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Review of longitudinal studies on immunity from SARS-CoV-2

1. Background

This overview is prepared as a response to an action PHE and VSCG received at SAGE 90 on 27 May 2021:

> **VSCG & PHE to review longitudinal studies on immunity underway to ascertain whether there are any gaps and if further work may need to be commissioned; and to identify the most appropriate group to analyse the combined output of these studies.**

This action resulted from a discussion at SAGE on waning immunity after infection with SARS-CoV-2. The discussion highlighted the importance of monitoring changes in immunity over long periods of time using both detailed smaller studies as well as larger surveillance studies.

2. PHE/UKSHA normal remit in the area of the request

- Support for JCVI
- Vaccine Safety monitoring
- Monitoring of population immunity through sero-surveillance
- Monitoring of vaccine effectiveness through provision of serological data
- Vaccine efficacy assessment using pre-clinical studies and in-vitro biological neutralisation assays
- Monitoring of vaccine effectiveness through population surveillance
- Risk assessment of viral variants on vaccine efficacy and/or escape
- Outbreak investigations
- Vaccine uptake in adults and in children
- Studies in schools and care homes

3. Studies in PHE that address the remit of the SAGE tasking

PHE is undertaking a number of research, evaluation, surveillance, sero-surveillance, clinical, population and pre-clinical studies on this topic, some funded externally by UKRI and NIHR, others funded as part of COVID response. Virtually all of these studies are short term duration of <18 months, addressing immediate information gaps in support of policy development, but not addressing fundamental mechanistic science (Table 1).

Several PHE sponsored studies will be suitable for longer term cohort development/partnership with academia. This requires further assessment of the existing studies

Outputs of population studies may be more directed towards underpinning NHS clinical service delivery or fundamental understanding of basic immunology through serial sampling. A spectrum of studies is needed to cover all areas.

Many stakeholders have an interest in this work, and rely upon data or cohorts established by PHE to generate surveillance information. Effort to minimise overlaps and fund complementary studies is necessary. PHE to continue dialogue with funding bodies regarding research gaps (e.g. UKRI, NIHR, CMO and other international funders).

Appendix 1 details the studies led or supported by PHE including those approved by PHE's Research Ethics & Governance Group. Pre-clinical studies are found in Annex 2, with Annex 3 showing an extract from the UK Collaborative on Development Research (UKCDR) and Global research collaboration for infectious disease preparedness (GLOPID-R) project tracker.

4. Gaps

Scientific gaps that can be identified:

- **Assessment of cellular immune response and its impact on vaccine efficacy *(longer term studies)***
- **Studies in immunocompromised/immune suppressed groups *(cohort based observational studies)***
- **Correlates of protection.** Finding a laboratory correlate which can predict necessity for re-vaccination or increased disease susceptibility ***(will need inputs from a range of studies)***
- **Duration of Immunity in children *(longer term studies)***
- **Duration of protective immunity in all ages and ethnic backgrounds *(longer term studies)***
- **Assessment of efficacy of vaccines not currently deployed in the UK, and potential for interaction with immunity generated by UK vaccines *(medium term)***
- **Protection conferred by prior infection *(all age groups meta analysis longer term)***
- **Impact of long COVID and/or vaccine enhanced disease *(longer term cohort)***

5. Recommendations

- Commitment to longer term cohort studies in various age groups and settings. Most studies are established for a short-term duration 6-18 months.
- Give consideration to which of these studies should be funded for the medium term (3-5 years), +/-partnership with academic consortia
- SAGE to commission a living evidence review on immunity studies to support early identification of evidence gaps and design of studies to address missing information.
- Commitment to niche studies enabling mechanistic basic science work in partnership with industry and academia

- Continued surveillance and evaluation of risk assessments from variants of concern
- Continued evaluation of vaccine efficacy through preclinical and clinical assessment
- Continue to work closely with UKG departments (e.g. BEIS/VTF and FCDO), international agencies (CEPI, WHO, BMGF, USG) and agreements (G7 Clinical Trial Charter)

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Table 1 – PHE studies mapped against coverage of population groups

