matched CC	N/a	Ukraine	15 to 29 years	714	Confirmed or epi-linked	At least one dose	91.8 (78.3-97.3)
Velicko I (2008)	Matched CC	N/a	Ukraine	15 to 29 years	670	Confirmed or epi-linked	Two doses	93.1 (80.5-98.0)
Velicko I (2008)	Matched CC	N/a	Ukraine	15 to 29 years	714	Confirmed or epi-linked	At least one dose	91.6 (78.5-97.1)
Velicko I (2008)	Matched CC	N/a	Ukraine	15 to 29 years	670	Confirmed or epi-linked	Two doses	92.0 (79.4-97.2)
Vitek CR (1999)	Cohort study	Attack rate	USA	5 to 10 years	625	Confirmed or epi-linked	One dose	92
Vitek CR (1999)	Cohort study	Attack rate	USA	5 to 10 years	625	Confirmed or epi-linked	Two doses	100
Vitek CR (1999)	Cohort study	Attack rate	USA	5 years	37	Confirmed or epi-linked	One dose	91 (73-97)
Weeks RM (1992)	Cohort study	Attack Rate	Uganda	9m to 35m	207	Clinical	One dose	75

Weeks RM (1992)	Cohort study	Attack Rate	Uganda	9m to 35m	207	Clinical	One dose	55
Wichmann O (2007)	Cohort study	Attack rate	Germany	10 to 21 years	235	Clinical	One dose	98.1 (92-100)
Wichmann O (2007)	Cohort study	Attack rate	Germany	10 to 21 years	597	Clinical	Two doses	99.4 (97-100)
Woudenberg T (2017)	Cohort study	Cox regression	Netherlands	6 to 12 months	1080	Confirmed	One dose	71 (-72-95)
Woudenberg T (2017)	Cohort study	Cox regression	Netherlands	6 to 12 months	1204	Clinical	One dose	43 (-12-71)
Wyll S (1971)	Cohort study	Unknown	USA	Unknown	Unknown	Clinical	One dose	91
Yadav RM (2024)	CC study	N/a	India	<5 years	141	Clinical	One dose	40 (5-62)
Yadav RM (2024)	CC study	N/a	India	<5 years	174	Clinical	Two doses	64 (23-73)
Yadav RM (2024)	CC study	N/a	India	5 to 15 years	30	Clinical	One dose	64 (17-84)
Yadav RM (2024)	CC study	N/a	India	5 to 15 years	117	Clinical	Two doses	70 (28-88)
Yaméogo KR (2005)	Matched CC	N/a	Burkina Faso	9m to 14years	361	Confirmed	One dose	99 (92-100)
Yang Z (2014)	TNCC	N/a	China	8m to 14years	578	Confirmed	At least one dose	94.8 (76.2-98.8)
Yang Z (2014)	TNCC	N/a	China	8m to 14years	497	Confirmed	One dose	89.1 (44.5-97.9)
Yang Z (2014)	TNCC	N/a	China	8m to 14years	499	Confirmed	Two doses	97.8 (88.3-99.6)
Yeung LF (2005)	Cohort study	Attack rate	USA	13 to 26 years	630	Clinical	Two doses	98.6 (92.0-99.4)
Yeung LF (2005)	Cohort study	Attack rate	USA	13 to 26 years	512	Clinical	Two doses	99.1 (95.5-99.8)
Yeung LF (2005)	Cohort study	Attack rate	USA	13 to 26 years	78	Clinical	Two doses	94.0 (69.6-98.3)
Yousif M (2022)	Cohort study	Attack rate	South Africa	1 to 4 years	3389	Confirmed	At least one dose	80
Zahidie A (2014)	Matched CC	N/a	Pakistan	<12 years	Unknown	Clinical - severe	One dose	87.4 (76.1-93.4)
Zahidie A (2014)	Matched CC	N/a	Pakistan	<12 years	Unknown	Clinical - severe	Two doses	93.0 (86.2-96.6)
Ziskin LZ (1976)	Cohort study	Unknown	USA	Unknown	Unknown	Confirmed or epi-linked	One dose	94
Ziskin LZ (1976)	Cohort study	Unknown	USA	Unknown	Unknown	Confirmed or epi-linked	One dose	87

