

**The University of Oxford's approach to COVID-19 testing:  
Principles, current plans and future testing strategies**

Chris Conlon, FRCP

Professor of Infectious Diseases, Nuffield Department of Medicine  
Chair, Health Measures Advisory Group (HMAG), University of Oxford

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## **1. Introduction**

In August, the University launched its in-house COVID-19 testing service for all staff and students of the University and colleges. The Testing for COVID-19: Early Alert Service is underpinned by a set of principles agreed by the Health Measures Advisory Group (HMAG), a group of medical experts from the University advising its Silver Group. Having adopted a testing method that aligns with these principles, HMAG continues to monitor potential alternative tests as they become available, including additional or enhanced testing strategies, as well as the testing environment generally to assess the ongoing suitability of its approach.

This paper is intended as a high-level review of the current testing situation and sets out:

- Principles and current plans for swab testing by RT-PCR
- The testing environment generally
- The COVID-19 testing service that the University has set up
- Potential alternative tests that may become available
- Additional and enhanced testing strategies

## **2. Principles**

The HMAG adopted the following principles to help guide its proposals for a University COVID-19 testing service:

- Select a validated and regulated test to match NHS standards
- Use testing to help identify infections to reduce spread in the community
- Link results to local public health services to facilitate contact tracing
- Avoid adverse impacts on NHS resources
- Ensure testing is available for all staff and students

## **3. The current COVID-19 testing environment**

The vast majority of tests being done in the UK at present are processed in the large Lighthouse laboratories. These are essentially testing factories with many PCR machines and staff, and the swabs are sent from the various NHS testing sites around the country, like the one at Oxford Parkway. This is called Pillar 2 testing. Because of issues to do with transport of swabs, the huge numbers being tested and difficulties with some of the informatics, the turnaround time for the test results has got longer, and is now usually more than 48 hours. These laboratories are having trouble dealing with the increased testing and have already advertised for more staff. Testing is only available to those with symptoms. The system is currently under severe strain.

NHS hospitals have diagnostic laboratories that can do COVID-19 testing on patients with symptoms (Pillar 1) and are also undertaking the testing for local care homes. In many hospitals, including in Oxford, there is a programme of testing asymptomatic healthcare workers as part of large study funded by the government. This is largely because of concerns about staff becoming positive and potentially infecting patients, and about staff sickness and absence due to the need to self-isolate.

The government is piloting a variety of different tests, including saliva tests, and is evaluating new tests, such as LAMP and point of care tests. None of these have been adopted for routine testing yet. There is some optimism that the LAMP technology will work but this will take time to introduce into diagnostic laboratories, and the costs to the NHS are not clear yet.

The HMAG is monitoring developments with a view to assessing new technologies that provide better outcomes as they become available.

#### **4. Oxford University's adopted COVID-19 testing method**

The HMAG decided the most reliable existing test at present was the naso-pharyngeal swab tested by RT-PCR. Also known as a reverse transcription polymerase chain reaction test, this is considered the 'gold standard' for detecting certain viruses. This is the test being used in clinical settings and in the national testing service. It requires a well-equipped laboratory with quality assurance and standard operating protocols. Good informatics are essential to ensure any test can be accurately linked to an individual.

Testing currently takes about 6–8 hours of machine time but several more hours of delivering, logging and tracking specimens, with tests undertaken in batches. The time this takes might be reduced in the near future as new technology becomes available. Moreover, it can be done to scale if sufficient staff or robotics are available.

The University is looking at the possibility of supplementing NHS analytical capacity with an in-house COVID-19 testing laboratory (*see section 6*).

##### *a. Modifications*

This method may also be conducted via self-swabbing or supervised self-swabbing. Self-swabbing is probably as accurate in symptomatic patients (though less so for those who are asymptomatic). The advantage of supervised self-swabbing is that it ensures the test relates to a known individual.

##### *b. Accuracy*

There is a false negative rate – possibly of the order of 20%. This can occur in the following circumstances:

- Very low viral load (likely in many asymptomatic patients, who are probably not very infectious)
- Incorrect technique used for swabbing
- Laboratory error (rare)

There can be a false positive rate (which is greater with low population prevalence). Most tests have a false positive rate of at least 1%. False positives can occur in the following circumstances:

- In those who have had COVID-19, some have detectable (non-infectious) viral RNA (ribonucleic acid) for up to 6 weeks after recovery – this is also true for some who never had symptoms
- Laboratory contamination (rare but has happened)

#### **5. Oxford University's current COVID-19 testing service:**

Within the framework of available and validated tests the University has put in place a comprehensive testing service for all staff and students who display COVID-19-like symptoms. There are two testing 'pods', one at the Old Road Campus and one at the Radcliffe Observatory Quarter. The latter opened in August and the former opened on 14 September. The University is funding this service fully.