Study Name	Maternity	Perinatal and infants	Young children / preschool	Primary school	Secondary school	Young adults / university	Working age	Healthcare workers	Healthy elderly	Frail elderly / care homes
PeriCOVID										
PregnaCOVID 1/2										
Evaluation of COVID-19 vaccines in pregnant women										
COVID-19 Surveillance in children attending pre-school, primary and secondary schools										
sKIDsPLUS										
COVID-19 Schools survey										
COVID-19 Vaccination in KIDS										
Serology in university settings										
UNICOVID										
Serosurveillance for coronavirus PHE/NHS staff										
SIREN										
Snapshot PCR surveillance										
LonGitudinal Evaluation of COVID-19										
DASH										
LondonCOVID										
Easter Six										
Pilot Point Prevalence Survey										
VIVALDI										
COVID-19 vaccine effectiveness in closed-setting outbreaks										
ArmyCOVID										
EDSAB HOME										
Infectiousness of immunosuppressed patients										
Evaluation of large-scale population programme										
Household contacts of confirmed patients (ATACCC)										
National enhanced surveillance of vaccination programmes										
CONSENSUS										
National surveillance of possible symptomatic COVID re-infection										
M&M COVID										
COVID LIV										

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APPENDIX 1 – CLINICAL AND POPULATION STUDIES LED OR SUPPORTED BY PHE

Study title	Classification	Overview & related publications	REGG approved
Maternity, perinatal and infants			
PeriCOVID. COVID-19 infection in pregnancy and in newborn	Sero-Surveillance	This surveillance study aims to answer important questions about the impact of the novel coronavirus on pregnant women and their infants, and the mode of transmission from mother to baby.	Y
Pregna COVID	Surveillance	Universal screening of pregnant women attending the labour ward for delivery in a New York Hospital found 7 of 8 SARS-CoV-2 positive women were asymptomatic and therefore, with a potential to transmit the infection to their infant as well as maternity staff providing their care during and after delivery. In England, maternity hospitals have implemented routine SARS-CoV-2 testing for pregnant women attending labour ward for deliver. This surveillance aims to collect anonymised routine data to assess the rate of symptomatic and asymptomatic SARS-CoV-2 infection among pregnant women attending maternity units with universal screening in place Khalil A, Hill R, Wright A, Ladhani S, O'Brien P. SARS-CoV-2-Specific Antibody Detection in Healthcare Workers in a UK Maternity Hospital: Correlation With SARS-CoV-2 RT-PCR Results. Clinical Infectious Diseases. 2021 May 4;72(9):1680-1681. https://doi.org/10.1093/cid/ciaa893	Y
SARS-CoV-2 surveillance in the first trimester in pregnant women. PregnaCOVID 2	Surveillance	Public Health England is conducting surveillance of SARS-CoV-2 IgG infection in early pregnancy by testing 1200 stored booking blood (serum) samples during COVID-19 pandemic (between 1st February 2020 and 30th April 2020). Data on SARS-COV-2 IgG positivity, risk factors for infection, and outcomes of infection in pregnant women and their infants will be very useful in determining the natural history of SARS-CoV-2 IgG infection in early pregnancy. The results of this surveillance may lead to implementation of additional measures during pregnancy to monitor for potential adverse outcomes.	Y
Evaluation of COVID-19 vaccines in pregnant women receiving the extended immunisation schedule	Evaluation	Public Health England is responsible for monitoring the impact of national immunisation programmes in England, including COVID-19 vaccines. Current UK guidelines recommend that pregnant women should receive the vaccine if they are at increased risk of COVID-19 or its complications because of their age, an underlying medical condition or occupational exposure, especially those working in health and care settings. There are currently limited data on immune responses to COVID-19 vaccination in pregnant women, especially when given at the UK-recommended extended schedule of up to 12 weeks between doses rather than the 3-4 week authorised schedule. This investigation aims to assess	Y

