HOUSE OF LORDS

SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

COVID-19 Rapid Summary: Testing

Many members of the public are puzzled and anxious about aspects of the COVID-19 pandemic. These short summaries of our regular meetings are a record of evidence heard from scientists with internationally recognised expertise about what is known and unknown about the developing science, and which we hope will be helpful to the public.

Background

In its second session on 9 June, the Committee heard evidence about the science behind, and role of, testing in the UK's current and future response to the pandemic. This note summarises key points made by the witnesses. The full transcripts and a recording of the sessions are available at the following links:

- Transcript of evidence session 6
- Parliament TV (from 11am)

Types of test

There are two main categories of testing that are being used during this pandemic:

1. Tests for the presence of parts of the virus, to diagnose if an individual currently has COVID-19 (**diagnostic tests**)
2. Tests to determine if an individual has been previously infected with COVID-19 (**antibody tests**)

Diagnostic tests

The gold standard diagnostic test for COVID-19 infection are reverse-transcription polymerase chain reaction (RT-PCR) tests**.** This type of test relies on collecting a very small sample of viral genetic material from the person suspected to be infected, via a nose and/or throat swab, and amplifying it in the lab to a point where it can be studied in detail. RT-PCR tests can only detect the virus while it is present in the person; it cannot tell if the person has had the virus but has since recovered.

In addition to diagnosing COVID-19 in individuals, diagnostic tests can be used to get an idea of the prevalence of the disease across the country. The Office for National Statistics is conducting a survey of infection in households in the UK, where households are randomly sampled on an ongoing basis to build up a picture of how many people are currently infected with COVID-19 across the country.

We also heard that there are hopes that a different type of diagnostic could be developed, which could produce results more quickly than RT-PCR tests. The idea is that these tests would identify some of the proteins (known as "antigens") a virus is made of. These antigen tests would use similar technology to pregnancy tests, and therefore be able to provide more rapid results.

Antibody tests
Antibody tests (sometimes referred to as serological tests) detect if a person has had the virus, and has developed antibodies to that virus as a consequence. Antibodies are proteins that are produced by the body in response to certain antigens that are unique to the virus. Most antibody tests are conducted using the same basic method: a sample of blood or serum (the fluid component of blood) is washed over a surface which holds particular antigens of the virus. If antibodies are present in the blood or serum sample, they bind to the target molecules, and the test gives a chemical reaction, such as a colour change.

Test reliability and accuracy

The reliability and accuracy of virus tests are usually discussed with reference to their sensitivity and their specificity:

- **Sensitive** means the test catches as many true cases as possible; that is, they don't return a negative result for a person who is infected (for a PCR test) or has been infected (for an antibody test)
- **Specific** means that the test returns as few false positives as possible; that is, they don't return a positive result for a person who isn't infected (for a PCR test), or hasn't been infected (for an antibody test)

RT-PCR tests are highly specific, meaning that it is rare for the tests to return false positives. The sensitivity of RT-PCR tests is lower than the specificity, meaning false negatives are more of a problem than false positives. We heard that inconsistencies in taking swabs may be a factor contributing to false negatives, particularly if not enough material if collected on the swab. In particular, it is not clear how good people are at taking swabs themselves when sent a home testing kit.

There is less certainty about the sensitivity and specificity of antibody tests. Many companies have developed antibody tests for COVID-19, but only two have been approved so far for use by the NHS in the UK. While these tests appear to be highly specific, we heard that they aren't really sensitive enough to be used to diagnose prior infection on an individual basis; that is, too many people will test negative who have in fact had the virus.

We heard that high sensitivity is less important when using antibody tests to understand the prevalence of infection across a population. Antibody tests can be particularly useful in detecting cases which were asymptomatic or where the person had very mild symptoms, and therefore is unlikely to have been tested while infected. However, it is not yet clear whether every infected person develops antibodies, and we heard there is preliminary evidence that people who have a mild infection, or are asymptomatic, may produce fewer antibodies than those who have severe illness.

Test evaluation processes
To determine the sensitivity and specificity of different types of test, they need to be evaluated. Testing samples known to be COVID-19 antibody-negative (such as blood samples taken before the virus was in circulation) gives information about specificity, while testing samples that are known to be antibody-positive gives information about sensitivity. However, we heard that it is also important to check the sensitivity of the test in samples where the virus state is unknown, such as in samples from the wider population. This is

known as clinical sensitivity, and is usually a lower value of sensitivity than is obtained from known positive samples (known as analytical sensitivity). If only the analytical sensitivity is reported, we heard it could give a false sense of the test's accuracy in the wider population.

