Performance of the Innova SARS-CoV-2 antigen rapid lateral flow test in the Liverpool asymptomatic testing pilot: population based cohort study

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ABSTRACT

OBJECTIVE
To assess the performance of the SARS-CoV-2 antigen rapid lateral flow test (LFT) versus polymerase chain reaction testing in the asymptomatic general population attending testing centres.

DESIGN
Observational cohort study.

SETTING
Community LFT pilot at covid-19 testing sites in Liverpool, UK.

PARTICIPANTS
5869 asymptomatic adults (≥18 years) voluntarily attending one of 48 testing sites during 6-29 November 2020.

INTERVENTIONS
Participants were tested using both an Innova LFT and a quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR) test based on supervised self-administered swabbing at testing sites.

MAIN OUTCOME MEASURES
Sensitivity, specificity, and predictive values of LFT compared with RT-qPCR in an epidemic steady state of covid-19 among adults with no classic symptoms of the disease.

RESULTS
Of 5869 test results, 22 (0.4%) LFT results and 343 (5.8%) RT-qPCR results were void (that is, when the control line fails to appear within 30 minutes). Excluding the void results, the LFT versus RT-qPCR showed a sensitivity of 40.0% (95% confidence interval 28.5% to 52.4%; 28/70), specificity of 99.9% (99.8% to 99.99%; 5431/5434), positive predictive value of 90.3% (74.2% to 98.0%; 28/31), and negative predictive value of 99.2% (99.0% to 99.4%; 5431/5473). When the void samples were assumed to be negative, a sensitivity was observed for LFT of 37.8% (26.8% to 49.9%; 28/74), specificity of 99.6% (99.4% to 99.8%; 5431/5452), positive predictive value of 84.8% (68.1% to 94.9%; 28/33), and negative predictive value of 93.4% (92.7% to 94.0%; 5431/5814). The sensitivity in participants with an RT-qPCR cycle threshold (Ct) of <18.3 (approximate viral loads >10^6 RNA copies/mL) was 90.9% (58.7% to 99.8%; 10/11), a Ct of <24.4 (>10^4 RNA copies/mL) was 69.4% (51.9% to 83.7%; 25/36), and a Ct of >24.4 (<10^4 RNA copies/mL) was 9.7% (1.9% to 23.7%; 3/34). LFT is likely to detect at least three fifths and at most 998 in every 1000 people with a positive RT-qPCR test result with high viral load.

CONCLUSIONS
The Innova LFT can be useful for identifying infections among adults who report no symptoms of covid-19, particularly those with high viral load who are more likely to infect others. The number of asymptomatic adults with lower Ct (indicating higher viral load) missed by LFT, although small, should be considered when using single LFT in high consequence settings. Clear and accurate communication with the public about how to interpret test results is important, given the chance of missing some cases, even at high viral loads. Further research is needed to understand how infectiousness is reflected in the viral antigen shedding detected by LFT versus the viral loads approximated by RT-qPCR.

WHAT IS ALREADY KNOWN ON THIS TOPIC

The Innova SARS-CoV-2 antigen rapid lateral flow test (LFT) was adopted for large scale UK pilots of community testing in response to covid-19, including open access testing for asymptomatic residents of Liverpool, UK

Although the evaluation of the test's accuracy in people with symptoms is well documented, limited data are available for its use in asymptomatic people

WHAT THIS STUDY ADDS

Innova LFT results were positive for most people with high viral load (likely to be infectious) who tested positive using reverse-transcriptase polymerase chain reaction (RT-qPCR), whereas results were negative for most people with viral load <10^4 RNA copies/mL (expected to be less infectious)

Policy makers need to consider LFT utility in context sensitive ways, regarding population levels of infection, phases of epidemic curves, and the transmission risks and consequences in specific settings

Introduction

The global SARS-CoV-2 pandemic has been responsible for many deaths and has had a profound, enduring effect on the livelihoods and life chances of people worldwide. Identifying those with covid-19 has become a key strategy for limiting the spread of the disease, with quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR) testing being used as the reference standard in the diagnosis of covid-19. In a public health rather than clinical context, however, the hours or days taken to receive a RT-qPCR test result is time when infected people might be transmitting the virus to others. The cost and capacity of RT-qPCR testing also limit its value for public health uses. As a consequence, low cost, rapid lateral flow technology (LFT), such as that used in pregnancy test kits, was developed to detect the nucleocapsid protein antigen

of SARS-CoV-2, the virus responsible for covid-19.[1] The LFT provides results within 30 minutes and can be carried out without the need for a laboratory, offering the potential to rapidly identify people with covid-19, ideally leading to quick isolation, and breaking transmission chains.

