



Public Health
England

Protecting and improving the nation's health

COVID-19 vaccine surveillance strategy

March 2021

Contents

COVID-19 vaccine surveillance strategy	1
Contents.....	2
Document revision information.....	3
1. Background.....	4
2. Aims of post-implementation surveillance	6
3. Vaccine coverage	7
3.1 Existing models for vaccine coverage reporting	7
3.2 National Immunisation Management System	7
3.3 Proposed model for COVID-19 vaccine coverage monitoring	7
4. Safety.....	8
4.1 Signal detection.....	8
4.2 Rapid assessment.....	8
4.3 Signal evaluation	9
4.4 Vaccination in pregnancy	9
5. Vaccine effectiveness	11
5.1 Approaches to estimating vaccine effectiveness	11
5.2 Outcomes	11
5.3 Duration of protection	12
5.4 Surveillance systems and study designs	12
5.5 Reporting of vaccine effectiveness data	16
6. Vaccine failure	17
7. Programme impact.....	18
8. Sero-surveillance	19
8.1 CONSENSUS study	20
9. Attitudinal research	21
10. References.....	22

Document revision information

Version number	Details	Date
1	Document created	11 January 2021
2	Added information about the CONSENSUS study	26 March 2021

1. Background

Roll out of the UK COVID-19 immunisation programme began in December 2020. Three vaccines have now received emergency use authorisation and there are further vaccines in the late stages of clinical evaluation which may be introduced over the course of 2021 (1). The Joint Committee on Vaccination and Immunisation (JCVI) has provided interim advice on priority groups for vaccination which include older adults, care home residents and staff, health and social care workers and individuals in clinical risk groups (2).

Phase 1 to 3 clinical trials have been undertaken by the vaccine manufacturers to estimate the immunogenicity, safety and efficacy of the vaccine in clearly defined populations against specific end points. These provide evidence on common adverse reactions and the early efficacy of the vaccine against laboratory confirmed disease within the study population. This has informed decision making on vaccine choice and target groups for a national programme. Nevertheless, these studies are undertaken in ideal delivery conditions, tend to exclude certain populations, such as individuals with underlying medical conditions, and typically have a relatively short follow-up period.

With vaccines now being offered to several million people, comprehensive 'real world' post-implementation surveillance systems are required to monitor delivery of the vaccination programme and evaluate its impact on health. This involves using existing disease surveillance systems and electronic health data, capturing vaccination data and active follow-up of vaccinated individuals and cases of COVID-19 within vaccine eligible cohorts. JCVI have made recommendations on the need to monitor the effectiveness and impact of vaccines against a broad range of outcomes and the need to integrate monitoring of inequalities in uptake, acceptability and outcomes in key underserved groups and across protected characteristics as a core component of the post-implementation surveillance.

The UK is a world leader in post-implementation vaccine surveillance and has been a pioneer in methodological advances in vaccine evaluation and providing evidence on new vaccines, including being the first country to show that the Meningococcus C, maternal pertussis and meningococcus B vaccination programmes prevent death and cases of serious disease; the first country to provide evidence that the live attenuated influenza vaccination programme in children offers indirect protection to the wider population including older adults; and the first country to provide evidence of the emergence of non-vaccine serotypes of after the 13 valent pneumococcal conjugate vaccination programme. Post-marketing vaccine coverage, disease surveillance and seroprevalence data have been used to adapt existing vaccination programmes, including recommending national and regional measles catch-up vaccination campaigns and introducing a teenage booster programme for meningococcus ACWY. Investigations have also been undertaken into a broad range of potential safety signals, the vast majority of which showed no association with vaccination.

COVID-19 Post-implementation vaccine surveillance strategy

In order to maintain public and healthcare professionals' confidence in the vaccine and to ensure that surveillance systems are in place for long-term monitoring of the programme, it is important that post-marketing surveillance is led by independent public health agencies without association with vaccine manufacturers.

This document provides a high-level oversight of the post-implementation surveillance strategy that PHE will be implementing, in collaboration with the MHRA, NHSEI and academic partners, to monitor and evaluate a future COVID-19 vaccination programme. The outcomes of this surveillance will be reported as soon as they become available to the JCVI, to support vaccine policy recommendations, and to SPI-M to support dynamic modelling to understand the impact of the vaccination programme on the need for non-pharmaceutical interventions.

