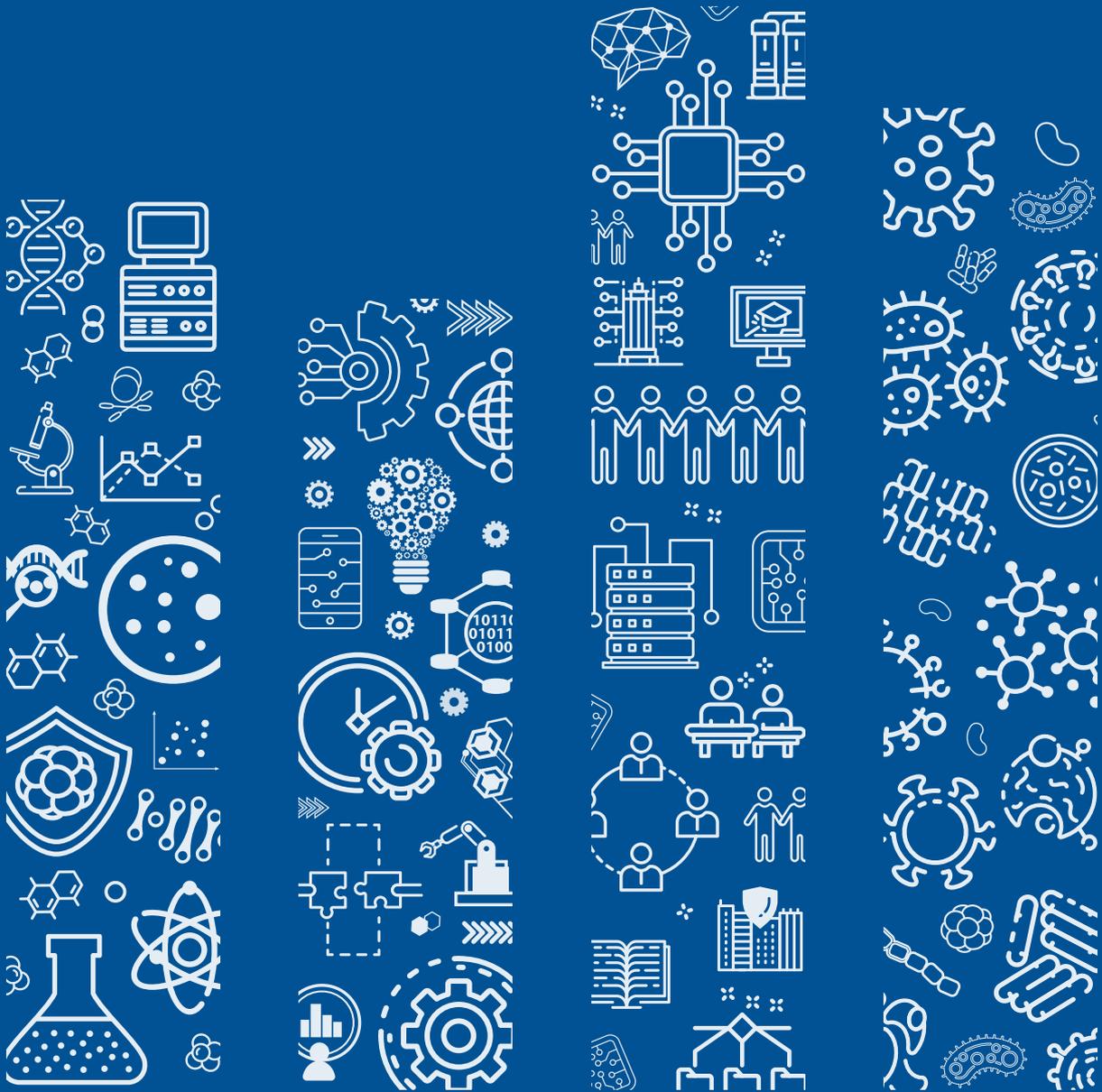




The Royal College of Pathologists

Pathology: the science behind the cure

COVID-19 testing: a national strategy



June 2020

This document was written by Professor Jo Martin, President of the Royal College of Pathologists, on behalf of the College's Trustee Board.

