



By email only

National Core Studies

28 October 2020

Dear all,

I am writing to inform you of the commencement of the **National Core Studies**, which will be crucial parts of the UK's response to the next phase of the Covid-19 pandemic.

Over the past few months, experts and key funders have identified a number of key areas where the UK must increase research scale to respond to near term strategic, policy and operational needs, and ultimately maintain resilience against Covid-19 through the winter and beyond. These are the National Core Studies. The aim is not to try to answer every question or to cover all the research needed and supported in the usual way through UKRI, NIHR, Wellcome Trust and others. The aim is to make sure we have the key information we need now and for the next few months to help guide policy and operational matters.

- **Epidemiology and Surveillance** led by Professor Ian Diamond (ONS). *Collecting and analysing data to inform appropriate levels of restrictions and protection against imminent outbreaks (the existing ONS study expanded).*
- **Clinical Trials Infrastructure** led by Professor Patrick Chinnery (MRC) and Divya Chadha Manek (Vaccines Task Force/NIHR). *Building on established NIHR infrastructure (and equivalent in DAs) to accelerate delivery of large scale Covid-19 trials for drugs and vaccines.*
- **Transmission and Environment** led by Professor Andrew Curran (HSE) *Understanding and mitigating transmission of the disease in workplace, transport and public places.*
- **Immunity** led by Professor Paul Moss (University of Birmingham) *Understanding immunity against Covid-19 to inform back-to-work policies.*
- **Longitudinal Health** led by Nish Chaturvedi (UCL) *Understanding the impact of Covid-19 on long term health to inform the design of mitigating policies (this is about bringing together information from existing studies and cohorts).*
- **Data and Connectivity** led by Professor Andrew Morris (HDR UK in partnership with ONS) *Making UK-wide health and administrative data available for linkage and accessible to catalyse Covid-19 research.*

This will be a truly four-nation endeavour. First, in study design: representatives from Scotland, Wales, England and Northern Ireland are members of the National Core Studies Oversight Committee (Annex 2), which ensures the programmes of work are scoped, shaped and delivered in a UK-wide manner. Second, in inputs: our vision is for data from across the UK to feed into the studies. Third, in outputs: the insights generated in the National Core Studies will feed into policy making and operational decisions in all relevant parts of government across the United Kingdom.

For the National Core Studies to achieve their full potential, we will need to continue the collaborative approach we have taken since the pandemic began. In this respect, your endorsement and support of the National Core Studies as it gathers pace would be greatly appreciated.

Yours sincerely,

A handwritten signature in blue ink, appearing to read 'P. Vallance', with a horizontal line extending to the right.

Patrick Vallance

Annex 1: Study details

1. Surveillance

These studies are vital to inform the safe level of restrictions and operation of the economy, inform the need for rapid local interventions, get a better understanding of transmission risks and minimise these to enable the spread to be controlled and reduced while increasing economic activity. Information on surveillance studies in detail, including protocol and data summaries can be found at this link: <https://www.gov.uk/government/publications/covid-19-surveillance/covid-19-surveillance>

Outputs over next 6 months include but are not limited to with updates provided here (<https://www.gov.uk/government/publications/covid-19-surveillance/covid-19-surveillance>):

- Establish a study in schools and provide answers on role of schools in transmission of Covid-19 during Autumn term. with regular results informing this crucial issue.
- Finalise and publish research on antibody titre levels with UK Biobank.
- Continue publishing weekly ONS COVID Infection Survey statistical bulletins.

2. Clinical Trials Infrastructure

This study aims to enhance existing infrastructure to help deliver clinical trials at the right scale. This aims to help achieve robust results (e.g. large enough sample size, etc) and return results in a faster timeframe.

The infrastructure will help support a platform for studies to determine which existing and novel therapeutics are effective against Covid-19.

3. Transmission and Environment

This will build on existing knowledge to address key questions about transmission of Covid-19 in the environment. For example:

- How is the virus transmitted?
- Do certain work environments cause a greater risk of infection? (as seen in meat packing or warehouses)
- What activities generate different levels of aerosolised particles?
- How can this be mitigated?

Outputs over the next 6 months

With the return to work these studies will yield information continually over the period, improving understanding of a 'Covid-19 secure workplace' and allowing adjustments to be made:

- Establish a multi-agency, rapid response team for environmental / patient sampling in outbreak investigation (including associated data collection protocols and Research Ethics approval) who will be deployed to the location of outbreaks in real-time in order to collect samples and environmental data.
- Develop a general data framework and a set of core analysis tools to support data acquisition/compilation, visualisation of key statistics and consistent reporting across outbreaks
- Enable information connectivity across the other themes and other data sources such as track and trace and the epidemiological/surveillance national core study.
- Enable the identification of factors that influence the transmission of the virus in specific settings.