2. Aims of post-implementation surveillance

The aims of post-marketing surveillance are:

- to monitor coverage of the vaccine in targeted populations and identify undervaccinated groups
- to rapidly detect and evaluate possible adverse events associated with vaccination
- to estimate the effectiveness of the vaccine at preventing a spectrum of disease outcomes and onwards transmission in different targeted populations, and against different viral variants, as well as the duration of any protective effect
- to identify risk factors for and outcomes of vaccine failure, including any impact on strain evolution
- to monitor the overall impact of the vaccination programme on COVID-19 in the wider population including the indirect effect on groups not targeted by the vaccination programme
- to monitor the impact of the vaccination programme on prevalence of antibodies against COVID-19 as an indicator of population level immunity, and to monitor antibody waning in the population
- to monitor attitudes to vaccination and identify barriers to high vaccine uptake
- to monitor inequalities in each of these outcome measures

3. Vaccine coverage

Vaccine coverage is a key indicator of the performance of the immunisation delivery system. Moreover, data on vaccine coverage are used to estimate the level of susceptibility in the population and identify areas or populations at increased risk of outbreaks. Identification of undervaccinated groups can be used to adapt delivery of the programme. Vaccination data at an individual and population level are also used to support the analysis of vaccine effectiveness, impact and safety.

3.1 Existing models for vaccine coverage reporting

PHE is responsible for monitoring coverage of all vaccines in the national immunisation schedule. Aggregated data are reported by the vaccine providers or from Child Health Information Systems are reported and analysed by PHE and published on a regular basis. (3). Most vaccines are delivered via primary care and uptake data are extracted automatically from GP electronic health record systems onto the ImmForm platform. Delivery through other providers, such as NHS trusts for vaccination of healthcare workers, or school immunisation teams for vaccines delivered in school, is typically monitored through regular manual reporting by the provider.

3.2 National Immunisation Management System

The COVID-19 vaccination programme is being delivered through a range of models including hospital trusts, mass vaccination centres and primary care networks. NHS Digital have led the development of a new national vaccination register and call/recall system for COVID-19 and influenza vaccination – the National Immunisation Management System (NIMS). Demographic data, GP data and employee data (for NHS staff) will feed into the NIMS to identify vaccine eligible groups so that they can be invited for vaccination and individual vaccination data feeds into the NIMS from the vaccine providers. Data from the NIMS also feeds back into GP systems to update the individual's electronic health record with their vaccination history.

3.3 Proposed model for COVID-19 vaccine coverage monitoring

COVID-19 vaccine coverage will initially be monitored using both the existing approaches outlined in section 2.1 as well as data extracts taken directly from the NIMS. It is anticipated that vaccine coverage monitoring through the NIMS will ultimately replace the existing approaches once data flows are established and data validation has been completed for all vaccine eligible groups.

4. Safety

Rapid detection and evaluation of possible adverse events associated with vaccination is vital for providing reassurance that the vaccine does not cause harm. Major safety concerns that are common and occur within a short period of vaccination are likely to be detected through the clinical trials. Rarer or more delayed adverse events require continuous post implementation monitoring. Safety surveillance will be undertaken in collaboration with the MHRA, further details on the MHRA proactive vigilance of COVID-19 vaccines are available [here](#).

4.1 Signal detection

A signal of a potential adverse events may come from a range of sources such as the pre-licensure clinical trials, MHRA assessments of Yellow Cards reports, active follow up of cohorts vaccinated during the implementation of the national programme or from other countries or specialist health care professionals seeing increases in consultations for specific conditions.

PHE will work with the MHRA and the Health Protection Research Unit (LSHTM) using the Clinical Practice Research Datalink (CPRD) to identify any potential safety signals using sequential testing methods for a pre-specified set of events of interest. Another component of the signal detection will be identifying whether the number of reports has exceeded the expected number for that specific condition in the same population in the absence of vaccination, to evaluate any potential signals compared to a historic baseline. This work will be led by MHRA and PHE and will generate background rates using hospital admission data (Hospital Episode Statistics (HES) for a list of prespecified conditions of interest.