The Innova LFT was adopted for large scale English pilots of community testing in response to covid-19, including open access testing for asymptomatic residents of Liverpool in England. An initial evaluation, undertaken as part of the test development and evaluation programme commissioned by the Department of Health and Social Care, and conducted by Public Health England Porton Down laboratory and the University of Oxford, reported test sensitivity compared with RT-qPCR of 79% when the LFT was read by laboratory scientists, 73% when read by trained healthcare workers, and 58% when read by self-trained staff members at a test and trace centre.[2] The study considered both people with and without symptoms and found no evidence of a difference in sensitivity. However, the study participants were part of a testing service for people with symptoms and details are lacking as to why asymptomatic people were tested. A recent review suggested that LFT can be less accurate in asymptomatic people than in those with symptoms.[3]

We assessed the performance of LFT to detect current SARS-CoV-2 infection in the general population without symptoms attending covid-19 testing centres. The use of RT-qPCR as the reference standard test is, however, questionable because RT-qPCR can detect

SARS-Cov-2 for an average of 17 days, and often for longer. For much of this period, the individual is likely to have stopped being infectious.[4-6] The RT-qPCR cycle threshold (Ct) offers an indication of viral load, which is understood to be linked to the level of infectiousness of someone with covid-19. Nevertheless, the precise relation in any individual between Ct and viral load, and between viral load and infectiousness is still unclear.[7 8] The PHE evaluation[2] indicated that LFT was able to identify more than 90% of people with a Ct <25, corresponding approximately to a viral load of >10^5 RNA copies/mL, indicating that the LFT has the potential to identify most of those who are infectious. Some concerns remain about the use of LFT, however, most noticeably about the accuracy reported by self-trained or non-expert readers in the asymptomatic population.[9]

On 6 November 2020 a community testing programme, piloted in Liverpool and sponsored by the Department of Health and Social Care, started with the aim of identifying more infected people earlier in their infection cycle so they could self-isolate and break transmission chains. To assess the performance and appropriate implementation of the Innova LFT in Liverpool, we performed a quality assurance exercise. We compared the sensitivity, specificity, and predictive values of the LFT with a RT-qPCR test sampled within minutes of self-administered swabbing by the same individual at the testing site. The sensitivity of the LFT as a function of PCR Ct (viral load proxy) was also investigated.
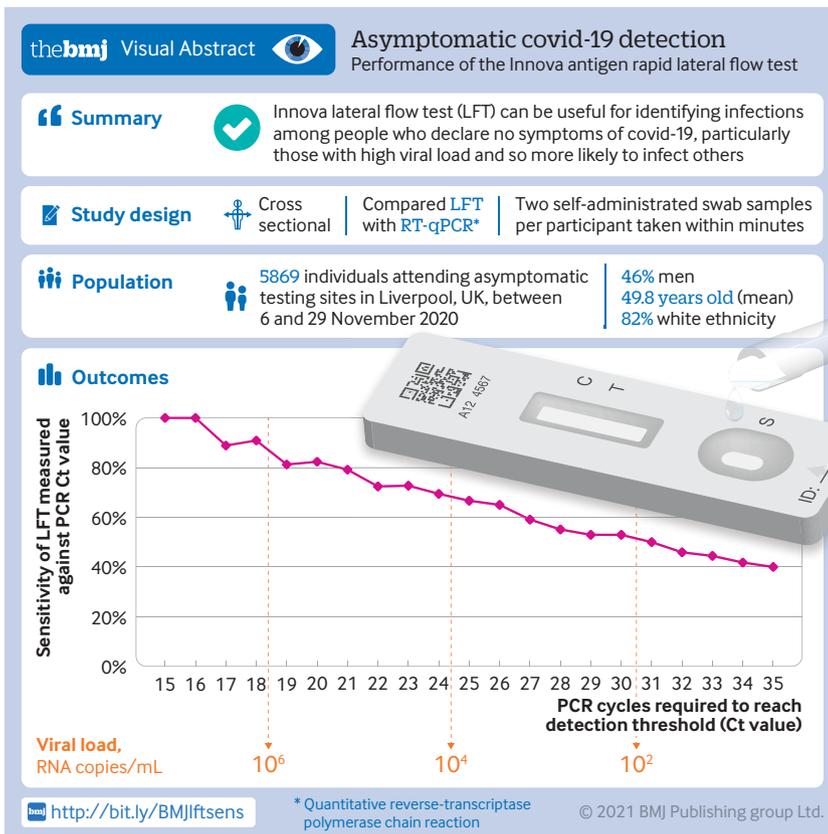
Some initial results from this Liverpool pilot have been reported previously[10 11] and have been debated in the literature,[12-19] but to date have not been published in the peer reviewed literature. We report the quality assurance findings of that study.