Bookings are made online; the individual gets a timed appointment and is swabbed by a healthcare worker in the pod. The swab is transported to the John Radcliffe Hospital Laboratory in a batch at the end of the session. The result (achieved by RT-PCR), if negative, is emailed to the individual. A positive result is communicated by telephone and email to the individual, but is also communicated to their college and/or department. Consent for this communication is part of the booking process. The result also triggers a call to the local public health team. In addition, the laboratory automatically notifies the National Test and Trace public health team.

Working seven days a week, the two pods have a maximum capacity to test in the region of 1000 people a week. Should this be exceeded, we can access local testing units set up by the NHS. The greatest constraint on capacity is the laboratory analytical capacity. In agreement with the Hospital Trust, University tests are being carried out in the John Radcliffe Hospital laboratories (Pillar 1), which have a faster turnaround time than the Lighthouse laboratory at Milton Keynes (Pillar 2). Speed of turnaround is crucial for effective disease control, but capacity in the John Radcliffe Hospital laboratories is limited to about 600–1000 tests a day.

## **6. University in-house laboratory COVID-19 testing facility option**

In light of potential capacity issues, and given emerging information about the possible rationing of NHS laboratory testing capacity, the University is looking at the possibility of setting up an in-house COVID-19 laboratory testing facility.

The issues limiting capacity are likely to be the acquisition of enough RNA extraction kits and PCR machines, along with consumables (gloves, gowns, masks, syringes, etc.). Because the University has limited experience in setting up laboratories of this type, it will need to find a way of resourcing (both financially and with personnel) the laboratory to run the tests.

In principle, an in-house facility would be able to carry out several thousand tests a week, although it would not be able to deliver enough tests for asymptomatic screening.

## **7. Other COVID-19 testing platforms**

There are various alternative testing platforms being developed by Oxford academics and others. The University is considering how it can help these platforms develop and make use of them in due course. These include:

### *a. DnaNudge*

This is an Imperial College spin-out company, initially set up to sell gene tests to the public to help them with food choices. The same technology has been repurposed to test for COVID-19 genes to detect infection. It uses a swab stuck into a cartridge, which goes into a benchtop machine. The result is sent to a secure DnaNudge cloud, which sends the result to the clinician via an Operator App. There is no direct readout from the machine. The process takes about 90 minutes, so is relatively quick. It processes swabs individually, so it cannot do many per day (unless you have hundreds of machines), and is not linked into an informatics system. It has been validated and there is one peer-reviewed publication in the press. The Medicines and Healthcare products Regulatory Agency (MHRA) has now approved this method and it is being used in a few London hospitals as a rapid test in certain settings (e.g. pre-op in emergency surgery).

This would be very difficult to scale up for larger testing settings so there are doubts about its suitability for surveillance testing. In terms of cost, we do not have any information currently. This technology is not available other than via national procurement processes.

### *b. LAMP tests (loop-mediated isothermal amplification)*

This is a two-step test. The RNA has to be extracted from virus in the swab, and is then put into a chamber and heated. LAMP is not a PCR-based test so does not involve multiple cycles of heating; hence it is quicker – possibly as rapid as 30 minutes – but it requires an RNA extraction process beforehand. The readout is a fluorescent signal that is either positive or negative.

The only UK commercial company promoting this is Oxford Nanopore. They claim to be able to do over 10,000 tests per day (again, it depends on how many machines are used). However, this technology has not been completely validated yet and is not MHRA-approved. Currently, our understanding is that they have not solved the informatics issues, so results cannot be linked reliably to patients.

If the informatics problems were solved, along with the RNA extraction step (and the test worked in a clinical setting), this could be scaled up.

There is also an Oxford spinout company in Engineering (OxSed Ltd) that has a LAMP test developed by Professor Cui Zhang (Oxford University). However, they have not completely evaluated the test and are some way from regulatory approval. There are also issues of how to scale the test and resolve the testing informatics. The group is developing a research protocol for HMAG to consider.

