Abstract

Objective To illustrate how data triangulation involving routine data sources can optimize data usage and provide insights into vaccine programme effectiveness by considering measles vaccination and disease incidence data in England.

Methods We obtained data on measles, mumps and rubella (MMR) vaccine coverage in birth cohorts from 1985 to 2016 from child health records and adjusted for under-ascertainment and catch-up campaigns. We assumed that the population had no natural immunity and that vaccine effectiveness was 95% for one dose and 99.75% for two doses. Vaccinations performed outside the routine schedule and in people who entered England after immunization age were identified from primary care records. Measles susceptibility was defined as the percentage of individuals who were not immune despite all vaccination activities. We triangulated measles susceptibility and incidence data.

Findings Median susceptibility was 4.6% (range: 1.2–9.2). Among cohorts eligible for two MMR vaccine doses, those born between 1998 and 2004 were most susceptible. Measles incidence was highest in these cohorts. Data from primary care and child health records were comparable for cohorts after 2000, suggesting that little supplementary vaccination took place. For cohorts before 2000, primary care data quality was insufficient for accurately estimating coverage.

Conclusion Triangulating routine data on measles vaccination coverage and disease surveillance provided new insights into population immunity and helped identify vulnerable groups, which was useful for prioritizing public health actions to close gaps in immunity. This approach could be applied in any country that routinely records vaccine coverage and disease incidence.

Introduction

A considerable amount of immunization coverage and surveillance data are available nationally, regionally and globally. Often, however, these data could be better used to aid decision-making on national and subnational immunization programmes, particularly where a disease is close to being eliminated and the remaining few percent of susceptible individuals
are being targeted – the need for accurate data increases as vaccine coverage increases. Synthesizing data from two or more sources (i.e. data triangulation) is a pragmatic approach to optimizing the use of existing data, thereby improving data quality and gaining insights into the performance of vaccine programmes. In this study, we used the example of measles in England to illustrate how the triangulation of routine data sources – namely different sources on coverage of the combined measles, mumps and rubella (MMR) vaccine and measles incidence data – can help evaluate data quality and provide estimates of population immunity, which can be used to inform a national measles elimination strategy. As these data sources are available in most settings and for many diseases, with varying degrees of granularity and quality, our approach should be broadly replicable.

Measles is a viral infection transmitted by the respiratory route and one of the most contagious human diseases. In 2016, approximately 90,000 deaths were attributable to the disease globally, down from more than 550,000 in 2000 thanks to the accelerated roll-out of measles immunization programmes. The commitment to eliminate measles (and rubella) is an important part of global efforts to improve health and reduce inequality. To achieve and maintain elimination, the World Health Organization (WHO) recommends that countries attain 95% coverage with two doses of measles-containing vaccine by the time children are 5 years of age. Modelling suggests that measles can be eliminated in most contexts if the proportion of children younger than 5 years susceptible to measles is less than 15% and the proportion of susceptible individuals aged 5 years and older is less than 5%.

In England, before measles vaccine was introduced in 1968, 160,000 to 800,000 cases of measles were notified and around 100 deaths from acute disease were recorded each year. After the combined MMR vaccine was introduced in 1988, coverage rapidly reached 90% and disease incidence fell to a very low level. In 1994, a large catch-up programme was undertaken with measles–rubella vaccine and, in October 1996, a second MMR vaccine dose was added. However, in 1998 a British doctor published a now-discredited study suggesting a link between MMR vaccine and autism. The resulting intense media interest had a substantial impact on MMR vaccine coverage, which dropped to about 80% in the late 1990s and early 2000s and took many years to recover. Since this fall, several catch-up campaigns have been implemented to address gaps in population immunity. Measles cases continued to rise and, in 2006, endemic transmission became re-established in the United Kingdom of Great Britain and Northern Ireland. The incidence peaked at 3.2 per 100,000 population in 2012 and decreased to 1.0 per 100,000 in 2016. The United Kingdom is committed to measles elimination and has developed a national strategy in line with the European Vaccine
Action Plan 2015–2020.\textsuperscript{11,12} Since 2012, coverage for the first MMR vaccine dose in children aged 24 months has been consistently over 90%.\textsuperscript{9,10} In 2016 and 2017, coverage for the first dose in children aged 5 years reached 95% for the first time.\textsuperscript{9} Since 2016, imported cases of measles have led to several outbreaks, with some limited spread in the population, particularly among individuals who missed the MMR vaccine when they were younger and in undervaccinated communities.\textsuperscript{13} Overall, the incidence of measles in England quadrupled between 2017 and 2018.\textsuperscript{14}