4.2 Rapid assessment

To assess any signal coming from these sources a more detailed investigation is needed before a full epidemiological study is performed. This investigation may include ecological studies using large routinely collected national datasets, such as HES, Secondary Uses Service (SUS) or the Emergency Care Dataset (ECDS), which may be undertaken assuming coverage of the vaccination is high in the population of interest. These analyses will be used to compare trends in disease rates before and after the introduction of the vaccination programme in defined vaccine targeted and comparator populations without requiring individual vaccination status. These studies cannot establish causation or quantify a risk but are seen as a rapid exploratory analysis with the view to inform the epidemiological hypothesis-testing stage of the assessment and to

complement other rapid assessment of signals for prioritisation of those requiring hypothesis testing studies.

4.3 Signal evaluation

To establish whether the signal seen is associated with the vaccine and to quantify the risk a formal epidemiological study is needed to test the specific hypothesis. This requires a pre-specified protocol detailing the population under study, the case definition of the outcome of interest, the period after vaccination in which an elevated risk is suspected and the methods for case identification and statistical analysis. Most importantly the ascertainment of the condition of interest must be unbiased with respect to vaccination history. There are a range of data sources which PHE will utilise to evaluate and test a signal. These include GP data (such as CPRD, THIN and Open Safely). These datasets are best for events presenting at GPs where coding has reasonable specificity. Some of these datasets are linked to hospital data for either a subset (CPRD) or for all the data (Open Safely). Analyses will include cohort, case-control and self-controlled case series designs. For hospitalised conditions the HES or SUS and ECDS can be utilised and linked to the National Immunisation Management System (NIMS) or the individuals' vaccination history can be obtained by linkage to GP electronic health records or contacting the GP. Methods employed here typically include the self-controlled case-series and case-coverage methods.

In addition, specialist registers may be established for particular events that have been identified as a possible safety signal where routine data sources are inadequate. The validation of a subset of cases from these existing data sources can be performed through hospital visits and the use of expert panels.

The data source used to identify the condition of interest and statistical methods employed will depend on the condition under investigation. PHE will use their range of available data sets and experience, which has been built over the past 25 years with more than 40 vaccine safety studies performed which have focused on a number of different safety concerns, to robustly investigate vaccine safety concerns.

4.4 Vaccination in pregnancy

There is no known risk associated with giving non-live vaccines during pregnancy. On a precautionary basis, pregnant women have been excluded from most COVID-19 vaccine trials. This means that there is a deficit of information on the safety of COVID-19 vaccines in this group. JCVI have advised that there is insufficient evidence to recommend routine use of COVID-19 vaccines during pregnancy, however, vaccination should be considered for pregnant women at high risk of exposure or of serious complications. PHE has already established surveillance of inadvertent vaccination in pregnancy (VIP) currently covering the live MMR, chickenpox and varicella vaccines.

COVID-19 Post-implementation vaccine surveillance strategy

This is collaborative UK-wide surveillance and any healthcare professional can report to this surveillance if they become aware of a woman who has received one of these vaccines in pregnancy. VIP surveillance has been established for COVID-19 vaccination in pregnancy (inadvertent or intentional) (4). Background information on the medical history of the pregnant women including prior pregnancies is collected at the time of reporting and these are then followed 10 weeks post estimated date of delivery to determine the pregnancy outcome and initial information for all live births with a final follow up when the baby reaches their first birthday.

Reports of exposure may also be submitted to the MHRA and to the UK teratology information service (UKtis) and there is agreement between PHE, the MHRA and UKtis that all reports will be transferred to PHE so that a standardised surveillance approach can be undertaken. These 3 organisations will also be involved in later evaluation of the collected data.

5. Vaccine effectiveness

Phase 3 vaccine trials are undertaken in clearly defined populations that may exclude some groups, such as those with immunosuppression, pregnant women and children. These trials are undertaken in ideal conditions, with perfect storage and maintenance of cold chains and ensure that the recommended interval between doses is strictly adhered to. It is important to evaluate the effectiveness as used in practice, ie 'real world', as this may differ to clinical trial efficacy. Clinical trials are also typically powered for a primary endpoint of virologically confirmed symptomatic disease within a relatively short follow-up period so that effective vaccines can be introduced as rapidly as possible. Nevertheless, understanding the effectiveness against different end points (such as disease severity and onwards transmission), effectiveness in different subgroups of the population and understanding the duration of effectiveness are equally important in decision making around which vaccines should be implemented as the programme evolves, who they should be offered to and whether booster doses are required.

