



Department  
of Health &  
Social Care

# **Asymptomatic testing for SARS-CoV-2 using antigen-detecting lateral flow devices**

**Evidence from performance data October 2020 – May 2021**

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# 1. Introduction to asymptomatic testing for COVID-19

Testing of symptomatic individuals to diagnose COVID-19 supports identification and self-isolation of positive individuals<sup>1</sup>. However, approximately one in three people never develop symptoms<sup>2</sup> <sup>3</sup>. Asymptomatic testing supports finding and identifying infectious cases to reduce community transmission. Unlike symptomatic testing, testing of asymptomatic people is not to diagnose as part of clinical care - if people need medical advice about their symptoms it is important they continue to follow the relevant channels or call 999 if they feel very unwell or think there's something seriously wrong.

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<sup>1</sup> Testing of symptomatic individuals is currently performed via NHS Test and Trace drive-through and walk-in testing sites, mobile outbreak response units, home PCR testing, and within care homes.

<sup>2</sup> Beale et al. A Rapid Review of the Asymptomatic Proportion of PCR-Confirmed SARS-CoV-2 Infections in Community Setting. Pre-print published 23 May 2020. DOI:<https://doi.org/10.1101/2020.05.20.20108183>

<sup>3</sup> Public Health England: <https://publichealthmatters.blog.gov.uk/2020/12/08/lateral-flow-testing-new-rapid-tests-to-detect-covid-19/>

## 2. The role of PCR for COVID-19 testing

RT-PCR (often referred to as just ‘PCR’) is the current standard used for testing people with symptoms. Genetic material from the virus is looked for in a sample – this material is known as RNA and is similar to DNA. PCR can detect very small amounts of the material and gives an indication of how much of it is present. It does not tell you whether the genetic material has come from a ‘living’ or ‘dead’ virus and does not distinguish whether the virus is capable of infection. This is why current guidance says only to re-test within a 90-day period if, for example, new symptoms develop<sup>4</sup>.

### 2.1 PCR testing of symptomatic individuals

PCR is essential for clinical diagnosis and surveillance of people with symptoms. It is used to detect current or recent infection with SARS-CoV-2. This is so they can seek treatment necessary, and their contacts can be traced.

We know that, over the course of infection, the amount of the viral material increases substantially to a peak and then declines more slowly (as shown in Figure 1 schematic)<sup>5</sup>. It is during the first part of this increase that the highest level of live replicating, or ‘infectious’ virus, is detected. Once the level begins to reduce, non-infectious virus starts to dominate and persist. The time for which this persists can vary substantially between people with most clearing by 6 weeks<sup>6</sup>.

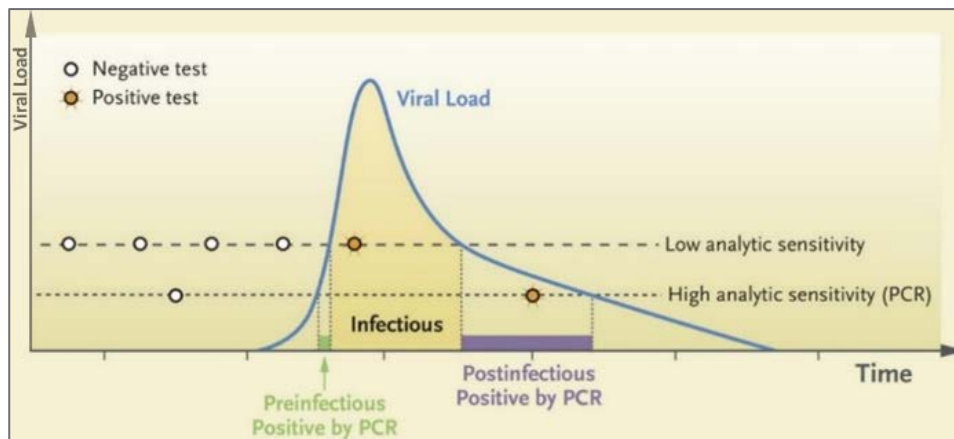
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<sup>4</sup> [Stay at home: guidance for households with possible or confirmed coronavirus \(COVID-19\) infection - GOV.UK \(www.gov.uk\)](https://www.gov.uk/guidance/stay-at-home-guidance-for-households-with-possible-or-confirmed-coronavirus-covid-19-infection)

<sup>5</sup> Mina et al. Rethinking Covid-19 Test Sensitivity — A Strategy for Containment. N Engl J Med. 2020 Nov 26;383(22):e120. DOI:10.1056/NEJMp2025631. Epub 2020 Sep 30

<sup>6</sup> PHE: Understanding cycle threshold (Ct) in SARS-CoV-2 RT-PCR: A guide for health protection teams.

Figure 1 - Adapted from Mina et al (4). Schematic representation with hypothetical test illustration. The duration of viral load ramp up and down will vary by individual and symptom status (asymptomatic and symptomatic).