Public Health England has evaluated a number of different antibody tests, and has so far approved two for use in the NHS in the UK. However, we heard concerns that there is not yet a common framework for evaluating and regulating antibody tests, either in the UK or in Europe more widely.

Current and future testing strategies

Test and trace

Like many countries, the UK has adopted a "test and trace" approach as it begins to ease some of the restrictions that have been in place since late March. Under this system, anyone with COVID-19 symptoms must request a test, and if it is positive, they must isolate for seven days, and their household and other close contacts must isolate for 14 days.

Test and trace approaches are particularly important when trying to contain the spread of a virus. We heard that ideally, test results should be returned on the same day, so that the infected person and their contacts can isolate, and onward transmission of the virus can be reduced. However, there are some logistical challenges to this, such as the time it takes to transport samples to dedicated testing labs across the country. We heard that increasing capacity for "in-house" testing in hospitals will help improve the turnaround time for testing. There are also "point-of-care" tests in development that could be used in hospitals and cares homes to provide rapid test results. It may be that these tests are less sensitive, but overall it might be a worthwhile trade-off for faster turnaround of results.

Who should be tested?

The current strategy in the UK is to test those who have any of the following COVID-19 symptoms: a high temperature; a new, continuous cough; or a loss or change to sense of smell or taste. However, this will only capture a proportion of new infections each day, as many people appear to be asymptomatic, or experience other symptoms. The current strategy does not include testing of any of the infected person's contacts, unless they also develop symptoms. We heard that one approach could be to test each contact at least once during the 14-day isolation period. This would allow people to stop isolating and return to work and other activities if they test negative. It would also improve the data on both the prevalence of the disease in the population, and the proportion of cases that are asymptomatic. Expanding the sample size of the Office for National Statistics infection survey will also be important for gathering information on prevalence and asymptomatic cases.

Antibody testing and immunity

There has been much discussion about the possibility of "immunity passports", where people who test positive for antibodies can be assumed to be immune and do not have to follow the same restrictions on daily life. In addition to issues around the sensitivity of these tests for individual diagnoses, we also heard there is not yet any clear evidence to suggest that the presence of antibodies means a person cannot be re-infected with COVID-19 (known as "protective immunity"). We heard that it will be important to continue to measure antibodies across the population, because if there is another wave of the virus, this

data can be used to determine the extent to which individuals with antibodies are protected.

Witnesses

- Professor Sir John Burn, Professor of Clinical Genetics, Newcastle University
- Professor Jon Deeks, Professor of Biostatistics, University of Birmingham
- Professor Andrew Hayward, Director, UCL Institute of Epidemiology and Health Care
- Professor Sheila Bird, Honorary Professor, College of Medicine and Veterinary Medicine, University of Edinburgh

Glossary

Antibodies
Antibodies are proteins produced by the immune system in response to an unknown substance encountered by the body (known as an antigen).

Coronaviruses
Coronaviruses are a type of virus that can cause respiratory and intestinal illnesses in humans and animals. There are seven known types of coronavirus that affect humans. Four are common and contribute to a third of common-cold infections globally. Three (SARS-CoV-1, MERS-CoV and SARS-CoV-2) are known to cause more severe illness and sometimes death.

COVID-19
COVID-19 is the illness causes by the SARS-CoV-2 virus, in the same way as the SARS-CoV-1 virus causes SARS (severe acute respiratory syndrome) and the MERS-CoV virus causes MERS (Middle East respiratory syndrome). COVID-19 illness tends to be milder than SARS or MERS, but the virus is more infectious.

Reproduction number
The reproduction number of a virus is the average number of people an infected person will go on to infect.

The *basic* reproduction number, R0 ("R nought"), is the average number of people infected by each single infected person at the start of a pandemic, before any interventions have taken place. If R0 is greater than one then an infection will spread exponentially. Early R0 figures in Wuhan were between 2 and 3, i.e. each infection led to two or three further infections. In the UK this would lead to 80% of the population being infected. Current estimates places R0 at between 2.5 and 3.1, which is higher than SARS or MERS.

The *effective* reproduction number, R, is used to describe the reproduction number through the course of the pandemic, in response to various interventions. The aim of many interventions is to reduce R below one, so that the spread of the virus cannot be sustained.

RNA
RNA is a type of genetic material, like DNA. Coronaviruses have RNA as their genetic

material. The genetic material of some viruses, like chickenpox and smallpox, is made of DNA

SARS-CoV-2

SARS-CoV-2 is a new type of coronavirus that was first identified in December 2019 in Wuhan, China.