Organisations that support this document include:

- Academy of Medical Royal Colleges
- The Association for Clinical Biochemistry and Laboratory Medicine
- The Association of Clinical Pathologists
- British Blood Transfusion Society
- British Division of the International Academy of Pathology
- British Infection Association
- British In Vitro Diagnostics Association
- British Society for Haematology
- Institute of Biomedical Science
- Faculty of Dental Surgery of the Royal College of Surgeons of England
- The Faculty of Intensive Care Medicine
- Faculty of Occupational Health
- Faculty of Public Health
- Public Health England
- The Royal College of General Practitioners
- The Royal College of Obstetricians and Gynaecologists
- The Royal College of Paediatrics and Child Health
- The Royal College of Physicians
- The Royal College of Physicians and Surgeons of Glasgow
- The Royal College of Radiologists
- The Pathological Society of Great Britain and Ireland.

Very helpful individual support in the development of this document has been received from:

Dr Marion Wood, Dr Martin Myers and Dr Tom Lewis (NHS Improvement Pathology GIRFT team), Dr Penny Wilson (UK Research Institute), David Wells (NHS England and NHS Improvement), Professor Carrie MacEwen and Professor Helen Stokes-Lampard (Academy of Medical Royal Colleges), Ros Levenson (Academy Patient and Lay Committee).

Looking forwards: planning for the future

As the UK moves forwards from the first wave of the COVID-19 epidemic, the approach to SARS-CoV-2 testing is also moving rapidly, both for viral detection and for testing the immune and protective immune responses to it. The initial wave has impacted, but further cases are likely unless and until an effective vaccine with long-term protective efficacy becomes available and widely used.

Testing is not something that is just done and counted. It is a process with clinical purposes for individual patients, for those who care for them and for the population at large. It is a conscious and targeted use of valuable materials and skilled professionals within the context of a pathway and purpose.

This document sets out a vision for a future strategy with which clinical, scientific and policy stakeholders, including patient advocacy groups, can align. It forms the basis for a roadmap to delivery. It applies equally to all settings in which care is delivered, across all the population and all age groups.

Due to the emerging situation, the strategy for testing will be iterative. There is a lack of data and questions remain about the virus and our immune response to it. This strategy will therefore evolve as evidence emerges.

This strategy is based on a set of seven principles, which underpin four key workstreams:

- testing matched to purpose and pathways
- innovation to adoption at pace
- infrastructure and workforce for a stable future
- SARS-CoV-2 is not the only virus.

Principles of a national strategy

The following seven principles underpin any form of diagnostic assessment and must be applied to a national testing strategy.

1. **The test is the right one, at the right time, and with the correct result.** This result includes the appropriate clinical interpretation and, where not specifically designed and validated for home use, a test carried out by skilled trained laboratory professionals to recognised and accredited quality and service standards.
2. **Testing must be carried out for a purpose:** for diagnosis, for screening or for gathering data to understand the spread, or level, of disease in a population. Any testing programme must be clear as to its purpose, and the tests chosen appropriate for that purpose.
3. **Problems in testing result in problems with care.** With an infectious disease, this can have significant impact on disease spread, risk assessment, morbidity, mortality and population health. These problems arise from a range of issues including poor specimen taking, poor labelling or poor transcription of details, slow turnaround of results, poor quality control, ineffective communication of the result, inappropriate application of the result, and lack of clinical input or oversight. Many of these issues have been seen in recent times, all of which must be urgently addressed.
4. **Data connectivity is a cornerstone of testing.** It is a key aspect of improving quality, and great strides have been made in this area through the rapid connection of labs via NPex across much of the UK. Consistent test coding will aid this, and should be rolled out at speed. Links that connect primary and secondary care and public health bodies should be strengthened to ensure all results are available to clinicians when required, form a part of individuals' permanent health records and can be used, in an appropriate and legal framework, for public health purposes.
5. **Testing standards must be upheld.** Testing will be carried out in many settings, but must be carried out as part of a quality assured system, meeting accredited standards in regulated or approved settings. Accredited standards will apply to both laboratory and point-of-care testing. Different technologies will be used, depending on the clinical setting, clinical pathways and public health need.
6. **People being tested should be informed** about why they are being tested, and the implications and limitations of their results. They should have access to those results. Individuals should be informed if their data becomes part of a research programme and of their rights to be excluded if they so wish, within the context of public health needs.
7. **At societal level, the more people who understand about the testing being performed, the more informed their consent will be.** Information needs to be in plain language and accessible to all in a range of formats. National and international awareness is raised by media, professional bodies and programmes such as Lab Tests Online, but broader education, including in schools, has a role also. It is important that sampling is not mistaken for testing – the language used must be accurate to give the public confidence in test results.