5.1 Approaches to estimating vaccine effectiveness

Vaccine effectiveness is estimated by comparing rates of disease in vaccinated individuals to rates in unvaccinated individuals. Typically, observational study designs are employed for monitoring real world effectiveness, either using routine data sources or individual follow-up of cases in vaccine eligible cohorts. Approaches include cohort studies, whereby vaccine eligible cohorts are followed up prospectively to monitor disease outcomes; retrospective designs, whereby vaccination history is compared in cases of COVID-19 to a control group, for example individuals testing negative (a test negative case control design) or comparing to uptake in the wider population (the screening method); and ecological designs whereby outcomes at a population level are observed, for example the impact of the vaccination programme on outbreaks in defined settings.

5.2 Outcomes

PHE will be monitoring the effectiveness of COVID-19 vaccines against:

- virologically confirmed symptomatic disease using PCR
- hospitalisation
- mortality
- laboratory confirmed infection (symptomatic or asymptomatic) using PCR or by demonstrating seroconversion due to disease
- markers of infectiousness and transmissibility – viral load (CT value) and culturable virus
- onwards person to person transmission

5.3 Duration of protection

Vaccine effectiveness against symptomatic disease and other outcomes will continue to be monitored regularly as the programme is rolled out and beyond with an increasing follow-up period after vaccination of the initial cohorts. Analyses will be stratified into 3 month follow-up periods for the first year, 6 month periods, for the following year and annually thereafter, subject to the number of cases being sufficiently high for an adequately powered analysis. Splines will also be used to model VE by time since vaccination. This will provide early warning of any waning of effectiveness and the need for booster doses.

5.4 Surveillance systems and study designs

PHE will monitor vaccine effectiveness in different targeted groups using a range of existing surveillance systems, new enhanced surveillance and by building upon established research studies in specific populations. This work will be undertaken in collaboration with academic partners at the University of Oxford, London School of Hygiene and Tropical Medicine, the University of Nottingham, University College London and the University of Bristol. The approaches that will be used are described below:

5.4.1 Vaccine effectiveness against symptomatic disease

The phase 3 clinical trials provide evidence of vaccine effectiveness against symptomatic disease; however, further evidence is needed on how effectiveness varies by subgroup (such as by age or clinical risk groups), viral variants, number of doses administered, timing of doses, and the comparative effectiveness of different vaccines in the real world. Evidence on these outcomes will be generated through routine data sources, including routine testing data and GP electronic health records, as well as through enhanced surveillance.

5.4.1.1 Routine testing

Routine COVID-19 testing data through Pillar 1 and Pillar 2 is available through the Second Generation Surveillance System (SGSS). This will be linked to vaccination data from the NIMS. This provides a dataset for monitoring vaccine effectiveness using a test-negative case control approach by vaccine, age group, clinical co-morbidities and different dosing schedules that may be used in the programme. While details of symptoms and clinical history are limited, through pillar 2 testing, those requesting tests report their symptom status and date of symptom onset. The routine testing data has the advantage that it provides a very large dataset for rapid analysis of vaccine effectiveness against symptomatic disease.

5.4.1.2 Enhanced surveillance

Once a vaccination programme is implemented and the earliest eligible groups have been offered a full course of vaccination, PHE will begin enhanced surveillance of a subset of cases in vaccine eligible groups identified through the routine testing. Clinical questionnaires will be completed with the case and their GP or hospital clinician on vaccination history, past medical history, symptoms and outcomes. Repeat nose and throat swabs and acute and convalescent serum and oral fluid samples will be taken, these will be used to:

- confirm recent infection
- provide evidence of immune response following vaccination and identify primary and secondary vaccine failures
- estimate viral load, viral replication and culturable virus as markers of infectiousness
- test for other respiratory viruses
- undertake sequencing to identify nucleotide changes that may favour vaccine escape and differences in phenotype

The enhanced surveillance will be used for monitoring age-specific vaccine effectiveness in targeted groups using a screening and test-negative case control design and identifying risk factors for, and outcomes of, vaccine failure.