Methods

Study design and participants

Asymptomatic people attending testing sites in Liverpool between 8 and 29 November 2020 were invited to participate in this prospective quality assurance exercise. Eligible participants were adults (≥18 years) who did not display any of the UK government's list of symptoms for covid-19 (new continuous cough, high temperature, or loss of, or change in, normal sense of taste or smell). Participants provided verbal consent (recorded) to take part. Recruitment rotated between 48 test sites until the team had either recruited 200 participants at a site, or two days of recruitment at that site had elapsed without the target being reached. Reasons for not being invited to participate were age younger than 18 years old or the volume of people at a test centre prohibited this additional recruitment step. Otherwise all individuals consecutively attending the relevant test centres were invited to participate.

Sample size was predefined by NHS Test and Trace service at 200 in each testing site and not based on statistical calculations from the evaluation team. This balance was pragmatic to account for potential

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Asymptomatic covid-19 detection
Performance of the Innova antigen rapid lateral flow test

Summary — Innova lateral flow test (LFT) can be useful for identifying infections among people who declare no symptoms of covid-19, particularly those with high viral load and so more likely to infect others

Study design — Cross sectional | Compared LFT with RT-qPCR* | Two self-administered swab samples per participant taken within minutes

Population — 5869 individuals attending asymptomatic testing sites in Liverpool, UK, between 6 and 29 November 2020 | 46% men | 49.8 years old (mean) | 82% white ethnicity

Outcomes

Viral load, RNA copies/mL: 10^6 | 10^4 | 10^2

http://bit.ly/BMJlftsens

* Quantitative reverse-transcriptase polymerase chain reaction

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variability across sites (eg, differences in personal and socioeconomic characteristics). Similar numbers of participants (n=200) were recruited in each site. Assuming about a 1% prevalence for covid-19, the sample size was anticipated to provide on average one or two positive test results in each test site. Participants received both an Innova LFT and an RT-qPCR test to be self-administered swabs (combined throat and nose) under supervision and taken at the same appointment within minutes. The LFT test was always taken first and graded within 30 minutes. Trained observers monitored this process to ensure that the manufacturer's instructions were followed. The site team analysed the LFT directly according to the Department of Health and Social Care standard protocol, with the result confirmed by the quality assurance team. The team were members of the armed forces who were provided with a set of standard operating instructions, detailing how to process the swab sample and how to interpret the results. The same version of the Innova LFT (product code BT1309) was used for the city-wide testing pilot. The second swab was sent for RT-qPCR analysis at one of the Lighthouse laboratories using its standard RT-qPCR SARS-CoV-2 assay (TaqPath; ThermoFisher Scientific). Neither test result was graded with knowledge of the other test result. The results were sent from NHS Test and Trace to Liverpool's integrated health and social care and public health data system (www.cipha.nhs.uk) and analysed by an independent team at the University of Liverpool. The supplementary file provides further information on the quality assurance protocol developed by the Department of Health and Social Care.