The four pillars of the testing strategy

Testing matched to purpose and pathways

Tests differ in their performance characteristics and must be chosen with the intended use in mind – for epidemiology, diagnostic use or for screening. A screening test, even with very high specificity, may still have poor positive predictive value in a low-risk population, with detrimental consequences for people testing falsely positive.

Virus testing

Systems with more rapid turnaround will be needed for clinical care and resource management, as patients are screened for the virus prior to operations, cancer therapies or other care, and as they come into emergency care. This will be especially important for reducing risks to vulnerable patients from staff or other patients. Agile services should be available in conjunction with local pathology services and require a ramp-up in the volume of technology and skilled staff to support this.

High-quality testing for SARS-CoV-2 and associated biomarkers is also likely to be key to good antimicrobial stewardship, through reduction in broad spectrum antimicrobial use. This will reduce the potential for the pandemic to drive a further wave of antimicrobial resistance.

Targeted or routine screening of specific groups will include health and social care staff and vulnerable groups, such as those attending for dialysis, transplant recipients or the immunosuppressed. This will require medium-scale testing with rapid turnaround in laboratories. Near-patient or staff testing will enable risk management and more intensive infection control for key patient pathways, such as patients undergoing surgery or cancer therapy.

Rapid turnaround viral testing, as it becomes more widely available, will also be important for certain social settings, where rapid decision making is important, for example in schools, airports and workplaces. All such testing must be quality controlled by trained and experienced laboratory professionals.

The relationship between RNA detection and infectivity needs to be better understood to be able to manage the effective management of infection control and clinical pathways.

Immune response testing

Serology will be used as a companion diagnostic alongside viral detection-based screening in many of the examples previously outlined.

Serology will identify those who have been infected by SARS-CoV-2 and will be used to help understand whether the presence of antibodies translates into protection, and if so, for how long, as part of longitudinal data gathering. The relationship between the presence of antibodies to various viral antigens and immunity is still to be clarified.

Large-scale population serology testing data, with the use of phlebotomy methods less dependent on venous blood samples, as they are developed, will assist in national decision making.

Antibody assays will be helpful in specific clinical settings, such as where a patient has been ill for some time with a COVID-19-type illness, but has no detectable viral RNA. It is expected that refinements of assays, better understanding of comparability between assays and the discovery of other immunity markers will be important.

Cellular immunity and the interaction of cellular and humoral defences are becoming better understood, and this knowledge will feed into a national testing strategy.

Blood transfusion services are key in supporting testing, by helping to source quality assurance materials, and by providing sera for national sero-prevalence studies and convalescent plasma.

Staff testing

There is recognition that SARS-CoV-2 detection and immune response assessments will extend to many different clinical and healthcare settings.

Wider staff testing is required to understand infection prevalence and to inform infection prevention and control. This is key to controlling the spread and providing protection and reassurance to patients and staff coming into these environments. To inform planning and countermeasures, this will entail both viral and antibody testing to identify those who have, and those who had, COVID-19. At present, antibody tests should not be used as a signal of immunity, given the current state of knowledge on this subject.

It is important that gaps in knowledge are filled with sensible supportive data with accompanying guidance, to prevent unnecessary and potentially harmful untested technologies being used. Eventually, it is likely that vaccination and assessment of its outcome, in terms of the response achieved, will provide the best way forwards – as happens for many viral infections. However, lasting immune protection resulting from SARS-CoV-2 vaccination is not certain at this time.