5.4.1.3 GP electronic health record studies

GP electronic health record datasets typically contain data on:

- patient demographics and comorbidities that would place them in a vaccine eligible cohort
- vaccination history – for COVID-19 this would be via a feed from the NIMS (described in 2.2)
- laboratory confirmed SARS-CoV-2 infection - either through linkage to pillar 1 and 2 testing data or through sentinel swabbing
- hospitalisation and mortality – through linkage to Hospital Episode Statistics (HES) and ONS mortality databases

PHE has a longstanding collaboration with the Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) for monitoring influenza and other respiratory infections in primary care (5). In addition to monitoring clinical presentations with respiratory syndromes, the network undertake sentinel swabbing of patients presenting with influenza like illness. This system is used annually for monitoring influenza vaccine effectiveness using both test negative case control and cohort study designs. For the test negative design this has included aggregating data across UK wide sentinel networks to enhance power (6) and this can be done for COVID-19 vaccines as well. The RCGP network has been expanded since the start of the pandemic and the electronic health record data are also linked to testing data in SGSS which includes testing through both Pillar 1 and Pillar 2 (7). The RCGP RSC will be used for routine

reporting of vaccine effectiveness against symptomatic infection in vaccine eligible groups and, if sample size allows, for monitoring of vaccine effectiveness against hospitalisation with COVID-19 and COVID-19 mortality.

A similar approach will be taken using OpenSAFELY and/or the Clinical Practice Research Datalink (CPRD) in collaboration with the University of Nottingham and the London School of Hygiene and Tropical Medicine (8) (9). These datasets are also linked to SGSS and HES and offer a larger quality assured cohort so may be more suitable for estimating vaccine effectiveness in smaller subgroups, estimating vaccine effectiveness against rarer outcomes, or estimating relative effectiveness of different vaccines.

5.4.2 Vaccine effectiveness against severe disease

5.4.2.1 Hospitalisation

Hospitalisation will be used as a marker of how effective the vaccine is at preventing severe disease. Hospitalised patients with COVID-19 are reported daily by sentinel hospital trusts to the PHE Severe Acute Respiratory Infection (SARI) -Watch surveillance system. A question has been added to this surveillance system on COVID-19 vaccination history. The hospitalisation data will also be linked to the NIMS. Vaccine uptake in hospitalised cases can be compared to uptake in the general population to estimate vaccine effectiveness using the screening method. The effect of vaccination on hospitalisation will also be monitored through the national Secondary Users Service (SUS) hospitalisation dataset linked to testing data through SGSS and vaccination data through the NIMS so that a test-negative case control design can be used. The population will be restricted to those with respiratory admissions. SUS data follows a 1-2-month lag therefore the SARI-Watch approach will be used in the early stages of the vaccination programme.

The University of Bristol have an established study of pneumonia hospitalisations which is being adapted to collect information on COVID-19 testing and vaccination. This has the advantage of including clearly defined respiratory admissions and a collection of more in-depth data on the hospital admission and clinical history.

5.4.2.2 Mortality

Vaccine effectiveness against mortality from COVID-19 will also be monitored. The surveillance systems described in 5.4.1 will all be linked to NHS and ONS mortality data and this will form an integral part of the analysis.

5.4.3 Vaccine effectiveness against infection

The majority of clinical trials have only provided data on effectiveness against symptomatic disease without including asymptomatic infection. Understanding the overall effectiveness against infection is important because infected individuals may continue to transmit the virus even if they do not display symptoms. In order to monitor

vaccine effectiveness against infection repeat asymptomatic PCR testing or antibody testing is required. A number of studies have been established since the start of the pandemic with routine asymptomatic infection and these will be used to monitor vaccine effectiveness against infection.

5.4.3.1 SIREN (Sarscov2 Immunity & REinfection EvaluationN) study

The SIREN study is a PHE led cohort study of approximately 40,000 healthcare workers. Participants undertake symptom questionnaires and respiratory swabs every 2 weeks and a serum sample is taken every 4 weeks. Healthcare workers are one of the earliest groups to be offered the vaccine therefore this study is likely to provide one of the earliest estimates of vaccine effectiveness against infection.

5.4.3.2 Vivaldi study

Similarly, care home residents and staff are also one of the JCVI priority groups for vaccination (2). PHE is working with the Vivaldi study team at University College London to monitor vaccine effectiveness in care home residents and staff (10). Care home residents and staff are offered PCR testing on a weekly basis and these results are captured through pillar 2 and linked to study participants. This would allow us to monitor the effectiveness against symptomatic or asymptomatic PCR confirmed infection. In addition, participants have serum samples taken every 3 months for the first year which may allow us to monitor vaccine effectiveness against infection identified through either PCR or seroconversion. Ideally more frequent antibody testing would be used and options for increasing the frequency of testing are being explored.