Appendix 6. Summary of mumps vaccine effectiveness studies identified in published literature

Study	Study type	Analysis note	Country	Age group	Study size	Outcome	Dose	VE
Amaro Labrador J (1990)	Unknown	Unknown	Cuba	Unknown	Unknown	Unknown	One dose	97.4
Braeye T (2014)	Cohort study	Attack rate	Belgium	17 to 59 years	717	Clinical	Two doses (relative VE)	68 (-24-92)
Buxton J (1999)	Matched CC	N/a	Canada	All ages	95	Clinical	One dose	80 (29-96)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Third dose vs. two (7 days after MMR3)	60.0 (38.4-74.0)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Third dose vs. two (14 days after MMR3)	63.2 (42.3-76.5)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Third dose vs. two (21 days after MMR3)	68.3 (48.6-80.4)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Third dose vs. two (28 days after MMR3)	78.1 (60.9-87.8)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Two doses (<13years previous)	89.4 (-2.5-98.9)
Cardemil CV (2017)	Cohort study	Cox regression	USA	18 to 24 years	20496	Clinical	Two doses (>12years previous)	31.8 (-388.9-90.5)
Castilla J (2009)	Matched CC	N/a	Spain	1 to 10 years	1205	Clinical	At least one dose	72 (39-87)
Castilla J (2009)	Matched CC	N/a	Spain	1 to 10 years	875	Clinical	One dose	83 (54-94)
Castilla J (2009)	Matched CC	N/a	Spain	1 to 10 years	353	Clinical	Two doses	66 (25-85)
CDC (1983)	Cohort study	Attack rate	USA	11 to 13 years	357	Clinical	One dose	37
CDC (1983)	Cohort study	Attack rate	USA	11 to 13 years	357	Clinical	One dose	70
CDC (1983)	Cohort study	Attack rate (HH)	USA	All ages	99	Clinical	One dose	85
CDC (1984)	Cohort study	Attack rate	USA	11 to 12 years	165	Clinical	One dose	91 (77-93)
Chamot E (1998)	Cohort study	Attack rate (HH)	Switzerland	0 to 16 years	Unknown	Clinical	One dose	6.3 (-45.9-39.8)
Chamot E (1998)	Cohort study	Attack rate (HH)	Switzerland	0 to 16 years	Unknown	Clinical	One dose	61.6 (0.0-85.4)
Chamot E (1998)	Cohort study	Attack rate (HH)	Switzerland	0 to 16 years	Unknown	Clinical	One dose	73.1 (41.8-87.6)
Cohen C (2007)	screening method	N/a	UK	2 years and 5 to 12 years	N/a	Confirmed	One dose	87.8 (83.1-91.1)
Cohen C (2007)	screening method	N/a	UK	2 years and 5 to 12 years	N/a	Confirmed	Two doses	94.6 (92.9-95.9)
Compés-Dea C (2015)	Cohort study	Attack rate	Spain	12 to 16 years	Unknown	Clinical	One dose	34 (-44-70)
Compés-Dea C (2015)	Cohort study	Attack rate	Spain	12 to 16 years	Unknown	Clinical	Two doses	67 (28-83)
Deeks SL (2011)	screening method	N/a	Canada	25 to 29 years	N/a	Confirmed or epi-linked	One dose	81.6 (0-96.4)