Evaluation led by Public Health England and academics from the University of Oxford shows a strong relationship between higher viral loads and risk of transmission of the virus to others. While it is important for public health surveillance purposes to understand what proportion of people have any SARS-CoV-2 infection, it is most relevant to identify people with the infectious and transmissible stage of the virus. This will break the chain of infection by identifying people earlier than they would otherwise have been diagnosed, or who may never have been diagnosed at all, who could have then gone on to infect others.

While various groups are working on a direct standard to measure infectiousness, there is currently no generally accepted direct measure. To establish the relationship between how much virus an individual is *infected* with and how *infectious* they are, the study led by academics from the University of Oxford and Public Health England used non-identifiable NHS Test and Trace data on the contacts of over 700,000 confirmed SARS-CoV-2 infections<sup>7</sup>. This study took advantage of a property of the PCR test result called the 'CT value'. This is a measure of how much virus was in the individual's samples and can be mathematically converted to the concentration of virus particles present in the sample<sup>8</sup> - this is a proxy for how 'present' they are in the individual, although it can also be affected by how well the sample has been collected. This concentration is called the 'viral load'.

<sup>7</sup> Lee et al. SARS-CoV-2 infectivity by viral load, S gene variants and demographic factors and the utility of lateral flow devices to prevent transmission. Pre-print published 31 March 2021. DOI:<https://doi.org/10.1101/2021.03.31.21254687>

<sup>8</sup> In this study by Lee et al., to enable the comparison of data across PCR assays "the Qnostics SARS-CoV-2 Analytical Q Panel 01 (Qnostics, Glasgow, UK) was used to calibrate CT values from the Thermo Fisher assay into equivalent synthetic RNA viral load (VL) in copies per ml. The resulting equation for converting CT values into viral loads for the Thermo Fisher TaqPath assay was  $\log_{10}(\text{VL}) = 12.0 - 0.328 \cdot \text{Ct}$ ."

While there is no specific cut-off viral load, below which someone will definitely not be infectious, and above which they definitely will, expert advice from Public Health England and University of Oxford academics suggests the following broad cut-off points can be used:

- People with a viral load above 1,000,000 copies per millilitre<sup>9</sup>: These people are highly likely to be infectious.
- People with a viral load between 10,000 and 1,000,000 copies per millilitre: The majority of which will have little infectious virus.
- People with a viral load of less than 10,000 copies per millilitre: The majority will have negligible to zero infectious virus.

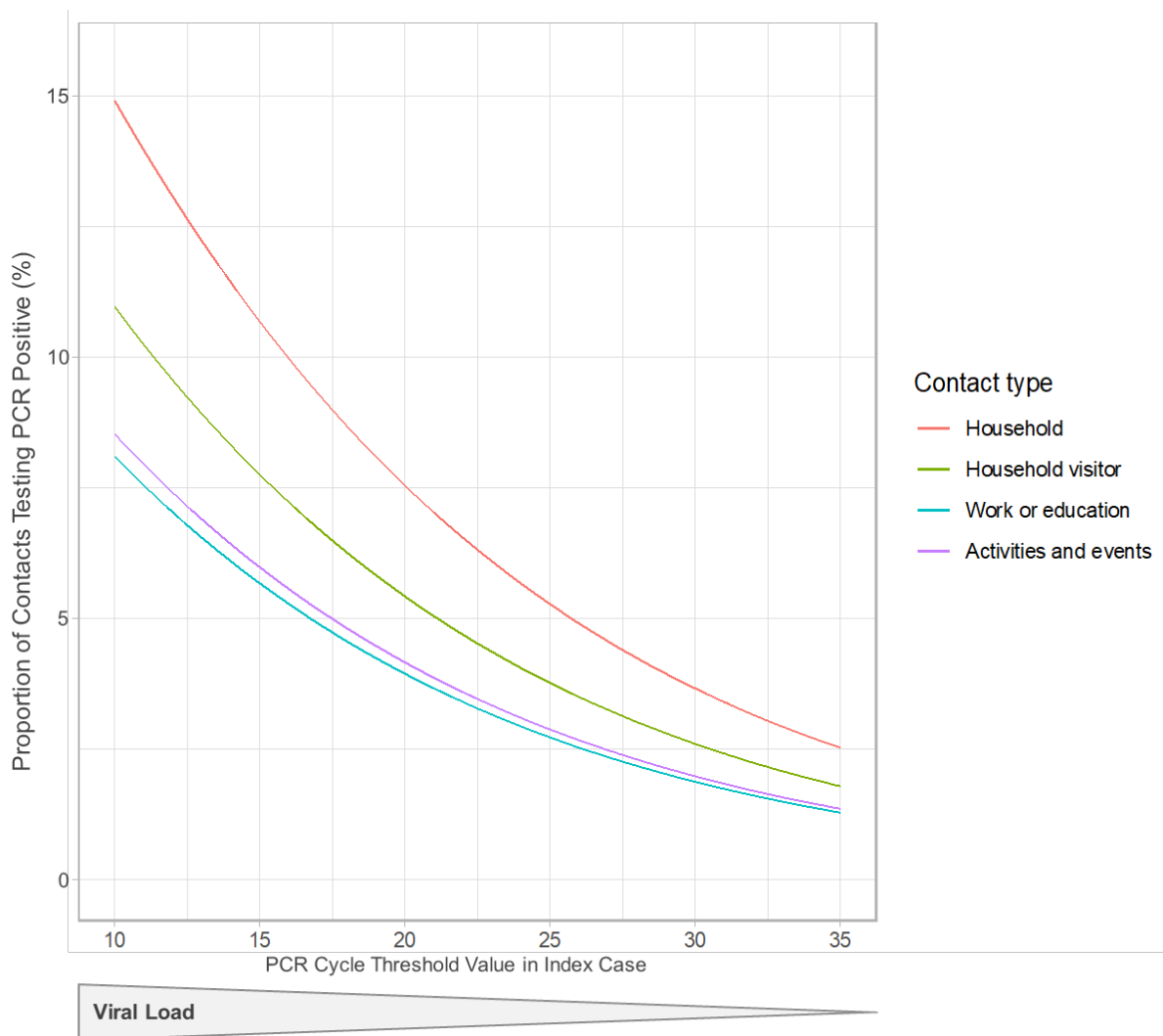
In the study data analysis, comparison was made between the number of SARS-CoV-2 positive contacts each of the 700,000 initial positive 'index cases' had (i.e. how many people they were known to have transmitted the virus to), and how this varied by the viral load of the original index case. This analysis combined NHS Test and Trace PCR results and contact tracing data between May and December 2020. Contacts were classified by the degree of closeness, specifically household members, household visitors, work/education, and other activities to take into account that different types of contacts are more or less likely to be infected because of their degree of contact with the original infected person<sup>10</sup>. Figure 2 shows that as viral load increases, the infectiousness of a person increases. As expected, this is dependent on the 'closeness' of the contact, with household contacts being most at risk.