\textbf{Routine coverage and surveillance data in England}

Vaccine coverage in England is estimated by two methods: the first uses data from local Child Health Information Systems, which provide data to the cover of vaccination evaluated rapidly (COVER) programme;\textsuperscript{15} and the second involves an online platform called ImmForm that automatically extracts immunization data from approximately 95% of primary care facilities (i.e. general practices).\textsuperscript{16} The COVER programme is designed to collect data on coverage by specific target ages (i.e. by children’s second and fifth birthdays) and, because it includes the entire population eligible for vaccination, provides the most accurate estimates of coverage at the time of data collection. As coverage is not routinely assessed again, COVER data will not accurately reflect the current status of a given birth cohort many years later: vaccines given at an older age may not be recorded and neither the numerator nor denominator in the coverage calculation will include individuals who arrived in England after their fifth birthday. Nevertheless, COVER data are used for reporting to WHO on the WHO and United Nations Children's Fund’s (UNICEF’s) Joint Reporting Form. By contrast, ImmForm data represent vaccine coverage recorded by general practices at the time of data extraction and include anyone in a specific birth cohort who was registered with the practice at that time (i.e. 2017 to 2018 for our study). Consequently, the data should cover vaccinations given either through routine vaccination programmes, during national catch-up campaigns, opportunistically, or outside England to any individual of any age. The accuracy of ImmForm data depends on the quality and completeness of clinical coding at each facility – these characteristics are known to have the greatest influence on immunization data quality globally.\textsuperscript{1} In the United Kingdom, clinicians are legally required to report suspected measles cases to the public health services. In addition, national surveillance systems require all suspected cases to be confirmed by laboratories using either an immunoglobulin-M antibody test on a serum or oral fluid specimen or a polymerase chain reaction technique.\textsuperscript{11}
Data triangulation

Data triangulation involves the synthesis of two or more data sources with the aim of assisting programme planning and decision-making. The process can identify and address limitations in any single data source or data collection method. In addition, deeper insights can be achieved by examining complementary data and putting them into a broader context. A recent report from a WHO-commissioned expert group on immunization data quality recommended that data triangulation should become the default approach to data analysis and use in its Expanded Programme on Immunization.¹

The aim of our study was to use the example of measles elimination in England to demonstrate how data sources that are routinely available as part of the Expanded Programme on Immunization can be synthesized to improve vaccination data quality and to generate new information, for example on measles susceptibility and gaps in immunity, that can help guide decision-making on vaccine policy.

Methods

In calculating the proportion of the English population susceptible to measles, we assumed a vaccine effectiveness of 95% for one MMR vaccine dose and 99.75% for two doses.¹⁷–¹⁹ In addition, we assumed there was no natural immunity because the level of circulating disease in the country over the past 30 years was low.

To estimate coverage of routine immunization for each birth cohort between the year from April 1985 to March 1986 (i.e. 1985–1986) and the year from April 2015 to March 2016 (i.e. 2015–2016), we used COVER data on the first and second MMR vaccine doses. Data collected at children’s fifth birthdays were generally available for birth cohorts from 1992–1993 until 2012–2013. We used data collected at the second birthday for individuals in birth cohorts after 2012–2013, who were too young during our study period to have had coverage of two doses assessed at 5 years of age, and for individuals in birth cohorts before 1992–1993, who were born before the second dose was included in the vaccination schedule. We applied a 50% coverage underestimate correction factor to COVER estimates. This percentage was based on a study that examined the extent of underestimation by checking the vaccination status of individuals not recorded as vaccinated in Child Health Information Systems.²⁰ Further, to consider the possibility that the 50% correction factor was too high, we examined the effect of a 25% correction factor in a sensitivity analysis.

Several birth cohorts included in the study were eligible for supplementary immunization in national catch-up campaigns (Table 1). Coverage data have been published
for the 1994 and 2013 campaigns;\textsuperscript{21,22} for other campaigns, we used the best estimates from Public Health England (unpublished data). Fig. 1 describes how we determined the level of protection from measles among cohorts that were eligible for participation in catch-up campaigns. To ascertain the level of opportunistic vaccination after the routine vaccination age and outside of catch-up campaigns, we triangulated vaccine coverage data from the COVER programme (i.e. routine vaccination data only) with data from ImmForm, which potentially captures any vaccinations given up to the time of data extraction.