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Study title	Classification	Overview & related publications	REGG approved
		antibody and cellular responses in pregnant women receiving a COVID-19 vaccine as part of the national immunisation programme in England.	
School-age children			
COVID-19 Surveillance in Children attending preschool, primary and secondary schools	Surveillance	Public Health England is undertaking SARS-CoV-2 surveillance in staff and children of key workers attending preschool, primary and schools across England. Very little is known about SARS-CoV-2 carriage and transmission in children and whether they develop protective antibodies even if they are asymptomatic. We need to better understand the role of children in SARs-CoV-2 transmission in educational settings. Participating staff and children will be asked to provide nose, throat and saliva swabs as well as a blood sample to test for SARS-CoV-2 and antibodies against the virus at recruitment, around 2 months and 4-6 months later. A convenience sample of at least 200 children and as many staff members will be recruited at each participating preschool/school.	Y
COVID-19 Surveillance in Secondary Schools (code: sKIDsPLUS)	Surveillance	Public Health England is undertaking SARS-CoV-2 surveillance in staff and children attending secondary schools across England. Very little is known about SARS-CoV-2 infection and transmission in children and whether they develop antibodies even if they are asymptomatic. We need to better understand the role of children in SARS-CoV-2 transmission in educational settings. Participating staff and children will be asked to provide nose swabs as well as a blood sample to test for SARS-CoV-2 and antibodies against the virus at recruitment and at the end of each term in the school year. A convenience sample of at least 225 children and about 75 staff members will be recruited at each participating secondary school.	Y
COVID-19 Schools Infection Survey	Surveillance	The COVID-19 Schools Infections Survey (SIS) is being conducted by Public Health England in partnership with the Office for National Statistics, and the London School of Hygiene and Tropical Medicine. A total of 150 primary and secondary schools will be recruited across England to monitor SARS-CoV-2 infection and transmission in educational settings. We need to find out how many school pupils and staff have already SARS-CoV-2 infection and develop antibodies against the virus and how this changes over the course of the academic year. The information we collect will help inform policies to help protect pupils and staff in educational settings.	Y
Surveillance and monitoring of Antibody kinetics, Feasibility and Effects of COVID-	Surveillance	Public Health England conducts enhanced surveillance for vaccine preventable diseases in England. In response to the current COVID-19 pandemic, the UK implemented a national COVID-19 vaccine programme, primarily targeting older adults and those with underlying medical problems. Compared to adults, children have a lower risk of COVID-19 and severe disease. They are, therefore, not prioritised for vaccination in the early vaccine deployment phase of the current COVID-19 immunisation programme. Some children with underlying medical conditions, especially those with severe	Y

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Study title	Classification	Overview & related publications	REGG approved
19 Vaccination in KIDS		neurodisabilities, have an increased risk of hospitalisation, intensive care requirement and death due to COVID-19. This group has been recommended for vaccination by the UK Joint Committee on Vaccination and Immunisation (JCVI). There are, however, limited data on the immunogenicity of COVID-19 vaccines in children, especially under the current extended schedule of up to 12 weeks between the two doses. PHE is undertaking a service evaluation of COVID-19 in high-risk children in England. Participants will provide blood samples to test immune response after the first and second dose of COVID-19 vaccine. The samples will be tested on multiple assay platforms and the findings which be used to inform national guidance.	
Universities			
SARS-CoV-2 investigations using serology in university settings and UNICOVID: A rapid university seroprevalence study to establish extent of transmission in university settings which experienced outbreaks in Sept-Nov 2020.	Cross sectional survey	Public Health England is undertaking SARS-CoV-2 investigation using serology in university settings across England. Many universities in England have experienced outbreaks and serologic evaluation to determine the student population prevalence of antibodies to the virus in these universities will provide valuable information on the extent of transmission within these settings and the risk of future outbreaks and have implications for future outbreak management. Participating students will be asked to provide a blood sample to test for antibodies against the virus. A convenience sample of at approximately 1000 students will be recruited at each participating university. Mensah AA, Sinnathamby M, Zaidi A, Coughlan L, Simmons R, Ismail SA et al. SARS-CoV-2 infections in children following the full re-opening of schools and the impact of national lockdown: Prospective, national observational cohort surveillance, July-December 2020, England. Journal of Infection. 2021 Apr;82(4):67-74. https://doi.org/10.1016/j.jinf.2021.02.022 Ladhani S, Baawuah F, Beckmann J, Okike IO, Ahmad S, Garstang J et al. SARS-CoV-2 infection and transmission in primary schools in England in June–December, 2020 (sKIDs): an active, prospective surveillance study. The Lancet Child and Adolescent Health. 2021 Jun;5(6):417-427. https://doi.org/10.1016/S2352-4642(21)00061-4 Ismail SA, Saliba V, Lopez Bernal J, Ramsay M, Ladhani S. SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in	Y