Ct values and connection with viral load

Ct is defined as the number of cycles required for the sample fluorescence in the laboratory to exceed a chosen threshold for positivity. Ct values provide an indication of the concentration of viral RNA in a sample tested by the RT-qPCR method, such that low Ct values tend to be linked to high viral loads and, conversely, high Ct values tend to be linked to low viral loads. Lack of standardisation of Ct values across different laboratories and equipment makes it challenging to compare Ct values between studies using difference laboratories. The RT-qPCR test used here corresponds to the standard test used in UK Lighthouse laboratories studies, and we have used the same Ct thresholds to calculate sensitivity of LFT compared with RT-qPCR to allow easy comparison.[8] Our study protocol had no prespecified Ct cut-offs. Ct values were converted into approximate viral loads using the calibration curve performed for the Glasgow laboratory ($\log_{10}$(viral load)=$12-0.328\times$Ct), since it is understood to be generalisable to other Lighthouse laboratories using similar methods.[8]

Statistical analysis

We used the Clopper-Pearson exact method to estimate the sensitivity, specificity, positive predictive value, and negative predictive values along with corresponding 95% confidence intervals. For the purposes of this analysis, we regarded RT-qPCR as the reference standard, although we acknowledge that viral shedding (reflected by LFT) and viral loads (reflected by RT-qPCR Ct) are temporally aligned processes. Estimates of sensitivity were provided for each Ct interval, which we calculated as the combined average of existing genes (such that if a particular gene had a missing value, the average was calculated over the remaining Ct scores). Void results were not included in calculation of accuracy variables for the main analysis. However, for completeness, we also assessed accuracy taking into account void results (for either test) by grouping them with the negative results.[20] A voided RT-qPCR test is one that is either operationally non-analysable (eg, insufficient sample for analysis) or has an analytically inconclusive fluorescence amplification curve. In some of these cases amplification might have been observed for one of the target genes, but this was determined to be based on either background signal or sample contamination. A voided LFT test result is one where the control line fails to appear within 30 minutes. Estimates of sensitivity were also generated based on the N gene (the nucleocapsid antigen that LFT is designed to detect) as well as based on the S (spike protein) gene and ORF1ab (open reading frame 1ab) for completeness.

When multiple LFT and RT-qPCR tests were identified from the same participant, we included only one pair of test results in the main analysis following predefined selection criteria (see supplementary file). Sensitivity analyses were performed to consider scenarios where agreement between LFT and RT-qPCR results was maximised and minimised based on the results from multiple tests for each individual. An additional analysis including all multiple tests (assuming independence) was also conducted. Statistical analyses were carried out in R (version 3.6.1 or later) and checked by a second statistician using SAS software (version 9.4).

Patient and public involvement

This study uses data from Liverpool's integrated health and social care and public health data system, and it is an urgent public health research study in response to a public health emergency of international concern. Patients and the public were not involved in the design, conduct, or reporting of the study.

Results

Personal characteristics of the participants were not collected as part of this quality assurance study. It was, however, possible to use the Combined Intelligence for Population Health Action platform to access results for all but 116 of the LFT tests conducted in the study to extract basic personal information. The mean age of the participants was 50 years (SD 18 years), 54% were women, and most were of white ethnicity (82%). Supplementary table S4 and figures S1-S4 provide additional information on the characteristics of the study cohort, flowchart, distribution of the number of

tests by test centre, and test results over time. Personal characteristics were similar between the study participants and those who attended the test centres on the same day as the study team (supplementary table S5).

Forty participants had taken part in the study on more than one occasion—30 had the same LFT and RT-qPCR paired results and 10 showed inconsistent results for LFT or RT-qPCR, or both (see supplementary file).