5.4.3.3 Community infection survey

PHE are also working with the Office for National Statistics (ONS) to monitor vaccine effectiveness against infection through the community infection survey. This can be estimated through the existing asymptomatic PCR testing. A cohort for longer term follow-up is also being expanded for repeat serology over at least a 12 month period. This will be used to monitor vaccine effectiveness against infection in a general population cohort.

5.4.3.4 Routine data sources

Repeat testing data will also be available through SGSS and GP datasets and will be used for monitoring vaccine effectiveness against infection. Repeat serum samples are also being collected through the RCGP RSC network and will be used to monitor both seroconversion and antibody waning.

5.4.4 Effect of vaccination on transmissibility

As well as understanding the impact of vaccination on disease outcomes and infection it is also important to understand whether it reduces the risk of onwards transmission. This will inform policy decisions around whether to prioritise vaccination of those with worse outcomes or those who transmit more.

Analysing CT values, culturable virus and duration of PCR positivity in vaccinated cases will provide an indication of infectiousness.

To directly monitor the effect on transmission, a sample of cases identified through enhanced surveillance as well as healthcare workers and care home staff identified through the SIREN (Sarscov2 Immunity & REinfection EvaluationN) study and the Vivaldi study (described below) will be recruited to monitor the effect of vaccination on their risk of onwards transmission. This would ideally include asymptomatic cases identified by seroconversion or routine swabbing. The approach to monitoring transmission will build on the existing PHE Household Contact (HoCo) study. Symptom questionnaires will be undertaken with the household contacts at baseline and 14 days. They will also have repeat nose and throat swabs as well as baseline and 35-day serum samples and oral fluid tests. This will identify symptomatic and asymptomatic secondary cases in the household. Secondary infection rates where the primary case has been vaccinated will be compared to those where the primary case was unvaccinated.

Routine testing data will also be used to monitor the number of secondary cases in households where the first case identified in the household is vaccinated using the PHE HOSTED dataset with linkage to the NIMS data.

5.4.5 Outbreaks

Protocols have also been developed for monitoring vaccine effectiveness in outbreaks in closed settings. This may also be used for studying the effectiveness of vaccination as post exposure prophylaxis.

5.5 Reporting of vaccine effectiveness data

Vaccine effectiveness monitoring in the cohorts described above will begin once sufficient time has elapsed for the earliest vaccine eligible cohorts to have received a full course of vaccine and mounted an immune response (this is anticipated to be 7 days after the second dose). Effectiveness of a single dose will also be monitored from 14 days after the first dose. Estimation of vaccine effectiveness will require a sufficient sample size for an adequately powered analysis. This will depend on the disease epidemiology at the time, how effective the vaccine is and the level of vaccine uptake, it is anticipated that the earliest estimates will be reported in the first quarter of 2021. Vaccine effectiveness will be reported by demographic and clinical characteristics (such as age group and clinical risk group) and vaccine brand. Depending on how the programme is delivered and where adequately sample sizes are available, relative effectiveness of different vaccines and effectiveness of different dosing schedules may be estimated.

6. Vaccine failure

Even with a highly effective vaccine, it is anticipated that some vaccinated individuals will develop COVID-19. This may either be due to primary vaccine failure, where the individual did not mount an immune response to vaccination, or secondary vaccine failure where an individual developed disease despite evidence of an immune response to vaccination. Understanding factors associated with vaccine failure is important in ensuring the success of the vaccination programme.

Possible vaccine failures will be followed up through the enhanced surveillance described in section 5.4.1.2 , including viral whole genome sequencing to identify nucleotide changes that may be associated with vaccine escape, identifying patient factors or programme delivery factors associated with vaccine failure and monitoring disease outcomes. This will be used to understand whether there is any evidence of vaccine-induced immune enhancement, whereby disease outcomes are more severe in vaccinated cases.

Clinicians and immunisation teams will also be asked to report cases of breakthrough infection where there is a suspicion of enhanced disease.

7. Programme impact

Vaccines typically have both direct effects on those who are vaccinated and indirect effects on those who are unvaccinated due to a reduced probability that they will come into contact with an infected individual. The overall impact of the vaccination programme may therefore extend beyond that estimated through vaccine effectiveness analysis. This is not captured in clinical trials which are designed to estimate individual protection.

Estimating the impact of a vaccination programme is challenging without, for example, randomised roll-out of the programme to different areas at different times. Ecological assessments will be used to estimate the impact of the programme using before and after analyses, comparing targeted to non-targeted groups and by using any variation in the timing of delivery or level of uptake in different groups. The impact on different disease indicators including case detections, outbreaks, hospitalisations and mortality will be monitored using these approaches.