### *c. Saliva tests*

Saliva will contain COVID-19 in infected individuals, and detection is probably as good as from a nasopharyngeal swab. There are trials of saliva tests being conducted in the UK at present. Yale University has developed an in-house saliva test that they have published, but the capacity is currently small. Saliva samples can be run through the RT-PCR (reverse transcription polymerase chain reaction) platforms, but data is lacking for the other platforms. One of the problems with using saliva is that, because of its viscosity, it is difficult to handle in robotic systems. There may also be more PCR inhibitors in saliva. Nevertheless, saliva sampling is easy and less intrusive for the individual, and it dispenses with the need for a physical swab. However, NHS laboratories are not geared up to handle saliva samples at present and there do not appear to be any validated commercial test kits. Unlicensed (in the UK) tests are being used in some settings in the US.

### *d. Blood tests*

COVID-19 only appears in the blood transiently, if at all, and is probably only detectable early in sick patients. Thus, it is not a suitable substance to test.

### *e. Point of Care (POC) tests*

These were recently highlighted by the government. Lots of companies are trying to develop POC tests, and many have been evaluated by the University. They generally use what is called 'lateral flow' technology, a bit like a pregnancy test, where a saliva sample is put into a well, a liquid reagent is added and a line appears in a window indicating positive or negative. The result could be available within minutes. This sort of test is the 'holy grail' but none of the examples evaluated to date have been adequate. It seems likely that some sort of test like this will become available in the next year, but probably not before mid-2021. The cost of the test would clearly be important if it were to be widely used. POC tests cannot be linked automatically to an information system, so notification would rely on an app or website the individual could access. These tests tend to be of relatively low sensitivity but might pick up the most highly infectious individuals.

## **8. Alternative COVID-19 testing strategies**

### *a. Pooling of samples*

Theoretically, samples can be tested in pools (this is the system that Cambridge has just announced); for example, 10 swabs can be put into one sample well for testing in the laboratories. This reduces costs and increases capacity. However, there are logistical problems (for example transporting the samples), and if one or more of the swabs is positive, they all have to be re-tested to work out which individual(s) are positive and need to be notified etc. This obviously takes time and resources, slowing down the recognition of positive cases. As infection rates increase, more and more pools are likely to be positive and more individual tests will be needed to unravel the issues. In addition, there might not be sufficient original sample left to retest, so a further sample might need to be obtained. Pooled testing is also not part of the standard operating protocols in NHS laboratories because it is more labour intensive and slower (i.e. difficult to automate), and it does not fulfil their primary aim, which is to diagnose individual cases.

Pooled testing is very good for surveillance of infections or conditions that are of low prevalence, that is where the expectation of a negative test is high. They are less good for identifying individual cases, as outlined above. The informatics aspect is also complicated.

### *b. Using unregulated, unvalidated tests*

This is clearly happening in the USA and might be happening in the UK at some universities. It carries some risk, largely because a clinical decision is being made on a poor test, so somebody might be told they are infected (and must isolate) when they are not, and *vice versa*. Affecting people's lives by providing incorrect clinical advice on the basis of a bad test could be criticised. Most practising clinicians would be uncomfortable doing this and might not be insured in this setting.

Such testing could be used for screening, followed by formal approved tests for those who flag positive. This could involve initial pooled testing with the unvalidated test. However, it would rely on good informatics for the unvalidated testing so that the right people are identified for further testing by the NHS. Again, this would be a relatively slow process involving two tests. There are also issues around laboratory capacity.

### *c. Commercial providers*

There are probably no commercial providers who have significant or required experience of COVID-19 laboratory testing, so this would be unknown territory. Exeter University has announced such a partnership, although it appears it will be limited to testing symptomatic individuals and is not yet up and running. This could work, depending on the platforms and company, so long as it gave a reasonable turnaround time and had good informatics. If it were used for mass screening, it would be costly.

## **9. Mass COVID-19 testing versus symptomatic COVID testing**

There are two possible reasons for doing regular testing at scale. The first is for surveillance, in order to understand the evolution of the epidemic and to find hotspots. This is what the Office of National Statistics (ONS) is undertaking in order to inform the government.