Overall, 5869 asymptomatic adults from 48 testing sites in Liverpool participated in this study. Table 1 shows the results for pairs of LFT and RT-qPCR tests for each participant. After excluding void test results, the sensitivity was found to be 40.0% (95% confidence interval 28.5% to 52.4%; 28/70), specificity 99.9% (99.8% to 99.99%; 5431/5434), positive predictive value 90.3% (74.2% to 98.0%; 28/31), and negative predictive value 99.2% (99.0% to 99.4%; 5431/5473). Positive and negative predictive values were directly estimated from the data, which showed a 1.3% prevalence; the Office for National Statistics reported a prevalence of 2.3% for West Lancashire, Liverpool, Knowsley, and Sefton on 20 November.[21] The lower percentage of positive test results in the current study reflects that all testing was conducted in people without covid-19 symptoms.

When the void results for either test were grouped with the negative results, a sensitivity was observed for LFT of 37.8% (26.8% to 49.9%; 28/74), specificity of 99.6% (99.4% to 99.8%; 5431/5452), positive predictive value of 84.8% (68.1% to 94.9%; 28/33), and negative predictive value of 93.4% (92.7% to 94.0%; 5431/5814). Including void results in this way provides a more conservative estimate of sensitivity, given that void LFT results linked to a positive PCR result are assumed to be negative.[20]

Figure 1 and table 2 present the results for sensitivity of the LFT against RT-qPCR by viral load. In the context of a positive RT-qPCR test result with high viral load (>10^6 RNA copies/mL) the LFT was able to detect 90.9% (58.7% to 99.8%; 10/11) of cases. The LFT detection rate of participants with a positive RT-qPCR result decreased substantially as viral load decreased. For example, for those with a viral load <10^4 RNA copies/mL the sensitivity was only 9.7% (1.9% to 23.7%; 3/34). Figure 2 shows LFT sensitivity against mean Ct value.

The LFT results assessed on site showed a high level of concordance (99.9%) with the quality assurance

team's readings, with 5845 concordant and two discordant samples (99.9% concordance, excluding voids, almost identical if voids are included; see supplementary table S2). Interobserver agreement did not differ noticeably across test sites.

Two additional analyses based on agreement or disagreement between LFT and RT-qPCR test results for those participants with multiple tests showed that the selection criteria followed had a minor effect on the accuracy variables (see supplementary table S3). Results remained similar when multiple tests were included (ie, treating multiple pairs of tests for the same individuals as if they were independent observations; supplementary table S4).

Discussion

We report a city-scale evaluation of Innova LFT versus RT-qPCR test results among the general population attending asymptomatic testing centres voluntarily in Liverpool between 8 and 29 November 2020. Participants declared that they did not have classic symptoms of covid-19 and we have drawn no conclusions about those who may have been (pre-; pauci-) symptomatic. The sample was representative of those attending asymptomatic testing centres concurrently (supplementary table S5). Contrasts with the wider population have been described elsewhere.[22]

The overall sensitivity of the Innova LFT was 40%—a potentially misleading statistic if RT-qPCR detects a large proportion of people post-infection.[18] RT-qPCR is exquisitely sensitive for detecting SARS-CoV-2 RNA in those with replicating virus or those whose immune systems have controlled the infection and are less likely to be infectious. So a substantial proportion (depending on the epidemic phase) of people with a positive RT-qPCR test result will no longer be infectious.[5 7] In our study, LFT achieved 90% sensitivity compared with people found to be positive by RT-qPCR testing with a high viral load >10^6 RNA copies/mL, and the corresponding 95% confidence interval indicated that LFT is likely to detect at least three fifths and at most 998 in every 1000 people with a positive RT-qPCR test result with high viral load. For comparison, LFT achieved a sensitivity of 72.4% (52.8% to 87.3%) in those with an approximate viral load >10^5 RNA copies/mL.