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Study title	Classification	Overview & related publications	REGG approved
		England. The Lancet Infectious Diseases. 2021 Mar;21(3):344-353. https://doi.org/10.1016/S1473-3099(20)30882-3 Vusirikala A, Whitaker H, Jones S, Tessier E, Borrow R, Linley E et al. Seroprevalence of SARS-CoV-2 antibodies in university students: Cross-sectional study, December 2020, England. Journal of Infection. 2021. https://doi.org/10.1016/j.jinf.2021.04.028	
Healthcare workers			
Serosurveillance for coronavirus among PHE and NHS staff	Sero-Surveillance	Seroprevalence study requesting participants at PHE and NHS sites at Colindale, Porton and Manchester to provide a monthly blood sample for six months to test for coronavirus antibodies.	Y
Impact of detectable anti-SARS-COV2 on the subsequent incidence of COVID-19 in healthcare workers. SIREN	Surveillance 18 months	In this study, we will recruit healthcare workers to be followed for at least a year and study their immune response to the virus causing COVID-19, called SARS CoV2. We will do this by collecting data on their history of COVID-19 infection and any new symptoms. All NHS staff who deliver care to patients are being asked to have a nose and throat swab every other week in order to detect mild cases or cases who do not have symptoms. This is the main test that is currently used to detect and diagnose infection. It looks directly for the virus in the nose and throat. Once the infection is cleared, we cannot detect virus in samples. Therefore, we will also ask these individuals to have blood samples taken every other week to determine whether they have antibodies to the infection. The aim of this study is to find out whether healthcare workers who have evidence of prior COVID-19, detected by positive antibody tests, compared to those who do not have evidence of infection (negative antibody tests) are protected from future episodes of infection. In the past year SIREN has carried out 519,465 PCR tests, 249,402 blood tests, with 44,549 participants across 135 sites. Participants are tested every 2-4 weeks using both PCR and antibody tests. Lumley SF, O'Donnell D, Stoesser NE, Matthews PC, Howarth A, Hatch SB et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. New England Journal of Medicine. 2021 Feb 11;384(6):533-540. https://doi.org/10.1056/NEJMoa2034545	Y

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Study title	Classification	Overview & related publications	REGG approved
		SIREN Study Group, Hall VJ, Foulkes S, Saei A, Andrews N, Oguti B et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. The Lancet. 2021 May 8;397(10286):1725-1735. https://doi.org/10.1016/S0140-6736(21)00790-X Shrotri M, Harris RJ, Rodger A, Planche T, Sanderson F, Mahungu T et al. Persistence of SARS-CoV-2 N-antibody response in healthcare workers, London, UK. Emerging Infectious Diseases. 2021 Apr;27(4):1155-1158. https://doi.org/10.3201/eid2704.204554 SIREN Study Group, Hall VJ, Foulkes S, Atti A, Monk EJM, Simmons R et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). The Lancet. 2021 Apr 17;397(10283):1459-1469. https://doi.org/10.1016/S0140-6736(21)00675-9	
Snapshot PCR Surveillance for SARS-CoV-2 in Hospital Staff.	Surveillance	A study to ascertain the proportion of NHS healthcare workers at work in whom SARS-COV-2, the virus that causes COVID-19 illness, can be detected by Polymerase Chain Reaction (PCR) (whether asymptomatic, pauci-symptomatic, or having completed self-isolation following an infection episode). This will be conducted across a purposive selection of NHS Acute Trusts. Participants will complete a health questionnaire and give a one-off, combined nose and throat swab which will be tested by PCR in PHE laboratories. PHE will undertake a descriptive analysis of the results.	Y
LOnGItudinal Evaluation of COVID-19: Symptoms, Virology & Immunity	Surveillance	Public Health England working with the University of Bristol and University Hospitals NHS Foundation Trust to evaluate the transmission of SARS-CoV-19 transmission among frontline healthcare staff working in the Emergency Department in Bristol. Around 150 participants will be recruited and ask to complete a daily symptom diary for 12 weeks, provide twice weekly viral swabs for 12 weeks and six blood samples over 12 months. The results of this evaluation will help provide an evidence base for guidelines to protect frontline healthcare staff and the patients attending the Emergency Department	Y
DASH COVID - Preliminary characterisation of the Development of the Antibody response and virus	Surveillance	This study is designed to obtain more information about the relationship between virus shedding and seroconversion and to determine if antibody level, measured using a serology assay, correlates with virus neutralising activity, suggesting the patient may be protected against infection. It will provide essential data to inform public health advice about how to act on the results of serology testing when it is rolled out more widely and in particular, whether antibody positive healthcare workers are likely to be protected from reinfection.	Y

