Options for enhancing capacity for testing in symptomatic individuals

Background
Access to timely and accurate COVID-19 testing is an essential component to support clinical management of cases, contact tracing, infection prevention and control, and disease surveillance. In this country to date, testing for the SARS-CoV-2 virus has been primarily based on a significant and agile PCR test capacity that has been built up by the HSE and which is appropriately targeted to support the pandemic response. The ECDC proposes five main objectives for testing including to control transmission; reliably monitor SARS-CoV-2 transmission rates and severity; mitigate the impact of COVID-19 in healthcare and social care settings; detect clusters or outbreaks in specific settings and maintain sustained control of COVID-19 once achieved.¹ Additionally, testing strategies should be flexible and rapidly adaptable to change, depending on the local epidemiology, transmission, population dynamics and resources.

Capacity
Current PCR testing capacity relies on both swabbing and laboratory testing capacity. Current standing capacity for swabbing is 32,400 nationally per day.² Surge capacity is expected to increase to 35,900 swabs by mid-December 2021. This includes community swabbing, serial testing, home and mobile, private providers and acute hospital swabbing. Current standing capacity for laboratory testing is 32,400 tests (27,400 community and 5,000 acute hospitals). Current surge capacity is 36,000+ daily tests (31,000 Community Tests and 5,000 acute hospitals), with potential to increase this by 2,000 on a short-term basis. Laboratory capacity at higher levels is contingent on offshore availability. In the week to 30 November 2021, approximately 211,332 community referrals were made, and 215,385 laboratory tests were completed.

Table 1. Overview of standing capacity and surge capacity (HSE) as at 29 November 2021

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Standing Capacity</th>
<th>Surge Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swabbing</td>
<td>32,400</td>
<td>35,900 (mid-December)</td>
</tr>
<tr>
<td>Swabbing – Community</td>
<td></td>
<td>21,500*</td>
</tr>
<tr>
<td>Swabbing – Home &amp; Mobile</td>
<td></td>
<td>2,400</td>
</tr>
<tr>
<td>Swabbing – Private Providers</td>
<td></td>
<td>3,000</td>
</tr>
<tr>
<td>Swabbing – Serial Testing**</td>
<td></td>
<td>500</td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td>5,000</td>
</tr>
<tr>
<td>Laboratory</td>
<td>32,400</td>
<td>Average 36,000+ daily tests (7-day notice period to access additional capacity)</td>
</tr>
<tr>
<td>Laboratory - Lab 1</td>
<td>17,400</td>
<td>17,000</td>
</tr>
<tr>
<td>Laboratory - Lab 2</td>
<td>6,000</td>
<td>8,000</td>
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<tr>
<td>Laboratory - Lab 2 (offshore)</td>
<td></td>
<td>2,000 (–)</td>
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<tr>
<td>Laboratory – Lab 3</td>
<td>4,000</td>
<td>4,000</td>
</tr>
<tr>
<td>Laboratory - Acutes</td>
<td>5,000</td>
<td>5,000***</td>
</tr>
</tbody>
</table>

* Short-term surge capacity, not sustainable beyond a number of days
** Serial testing programmes will commence on 6th Dec and expected volumes will be 21,000 per week with 7-day testing
*** Acute hospitals are running consistently at 5,000 presents significant challenges

² HSE. Test and Trace Paper – NPHET. 2nd December 2021
Expected demand for testing
The current epidemiological situation in Ireland clearly demonstrates high levels of community transmission, with high incidence and positivity rates. Increased socialisation is expected over the Christmas/New Year’s period, in addition to increased travel into Ireland. The emergence of the Omicron variant of concern (VOC), and increased detection of cases globally presents an uncertain threat. Both the ECDC and WHO have raised significant concerns in relation to potential increased transmissibility and immune escape with this VOC, due to the constellation of mutations it possesses.

Figure 1: Total tests reported per day

Figure 1 indicates that current testing levels are highest than at any previous point in the pandemic.

Figure 2: Demand for PCR in PH laboratories (optimistic scenario)
Existing modelling suggested that cases will peak in December 2021, and that demand for PCR will fall in January 2022 (figure 2). This scenario details the demand for testing in most optimistic scenario, which assumes a 10% reduction in effective social contact from Monday 29th October, and high prior population immunity. This scenario does not apply any adjustment for the Omicron variant.

Figure 3: Demand for PCR in PH laboratories (pessimistic scenario)

The demand for testing in the most pessimistic scenario is illustrated in figure 3. This assumes a 10% increase in effective social contact from last week onwards, and a Christmas surge in social contact. Additionally, this provides for emergence of the Omicron variant, with assumptions including a 30% reduction in vaccine effectiveness and a 1.4x transmission advantage compared to delta, on the background of low prior population immunity. While the demand follows a similar trajectory, albeit with latter peak, the absolute demand is approximately twice that of the optimistic scenario.