This will inform and target policies and interventions to support the economy opening up faster.

- Pilot data collection in outbreaks from two key areas: food processing and warehousing.
- Develop and apply new approaches to understand and quantify Covid-19 transmission through different routes and evaluate strategies to control transmission with an aim to quantify “Covid-19 secure” from a combined mechanistic and epidemiological perspective. This will enable the identification of features of settings that increase risk to, or the protection of, workers.
- Understand and characterise respiratory droplet dispersal by building computational and experimental models to quantify how respiratory droplets are emitted and dispersed into the environment and the environmental contamination that results.
- Commence programmes of work to undertake ‘deep dives’ into environmental and transmission issues in key sectors of the economy including transport, education and food processing.
- Establish a ‘Face Mask Sampling’ (FMS) programme to analyse respiratory emissions of infectious virus using human subjects. Respiratory emission of virus is a process essential to airborne transmission, yet is currently very poorly understood. This programme will determine respiratory output of virus from infected individuals and, where possible, relate this directly to transmission.

This information will inform targeted policies and interventions to enable the safe resumption of further activities.

This work builds on work being undertaken by UKRI but will not overlap with any research being proposed under the UKRI agile call.

4. Immunity

This study will coordinate research programmes and infrastructure to ensure key questions on immunity are being answered, from basic understanding of the immune response, through duration and nature of immunity, to the impact of pre-existing immunity to other coronaviruses on Covid-19. It will build on results generated by previous UKRI studies but will not delve into new areas of research which falls under the UKRI agile call.

This information is required to inform specific policies related to immunity in individuals and policies that are impacted by the level and dynamics of immunity in the population.

As we enter winter the answer to these questions is vital to restrict spread of Covid-19.

It will inform policy relying on the results of specific antibody tests, and/or policies related to the likelihood of those who have previously been infected experiencing severe disease again. This risk is increased in the next 6 months.

Outputs over the next 6 months:

- What are historical infection rates in patients who have been shielding and which clinical groups will be at specific risk from Covid-19? How can we minimise and control this challenge?

Policy Outcome: DHSC. Guidance on shielding policy

- What are the features of the SARS-CoV-2 specific immune response and how does this differ in asymptomatic and severe infection? How can we use this information to improve protective immune responses in patient groups?

Policy Outcome: DHSC, UKRI. Building immunity into the power of the NCS cohorts to develop new prognostic and therapeutic opportunities for severely ill patients

- How does the magnitude, profile and duration of immunity compare within different demographic groups and does it prevent re-infection?

Policy Outcome: DHSC, UKRI. Insight into protection and potential transmission from different age groups, e.g. children and younger adults.

- Do immune responses contribute to early and late complications of SARS-CoV-2 infection, is this related to the severity of the first infection and how can this be managed optimally?

Policy Outcome: DHSC, Treasury. What will be the policy and cost implications of management of late-disease complications: 'long-Covid'

- What are the optimal cellular assays to measure immunity to Covid-19?

Policy Outcome: DHSC, Treasury: Development of reliable and effective tests to support policy of 'immune protection'.

Immunity underpins susceptibility, severity of disease and protection. These proposed studies of immunity have been designed to build around associated NCS investments (e.g. surveillance, data, transmission) to offer solutions 'at scale' that could NOT be addressed through traditional UKRI support mechanisms.

5. Longitudinal Health

This study will generate greater understanding of risk factors related to Covid-19 outcomes (e.g. from individual risk factors to wider environmental risk factors), as well as information on the burden of both short- and long-term health and wider outcomes related to Covid-19 and interventions.

This information is required to:

- better manage individual cases,
- understand and balance the impact of interventions
- stop direct Covid-19 transmission and,
- manage health impacts against unintended or negative effects of these on e.g. physical and mental health.

This will enable more targeted policy interventions that better consider overall outcomes.

Further studies will aim to examine the mechanisms under which different health outcomes are experienced and where best to target public policies.

Outputs over next 6 months:

- Establish the determinants of C-19 re-infection in the community
- Identify the short- and medium-term health (physical and mental) health impacts of those who have had C-19 infection
- Establish the impacts of NPIs on health behaviours (e.g. exercise, diet), and on health (e.g. obesity, mental distress)?

These outputs will specifically help:

- identify high risk groups that may require protective measures
- determine target interventions to avoid or diminish health effects of infection in high risk groups
- Quantify the early health risks of viral suppression measures and inform policy to mitigate these risks.