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<sup>9</sup> The term 'copies per millilitre' refers to the number of genetic material fragments (RNA) in a millilitre of sample.

<sup>10</sup> Lee et al. An observational study of SARS-CoV-2 infectivity by viral load and demographic factors and the utility lateral flow devices to prevent transmission. Pre-print published 20 January 2021. <https://bit.ly/36fquXt>

Figure 2 - Infectivity for different index case viral loads and contact types; derived from modelling of raw experimental data



### 3. Detecting COVID-19 in asymptomatic individuals

Around one in three people with SARS-CoV-2 never develop symptoms<sup>11</sup>. Asymptomatic individuals may represent a large proportion of the infected population who are unwittingly contributing to large-scale transmission.

Asymptomatic testing at scale allows us to find more people with transmissible virus. Modelling data, such as that commissioned for the SPI-M academic group, shows that testing in a number of community settings has the potential to break the chain of transmission<sup>12 13</sup>:

- Identification of infectious asymptomatic individuals through large scale testing of high prevalence areas;
- Supporting the regular testing of groups including health care and critical workers;
- Testing within educational institutions (for example, schools, further education and higher education), factories, and businesses;
- Intermittent pre-event testing in low prevalence populations.

In order to identify asymptomatic infectious people, so they can self-isolate and interrupt viral transmission, testing needs to be delivered at a much greater scale than currently exists for symptomatic testing. Additionally, people who are tested need to be told their COVID-19 status as fast as possible to minimise unnecessary isolation and improve overall compliance. While tests undertaken in centralised laboratories can theoretically achieve this scale, the transport of samples from person to lab for processing increases the turnaround time for an individual's results.

**In general, this turnaround time and the logistics of sourcing, electronically tracking, couriering, receipting, and robotically processing the large number of samples makes laboratory-based tests impractical for asymptomatic testing at the scale required. This makes tests that do not require a laboratory attractive for mass testing. However, it is worth noting that even in a mass testing setting, PCR and other laboratory-based tests are still essential for confirmatory testing when**

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<sup>11</sup> Beale et al. A Rapid Review of the Asymptomatic Proportion of PCR-Confirmed SARS-CoV-2 Infections in Community Setting. Pre-print published 23 May 2020. DOI:<https://doi.org/10.1101/2020.05.20.20108183>

<sup>12</sup> Rapid testing strategies for traced contacts: comparing quarantine, quarantine and testing, and daily testing, 16 November 2020. Scientific Advisory Group for Emergencies.

<sup>13</sup> SPI-M: Mass testing of the whole population, 25 November 2020. Scientific Advisory Group for Emergencies.