8. Sero-surveillance

The SARS-CoV-2 genome encodes 4 major structural proteins including the spike (S) glycoprotein, envelope (E), membrane protein (M) and the nucleoprotein (N). Most serological studies are based on assays which target either the N or S proteins. PHE has been using a range of commercial assays targeting both the N and S proteins for sero-surveillance activities to date. This currently includes the Abbott assay targeting N protein (SARS-CoV-2 IgG chemiluminescent microparticle immunoassay (CMIA)) and the Euroimmun assay targeting the S protein (Anti-SARS-CoV-2 ELISA IgG).

Although the timing and sensitivity and specificity will vary by assay, typically an antibody response to N and S following infection is detectable from the first week from symptom onset and peaking at around 28 days. Given the delay between natural infection and antibody response, seroprevalence studies measure infections acquired at least 3 weeks earlier. Whilst there is no agreed correlate of protection, sero-surveillance provides valuable information on the proportion of the population that has been exposed to SARS-CoV-2 and includes asymptomatic infections that generally remain undetected using other surveillance systems.

All the currently proposed vaccines for use in the UK target the spike protein only and therefore it is not expected that there will be an antibody response to the other SARS-CoV-2 proteins, especially the N protein. Immunological responses following vaccination appear to be strongly detected at 28-35 days following the first dose vaccine. It is proposed that the differential antibody response to N and S can be used to distinguish between antibody response to vaccine or to natural infection, and therefore testing samples collected through the existing PHE sero-surveillance programme by multiple assays will support the evaluation of the vaccine programme as vaccine is rolled out.

These collections include:

- NHSBT collection – adult blood donor samples (aged 17 years and above) provided by NHS Blood and Transplant
- RCGP collection – samples collected from patients (aged 10 years and above) attending one of the participating Royal College of General Practitioners' practices for routine blood tests; additional demographic and clinical information including vaccine status will be available for samples collected through this scheme
- PHE Seroepidemiology Unit (SEU) collection – residual sera (all age groups) provided by participating laboratories across England

Outcomes

Proportion of population seropositive to (a) N protein and (b) S protein by age group, gender, region, time period.

Prevalence of antibodies to S protein will be compared with data on vaccine uptake (see earlier section). Prevalence to N or S protein will help assess overall population immunity and changes in N protein seroprevalence will help assess incidence of infection in both vaccine-targeted and non-targeted populations, which will contribute to understanding whether the vaccine offers direct and indirect protection.

8.1 CONSENSUS study

Authorisation for the Pfizer BioNTech vaccine was based on a two-dose schedule administered 21 days apart and, for the Oxford AstraZeneca vaccine, 4 to 12 weeks after the first dose. In light of the UK COVID-19 epidemiology in late 2020 with rapid increase in cases, hospitalisation and deaths, updated advice from the UK JCVI was issued to extend the interval between the first and second doses to up to 12 weeks for both vaccines so that as many people within the priority groups for Phase 1 are vaccinated quickly with at least one dose. A single dose is expected to provide high levels of protection until the second dose is given to provide more long-term protection. With most vaccines, an extended interval between the prime and booster doses leads to a better long-term immune response.

As part of the evaluation of the vaccine programme, PHE is rapidly monitoring the development and persistence of antibody levels and T cell responses in individuals who have received the extended schedule of either the Pfizer or Oxford AstraZeneca vaccine. Immune responses will be compared with individuals who have received the authorised schedule for Pfizer BioNTech vaccine (2 doses administered 21 days apart). Findings will be reported to the UK JCVI and Department of Health and Social Care.

9. Attitudinal research

Attitudinal research is important for understanding views on vaccination and the barriers and drivers to uptake. This information can be used to adapt delivery models, patient information leaflets and wider communications on the vaccine.

PHE Immunisation and Countermeasures Division currently commission 2 annual attitudinal surveys exploring awareness of and confidence and trust in the national childhood and adolescent vaccination programmes. Expansion of this work to enable confidence in the vaccination programme to be monitored across the life course is planned.