For each birth cohort, we calculated susceptibility ($S$) to measles, which was defined as the percentage of individuals in the birth cohort who had not been vaccinated or who were probably not immune despite routine, supplementary or opportunistic vaccination, using the equation:

\[
S = 100 - [(X \times 0.9975) + (Y \times 0.95)]
\]

Where $X$ is the percentage of birth cohort who received $\geq 2$ vaccine doses and $Y$ is the percentage of birth cohort who received 1 dose. Then, using the size of the population in each age band in 2017 obtained from the Office of National Statistics,\textsuperscript{23} we calculated the number of susceptible individuals in the population and overall population susceptibility. Susceptibility in each birth cohort was compared to the target immunity level required to keep the reproductive number ($R_0$) below one and, therefore, interrupt transmission in the population ($R_0$ is the number of additional cases each disease case generates in a susceptible population; if $R_0 < 1$, transmission will not carry on).\textsuperscript{6} Table 1 shows whether each cohort achieved this target or not. To further validate our susceptibility estimates, we compared the age-specific incidence of laboratory-confirmed cases of measles by year of diagnosis (restricted to cases with an onset between 2010 and 2018) with age-specific susceptibility. We focused on age-specific incidence and susceptibility rather than on annual incidence to identify reported cases that occurred in birth cohorts eligible for vaccination and to help us discover underprotected groups that could be targeted by practical changes to vaccination programmes (for example, by identifying appropriate age groups for a catch-up campaign).

All susceptibility calculations were performed using Microsoft Excel (Microsoft Corporation, Redmond, United States of America). All coverage and surveillance data were collected through national routine surveillance systems and the study was conducted using aggregated data as part of routine surveillance activities. No specific funding or formal ethical approval was required.
Results

Table 1 shows coverage of the first and second MMR vaccine doses in birth cohorts between 1985–1986 and 2015–2016. The small differences between COVER and ImmForm estimates for birth cohorts between 2000–2001 and 2012–2013 (Fig. 2; ImmForm data at the children’s fifth birthday were not available after this date) suggest that little opportunistic vaccination took place after routine immunization and that no large groups of unvaccinated foreign-born children were registered with general practices in England. Because the quality of primary care data (i.e. ImmForm data) was low for birth cohorts before 2000–2001, coverage estimates were uncertain (Fig. 2).

Overall, measles susceptibility among people born between 1985 and 2016 was 4.6% (range: 1.2–9.2), which corresponds to 975,920 individuals in these birth cohorts in 2019 (Table 1). Of individuals who were eligible for the second MMR vaccine dose from October 1996 onwards, those born between 1998 and 2004 were in birth cohorts classified as not having a sufficiently high level of immunity to prevent measles transmission (Table 1). Surveillance data on measles cases confirmed that, among birth cohorts eligible for full vaccination, the incidence was highest in these cohorts (Fig. 3). Likewise, birth cohorts between 1989–1990 and 1991–1992 did not appear to achieve a sufficiently high level of immunity. However, high susceptibility in those cohorts was not matched by high disease incidence (Fig. 3), which indicates that coverage of the 1996 catch-up campaign was probably underestimated. The incidence of disease in individuals born in 2010 and 2011 was higher than that in more susceptible individuals born between 2000 and 2003 (Fig. 3). However, most cases in those born in 2010 and 2011 occurred before all children in their birth cohort became eligible for the first MMR vaccine dose (Fig. 3).

When a coverage underestimate correction factor of 25% rather than 50% was applied in the sensitivity analysis, susceptibility estimates suggested that no birth cohort between 1989–1990 and 2006–2007 achieved a sufficiently high level of immunity to prevent measles transmission. However, this apparently high susceptibility was not matched by a high observed disease incidence. Consequently, the correction factor of 50% was more likely to be correct.