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**required, and as a source of viral genetic material to allow genome sequencing and identification of Variants of Concern (VOC).**

## 4. Lateral flow antigen testing devices as a technology for mass testing programmes

Lateral flow antigen testing devices (LFD) are a novel testing technology that offers several advantages over lab-based tests for mass testing programmes and asymptomatic testing. They are sometimes referred to as “rapid tests”. The devices are intuitive, require minimal infrastructure and training to operate compared to laboratory-based testing – although training remains important<sup>14</sup>. This means we can offer wide-spread and repeat testing for people that would not otherwise have been tested.

**Testing asymptomatic people regularly requires a test that can identify people at the infectious stage of COVID-19, which poses a challenge in itself. There is currently no gold standard test for transmissible virus<sup>15</sup>. LFD antigen tests detect the viral antigen (a protein found on the virus). As antigens form part of the wall of the ‘replicating’ infectious virus, this antigen test provides a method for detecting infectious virus.**

Results of validation experiments performed by Public Health England and academics from the University of Oxford show these LFD antigen tests have suitable sensitivity and specificity for use within the community setting across the range of viral prevalence levels likely to exist<sup>16</sup>. The Innova SARS-CoV-2 Antigen Rapid Qualitative Test was one of the first to be piloted in the UK with a number of evaluation studies supporting the current evidence base<sup>17</sup>. The test is available in sufficient quantities to meet the scale required for asymptomatic testing and has been assessed on its ability to pick up new variants with no evidence to suggest decreased sensitivity against the Alpha, Beta and Gamma variants<sup>18</sup>.

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<sup>14</sup> Survey of participants (including university students) found that they were confident with the use of the device – 88% agreeing or strongly agreeing it was acceptable to use regularly.

<sup>15</sup> Viral genetic material is detected by RT-PCR – representing infectious and non-infectious virus.

<sup>16</sup> Peto et al. COVID-19: Rapid Antigen detection for SARS-CoV-2 by lateral flow assay: a national systematic evaluation for mass-testing. E Clinical Medicine 2021 May 30;100924.  
DOI:10.1016/j.eclinm.2021.100924

<sup>17</sup> Studies and pilots for other manufacturers are ongoing. Latest data and guidance for the assessment and procurement of coronavirus (COVID-19) test available from: [Assessment and procurement of coronavirus \(COVID-19\) tests - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/assessment-and-procurement-of-coronavirus-covid-19-tests)

<sup>18</sup> Lateral flow tests are routinely assessed on their ability to pick up new variants. The lateral flow devices (LFD) deployed nationally have been assessed against Variants of Concern (VOC) Alpha and Beta at PHE Porton Down. They include a large number of changes in the spike protein but less in the nucleocapsid protein. The antigen target of the LFDs deployed is nucleocapsid protein and they have successfully detected these variants. There is currently no evidence to suggest LFD tests have decreased sensitivity against Alpha, Beta and Gamma variants. As part of the ongoing validation programme, LFDs that reach Phase 3 of the process are tested against variants. Further information can be found on the gov.uk webpage: <https://www.gov.uk/government/publications/sars-cov-2-lateral-flow-antigen-tests-evaluation-of-voc1-and-voc2>

Following this, additional LFD antigen tests have passed through to piloting, for example Orient Gene Coronavirus Ag Rapid Test Cassette. The remainder of this document summarises the current evidence underpinning the use of LFD antigen test devices for asymptomatic COVID-19 testing – as published in the preliminary evidence report<sup>19</sup> and latest DHSC Service Evaluation Evidence Reports.

## 4.1 Considerations for determining the suitability of a COVID-19 test

DSHC considers the suitability of new COVID-19 tests such as the LFD antigen test prior to use within a variety of settings. An initial portfolio of real-world field studies is run to provide evidence that may be generally applicable across different uses. This allows limited piloting in those settings to better understand how to operationalise testing and provide evidence for regulatory bodies where new use types may be considered (for example, self-test LFD antigen devices). Further to this, based on the findings of pilots, broader roll out with ongoing evidence generation from quality assurance processes and bespoke evaluations is possible. Key factors in determining suitability are the test's accuracy (how likely is it to provide a correct result) and the overall individual clinical, public health, economic, social and well-being risks and benefits of testing compared to not testing.

The accuracy of a test is determined by:

- The **sensitivity** of a test is a measure of how good the test is at detecting true positive cases. A high sensitivity test is unlikely to return a negative result for someone who is truly positive (a 'false negative').
- The **specificity** is a measure of how good the test is at discerning true negative cases. A high specificity test is unlikely to return a positive result for someone who is truly negative (a 'false positive').
- The disease **prevalence**, which is a measure of how many positive cases there are in a population at any one given time. This interacts with a test's sensitivity and specificity to determine the absolute number of false negative and false positive returned by a test. In general, for any given test, the number of false negative results is higher when prevalence is higher. By contrast, when prevalence is lower the number

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<sup>19</sup> Preliminary report from the joint PHE Porton Down & University of Oxford SARS-CoV-2 LFD test development and validation cell: Rapid evaluation of Lateral Flow Viral Antigen detection devices (LFDs) for mass community testing. 8 November 2020. [UK evaluation\\_PHE Porton Down University of Oxford\\_final.pdf](#)

of false positives is higher, while the total number of true positive tests results will be lower, making false positives a greater share of all positive test results.