Comparison with other studies
Other rapid antigen tests have been assessed for their ability to detect people with confirmed covid-19 by RT-

Table 1 | Results of rapid lateral flow test (LFT) and quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR) tests in quality assurance dataset (5869 participants)

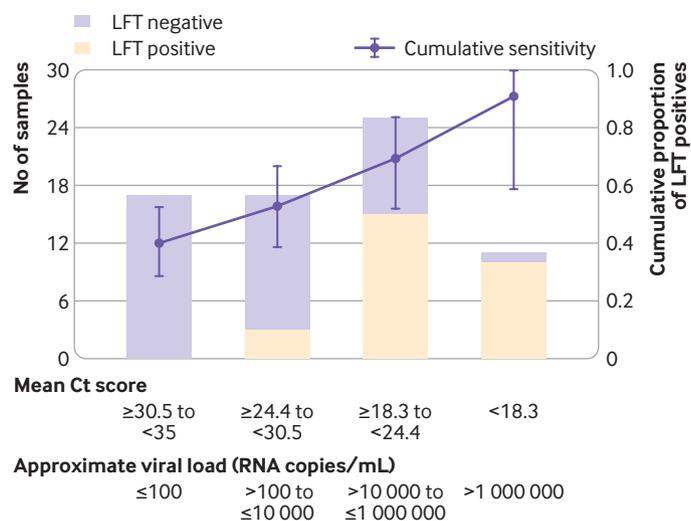| LFT result	RT-qPCR result			Total (%)	Predictive values
	Positive	Negative	Void		
Positive	28	3	2	33 (0.6)	90.3 (74.2 to 98.0)
Negative	42	5431	341	5814 (99.1)	99.2 (99.0 to 99.4)
Void	4	18	0	22 (0.4)	
Total (%)	74 (1.3)	5452 (92.9)	343 (5.8)	5869	
Sensitivity (%, 95% CI)	40.0 (28.5 to 52.4)				
Specificity (%, 95% CI)		99.9 (99.8 to 99.99)			

Fig 1 | Number of participants with negative and positive lateral flow test (LFT) results by quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR) viral load (based on mean cycle threshold (Ct) score across three gene targets). Intervals show the 95% confidence interval for the cumulative sensitivity to detect viral loads >1, >10², >10⁴, and >10⁶ RNA copies/mL

qPCR testing, reporting broadly similar sensitivity and specificity in asymptomatic people as we report for the Innova LFT in the Liverpool pilot.[23-25] All three studies also report similar ability to detect lower Ct values with higher sensitivity. Although our study involved mainly white British people, comparable results have been recorded in other countries and ethnic groups.[26 27]

The association between covid-19 viral load and infectiousness has not yet been fully characterised.[8 28] Analysis of NHS Test and Trace contact data suggests that a lower Ct in the index case (ie, higher viral load) increases the likelihood of contacts testing positive for covid-19.[8] This study traced 64% of all contacts and observed that 13% of case-contact pairs with a contact who tested positive by RT-qPCR had case viral loads <10⁴ RNA copies/mL, 40% of case-contact pairs had case viral loads between 10^4 and 10^6 RNA copies/mL, and around 47% of case-contact pairs with contacts who tested positive by RT-qPCR- had case viral loads >10⁶ RNA copies/mL. A recent Spanish contact tracing study[28] identified that more than 85% of transmission events occurred in clusters linked to an index case with a viral load of >10⁵ RNA copies/mL. These studies indicate that LFT can identify most of the those with a

Table 2 | Results of rapid lateral flow test (LFT) with a breakdown by cycle threshold (Ct) value