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Shedding after SARS-CoV-2 infection			
LondonCOVID COVID 19 infection in NHS healthcare staff in a clinical setting.	Seroincidence	A seroincidence survey of NHS healthcare staff working in a clinical setting in participating London hospitals. This involves taking a blood sample from participants every two weeks for 6 months to monitor how rapidly SARS-CoV-2 is transmitted among NHS staff working on the frontline. This study closed on 3/6/20 and participants transferred to the SIREN study.	Y
Social care (care homes, domiciliary care)			
EASTER 6: Outbreak Investigation using serology to monitor COVID-19 in care home residents and staff	Surveillance	Six London care homes with COVID-19 outbreaks were investigated during the Easter weekend (EASTER6) and found high rates of infection with SARS-CoV-2 were found in residents and staff members. Many did not have any symptoms at the time. The investigation will be continued through the measurement of antibodies against SARS-CoV-2 in residents and staff at the six care homes around one month after initial investigation Jeffery-Smith A, Iyanger N, Williams SV, Chow JY, Aiano F, Hoschler K et al. Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020. Eurosurveillance. 2021 Feb 4;26(5). 2100092. https://doi.org/10.2807/1560-7917.ES.2021.26.5.2100092 Tang S, Sanchez Perez M, Saavedra-Campos M, Paranthaman K, Myers R, Fok J et al. Mass testing after a single suspected or confirmed case of COVID-19 in London care homes, April-May 2020: implications for policy and practice. Age and Ageing. 2021 May 5;50(3):649-656. https://doi.org/10.1093/ageing/afab054 Rowland TAJ, Whitaker H, Jeffery-Smith A, Lang N, Sendall K, McLaren R et al. Seropositivity and risk factors for SARS-CoV-2 infection in staff working in care homes during the COVID-19 pandemic. Journal of Infection. 2021 Apr;82(4):84-123. https://doi.org/10.1016/j.jinf.2020.10.035	Y

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Study title	Classification	Overview & related publications	REGG approved
		Ladhani S, Jeffery-Smith A, Patel M, Janarthanan R, Fok J, Crawley-Boevey E et al. High prevalence of SARS-CoV-2 antibodies in care homes affected by COVID-19: Prospective cohort study, England. EClinicalMedicine. 2020 Nov;28. 100597. https://doi.org/10.1016/j.eclinm.2020.100597 The London Care Home Investigation Team. Increased risk of SARS-CoV-2 infection in staff working across different care homes: enhanced CoVID-19 outbreak investigations in London care Homes. Journal of Infection. 2020 Oct;81(4):621-624. https://doi.org/10.1016/j.jinf.2020.07.027 Ladhani S, Chow JY, Janarthanan R, Fok J, Crawley-Boevey E, Vusirikala A et al. Investigation of SARS-CoV-2 outbreaks in six care homes in London, April 2020. EClinicalMedicine. 2020 Sep;26. 100533. https://doi.org/10.1016/j.eclinm.2020.100533	
Pilot Point Prevalence Survey of COVID-19 among Domiciliary Care Staff in England	Surveillance	The aim of this study is to estimate the prevalence of COVID-19 infection among domiciliary care workers. The latest surveillance information in the England has estimated prevalence of COVID-19 in the general population to be 0.25%. 1 There is evidence that some occupational groups have a higher risk of exposure and therefore of acquiring COVID-19. Health and social care staff are thought to be at risk of exposure due to the nature of their work where they work closely with individuals to provide personal or health care. A recent study of health care workers in acute trusts in England estimated prevalence among front line health care workers to be 2.0%.2 A study of 250 care staff working in six of care homes with known outbreaks of COVID-19 in London found that 20.4% were SARS-CoV-2 positive. Despite these recent studies, to date there have been no studies of the prevalence of COVID-19 infection or risks of transmission in domiciliary care staff in England. This pilot study will provide the first estimate of the prevalence of COVID-19 infections among domiciliary care. It will inform testing strategies for domiciliary care staff and measures to reduce the risk of transmission of COVID-19.	Y
VIVALDI (UCL led; PHE collaborating)	Ends December 2021 (18 Months)	The aim of the study is to find out how many care home staff and residents have been infected with COVID-19, to inform decisions around the best approach to COVID-19 testing in the future. By testing around 6500 staff and 5000 residents across >100 care homes in England, we will estimate the proportion who have been infected with COVID-19 in the past and have antibodies, and the proportion who are infected now. These tests will be repeated over time to learn how COVID-19 spreads in care homes and how long the antibody response lasts and whether this helps to prevent re-infection with the virus.	