When evaluating the accuracy and suitability of a test it is important to consider what would be the real life impact of false negatives and positives *in the situation the test will be used*, and how this impact is mitigated by other aspects of the overall public health response. Both false negatives and false positives have an undesirable impact, with the former leading to false reassurance and possible risky behaviour, and the latter an avoidable period of self-isolation. No test is perfect, and the risks of a false negative should continue to be mitigated through adherence to national guidance on measures including social distancing, hand washing, and face coverings. When prevalence is low, the risks associated with false positives are mitigated by using a different test to confirm an initial positive result.

## **4.2 Lateral flow antigen device testing as a test to detect infectious asymptomatic individuals**

There is no simple way to test and detect an infected infectious individual who is likely to spread the virus over an infected individual where the virus is unlikely to spread. As described earlier, the amount of virus present (viral load) can be used to assess an individual's infectious state and their likelihood to spread the virus<sup>20</sup> – where high viral loads are more infectious than low or minimal viral loads. Although PCR tests normally give a simple positive or negative result, the test can also be used to measure this viral load. In the following real-world evaluations, the viral load of an individual was measured and used to provide an indicative link between the LFD antigen test results and the corresponding infectiousness of an individual. Using this link the proportion of people with different viral loads (and therefore infectiousness) that were correctly identified by LFD antigen tests, was measured in these real-world evaluation settings. In this context, inclusion of symptomatic based studies is relevant as it is the viral load that is assessed and the detection ability of the LFD antigen test at different viral load levels, regardless of presence or absence of symptoms *per se*. The following summary discussion of results relates to the evaluation studies outlined in Table 1 (professional user) and Table 2 (experienced and inexperienced lay users).

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<sup>20</sup> Because of differences in practice between different laboratories performing PCR tests the number of viral particles represented by a given CT value can be different between different laboratories. Therefore, it is important to convert CT values to viral loads when comparing results data from different laboratories.

**Table 1 - Summary outline of professional user evaluation studies referenced within this paper (Public Health England - Porton Down)<sup>21</sup>**

<b>Reference:</b>	<b>PHE Field Test 1</b>	<b>PHE Field Test 2</b>
LFD antigen test:	Innova	Innova
Evaluation:	Professional Use	Professional Use
Setting:	Swab: RTS Site Process: PHE PD	Swab: RTS Site Process: PHE PD
Symptom status:	Symptomatic	Symptomatic
Swabbing and LFD use scenario:	Assisted Swab - Assisted Testing	Assisted Swab - Assisted Testing
Personnel using the test:	Professional (Laboratory Scientist)	Professional (Clinical Research Nurse)
Training:	Professional	Professional
Total subjects:	199	242

**Table 2 - Summary outline of experienced and inexperienced lay user evaluation studies referenced within this paper<sup>22</sup>**

<b>Reference:</b>	<b>ATS Field Test 1 (University)</b>	<b>ATS Field Test 2 (Community)</b>	<b>RTS Field Test 1 (Assisted)</b>	<b>RTS Field Test 2 (Assisted)</b>
LFD antigen test:	Innova	Innova	Innova	Orient Gene
Evaluation:	University ATS	Community ATS (Liverpool SMART mass testing programme)	RTS Trained Staff	RTS Trained Staff
Setting:	University Pilot ATS	Community ATS	RTS Site	RTS Site
Symptom status:	Asymptomatic	Asymptomatic	Symptomatic	Symptomatic

<sup>21</sup> Innova = SARS-CoV2-Antigen Rapid Qualitative Test; Orient Gene = Coronavirus Ag Rapid Test Cassette (Swab)

<sup>22</sup> RTS = Regional Testing Site (i.e. drive-in site for people with symptoms of COVID-19); ATS = Asymptomatic Testing Site (i.e. walk-in site for people without symptoms)

<b>Reference:</b>	<b>ATS Field Test 1 (University)</b>	<b>ATS Field Test 2 (Community)</b>	<b>RTS Field Test 1 (Assisted)</b>	<b>RTS Field Test 2 (Assisted)</b>
Swabbing and LFD use scenario:	Self Swab - Assisted Testing	Self Swab - Assisted Testing	Assisted Swab - Assisted Testing	Assisted Swab - Assisted Testing
Personnel using the test:	Experience User Assisted Use	Experience User Assisted Use	Experience User Assisted Use	Experience User Assisted Use
Training:	Training Video	Training Video	Information Manual	Information Manual
Total subjects:	579	6,076	4,356	2,635