Deeks SL (2011)	screening method	N/a	Canada	20 to 24 years	N/a	Confirmed or epi-linked	One dose	59.4 (0-86.2)
Deeks SL (2011)	screening method	N/a	Canada	23 to 22 years	N/a	Confirmed or epi-linked	One dose	76.7 (0-94.6)
Deeks SL (2011)	screening method	N/a	Canada	21 to 19 years	N/a	Confirmed or epi-linked	One dose	49.2 (0-97.4)
Deeks SL (2011)	screening method	N/a	Canada	18 to 11 years	N/a	Confirmed or epi-linked	One dose	76.5 (0-99.7)
Deeks SL (2011)	screening method	N/a	Canada	23 to 22 years	N/a	Confirmed or epi-linked	Two doses	88.0 (0-98.6)
Deeks SL (2011)	screening method	N/a	Canada	21 to 19 years	N/a	Confirmed or epi-linked	Two doses	66.3 (0-94.7)
Deeks SL (2011)	screening method	N/a	Canada	18 to 11 years	N/a	Confirmed or epi-linked	Two doses	83.9 (0-98.2)
Domínguez A (2010)	screening method	N/a	Spain	2 to 12 years	N/a	Confirmed or epi-linked	One dose	85.4 (67.3-93.4)
Domínguez A (2010)	screening method	N/a	Spain	2 to 12 years	N/a	Confirmed or epi-linked	Two doses	88.5 (78.1-93.9)
Fernández de la Hoz Zeitler K (1997)	Cohort study	Attack rate	Spain	10 to 17 years	4275	Unknown	One dose	76 (66-87)
Fernández de la Hoz Zeitler K (1997)	Cohort study	Attack rate	Spain	10 to 13 years	Unknown	Unknown	One dose	87 (76-93)
Fernández de la Hoz Zeitler K (1997)	Cohort study	Attack rate	Spain	14 to 17 years	Unknown	Unknown	One dose	46 (20-76)
Fu C (2008)	Matched CC	N/a	China	8m to 12 years	938	Clinical	One dose	86.0 (77.2-91.5)
Fu C (2013)	Matched CC	N/a	China	8m to 12 years	3966	Clinical	One dose	53.6 (41.0-63.5)
Fu CX (2009)	Matched CC	N/a	China	8m to 12 years	388	Clinical	At least one dose	83.3 (68.4-91.2)
Fu CX (2009)	Matched CC	N/a	China	8m to 12 years	344	Clinical	One dose	80.4 (60.0-90.4)
Fu CX (2009)	Matched CC	N/a	China	8m to 12 years	109	Clinical	Two doses	90.0 (-123.7-97.2)
Fu CX (2009)	Matched CC	N/a	China	8m to 9 years	168	Clinical	One dose	81.8 (47.2-93.7)
Fu CX (2009)	Matched CC	N/a	China	10 to 12 years	176	Clinical	One dose	79.2 (45.4-92.1)
González PP (2012)	Cohort study	Attack rate	Spain	14 to 16 years	111	Unknown	One dose	80.4 (59.1-90.6)
González PP (2012)	Cohort study	Attack rate	Spain	14 to 16 years	111	Unknown	Two doses	71.0 (55.9-81.0)
González PP (2012)	Cohort study	Attack rate	Spain	16 to 18 years	116	Unknown	One dose	93.3 (78.9-97.9)
González PP (2012)	Cohort study	Attack rate	Spain	16 to 18 years	116	Unknown	Two doses	98.0 (85.4-99.7)