The second reason would be to control the spread of the virus. The consensus is that to have a chance of achieving this, testing would have to be conducted at least twice a week in order to catch cases before they had transmitted the virus too widely. This is theoretically possible, but for a number of reasons, it would be logistically very difficult and uncertain. For example:

1. **Behavioural effects:** Such testing gives a snapshot of one day – a negative test might be positive tomorrow. This could be falsely reassuring and might lead to those with symptoms assuming they don't have COVID-19 and not isolating or getting retested.
2. **Logistics:** The laboratories would not have the capacity to process the swabs and, in any case, would not be permitted to do so using NHS laboratory capacity as asymptomatic screening is only authorised for healthcare workers (as part of a national research programme) and those in care homes. In addition, oversight of the results would be very difficult. Testing such large numbers might take several weeks to complete.
3. **NHS resources:** It is important to balance the need to prevent a local outbreak emanating from the University with ensuring that we do not drain resources from the NHS and the City of Oxford.
4. **Disruption:** The University would face enormous disruption through regular testing, which would see hundreds of staff and students self-isolating needlessly (in the case of false positives), or not self-isolating when they should (in the case of false negatives).
5. **Cost:** Given the limited accuracy of the tests and the major disruption this would cause to the University without commensurate benefit, the enormous cost would not be justified.

At present, therefore, the University have decided not to do mass testing on all students and staff, including at the start and end of terms. Instead, and in line with current NHS policy, we are testing all those who come forward with symptoms. However, one of the challenges the University faces is staff and students with no COVID-19 symptoms asking for tests unnecessarily. As is the current case nationally, this could lead to capacity problems; it is important to be clear that only those with symptoms should be booking a test.

## 10. Examples of other university and research institute approaches

Different universities and research institutes are approaching the problem of testing and tracking students and staff in a wide variety of ways. There is no clear best approach and each institution should be open to learning from others.

### *a. University of Cambridge*

The University of Cambridge has a single testing pod in the city for symptomatic cases and can turn around up to 50 per day. However, they have recently announced they will test all asymptomatic students in colleges. It is understood that college students living outside of colleges cannot get tests, nor can college staff or other university staff. There is a separate testing service for staff. Cambridge has one of the Lighthouse laboratories (in partnership with AstraZeneca) that processes NHS tests for the national test and trace programme. Because this is on University of Cambridge land, the university has negotiated for 300 tests per day to be processed there. They plan to pool household swabs (the students in each household in college will all put their swabs into one bottle per household), and send the pooled sample to be tested. If it comes back positive, the whole household will have to isolate and the individuals will be encouraged to get an NHS test to facilitate contact tracing. This is an interesting experiment and might reassure those student groups who test negative, but it will be a slow way to pick up positive cases. It is also subject to the Lighthouse laboratory having capacity as NHS testing increases – it may reach the stage where there is no longer capacity to carry out the asymptomatic pooled testing.

### *b. University of Exeter*

The University of Exeter has announced a partnership with a new biotech company, Halo. From the information available, it seems the company is using an unvalidated, unapproved saliva test, and Exeter is their first major client. It is thought that the tests are carried out in the Halo Laboratory in



London, but the informatics are unclear. The plan is to offer tests to symptomatic students. If a student tests positive, they will then be told to seek a Pillar 2 test (with all the consequent delays etc.). There is no direct public health link. It is also not clear how much this system costs.

*c. University of Leicester*

The University of Leicester announced that it will offer tests to all of its 17,000 students on a voluntary basis. From the information available, it appears that they will offer to test asymptomatic students – we believe using the Nanopore (to date unlicensed) LAMP test. It is currently unclear whether staff are being offered tests. Testing on this scale will be a challenge.

*d. Oxford Brookes University*

After discussions with our local public health team, a local testing unit (LTU) has been set up at Brookes University in the old restaurant at the Gypsy Lane Campus in Headington. This is open to the general public with booked slots. It is Pillar 2 testing so the results go to the individual, not to an employer or a university. There are plans to have another LTU in the city centre if a suitable site can be found. Although this enhances testing access, it is still dependent on Pillar 2 with its attendant, well-publicised problems and is not easily linked to the local public health team.

There are also plans to roll out mobile testing units (MTU) in the event of localised outbreaks in the city and county. Again, these are Pillar 2 tests, but testing capacity might be limited.

*e. The Francis Crick Institute*

This is a stand-alone research institute in London that offered testing facilities to the NHS. They have set up a laboratory to provide extra testing capacity for University College Hospital (UCH). They also test their own staff (n=800) once a week. The Crick staff do a self-swab at home and bring it to the institute, where the swab is registered on the UCH laboratory management system and processed in the Crick laboratory. Currently, this laboratory is run by volunteer scientists using the Crick's own machines. As non-COVID-19 research gets under way again, it is not certain how the system can be maintained as staff and machines might no longer be available.

## **11. Concluding remark**

The University's approach is taken with the best evidence in mind, and our knowledge and experience of COVID-19 and tests for COVID-19 are evolving all the time. HMAG will continue to evaluate and make recommendations to the University on various future options for better and wider testing.