<b>Reference:</b>	<b>RTS Field Test 3 (Self Use)</b>	<b>RTS Field Test 4 (Self Use)</b>	<b>RTS Field Test 5 (Self Use)</b>
LFD antigen test:	Innova	Innova	Orient Gene
Evaluation:	Full Self Use (York)	Full Self Use (Manchester)	Full Self Use (RTS)
Setting:	York RTS	Manchester RTS	RTS (Manchester & Slough)
Symptom status:	Symptomatic	Symptomatic	Symptomatic
Swabbing and LFD use scenario:	Full Self Use	Full Self Use	Full Self Use
Personnel using the test:	Self Use	Self Use	Self Use
Training:	Instructions for Use	Instructions for Use	Instructions for Use
Total subjects:	1,619	963	1,877

The evaluations include over 1,500 LFD antigen test positive individuals from a total population of over 18,000.

In the initial two professional use evaluations (PHE Field Tests 1 and 2), individuals swabbed themselves and these samples were analysed on the LFD antigen test by highly

experienced professionals. Each participant also had a PCR test to allow their viral load to be calculated. The sensitivity of the test increased as the viral load (and chances of infectiousness) increased:

- For people with sample viral loads above 1,000,000 copies per millilitre, 96% (66/69) were detected by the LFD antigen test;
- For individuals with sample viral load between 10,000 – 1,000,000 copies per millilitre, 92% (180/195) were detected;
- For those with sample viral loads under 10,000 copies per millilitre, 43% (55/127) were detected.

Applying the observed performance of LFD to the data obtained from the NHS Test and Trace study on infectiousness, it was calculated that LFD tests would detect 83-89% of cases with PCR-positive contacts (7).

Following this, a small scale university-based evaluation (ATS Field Test 1) showed increasing likelihood of a positive result for the LFD antigen tests with higher ‘infectious’ viral load levels. Out of 571 individuals who were tested with both an LFD antigen test and PCR; 2 had a high viral load<sup>23</sup>, 4 had a low viral load<sup>24</sup>, and 11 had minimal viral load<sup>25</sup>. The LFD antigen test detected 100% of the most infectious high viral load, 50% of people with a low viral load, and 9% of those with minimal viral load.

Similar results were found in LFD quality assurance data (ATS Field Test 2), analysed as part of the preliminary evaluation of the Liverpool SMART mass testing programme. The proportion of people identified as positive by the LFD antigen test increased with viral load. A blinded reappraisal of the results including device photographs was performed by DHSC to ensure validity of the results derived from the initial onsite reading of the tests. The reappraised results rise to 100% detection for those with a high viral load, as shown in Table 3.

**Table 3 - Liverpool SMART mass testing programme (ATS Field Test 2). This shows the impact of reassessing the results based on blinded reappraisal of device photographs.**

		Onsite	Reappraised
Sensitivity (%):	High Viral Load VL > 1M RNA copies/ml	91% (10/11)	100% (11/11)

<sup>23</sup> High viral load is over 1,000,000 RNA copies per millilitre.

<sup>24</sup> Low viral load is 10,000 – 1,000,000 RNA copies per millilitre.

<sup>25</sup> Minimal viral load is less than 10,000 RNA copies per millilitre.

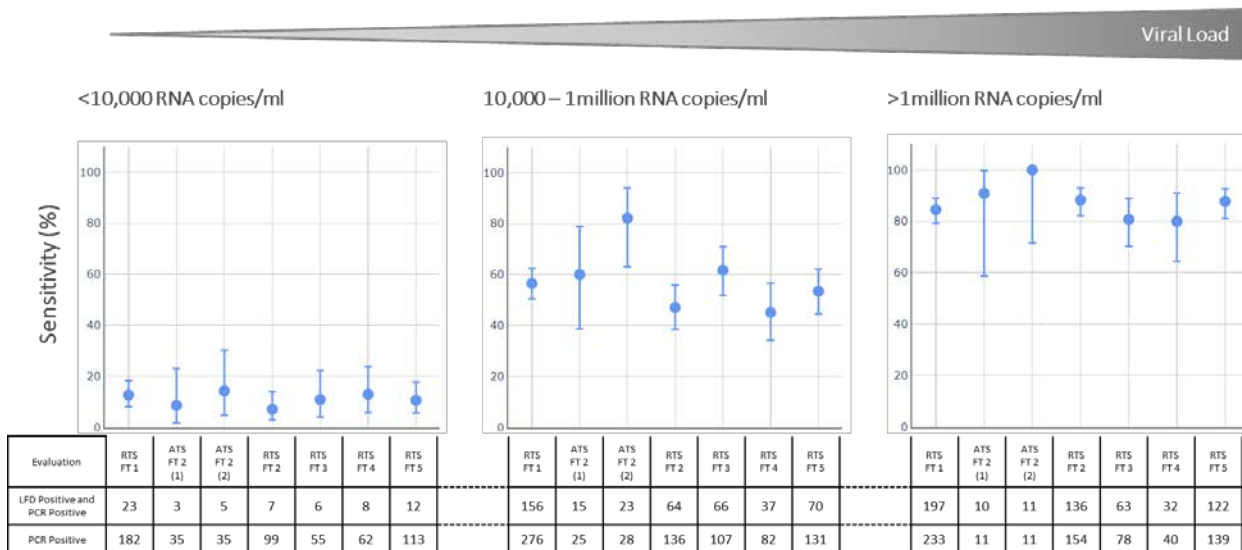
	<b>Onsite</b>	<b>Reappraised</b>
Low Viral Load VL 10,000 - 1M RNA copies/ml	60% (15/25)	82% (23/28)
Minimal Viral Load VL < 10,000 RNA copies/ml	9% (3/35)	14% (5/35)