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Study title	Classification	Overview & related publications	REGG approved
		Krutikov M, Palmer T, Donaldson A, Lorencatto F, Forbes G, Copas A et al. Study Protocol: Understanding SARS-Cov-2 infection, immunity and its duration in care home residents and staff in England (VIVALDI). Wellcome Open Research. 2021;5. 232. https://doi.org/10.12688/wellcomeopenres.16193.2 https://www.gov.uk/government/publications/vivaldi-2-coronavirus-covid-19-care-homes-study-report/vivaldi-2-covid-19-care-homes-study-report	
Determining COVID-19 Vaccine Effectiveness in closed-setting outbreaks	Public health outbreak investigation	During the COVID-19 pandemic, outbreaks are occurring in closed settings such as care homes where residents and staff are currently being vaccine against SARS-CoV-2. Outbreaks in closed settings provide an important opportunity to assess vaccine effectiveness, by comparing COVID-19 rates in vaccinated and unvaccinated individuals who are likely to have high exposure rates within the closed setting. This investigation aims to provide public health specialists with information evaluating vaccine effectiveness in closed settings experiencing a COVID-19 outbreak.	Y
Other frontline workers			
ArmyCOVID. COVID-19 surveillance among army personnel	Sero-Surveillance	In March 2020, a case of COVID-19 was confirmed in a soldier at the Household Cavalry Mounted Regiment in London where around 300 soldiers, their family and civilians reside, resulting in self isolation of 29 close contacts. To understand the transmission dynamics of SARS-CoV-2, PHE is working with the Household Cavalry Mounted Regiment to conduct surveillance of staff and residents within the barracks.	Y
EDSAB - Evaluating Detection of SARS-CoV-2: AntiBodies at HOME study		The EDSAB-HOME study is a study aiming to evaluate the detection of SARS-CoV-2 antibodies using home testing kits detecting antibodies against the SARS-CoV-2 virus. These kits are called lateral flow immunoassays, appear similar to a pregnancy test kit, and analyse a small amount of blood obtained from a finger prick. The study is being run by Public Health England at the request of the Department of Health and Social Care. https://www.gov.uk/government/publications/evaluating-detection-of-sars-cov-2-antibodies-at-home-study Mulchandani R, Taylor-Philips S, Jones HE, Ades AE, Borrow R, Linley E et al. Association between self-reported signs and symptoms and SARS-CoV-2 antibody detection in UK key workers. Journal of Infection. 2021 May;82(5):151-161. https://doi.org/10.1016/j.jinf.2021.03.019	
Immunosuppressed individuals			

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Study title	Classification	Overview & related publications	REGG approved
Infectiousness of immunosuppressed patients with persistently detectable SARS-CoV-2 RNA **General population**	Service evaluation / Research	Patients with COVID-19 may be infectious to others. However, particular characteristics, such as increasing time since symptom onset, decreasing viral load and detection of antibodies, are linked to lower likelihood of infectiousness. These findings were obtained from patients with healthy immune systems. However, PHE is receiving increasing reports of patients with weakened immune systems, such as bone marrow transplant recipients, who have prolonged shedding of viral material. We will analyse samples from these patients, collected as part of routine care, to define their infectiousness. Results will directly inform patient care and national guidance on how to prevent spread of infection.	Y
Evaluation of SARS-CoV-2 large scale population testing programme	Service delivery assessment	the UK Government is currently planning two major initiatives under Workstream 3 (WS3) to detect antibodies against SARS-CoV-2, which, subject to confirmation of assay performance, will be made available to key workers and to the general public. The aim of the mass testing programme(s) will be to provide information to individuals on whether they have been previously exposed to the virus. The implementation of the programme is being led by the Department of Health and Social Care (DHSC), with PHE contribution on assay performance and the prioritisation of populations who might benefit from the POC test; currently the top priority group for testing comprises key workers. PHE, in collaboration with the HPRU in Behavioural Science and Evaluation, aims to lead on the rapid evaluation of the POC kits used in this programme, through evaluating the POC kits' performance in detecting anti-SARS-CoV-2 antibody. In addition, it will explore the acceptability and feasibility of the programme.	Y
Protocol and costings for the follow-up of house hold contacts of confirmed cases of 2019-nCov	Surveillance Protocol produced by WHO	WHO structured follow up of household contacts of the early cases of 2019nCov to provide key epidemiological and virological information relevant to understanding the spread and morbidity associated with 2019-nCov infection.	Y