González PP (2012)	Cohort study	Attack rate	Spain	14 to 16 years	122	Unknown	One dose	78.61 (24.87-93.91)
González PP (2012)	Cohort study	Attack rate	Spain	14 to 16 years	122	Unknown	Two doses	97.69 (90.63-99.43)
Greenland K (2012)	Cohort study	Attack rate	Netherlands	17 to 28 years	751	Clinical	Two doses	68 (40.6-82.2)
Guimbao Bescós J (1992)	Cohort study	Unknown	Spain	Under 30 years	Unknown	Unknown	At least one dose	74.7
Guo A (2023)	Cohort study	Generalized linear mixed effects model	USA	5 to 17 years	9272	Clinical	Third dose (relative VE)	52.7 (-3.6-78.4)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	134	Clinical - orchitis	One dose (relative VE)	66 (1-88)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	424	Clinical - orchitis	Two doses (relative VE)	74 (49-87)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	202	Clinical - other complication	One dose (relative VE)	12 (-14-95)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	688	Clinical - other complication	Two doses (relative VE)	25 (-5-91)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	213	Clinical - severe	One dose (relative VE)	30 (-312-88)
Hahné S (2012)	CC study	N/a	Netherlands	1 to 86 years	665	Clinical - severe	Two doses (relative VE)	57 (-84-90)
Harling R (2005)	CC study	N/a	UK	1 to 18 years	331	Clinical	At least one dose	69 (41-84)
Harling R (2005)	CC study	N/a	UK	1 to 18 years	<331	Confirmed	At least one dose	65 (25-84)
Harling R (2005)	CC study	N/a	UK	1 to 18 years	<331	Confirmed	One dose	88 (62-96)
Harling R (2005)	CC study	N/a	UK	1 to 18 years	<331	Confirmed	Two doses	64 (40-78)
Hersh BS (1991)	Cohort study	Attack rate	USA	13 to 18 years	Approx 500	Unknown	At least one dose	83 (57-94)
Kim-Farley R (1985)	Cohort study	Attack rate	USA	11 to 13 years	339	Clinical	At least one dose	37 (0-63)
Kim-Farley R (1985)	Cohort study	Attack rate	USA	11 to 13 years	339	Clinical	At least one dose	52 (0-74)
Kim-Farley R (1985)	Cohort study	Attack rate	USA	11 to 13 years	335	Clinical	At least one dose	65 (29-81)
Kim-Farley R (1985)	Cohort study	Attack rate	USA	11 to 13 years	270	Clinical	At least one dose	70 (51-81)
Kim-Farley R (1985)	Cohort study	Attack rate (HH)	USA	All ages	110	Clinical	At least one dose	74 (29-89)
Kim-Farley R (1985)	Cohort study	Attack rate (HH)	USA	All ages	99	Clinical	At least one dose	85 (39-94)
Latasa P (2019)	screening method	logistic regression models	Spain	Unknown	N/a	Clinical	Two doses	55 (-12-82)
Livingston KA (2014)	Cohort study	Generalized estimating equations (HH)	USA	5 years and older	828	Clinical	At least one dose	85.8 (62.7-94.6)
Livingston KA (2014)	Cohort study	Generalized estimating equations (HH)	USA	5 years and older	137	Clinical	One dose	82.9 (37.1-95.4)
Livingston KA (2014)	Cohort study	Generalized estimating equations (HH)	USA	5 years and older	711	Clinical	Two doses	86.3 (63.3-94.9)
Livingston KA (2014)	Cohort study	Generalized estimating equations (HH)	USA	5 years and older	540	Clinical	Unknown	83.7 (55.9-93.9)
López Hernández B (2000)	Cohort study	Attack rate	Spain	0 to 15 years	723	Clinical	One dose	46 (0-84)
López Hernández B (2000)	Cohort study	Attack rate	Spain	0 to 15 years	723	Clinical	Two doses	87 (27-99)
Ma C (2018)	Cohort study	Attack rate	China	6 to 13 years	1695	Clinical	One dose	40 (23-53)
Ma C (2018)	Cohort study	Attack rate	China	6 to 13 years	743	Clinical	At least two doses	44 (12-64)