Additionally, as detailed in Table 2, NHS Test and Trace has an ongoing programme of service evaluation run across NHS Test and Trace regional and community testing sites. The overall aim of this programme is to continually increase the quality of the testing service. These evaluations provide additional insight into the impact of experience and training of the person using the LFD antigen test on sensitivity.

Out of the further five evaluations: two evaluated LFD antigen test device performance when less experienced but trained individuals processed the test at Regional Test Sites (experienced users at an RTS) and three evaluated when the participant processed the test themselves ('full self use'). As in the other studies, participants also provided PCR tests so their viral load could be calculated. The sensitivity results for these studies, along with the Liverpool SMART mass testing programme evaluation, are shown in Figure 3 and comparison by evaluation according to viral load, split by experience level of the processing user, in Table 4.



Figure 3 - Comparison of LFD sensitivity by evaluation<sup>26</sup>



RTS FT = Regional Test Site Field Test  
 ATS FT = Asymptomatic Test Site Field Test  
 ATS FT 2 (1) = Onsite Community ATS (Liverpool SMART mass testing programme)  
 ATS FT 2 (2) = Reappraised Community ATS (Liverpool SMART mass testing programme)

Table 4 - Comparison of sensitivity by evaluation according to viral load split by experience level of the processing user<sup>27</sup>

	Evaluation	Device	Minimal viral load (VL < 10K copies/ml)	Low viral load (VL 10K-1M copies/ml)	High viral load (VL >1M copies/ml)
Experienced users	RTS Field Test 1	Innova	13%	57%	85%
	ATS Field Test 2	Innova	14%	82%	100%
	RTS Field Test 2	Orient Gene	7%	47%	88%
Inexperienced self-trained users (Self)	RTS Field Test 3	Innova	11%	62%	81%
	RTS Field	Innova	13%	45%	80%

<sup>26</sup> The circles and bars on this chart represent sensitivity estimates and 95% confidence intervals. See footnote 20 for details.

<sup>27</sup> Innova = SARS-CoV2-Antigen Rapid Qualitative Test; Orient Gene = Coronavirus Ag Rapid Test Cassette (Swab)

	Evaluation	Device	Minimal viral load (VL < 10K copies/ml)	Low viral load (VL 10K-1M copies/ml)	High viral load (VL >1M copies/ml)
Use)	Test 4				
	RTS Field Test 5	Orient Gene	11%	53%	88%

These results demonstrate (in the upward trend moving from left to right) that the LFD antigen test becomes more sensitive at viral loads that correspond to likely infectiousness. There is ongoing evaluation work to determine the duration and content of training to optimise the test performance.

The evaluation results also highlight the difficulties of interpreting an overall ‘top line’ sensitivity (i.e. proportion of all PCR-positive individuals identified as positive by a LFD antigen test), as this will be affected by mix of viral loads and therefore likely infectiousness of the individuals in the group studied. As described previously, trace RNA material can remain for weeks after infectious virus has been cleared<sup>28</sup>, so that the apparent ‘sensitivity’ of LFD antigen tests in a group of people infected weeks previously would appear to be low, when in reality these individuals are highly unlikely to be infectious<sup>29</sup>.

An independent study by Ferguson et al. at the University of Birmingham estimated a prevalence rate within the student population of 0.86%, and an LFD antigen test sensitivity of 3.2%. This was following 2 positive LFD antigen tests out of 7,185 asymptomatic university students tested<sup>30</sup>. For the study, a sample of 710 people who had tested negative with LFD antigen tests underwent confirmatory PCR analysis. Of these confirmatory tests, an additional 6 positive samples were identified by PCR.