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Study title	Classification	Overview & related publications	REGG approved
National Enhanced Surveillance of Vaccination Programmes targeting COVID-19 Disease in England	Surveillance	Vaccination against COVID-19 has been introduced in the UK. Clinical trials are undertaken by vaccine manufacturers before vaccines are approved for use to estimate the safety and efficacy of vaccines. These provide evidence of common early adverse reactions and how well the vaccine works in the trial participants for a particular endpoint such as symptomatic COVID-19 infection. "Real-world" post-marketing surveillance is required to monitor delivery of the vaccination programme and evaluate vaccine effectiveness on other end points such as asymptomatic infection, hospitalisation and onward transmission, and in specific population groups. As part of enhanced surveillance, a random sample of individuals identified from testing data for COVID-19 will be contacted by telephone and asked to complete a questionnaire on symptoms, vaccination status and outcomes, and provide additional laboratory samples to confirm infection and antibody status. This complements data sourced from routine electronic health records in order to improve the quality of data available from routine sources and provide robust estimates of vaccine effectiveness. For any vaccine, some individuals may develop a disease despite having received a vaccination previously (vaccine failures). In a national vaccination programme, it is important to monitor if this particularly affects a certain section of the population and whether these infections are different to normal infections (e.g. of differing duration, infectiousness or having particular viral genotypes), which may inform understanding of the impact of vaccination on transmission. Monitoring of vaccine failures also allows continued surveillance for any vaccine-mediated enhanced disease.	Y
Evaluation of the immune response following COVID-19 vaccines used in the National Immunisation Programme: CONSENSUS	Prospective Cohort Survey – 24 months	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 are compared with individuals who have received the authorised schedule for Pfizer BioNTech vaccine (2 doses administered 21 days apart. Findings regularly reported to JCVI. Public Health England carries out enhanced surveillance for several vaccine preventable diseases that are part of the immunisation programme for epidemiological surveillance and to understand vaccine efficacy. In order to understand the antibody and T cell kinetics following vaccination, a longitudinal study is being performed on vaccinated individuals. This has been prompted by the recent change in advice to extend the two dose schedule from 3 to 12 weeks apart. Whilst this would not be expected to reduce long term protection it is critical that we undertake such a robust study to verify this and to inform future vaccine policy. Participants will be asked to provide a blood samples to test response following vaccination. Samples will be collected at fixed intervals from participants receiving either the	Y

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		AZ or the Pfizer/BioNTech vaccine with participants recruited across different age bands prioritising those aged 60 years and above. A control group of participants receiving the approved schedule for the Pfizer/ BioNTech vaccine will be recruited with samples collected at 2 weeks post second dose for comparison. The samples will be tested on multiple assays and this information will additionally support the ongoing sero-surveillance activities at PHE. Sathyavani Subbarao 1, Lenesha A Warrener 2, Katja Hoschler 2, Keith R Perry 2, Justin Shute 2, Heather Whitaker 3, Michelle O'Brien 4, Frances Baawuah 4 1, Paul Moss 5, Helen Parry 5, Shamez N Ladhani 6 1, Mary E Ramsay 1, Kevin E Brown 1, Gayatri Amirthalingam 1 Robust antibody responses in 70-80-year-olds 3 weeks after the first or second doses of Pfizer/BioNTech COVID-19 vaccine, United Kingdom, January to February 2021 Euro Surveill . 2021 Mar;26(12):2100329. doi: 10.2807/1560-7917.ES.2021.26.12.2100329. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.12.2100329 Zuo J, Dowell AC, Pearce H, Verma K, Long HM, Begum J et al. Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection. Nature Immunology. 2021 May;22(5):620-626. https://doi.org/10.1038/s41590-021-00902-8 Zuo J, Dowell AC, Pearce H, Verma K, Long HM, Begum J et al. Author Correction: Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection (Nature Immunology, (2021), 22, 5, (620-626), 10.1038/s41590-021-00902-8). Nature Immunology. 2021. https://doi.org/10.1038/s41590-021-00957-7 Harris RJ, Whitaker H, Andrews N, Aiano F, Amin-Chowdhury Z, Flood J et al. Serological surveillance of SARS-CoV-2: Six-month trends and antibody response in a cohort of public health workers. Journal of Infection. 2021 May;82(5):162-169. https://doi.org/10.1016/j.jinf.2021.03.015 Wong BLH, Ramsay M, Ladhani S. Should children be vaccinated against COVID-19 now? Archives of Disease in Childhood. 2021. https://doi.org/10.1136/archdischild-2020-321225	