Discussion

Our application of data triangulation to measles vaccination in England, which considered data on vaccine coverage (including supplementary immunization) in individual birth cohorts and data on the age-specific incidence of measles, illustrates that the approach provides a
pragmatic, simple and useful way of generating and validating disease susceptibility estimates. The concordance between data sources we observed for specific birth cohorts confirmed that data quality was high in those years – such information is helpful for evaluating data-driven targeted vaccination. In contrast, we found that coverage and incidence data were discordant for individuals in birth cohorts between 1989–1990 and 1991–1992, which suggested that one of the two sources was inaccurate. Discordant findings can trigger further investigation and lead to improved data quality.

The use of triangulation also enabled us to determine that, despite good coverage overall, there was a high proportion of susceptible individuals among those born between 1998 and 2004 (who were aged between 15 and 22 years in 2019), even after adjusting for coverage under-ascertainment. This finding was consistent with disease incidence data, which showed that most cases and outbreaks in recent years occurred in this age group. In England, where vaccine coverage is assessed using various methods, our synthesis of data from two different vaccine coverage sources led to insights into the vaccination status of the population. This data synthesis enabled us to estimate the magnitude of opportunistic vaccination, as well as evaluate the data quality of primary care vaccination records. For example, we found that data quality was not sufficient to accurately estimate vaccine coverage among adults born abroad.

In addition to the limitations inherent in both COVER and ImmForm data, the study had several other limitations. First, coverage data for catch-up campaigns were less accurate than for routine immunization. In particular, data were not collected for the 2008 catch-up campaign (unpublished regional evaluations suggest coverage was low). Second, a London-only, catch-up campaign took place in 2004 and achieved a minimum of 24% coverage for individuals born between 1985 and 2004. This campaign was not included in our study because it was regional. Consequently, susceptibility in eligible birth cohorts may have been overestimated at the national level. Third, coverage in national catch-up campaigns was assumed to be the same in all areas and eligible birth cohorts. Fourth, although 95% of general practices contributed to ImmForm data, the proportion varied between cohorts. Moreover, only 50% of practices reported data on cohorts born before September 1995. However, as these practices were spread across the country, coverage estimates for these cohorts were unlikely to have been biased. Fifth, although COVER data included single-antigen measles vaccine for birth cohorts between 1985 and 1987, ImmForm data did not. This discrepancy may explain why estimated coverage in these birth cohorts was lower for ImmForm than COVER data (Fig. 2). Sixth, during the early to mid-2000s, a small number of
parents opted to have their children vaccinated using a private, unlicensed, single measles vaccine. This vaccine was not included in either COVER or ImmForm data. A 2007 study involving children born in 2001 and 2002 estimated that use of this vaccine could have increased coverage for all measles-containing vaccines by around 2% in individuals born in the early 2000s.

When high-quality census data that can be linked to age-specific disease susceptibility estimates are available, the number of susceptible individuals currently in the population can be deduced, thereby enabling the size and timing of future outbreaks to be modelled. Data triangulation can improve the accuracy and precision of coverage estimates, which is vital in areas where coverage is high, and increase confidence in data. In contrast, a recent study that used incomplete and inaccurate information overestimated the number of susceptible individuals in England by a factor of 1.8.

Our analytical approach involved only routinely available data sources, which are not exclusive to the United Kingdom or other high-income countries. Any country that routinely records disease incidence and vaccine coverage could consider a similar approach for measles and other diseases. However, the value of the information produced will depend on the accuracy and precision of the data available and on knowledge of how data quality varies over time. A comprehensive report on improving immunization data quality and use that was recently presented to WHO’s Strategic Advisory Group of Experts on immunization is available online. The report provides strategic guidance on improving data at the national level. In countries where data on individual years are not available, wider age ranges could be considered. Although the resulting insights would be less detailed, the analysis would still be useful for validating coverage and surveillance data and for identifying susceptible age groups. Currently, WHO is planning to publish a framework for, and guidance on, data triangulation to help countries routinely adopt the approach. One alternative to using routine data sources is to conduct much costlier and resource-intensive seroprevalence studies. In England, where the quality of both coverage and incidence data is relatively high, the added value of seroprevalence studies is limited. Current arrangements rely on residual blood samples from hospitals, which may not be representative of the general population, particularly for younger age groups.