	RT-qPCR test (mean across three gene targets)				Void tests with Ct value				
	Ct (RNA copies/mL)				Positive (NA)*	30-<35	≥35	No Ct values†	Negative
	‹18.3 (›10⁶)	18.3-‹24.4 (›10⁴-10⁶)	24.4-‹30.5 (›10²-10⁴)	30.5-‹35 (≤10²)					
RT-qPCR Ct									
LFT site results:									
Negative	1	10	14	17	5	8	328	5431	
Positive	10	15	3	0	0	0	2	3	
Void	0	4	0	0	0	0	0	18	
Sensitivity (%, 95% CI)	90.9 (58.7 to 99.8)	60.0 (38.7 to 78.9)	17.6 (3.8 to 43.4)	0.0 (0.0 to 19.5)					
Cumulative sensitivity‡ (%, 95% CI)	90.9 (58.7 to 99.8)	69.4 (51.9 to 83.7)	52.8 (38.6 to 66.7)	40.0 (28.5 to 52.4)					
N gene									
LFT site results:									
Negative	1	8	16	15	2	6	4	331	5431
Positive	7	17	3	1	0	0	0	2	3
Void	0	4	0	0	0	0	0	0	18
Sensitivity (%, 95% CI)	87.5 (47.3 to 99.7)	68.0 (46.5 to 85.1)	15.8 (3.4 to 39.6)	6.3 (0.1 to 30.2)					
Cumulative sensitivity‡ (%, 95% CI)	87.5 (47.3 to 99.7)	72.7 (54.5 to 86.7)	51.9 (37.6 to 66.0)	41.2 (29.4 to 53.8)					
S gene									
LFT site results:									
Negative	1	10	13	9	9	1	4	336	5431
Positive	10	15	3	0	0	0	0	2	3
Void	0	4	0	0	0	0	0	0	18
Sensitivity (%, 95% CI)	90.9 (58.7 to 99.8)	60.0 (38.6 to 78.9)	18.8 (4.0 to 45.6)	0.0 (0.0 to 33.6)					
Cumulative sensitivity‡ (95% CI)	90.9 (58.7 to 99.8)	69.4 (52.9 to 83.7)	53.8 (39.5 to 67.8)	45.9 (33.1t o 59.2)					
ORF1ab gene									
LFT site results:									
Negative	3	10	13	8	7	1	2	338	5431
Positive	12	14	2	0	0	0	0	2	3
Void	1	3	0	0	0	0	0	0	18
Sensitivity (%, 95% CI)	80.0 (51.9 to 95.7)	58.3 (36.6 to 77.9)	13.3 (1.7 to 40.5)	0.0 (0.0 to 36.9)					
Cumulative sensitivity‡ (%, 95% CI)	80.0 (51.9 to 95.7)	66.7 (49.8 to 80.9)	51.9 (37.8 to 65.7)	45.2 (32.5 to 58.3)					

RT-qPCR=quantitative reverse-transcriptase polymerase chain reaction; NA=not applicable (missing gene target).
*Implies PCR result was graded as positive but particular target gene was not detected for that sample.
†When void PCR results were returned, Ct value was observed for at least one target gene in a small number of participants, but this was determined to be inconclusive.
‡Defined using number of samples with Ct less than upper threshold.
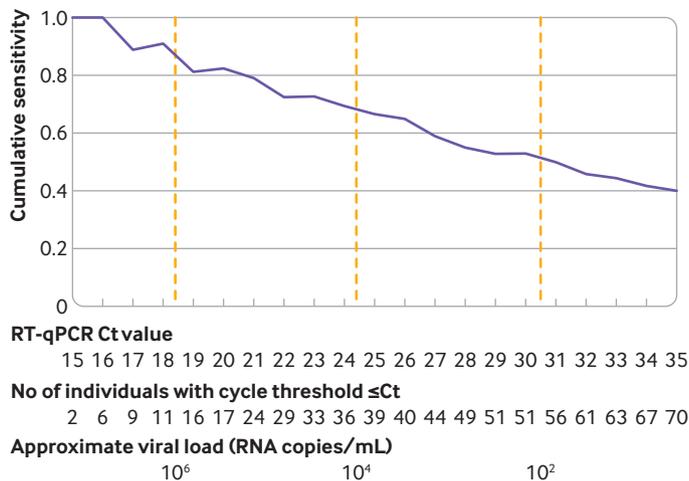
Fig 2 | Cumulative sensitivity of Innova lateral flow test (LFT) against quantitative reverse-transcriptase polymerase chain reaction (RT-qPCR) cycle threshold (Ct). Dashed orange lines show approximate viral loads (RNA copies/mL)

RNA and might be a better estimate of the actual number of genome copies per millilitre.[29] In our study we found an insubstantial reduction in sensitivity for detecting high viral loads when only the ORF1ab cycle thresholds were considered (table 2).