Ma R (2018)	screening method	N/a	China	7 to 14 years	N/a	Clinical	One dose	74.5 (65.6-81.3)
Ma R (2018)	screening method	N/a	China	7 to 14 years	N/a	Clinical	At least two doses	83.2 (78.6-86.3)
Man W (2012)	Cohort study	Attack rate	China	0 to 6 years	347	Clinical	One dose	36 (-12-63)
Man W (2012)	Cohort study	Attack rate	China	0 to 6 years	347	Clinical	One dose < 3 years ago	65 (19-85)
Man W (2012)	Cohort study	Attack rate	China	0 to 6 years	347	Clinical	One dose 3-6 years ago	15 (-52-52)
Man W (2012)	Cohort study	Attack rate	China	0 to 6 years	347	Clinical	Two doses	65 (-15-80)
Marin M (2008)	Cohort study	Attack rate	USA	18 to 36 years	235	Clinical	One dose	82 (0-98)
Marin M (2008)	Cohort study	Attack rate	USA	18 to 36 years	2141	Clinical	Two doses	79 (0-97)
Marin M (2008)	Cohort study	Attack rate	USA	18 to 36 years	235	Clinical	One dose	84 (48-95)
Marin M (2008)	Cohort study	Attack rate	USA	18 to 36 years	2141	Clinical	Two doses	80 (46-93)
Marin M (2008)	Cohort study	Attack rate (HH)	USA	18 to 36 years	<114	Clinical	One dose	64 (0-94)
Marin M (2008)	Cohort study	Attack rate (HH)	USA	18 to 36 years	<114	Clinical	Two doses	88 (63-96)
Marin M (2008)	Cohort study	Attack rate (HH)	USA	18 to 36 years	<114	Clinical	One dose	64 (0-94)
Marin M (2008)	Cohort study	Attack rate (HH)	USA	18 to 36 years	<114	Clinical	Two doses	76 (47-90)
Melgar M (2022)	screening method	N/a	USA	Unknown	N/a	Clinical	Two doses vs. one or 0	76.2 (63.7-84.4)
Melgar M (2022)	screening method	N/a	USA	Unknown	N/a	Clinical	Two doses vs. one or 0	67.0 (47.2-80.4)
Melgar M (2022)	screening method	N/a	USA	Unknown	N/a	Clinical	Two doses vs. one or 0	54.1 (42.2-63.5)
Melgar M (2022)	screening method	N/a	USA	Unknown	N/a	Clinical	Two doses vs. one or 0	31.6 (0.0-67.1)
Moon JY (2017)	Cohort study	Poisson regression	Korea	18 to 31 years	Unknown	Clinical	At least one dose	84.4 (84.1-88.2)
None (1998)	CC study	N/a	Italy	15m to 7years	301	Clinical	One dose	33 (11-49)
Ogbuanu IU (2012)	Cohort study	Attack rate	USA	11 to 17 years	2136	Clinical	Third dose (relative VE)	88.9 (-31.9-98.9)
Ong G (2005)	Cohort study	Attack rate	Singapore	Unknown	Unknown	Unknown	One dose	-55.3
Ong G (2005)	Cohort study	Attack rate	Singapore	Unknown	Unknown	Unknown	One dose	80.7
Ong G (2005)	Cohort study	Attack rate	Singapore	Unknown	Unknown	Unknown	One dose	54.4
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1633	Clinical - any complication	One dose (relative VE)	68 (9-89)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	9469	Clinical - any complication	Two doses (relative VE)	68 (61-75)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1039	Clinical - orchitis	One dose (relative VE)	66 (-16-100)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	5554	Clinical - orchitis	Two doses (relative VE)	72 (64-78)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1733	Clinical - meningitis	One dose (relative VE)	50 (-280-93)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	9567	Clinical - meningitis	Two doses (relative VE)	64 (46-79)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1733	Clinical - encephalitis	One dose (relative VE)	93 (66-98)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	9567	Clinical - Pancreatitis	Two doses (relative VE)	-18 (-186-51)

Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1733	Clinical - severe	One dose (relative VE)	68 (24-87)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	9567	Clinical - severe	Two doses (relative VE)	71 (65-76)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	1039	Clinical - severe	One dose (relative VE)	41 (11-90)
Orlíková H (2016)	CC study	N/a	Czech Republic	0-90 years	5554	Clinical - severe	Two doses (relative VE)	74 (67-79)
Povey M (2021)	CC study	N/a	UK	1 to 13 years	1213	Clinical	At least one dose	66.7 (48.1-78.6)
Povey M (2021)	CC study	N/a	UK	1 to 13 years	1213	Clinical - severe	At least one dose	-30.1 (-1731.0-90.8)
Povey M (2021)	CC study	N/a	UK	4 to 13 years	1213	Clinical	One dose	82.3 (32.7-95.3)
Povey M (2021)	CC study	N/a	UK	4 to 13 years	1213	Clinical	At least two doses	86.5 (64.0-94.9)
Qin W (2019)	Cohort study	Attack rate	China	6 to 15 years	825	Clinical	One dose	59 (36-74)
Qin W (2019)	Cohort study	Attack rate	China	6 to 15 years	254	Clinical	Two doses	76 (49-89)
Richard JL (2003)	CC study	N/a	Switzerland	Unknown	Unknown	Clinical	At least one dose	70.0
Rudnick W (2022)	Cohort study	Cox regression	Canada	> 1 year	3080	Clinical	At least one dose	63 (0-90)
Sane J (2014)	CC study	N/a	Netherlands	All ages	1492	Clinical - severe	One dose (relative VE)	57 (-60-89)
Sane J (2014)	CC study	N/a	Netherlands	All ages	1492	Clinical - severe	Two doses (relative VE)	82 (53-93)
Sane J (2014)	CC study	N/a	Netherlands	> 12 years	858	Clinical - orchitis	One dose (relative VE)	54 (2-78)
Sane J (2014)	CC study	N/a	Netherlands	> 12 years	858	Clinical - orchitis	Two doses (relative VE)	74 (57-85)
Sane J (2014)	CC study	N/a	Netherlands	All ages	1492	Clinical - severe	One dose (relative VE)	71 (38-86)
Sane J (2014)	CC study	N/a	Netherlands	All ages	1492	Clinical - severe	Two doses (relative VE)	76 (61-86)
Sartorius B (2005)	screening method	N/a	Sweden	5 to 24 years	N/a	Clinical	One dose	65
Sartorius B (2005)	screening method	N/a	Sweden	5 to 24 years	N/a	Clinical	Two doses	91
Schaffzin JK (2007)	Cohort study	Attack rate	USA	6 to 65 years	507	Confirmed or epi-linked	At least one dose	90.4 (82-95)
Schaffzin JK (2007)	Cohort study	Attack rate	USA	6 to 65 years	67	Confirmed or epi-linked	One dose	79.7 (42-93)
Schaffzin JK (2007)	Cohort study	Attack rate	USA	6 to 65 years	461	Confirmed or epi-linked	Two doses	91.6 (83-96)
Schwarz NG (2010)	Cohort study	Attack rate	Moldova	13 to 26 years	910	Clinical	One dose	-40 (-120-20)
Schwarz NG (2010)	Cohort study	Attack rate	Moldova	13 to 26 years	39	Clinical	Two doses	62 (-43-90)
Schlegel M (1999)	Cohort study	Attack rate	Switzerland	5 to 13 years	165	Clinical	At least one dose	-4 (-218-15)
Schlegel M (1999)	Cohort study	Attack rate	Switzerland	5 to 13 years	165	Clinical	At least one dose	78 (64-82)
Schlegel M (1999)	Cohort study	Attack rate	Switzerland	5 to 13 years	165	Clinical	At least one dose	87 (76-94)
Snijders BE (2012)	Cohort study	Poisson model	Netherlands	3 to 13 years	835	Clinical	One dose	92 (83-96)
Snijders BE (2012)	Cohort study	Poisson model	Netherlands	3 to 13 years	652	Clinical	Two doses	93 (85-97)
Snijders BE (2012)	Cohort study	Attack rate (HH)	Netherlands	0 to 34 years	106	Clinical	At least one dose	67 (-65-95)
Sullivan KM (1985)	Unknown	Unknown	USA	11 to 13 years	481	Clinical	One dose	81.2
Takla A (2014)	Cohort study	Attack rate	Germany	8 to 12 years	100	Clinical	Two doses	91.9 (81.0-96.5)
Takla A (2014)	Cohort study	Attack rate	Germany	18 to 46 years	44	Clinical	One dose	53.8 (-65.1-87.1)