Based on DHSC viral load analysis of the positive results, of the 2 positive samples detected by LFD antigen test, one was in the low viral load category (between 10k – 1million copies / ml) and the other had minimal viral load and so was most likely not infectious (<10k copies / ml). The additional six positive samples detected by PCR and not LFD antigen test were all in the category of minimal viral load. PCR positive students

<sup>28</sup> Cevik et al. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *Lancet Microbe* 2021; 2: e13–22. DOI:10.1016/S2666-5247(20)30172-5

<sup>29</sup> Cevik et al. Virology, transmission, and pathogenesis of SARS-CoV-2. *BMJ* 2020;371:m3862. DOI:<https://doi.org/10.1136/bmj.m3862>

<sup>30</sup> Ferguson et al. Validation testing to determine the effectiveness of lateral flow testing for asymptomatic SARS-CoV-2 detection in low prevalence settings. Pre-print published 24 December 2020. DOI:<https://doi.org/10.1101/2020.12.01.20237784>

therefore had low viral load at a time of falling COVID-19 incidence and the LFD antigen test could be described as working as expected.<sup>31</sup>

The authors of the University of Birmingham study also look at the theoretical performance of LFD antigen tests in a care home setting and conclude “the Innova LFD when compared to Pillar 2 samples [i.e. NHS Test and Trace community testing] from low-prevalence, asymptomatic population screening similar to student and care home surveillance, would successfully detect 84.56% of all infections.”

#### 4.2.1 Lateral flow antigen device testing swab type evaluation

As part of work to improve the tolerability of testing and overall access to testing, different swabbing techniques were assessed by DHSC as part of the evaluations using Orient Gene LFD antigen tests<sup>32</sup> (RTS Field Test 2). This evaluation compared standard throat-and-nose swabbing with ‘anterior nares’ swabbing (i.e. shallow swabbing at approximately 1 cm depth in both nostrils) for individuals taking part. Moving from throat-and-nose swab to anterior nares swabbing results in a reduction in test sensitivity across all viral loads, as shown in Table 5. However, in light of the likely improved tolerability from users of anterior nares swabbing, especially for a daily and/or weekly testing context, this reduction is deemed acceptable.

**Table 5 - Comparison of sensitivity by swab type for the Orient Gene LFD when used with assisted testing**

	Swab type	Device	Minimal viral load (VL < 10K copies/ml)	Low viral load (VL 10K-1M copies/ml)	High viral load (VL >1M copies/ml)
Sensitivity by viral load and swab site (%)	Throat-and-nose	Orient Gene	9%	59%	92%
	Anterior nares	Orient Gene	7%	47%	88%

<sup>31</sup> Mina et al. Clarifying the evidence on SARS-CoV-2 antigen rapid tests in public health responses to COVID-19. Comment in The Lancet 397;10283, p1425-1427. 17 April 2021. DOI:[https://doi.org/10.1016/S0140-6736\(21\)00425-6](https://doi.org/10.1016/S0140-6736(21)00425-6)

<sup>32</sup> Orient Gene = Coronavirus Ag Rapid Test Cassette (Swab)

### **4.3 Specificity of the lateral flow antigen testing devices for asymptomatic testing**

Results from evaluations carried out by Public Health England and University of Oxford estimated a high specificity of the Innova LFD antigen test of 99.7%. That is to say, for every thousand people tested who don't have the infection, three would test positive. These estimates were also supported by evidence from the six testing site-based Innova LFD antigen test evaluations. Like sensitivity, these studies suggested the level of experience of the LFD antigen test user influences the specificity. This ranged from 99.8% in experienced user field studies (RTS Field Test 1 and ATS Field Test 2) to 99.1% in inexperienced self-trained users (RTS Field Test 3 and 4). Similarly, for the Orient Gene LFD antigen test, specificity was found to increase from 99.3% for inexperienced users (RTS Field Test 5) to 99.8% for experienced users (RTS Field Test 2).

However, recent DHSC analysis of real-world positivity rates from approximately 25,000 Innova LFD Antigen tests delivered in the community as part of NHS Test and Trace testing, combined with mathematical modelling suggests that the Innova LFD devices are outperforming these initial estimates in mass testing use<sup>33</sup>. This larger analysis estimates the real-world specificity of the Innova LFD device to be greater than 99.97%. This means in every 10,000 people tested we would expect three people to receive a 'false positive' LFD result. As PCR is an imperfect gold standard, and these results are estimates based on a sample of individuals, it is possible that an equivalent improvement in specificity for Orient Gene is seen in the real world once larger sample sizes are collected through NHS Test and Trace ongoing quality monitoring.

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<sup>33</sup> Wolf et al. Lateral flow device specificity in phase 4 (post marketing) surveillance. March 2020. [Lateral flow device specificity in phase 4 \(post-marketing\) surveillance - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/864212/Lateral_flow_device_specificity_in_phase_4_(post-marketing)_surveillance_-_GOV.UK_(www.gov.uk).pdf)

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