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Study title	Classification	Overview & related publications	REGG approved
National surveillance of possible symptomatic COVID-19 re-infection	Surveillance	Covid-19 is a notifiable disease and all laboratories in England are therefore legally obliged to report positive results to PHE with all data on de-duplicated positive and negative results stored in a unified dataset. As part of PHE's COVID-19 surveillance, all SARS-CoV-2 testing undertaken in the hospital setting (pillar 1) and within the wider community (pillar 2) in England is included in this dataset. This surveillance will identify individuals from SGSS (2nd Generation Surveillance System) with two sequential positive samples at least 90 days apart in near real-time on a weekly basis. This was extended from initial criteria that identified a sixty-day interval between sequential positive results. Public Health England (PHE) holds permissions under section 251 of the 2006 NHS Act and Regulation 3 of the 2002 Health Service (Control of Patient Information) Regulations, to process patient information relating to this as a surveillance activity. The annual PHE Caldicott update includes this system as "ready" to be used in a pandemic situation. Under this national surveillance, COVID-19 cases tested through Pillar 1 will initially be followed up with the testing laboratory to collect clinical and laboratory data to help distinguish between persistent infection, residual RNA or a proven, probable or possible new COVID-19 episode. This will later move to passive reporting by laboratories and clinicians with a standard protocol. Cases that have been confirmed through Pillar 2 testing either at both episodes or the later episode will be contacted directly by the reinfection surveillance team using the email address used to request their test kit. Specific outcomes of interest for possible SARS-CoV-2 reinfections are similar to those identified for vaccine failures and aim to identify those with underlying immunodeficiencies and therefore other possible explanations for two positive results, even at a 90-day interval. Information on the symptoms and severity of disease at each episode will be collected. Those identified as symptomatic at each episode will be reviewed and may be invited to take part in further testing which aims to confirm reinfection through antibody profiles.	Y
Mixing & Matching of COVID-19 Vaccines (M&M-COVID)	Evaluation	Public Health England is responsible for monitoring the impact of national immunisation programmes in England, including COVID-19 vaccines. Current UK guidelines recommend that individuals receive the same COVID-19 vaccine brand for both their doses. In rare cases, however, some individuals may receive different vaccine brands if, for example, they developed significant side-effects from the first dose. There are currently no data on the immunogenicity of mixed COVID-19 schedules, especially when given at the UK-recommended extended schedule of up to 12 weeks between doses rather than the 3-4 week authorised schedule. This investigation aims to assess antibody and cellular responses in individuals receiving mixed COVID-19 schedules in order to inform national policy.	Y

Public Health England

Study title	Classification	Overview & related publications	REGG approved
COVID-LIV (led by HPRU GI)		Study addresses the transmission of SARS-CoV-2 between household members and how immunological response to the infection changes over time. Setiabudi W, Hungerford D, Subramaniam K, Vaselli NM, Shaw VE, Wilton M et al. Prospective observational study of SARS-CoV-2 infection, transmission and immunity in a cohort of households in Liverpool City Region, UK (COVID-LIV): A study protocol. BMJ Open. 2021 Mar 17;11(3). e048317. https://doi.org/10.1136/bmjopen-2020-048317	
ATTAC (HPRU/Imperial), with some follow up (reactivated study)			
Reinfection post-COVID infection – routine surveillance monitoring		Monitoring the number of cases of reinfection based on reporting through SGSS, antibody status and serological assessment. https://www.gov.uk/government/news/new-national-surveillance-of-possible-covid-19-reinfection-published-by-phe	

Public Health England

APPENDIX 2 – PRE-CLINICAL STUDIES LED OR SUPPORTED BY PHE

- NISEC sponsored studies including heterologous vaccination, Booster studies, vaccination of susceptible groups including pregnant women and at-risk patients
- Support pre-clinical and clinical trial studies (including externally sponsored) through assessment of vaccine efficacy and immune response
    - Oxford COVID Vaccine Trial Group. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. The Lancet. 2021 Mar 6;397(10277):881-891. https://doi.org/10.1016/S0140-6736(21)00432-3
    - the Oxford COVID Vaccine Trial Group. T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial. Nature Medicine. 2021 Feb;27(2):270-+. https://doi.org/10.1038/s41591-020-01194-5
- Perform risk assessment of Variants of Concern on vaccine efficacy and immunity through natural infection
- Support to UKRI funded studies on healthcare workers such as DIRECT study and COVIDsortium, PANTHER
- Surge and resilience support for serology testing to NHSBT, NIBTS and WBS.

APPENDIX 3 – FUNDED PROJECTS DATA EXTRACT FROM UKCDR PROJECT TRACKER (KEYWORDS: IMMUN*, LONGITUDINAL)

Funded Projects Immunity Global