Although RT-qPCR tests can detect small amounts of RNA, sensitivity can be affected by swabbing technique and by substantial and largely unexplained heterogeneity between studies in sensitivity to detect SARS-Cov-2 positivity in people who might have tested positive with a different swab sample. A recent systematic review identified 34 studies with RT-qPCR false negative rates (1−negative predictive value) ranging from 2% to 58%.[30] The sensitivity of the LFT is also substantially affected by the quality of the sample and swabbing technique.[2 31 32] The LFT was always done first. In theory this could have depleted the source material and hence virus nucleic acid available for the subsequent swab for RT-qPCR testing, although it is also possible that the second swab benefited from a training effect. In addition, variation in LFT device build quality, lack of quality assurance certification by batch of test, and storage temperatures are additional sources of heterogeneity that are poorly recorded.[10] The instructions for use of the LFT state that the tests should be stored between 2°C and 30°C and used at room temperature of between 15°C and 30°C. Given the relatively mild autumn temperatures in the UK, ambient storage conditions should have remained within these ranges and therefore we do not anticipate this had an impact on the performance of the LFTs.

Conclusions

Our study suggests that the LFT can be a useful tool among wider public health measures for the control of SARS-CoV-2 transmission and to mitigate risk of covid-19. The predictive value of testing, and in particular of LFT, varies with the phase of the epidemic curve and the population prevalence of infection,[33] which was declining at the time of this quality assurance study in Liverpool.[18] Our study also shows that about one 10th of the people with higher viral load (>10^6 RNA copies/mL) detected by RT-qPCR are missed, which highlights the need to assess the impact that false negative test results might have in specific contexts. Some false negative LFT results occur at a time when an individual's viral load is declining, and therefore they might no longer be highly infectious. A proportion of false negative LFT results are expected to correspond to the early phase of the infectious trajectory, when viral load might increase in the next 48 hours. For such individuals, serial testing could improve sensitivity, and optimal testing regimens need further study. Although false negative results might reflect those who are no longer infectious, there is a risk of false reassurance leading to behaviours that increase transmission. Careful communication is needed around all negative test results, and symptomatic people should continue to be encouraged to attend for PCR testing, allowing LFT to be seen to be an early screening for the most infectious cases.

higher chance of infecting others, but they also show that transmission of covid-19 can occur in those with low viral load. It is nevertheless possible that some of these instances of transmission were confounded by third party transmission, or that the transmission occurred when the individual's viral load was much higher. However, the evidence gathered to date suggest that people with a low viral load (about ≤10^5 RNA copies/mL) could still be infectious, although the chance of infecting others is lower than for those with a higher viral load. Although our study, conducted in an asymptomatic population, shows that LFT can detect most people with a high viral load, and therefore those at a higher risk of transmitting SARS-CoV-2, the LFT missed 10% of people with a high viral load >10^6 RNA copies/mL, 30% of cases with a viral load >10^4 RNA copies/mL, and most of the cases with a viral load <10^4 RNA copies/mL who might have contributed to virus transmission.[8] This suggests that care is needed when conveying negative LFT results so as not to give false reassurance.[15] Both of these contact tracing studies were in people with symptoms, who generally had higher viral loads than observed in our study. Contact tracing studies are currently the best instruments we have of transmission in whole populations. However, contact tracing systems evolve over time, and selection biases might be present related both to the recall of the original case and to the response of the contacts. In addition, these studies provide a snapshot of people at the point of PCR testing, so do not necessarily reflect the interaction between people or the progression of the virus in people before being tested. For these reasons caution is needed in using contact tracing studies to infer the proportion of infectious people detected by LFT.

Limitations of this study

A technical limitation is that RT-qPCR targeting the N gene might detect fragments of RNA and hence could overestimate the number of viral copies in a sample. The ORF1ab gene is only detected on viral genomic

The Innova LFT seems, in combination with other health protection measures, to be a valuable tool in wider public health responses to covid-19 for identifying those with higher viral loads who are more likely to be infectious but do not report classic symptoms. To maximise the value of LFT, care should be taken to train test operatives, communicate the meaning of results to tested people, target testing with reference to background case rates, and avoid single LFT results for access to vulnerable settings (such as care homes) where the consequences of infection are severe (unless comprehensive additional risk reduction measures are considered). Further studies are needed to understand the relation between LFT results and infectiousness.

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Supplementary information: additional information, tables, and figures

Supplementary information: quality assurance protocol developed by the Department of Health and Social Care