Takla A (2014)	Cohort study	Attack rate	Germany	18 to 46 years	44	Clinical	One dose	50.0 (-9.4-87.1)
Tizes R (1973)	Cohort study	Attack rate	USA	5 to 9 years	899	Unknown	One dose	79
Toscani L (1996)	Cohort study	Poisson model	Switzerland	4 to 12 years	195	Unknown	One dose	12.4 (-102-62.1)
Toscani L (1996)	Cohort study	Poisson model	Switzerland	4 to 12 years	195	Unknown	One dose	64.7 (10.6-86.0)
Toscani L (1996)	Cohort study	Poisson model	Switzerland	4 to 12 years	195	Unknown	One dose	75.8 (35.6-90.9)
Vandermeulen C (2004)	Cohort study	Attack rate	Belgium	5 to 11 years	1825	Clinical	One dose	64.0 (43.2-77.2)
Wang D (2021)	Cohort study	Attack rate	China	6 to 15 years	523	Clinical	At least one dose < 5 years ago	74.2 (9.7-92.6)
Wang D (2021)	Cohort study	Attack rate	China	6 to 15 years	523	Clinical	At least one dose >= 5 years ago	-30.0 (-143.2-30.3)
Wharton M (1988)	CC study	Modification of Bayes Theorem	USA	14 to 18 years	467	Clinical	One dose	57 (34-71)
Wharton M (1988)	CC study	Modification of Bayes Theorem	USA	14 to 18 years	433	Clinical	One dose	74 (59-84)
Wharton M (1988)	CC study	Modification of Bayes Theorem	USA	14 to 18 years	385	Clinical	One dose	78 (65-86)
Wharton M (1988)	CC study	Modification of Bayes Theorem	USA	14 to 18 years	467	Clinical	One dose	78 (65-86)
Wharton M (1988)	CC study	Modification of Bayes Theorem	USA	14 to 18 years	414	Clinical	One dose	81 (70-88)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	One dose	67.4 (59.5-73.8)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	Two doses	79.1 (72.3-84.2)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	One dose < 1 year ago	97.8 (96.8-98.4)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	One dose < 10 years ago	67.4 (59.5-73.8)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	Two doses < 1 year ago	98.3 (96.5-99.1)
Yin Z (2022)	screening method	N/a	China	10 to 14 years	N/a	Clinical	Two doses < 10 years ago	79.1 (72.3-84.2)
Zamir CS (2015)	Cohort study	Attack rate	Israel	All ages	3130	Clinical - severe	At least one dose (relative VE)	48.3
Zamir CS (2015)	Cohort study	Attack rate	Israel	All ages	3130	Clinical - orchitis	At least one dose (relative VE)	73.2
Zamir CS (2015)	Cohort study	Attack rate	Israel	All ages	3130	Clinical - meningitis	At least one dose (relative VE)	50.6
Zamir CS (2015)	Cohort study	Attack rate	Israel	All ages	3130	Clinical - any complication	At least one dose (relative VE)	72.0
Zamir CS (2015)	CC study	N/a	Israel	All ages	1661	Clinical - severe	One dose (relative VE)	28 (3.1-46.5)