Genome sequencing

Data will be collated for national and global monitoring, as it is for influenza, and will involve genome sequencing with sharing of data and information regarding mutations and emergence of strains, potentially with differing transmissibility or virulence. This will also inform future test and vaccine development, emergency planning and population-wide policies.

Genome sequencing at research level will also involve projects to sequence host genomes, study interactions between host and virus, and identify pathways that enhance or reduce the disease process, pinpointing particular areas for potential therapeutic intervention.

Post-mortem examination

The study of cells, tissues and organs after death is a key part of understanding the pathogenesis of disorders, including COVID-19. It allows for bio-banking and for research studies not otherwise possible, provided that appropriate consent is obtained. The Royal College of Pathologists has created an international post-mortem report submission portal to enable the systematic gathering of data that can be made available for a range of research purposes. Viral testing can be carried out after death in suspected cases, and testing should be made available for this purpose.

Innovation to adoption at pace

The pathology community has tremendous skill, expertise and experience in test development, assessment, adoption and whole-service rapid transformation for clinical benefit. This expertise crosses disciplines and is valuable in other areas of health services also. There is a wealth of expertise in service and research pathology laboratories that will need support for research at pace and scale.

Working with industry on validation and verification of new testing methods, but also in the implementation of innovation, is a key part of bringing in improvement. This should be supported by health provider organisations and universities.

Rapid implementation of new methods at scale and pace, without loss of impetus from procurement or business planning processes, has been successful in the emergency setting. A return to business as usual with slow and patchy adoption of innovation is not sensible. A happy medium between good governance and nimble adoption is ideal.

Sharing data and insights on the impact of innovation, test validation, clinical guidance and emerging evidence is important to prevent duplication and guide decision making. It is vital that government bodies and regulators seek advice from professional bodies when developing and implementing testing strategies and approaches.

Ongoing research into key clinical questions and uncertainties is essential. Public health bodies and other research organisations will be able to call for particular studies as priorities. Coordinating this activity to reduce duplication and gaps will be important. Open and timely access to data from these studies is crucial, and an iterative process for evidence summaries and dissemination will be important in this rapidly developing field.

Infrastructure and workforce for a stable future

In moving to a focused track-and-trace approach, with strengthened groups of infection prevention and control professionals and local public health teams, population groups with particular causative or associative risk factors will be identified and their household contacts will need additional testing. High incidence or outbreak settings will continue to have enhanced testing and surveillance. Current screening for the virus will be paired with antibody testing to enable more effective infection control, prevention and planning.

In the UK, the pop-up 'lighthouse' laboratories will eventually be stood down and the equipment returned to university use. As part of a return to normal, together with the increased requirement for SARS-CoV-2 PCR and serology testing, the NHS, in partnership with private-sector providers, will need to build sustainable capacity for the long term. Coordination across public health, community and NHS bodies will be essential in this planning.

Resilient supply chains will need to be secured for laboratory and near-patient equipment, personal protective equipment and consumables.

Data and laboratory systems infrastructure

National-level evidence collection through data analysis is key. Across the majority of the UK, an exemplary NHS system has been introduced at pace to link laboratories, and enormous work has been done on consistent coding in a very short period of time. Data concerning viral detection and antibody testing will be gathered, and full use should be made of this resource, together with safe havens for linking data with other clinical information. This should be extended at pace, to ensure the whole primary health record is linked to diagnostic and clinical data.

Despite this need, many laboratory information management systems are obsolete and require replacement. The impact of the loss of these key systems has been seen and has resulted in major incidents. Given the current urgency and need to use information to manage the pandemic, replacements must be expedited.

Digital transformation has the potential to mitigate some of the chronic severe workforce shortages in key specialties. No-one wants to see a return to, or exacerbation of, cancer backlogs because of histopathology workforce shortages. Digital pathology systems are part of the solution and need rapid rollout, including a national image-sharing platform to allow more rapid specialist expertise to be accessed alongside remote and networked working.