Although national estimates of disease susceptibility can help identify at-risk birth cohorts, they may not reflect inequalities at the local level. In England, vaccine coverage varies by ethnicity, social deprivation and geographical location. Consequently, coverage is heterogeneous and the burden of measles and rubella falls disproportionately on specific
communities.30,31 Herd immunity extends the benefits of national immunization programmes to unvaccinated individuals, thus intrinsically reducing inequalities, but its impact will depend on local and overall vaccine coverage and population mixing patterns. When a large number of unvaccinated individuals live in close proximity, their community becomes vulnerable to outbreaks. Better vaccine coverage across the whole population should be accompanied by targeted efforts to assess the risk, specific needs and characteristics of undervaccinated communities and, thereby, close any gaps in immunity.32

In conclusion, triangulating existing data sources on routine vaccination coverage and vaccine-preventable disease surveillance can generate new insights into a population’s level of immunity and help prioritize public health actions aimed at closing gaps in immunity. Use of this approach in England helped establish that, despite achieving high MMR vaccine coverage, measles susceptibility in particular age cohorts was sufficiently high to sustain disease transmission. Nevertheless, susceptibility in all population subgroups cannot be estimated using routine data sources alone. Ad hoc studies are needed for undervaccinated groups, such as adults born abroad. Triangulating coverage and incidence data, in particular, is a useful way of maximizing the quality of data on vaccine-preventable diseases and should be used more widely. Forthcoming guidance from WHO and its partners on the triangulation of data from the Expanded Programme on Immunization will help countries improve data use and quality and, ultimately, help control vaccine-preventable diseases.

Competing interests:
None declared.

References


25. Hitchen L. London’s catch-up vaccination campaign against measles, mumps, and rubella reaches less than a quarter of children who were unvaccinated. BMJ. 2008 09 24;337:a1797. https://doi.org/10.1136/bmj.a1797 PMID:18815174


### Table 1. Measles vaccination coverage and individuals susceptible to measles, by birth cohort, England, 1985–2016

<table>
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<th>Birth cohort</th>
<th>Applicable catch-up campaign</th>
<th>Coverage, %</th>
<th>Routine vaccination coverage, %</th>
<th>Adjusted routine vaccination coverage, %</th>
<th>Proportion susceptible to measles, %</th>
<th>Estimated no. of individuals in cohort in 2017</th>
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<th>Immunity level sufficient to interrupt transmission?</th>
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MMR: measles, mumps and rubella; MMR2: second dose of measles, mumps and rubella vaccine; NA: not applicable; ND: not determined.

a Birth cohorts included individuals born between April in one year and March in the following year.

b Catch-up campaigns were carried out in 1998, 2008 and 2013 with measles, mumps and rubella (MMR) vaccine, in 1994 with measles–rubella vaccine and in 1996 with the second MMR vaccine dose (MMR2; Fig. 2).
Vaccine coverage was determined using data from local Child Health Information Systems, which provide data to the cover of vaccination evaluated rapidly (COVER) programme.

Adjusted vaccine coverage was calculated using a 50% coverage underestimate correction factor: for example, if the estimated proportion of the cohort not covered by vaccination was 8%, 4% (i.e. 50% of 8%) was added to the unadjusted coverage.

The susceptibility calculation took into account both routine and catch-up vaccination, as described in the methods.

The immunity level was regarded as sufficient to interrupt measles transmission when the reproductive number (R0) was under 1, which corresponded to an immunity level over 85% in children aged under 4 years and over 95% in those aged 5 years and over.
Fig. 1. Flowchart for determining level of protection from measles in birth cohorts, England, 1985–2016

MMR1: first dose of measles, mumps and rubella vaccine; MMR2: second dose of measles, mumps and rubella vaccine.

For birth cohorts eligible for one catch-up campaign.

For birth cohorts eligible for more than one catch-up campaign.
Fig. 2. Measles vaccine coverage, by birth cohort, England, 1985–2016

COVER: cover of vaccination evaluated rapidly (programme); MMR: measles, mumps and rubella; MMR2: second dose of measles, mumps and rubella vaccine; MR: measles and rubella.

Notes: Estimates from the cover of vaccination evaluated rapidly (COVER) programme up to 1989 include coverage of both the single measles vaccine and the first measles, mumps and rubella (MMR) vaccine. For the COVER programme, coverage data were collected at the children’s second birthday for those in birth cohorts after 2012–2013 and before 1992–1993; otherwise data were collected at their fifth birthday. Birth cohorts included individuals born between April in one year and March in the following year.
Fig. 3. Measles susceptibility and incidence, by birth cohort, England, 1985–2018

MMR: measles, mumps and rubella.