The NIHR Health Protection Research Unit at the London School of Hygiene and Tropical Medicine have undertaken a survey of 18,000 people across the UK on their perceptions on both a novel COVID-19 vaccine and the seasonal influenza vaccine. They have also undertaken a survey of around 1200 parents (including 19 qualitative interviews) on their experiences of having their children vaccinated during the first lockdown period. This included questions on Covid-19 vaccine acceptance.

The PHE integrated marketing and communications team carried out qualitative insights work which has informed the planned messaging on vaccination through the deployment board.

PHE are also working closely with the NIHR Policy Research Unit at Newcastle University who have undertaken an online behavioural insights survey including those who are in high risk groups and minority ethnic communities who indicate they are unsure or do not want a Covid-19 vaccine to try and improve understanding on barriers to uptake in these communities.

Attitudes to vaccination will continue to be monitored through population surveys and qualitative interviews after the roll-out of the programme in order to adapt the communications and delivery strategy and maximise uptake in undervaccinated groups.

10. References

1. **World Health Organization.** Draft landscape of COVID-19 candidate vaccines,. [Online] 3 November 2020. <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>.
2. **Joint Committee on Vaccination and Immunisation.** JCVI: updated interim advice on priority groups for COVID-19 vaccination. [Online] 25 September 2020. <https://www.gov.uk/government/publications/priority-groups-for-coronavirus-covid-19-vaccination-advice-from-the-jcvi-25-september-2020/jcvi-updated-interim-advice-on-priority-groups-for-covid-19-vaccination>.
3. **Public Health England.** Vaccine uptake guidance and the latest coverage data. [Online] 21 October 2020. <https://www.gov.uk/government/collections/vaccine-uptake>.
4. —. Vaccination in Pregnancy. [Online] 18 December 2020. <https://www.gov.uk/guidance/vaccination-in-pregnancy-vip>.
5. *Emergence of a novel coronavirus (COVID-19): protocol for extending surveillance used by the Royal College of general practitioners research and surveillance centre and Public Health England.* **Simon de Lusignan, Jamie Lopez Bernal, Maria Zambon, Oluwafunmi Akinyemi, Gayatri Amirthalingam, Nick Andrews, Ray Borrow, Rachel Byford, André Charlett, Gavin Dabrera, Joanna Ellis, Alex J Elliot, Michael Feher, Filipa Ferreira, Else Krajenbrink, et al.** 2, s.l. : JMIR public health and surveillance, 2020, Vol. 6. DOI: 10.2196/18606.
6. *End of season influenza vaccine effectiveness in adults and children in the United Kingdom in 2017/18.* **Pebody Richard, Djennad Abdelmajid , Ellis Joanna , Andrews Nick , Marques Diogo F P , Cottrell Simon , Reynolds Arlene J , Gunson Rory , Galiano Monica , Hoschler Katja , Lackenby Angie , Robertson Chris , O'Doherty Mark , Sinnathamby Mary , et al.** 31, s.l. : Euro Surveill., 2019, Vol. 24. <https://doi.org/10.2807/1560-7917.ES.2019.24.31.1800488>.
7. **Department of Health & Social Care.** COVID-19 testing data: methodology note. [Online] 21 August 2020. <https://www.gov.uk/government/publications/coronavirus-covid-19-testing-data-methodology/covid-19-testing-data-methodology-note>.
8. *Data resource profile: Clinical practice research datalink (cprd) aurum.* **Wolf, Achim, Daniel Dedman, Jennifer Campbell, Helen Booth, Darren Lunn, Jennifer Chapman, and Puja Myles.** 6, s.l. : International journal of epidemiology, 2019, Vol. 48.
9. *OpenSAFELY: factors associated with COVID-19 death in 17 million patients.* **Williamson, E.J., Walker, A.J., Bhaskaran, K. et al.** s.l. : Nature, 2020. <https://doi.org/10.1038/s41586-020-2521-4>.
10. **Shallcross, L et al.** COVID-19 in care homes (VIVALDI). [Online] 05 June 2020. <https://doi.org/10.1186/ISRCTN14447421>.

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, research, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

Public Health England
Wellington House
133-155 Waterloo Road
London SE1 8UG
Tel: 020 7654 8000

www.gov.uk/phe

Twitter: [@PHE_uk](https://twitter.com/PHE_uk)

www.facebook.com/PublicHealthEngland

© Crown copyright 2020

Version 2

OGL

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit [OGL](http://www.ogil.gov.uk). Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

Published March 2021

PHE gateway number: GOV-7853



PHE supports the UN Sustainable Development Goals