Acute workforce shortages

Workforce shortages highlighted 'pre-COVID' remain. Especially urgent workforce shortages – those with the potential to impact on the functional capacity and performance of services – relate to transfusion and histopathology. Although recruitment into histopathology has increased, there remains a 25% shortfall in staff able to report results, with some regions having even higher shortages. Much more needs to be done, particularly with regard to the rapid rollout of digital pathology and increases in scientific and medical specialist training.

Many district general hospitals have been unable to fill microbiology posts over recent years, and workforce pressures are keenly felt. The epidemic has highlighted the essential need for near-patient infection expertise. Microbiology and infection prevention and control input into primary care, including the residential care sector, is extremely patchy and requires urgent investment and support.

The skills and expertise across the virology, microbiology, infection prevention and control, molecular pathology and biochemistry communities have enabled the rapid expansion of testing to date. These skills must be preserved and expanded as a stable workforce is urgently developed for the vastly extended capacity demands going forward. Investment in the scientific and medical workforce across these specialties must happen as a matter of urgency.

Learning and development

Open and timely access to data from emerging studies will be key to keeping professionals up to speed with developments, and an iterative process for evidence summaries and dissemination will be important in such a rapidly developing field.

Professional organisations have started to deliver programmes of learning related to the virus and the testing for it, but the broad community of laboratory professionals and pathologists need to have time for learning, as do all those who are using the tests. Technology-enhanced learning is helpful, but programmes of development will also be needed to ensure competence in the performance and use of these tests.

Training programmes across all disciplines will need to incorporate learning from this epidemic, including learning from those directly involved in delivering, requesting and interpreting testing.

Learning from incidents and events related to testing will also be needed, as part of a patient safety programme. All laboratories and settings where testing is taking place must feed into national incident reporting systems, with dissemination of learning through health services and professional organisational routes.

SARS-CoV-2 is not the only virus

SARS-CoV-2 PCR viral screening will need to be integrated into routine seasonal outbreak testing alongside influenza and other respiratory viruses, as well as gastrointestinal pathogen panels for patients on admission and potentially during their stay in hospital. This may be through near-patient testing or testing in local laboratories. Both will need to be quality controlled by experienced laboratory professionals and require short turnaround times.

Improvements in the sensitivity and range of testing should also enable COVID-19 to be ruled out in appropriate clinical settings, ensuring that alternative diagnoses are sought rather than missed and enabling operational optimisation in healthcare settings. Work with diagnostic industry partners will be needed to develop these multiplexed assays at pace. Procurement pathways will also need to support this in a timely manner.

Ongoing monitoring of virus prevalence will be required, supported by improved data connectivity and simpler reporting for all surveillance purposes.

Moving forwards: cohesion and collaboration

As the UK moves to the future, any diagnostic testing developments need to be aligned to this strategy to ensure a coherent and progressive approach. Everyone with a role in planning or decision making around testing, workforce and pathology services needs to think about the implications for what they can do.

The implementation of this strategy needs to be planned and executed with the same energy and sense of urgency with which the initial response was handled.

Our pathology professionals, working with partners in industry, the health service and public health bodies, have done exceptional work and deserve immense credit for the vast amount they have achieved. Pathology training and professionalism has stood healthcare in good stead in recent times, and will do so for the future.

The Royal College of Pathologists is a professional membership organisation with more than 11,000 fellows, affiliates and trainees worldwide. We are committed to setting and maintaining professional standards and promoting excellence in the teaching and practice of pathology, for the benefit of patients.

Our members include medically and veterinary qualified pathologists and clinical scientists in 17 different specialties, including cellular pathology, clinical biochemistry, haematology, immunology, medical microbiology, veterinary pathology and virology.

The College works with pathologists at every stage of their career. We set curricula, organise training and run exams, publish clinical guidelines and best practice recommendations and provide continuing professional development. We engage a wide range of stakeholders to improve awareness and understanding of pathology and the vital role it plays in everybody's healthcare. Working with members, we run programmes to inspire the next generation to study science and join the profession.

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