6. Data and Connectivity

The data and connectivity study sits across the other national core studies and aims to build a national health data research capability to support C-19 research questions. The study will ensure datasets are discoverable and accessible and linkages are established to answer the research questions prioritised in the other five National Core Studies.

Making data available for wider use by researchers will increase the scope of benefits beyond the specific studies above, likely leading to unexpected benefits and boosting UK research capacity more generally; and increasing return on investment for the NCS programme.

The integration of data and harmonisation of methods and standards, will also enable the rapid research and development of new interventions and technologies across the spectrum of the disease, as well as knowledge and technology transfer to other clinical and public health areas.

Outputs over the next 6 months:

- Map the initial high priority Covid-19 datasets required by the National Core Studies.
- Deliver the necessary data infrastructure and services (quality and timely data, ability to link the data and provide access to data for multiple researchers) in five Trusted Research Environments across the UK to allow the initial high priority research questions to be answered efficiently in a transparent and trustworthy way.
- Deliver a single “shop window” for the Covid-19 National Core Studies to ensure the priority datasets for Covid-19 research are findable, accessible, inter operable and reusable (FAIR) by enhancing the capability of the UK Health Data Research Innovation Gateway

The collation and linkage established between datasets is critical to bringing the core studies together and ensuring that each of them can deliver against their policy priorities.

For example, data from hospitals may not currently be linked with GP data and data about the wider community (e.g. socioeconomic data or data on housing and the built environment). Access, cleaning, linkage and use of these datasets together is needed to fully understand links between these factors and outcomes.

Annex 2: Oversight

The Study Leads will be guided by the Oversight Committee, chaired by Patrick Vallance.

- Patrick Vallance (Government Chief Scientific Advisor – Chair)
- John Bell (Oxford University – Independent Advisor)
- Jeremy Farrar (Wellcome Trust – Independent Advisor)
- Mike Ferguson (University of Dundee – Independent Advisor)
- Anne Johnson (UCL – Independent Advisor)
- Harpal Kumar (GRAIL – Independent Advisor)
- Ottoline Leyser (UKRI)
- Lynda Stuart (Gates Foundation – Independent Advisor)
- Chris Whitty (Chief Medical Officer for England)
- Rob Orford/David Crossman/Ian Young (Chief Scientists for Health, Wales, Scotland, Northern Ireland)

The Committee will ensure Study Leads' plans meet essential need and are linked to specific policy and operational needs that are best met through national Core Studies funding. It will also advise Leads on links and synergies, quality assurance, and rapid reviews of requests for new funding.

An international panel comprising Peggy Hamburg (Chair of the Board of the American Association for the Advancement of Science), Gagandeep Kang (Professor, Division of Gastrointestinal Sciences, Christian Medical College Vellore) and Gabriel Leung (Dean of Medicine, Hong Kong University) will provide further expert insight.

Annex 3: principles of participation

The National Core Studies have committed to a set of principles to enable delivery and share data in a way which builds public trust:

- Work collaboratively to actively share data to allow the scientific community to pool expertise, draw fresh insights, and increase our collective understanding.
- Ensure data is accessed through secure platforms which allow insights to be generated whilst maintaining privacy and data security.
- Demonstrate active and ongoing engagement with patients and the public in the design, development and governance of their activities, to provide assurance that these activities are in the public interest.
- Be transparent in the use of personal data and respect the privacy and confidentiality of individuals, complying with legal requirements and ethical expectations at all times.
- Make research outputs, observations, code and tools generated from the studies open-source, rapidly and freely accessible as a public good.
- Ensure all data and associated code and tools generated through the studies are Findable, Accessible, Interoperable and Reusable (FAIR).
- Demonstrate value for money by using existing UK infrastructure and research investments as far as possible and using open competitions where possible to develop new infrastructure capability.

Annex 4: Funding

1. Work can only be funded by the NCS programme if the work cannot be funded through standard peer review application systems.
2. -The vaccine component of the Clinical Trials Infrastructure and the Epidemiology and Surveillance studies are wholly funded through other means. They are involved in the programme to share resources and insights.
3. HMT has agreed to six months' initial funding to begin the programme, until the end FY 20/21.
4. This six months' funding totals £45.2m according to the following scheme:

F/Y	20/21 (£m)
Transmission & Environment	4.7
Immunity	7.2
Data & Connectivity	8.2
Clinical Trials	15.2
Longitudinal Health	9.9
Totals	45.2

5. Each study lead will be responsible for managing their agreed budget and reporting progress against stated aims to their respective Accounting Officers.
6. Funds will be drawn down on the agreement of the Accounting Officers on the Oversight Committee.
7. Funding from FY 21/22 will need to be secured through the Spending Review.