Zamir CS (2015)	CC study	N/a	Israel	All ages	2271	Clinical - severe	Two doses (relative VE)	43.7 (26.9-56.6)
Zamir CS (2015)	CC study	N/a	Israel	All ages	530	Clinical - orchitis	One dose (relative VE)	49.3 (-24.3-79.4)
Zamir CS (2015)	CC study	N/a	Israel	All ages	915	Clinical - orchitis	Two doses (relative VE)	77.1 (45-90.5)
Zamir CS (2015)	CC study	N/a	Israel	All ages	1661	Clinical - meningitis	One dose (relative VE)	74 (-44-95.5)
Zamir CS (2015)	CC study	N/a	Israel	All ages	2271	Clinical - meningitis	Two doses (relative VE)	43.5 (-82-82.4)
Zamir CS (2015)	CC study	N/a	Israel	All ages	1661	Clinical - any complication	One dose (relative VE)	52.1 (-4-78)
Zamir CS (2015)	CC study	N/a	Israel	All ages	2271	Clinical - any complication	Two doses (relative VE)	62.7 (25.7-81.3)

Appendix 7. Code lists used to identify complications from measles and mumps infection

List of ICD-10 codes used to identify measles related hospital admissions in the Patient Episode Dataset for Wales (PEDW) dataset

B051 Measles complicated by meningitis

A87% Viral meningitis

B050 Measles complicated by encephalitis

G049 Encephalitis, myelitis and encephalomyelitis, unspecified

B052 Measles complicated by pneumonia

J129 Viral pneumonia, unspecified

B053 Measles complicated by otitis media

H671 Otitis media in viral diseases classified elsewhere

H66% Suppurative and unspecified otitis media

Any code beginning with B05% (Measles) excluding B059 (Measles without complication)

List of ICD-10 codes used to identify mumps related hospital admissions in the Patient Episode Dataset for Wales (PEDW) dataset

B261 Mumps meningitis

A87% Viral meningitis

B262 Mumps encephalitis

G049 Encephalitis, myelitis and encephalomyelitis, unspecified

B263 Mumps pancreatitis

K858 Other acute pancreatitis

K859 Acute pancreatitis, unspecified

B260 Mumps orchitis

N45% Orchitis and epididymitis

Any code beginning with B26% (Mumps) excluding B269 (Mumps without complication)

List of Read v2 codes used to identify additional complications from measles related infections in the Primary Care GP (WLGP) consultations dataset

A553. Measles complicated by meningitis

F02.. Meningitis of unspecified cause

65VC. Notification of acute meningitis
F01z. Meningitis due to organism NOS
F011y Other viral meningitis
1471. H/O: meningitis
A550. Postmeasles encephalitis
F0351 Encephalitis following measles
F030z Encephalitis in viral disease NOS
65VB. Notification of acute encephalitis
F035z Postinfectious encephalitis NOS
F03z. Encephalitis NOS
1472. H/O: encephalitis
A551. Postmeasles pneumonia
H20z. Viral pneumonia NOS
H2z.. Pneumonia or influenza NOS
A552. Postmeasles otitis media
F52.. Suppurative and unspecified otitis media
F51.. Nonsuppurative otitis media + eustachian tube disorders
A554. Measles with intestinal complications
A55x. Measles with other specified complication
A55y. Measles with unspecified complication

List of Read v2 codes used to identify additional complications from mumps related infections in the Primary Care GP (WLGP) consultations dataset

A721. Mumps meningitis
F02.. Meningitis of unspecified cause
65VC. Notification of acute meningitis
F01z. Meningitis due to organism NOS
F011y Other viral meningitis
1471. H/O: meningitis
A722. Mumps encephalitis
F030z Encephalitis in viral disease NOS
65VB. Notification of acute encephalitis
F035z Postinfectious encephalitis NOS
F03z. Encephalitis NOS

1472. H/O: encephalitis
A723. Mumps pancreatitis
J6700 Acute pancreatitis unspecified
J670z Acute pancreatitis NOS
A720. Mumps orchitis
K240. Orchitis
A72x. Mumps with other specified complications
A72y. Mumps with unspecified complication