Current HSE antigen programmes
The HSE is currently running a number of antigen self-testing programmes. These include longstanding programmes in the further education setting, residential care facilities, food processing industry and other services identified as priorities by Public Health on a needs basis. More recently, programmes for fully vaccinated, asymptomatic close contacts, and asymptomatic children and staff in primary schools, who are identified as members of a pod with a confirmed Covid-19 case, have been launched. The HSE operates an antigen results website which is open to all and permits individuals to report the results of their antigen self-tests. Additionally, health-care worker administered antigen testing is available in acute hospitals and in outbreak settings. Further expansion of the programme to the childcare sector is expected in the next couple of weeks.

In the week to 26 November 2021, an average of 3,269 results were uploaded per day for past 7 days, of which 79% were confirmed on PCR. The fully vaccinated close contact pathway has dispatched 104,095 test kits being to date. Results have been reported for 31,850 of these (30.6%) with 10,271 recorded as positive of which 5,741 cases were confirmed on PCR testing, with between 4,000 and 5000 tests being utilised in the food processing industry testing per week. The schools' pathway launched on 29th November 2021, with over 12,000 antigen test kits
dispatched in the first 2 days. As such, it is estimated that the vaccinated close contact and schools’ pathways will collectively account for c.50,000 antigen test kits per week. In terms of supply, c.6 million tests (1.2m test kits) are expected for delivery on 17th December. It is unknown what impact expansion of the self-testing antigen pathways may have on PCR testing demands, particularly as vaccinated close contacts were not previously advised to undertake PCR testing (unless symptomatic).

**Options for increasing capacity**

Given current capacity demands, and based on modelling, additional demand for testing predicted over the next four to six weeks, the need to consider potential contingencies for increasing testing options is considered prudent. In doing so, the primary consideration is whether the role of antigen self-testing and/or use of self-collection PCR kits in symptomatic individuals should be explored further.

1. **Expansion of self-testing with rapid antigen detection tests to include symptomatic individuals**

As per ECDC’s most recent guidance rapid antigen detection tests (RADTs) can contribute to overall COVID-19 testing capacity, especially in situations in which Nucleic Acid Amplification Testing (NAAT) (e.g. RT-PCR) capacity is limited.\(^3\) Current guidance highlights that RADTs can help reduce further transmission through early detection of highly infectious cases, enabling a rapid start of isolation and contact tracing. RADTs are sensitive enough to detect cases with high viral load, early in the course of infection in pre-symptomatic and early symptomatic cases up to five days from symptom onset. The WHO advises that RADTs can play a significant role in this effort and may be more cost effective than NAAT in symptomatic populations.\(^4\) The predictive value of RADTs is highest in settings where SARS-CoV-2 prevalence is high.

**Advantages and disadvantages of self-testing with RADTs**

The advantages of RADTs include:

- RADTs can increase overall COVID-19 testing capacity
- Tests can be used at the point-of-care/at home and provide near real-time results
- Current SARS-CoV-2 prevalence is high and therefore the predictive value of RADTs is higher than previously
- The cost of initially isolating some false positives or risk of false negatives, may be offset by the fact that RADTs offer the fastest alternative to identify and isolate infectious individuals
- RADTs generally offer low-cost testing and relatively simple handling

The disadvantages associated with the use of RADTs include:

- Sampling relies mostly on nasopharyngeal specimens, however, self-sampling is not currently clinically validated for RADTs
- Self-sampling may be incorrectly conducted and may contribute to false negative results
- RADTs lack controls for confirmation of appropriate sampling
- As many of the RADTs are processed individually, monitoring of results is not possible, with no direct oversight of results by public health
- Specimens are not usually transported to laboratories, or may not be suitable, for further virus characterisation, such as sequencing or antigenic characterisation
- There is uncertainty as to the impact of N mutations of the Omicron variant on RADTs
- RADTs are less sensitive than NAATs, especially in asymptomatic patients
- The use of RADT as part of a scaled-up testing programme may accrue significant costs


\(^4\) https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2-infection-using-rapid-immunoassays
Use of antigen testing

RADTs detect the presence of a viral antigen in a specimen without amplification. RADTs are sensitive enough to detect cases with high viral load, including pre-symptomatic and early symptomatic cases up to five days from symptom onset, or low RT-PCR cycle threshold (Ct) value.

Currently available RADTs commonly demonstrate a lower sensitivity when compared to standard NAATs. While test sensitivities are variable, the validity of RADTs is best in symptomatic individuals and in the first five days after symptom onset, when viral load in the specimen is high and the person is likely to be most contagious. RADTs demonstrate high specificity, that is typically similar to NAATs, meaning that false positive test results are unlikely when the manufacturer’s instructions are followed in test use. The likelihood of false positive results is higher when used in settings where the prevalence of infection is low. However, this applies to all in vitro diagnostic tests that have specificity below 100%, including the NAATs (e.g. RT-PCR). The predictive values of all tests are dependent on the epidemiological situation in combination with test performance (i.e. sensitivity and specificity).

The WHO currently recommends the use of RADTs with a minimum performance requirement of ≥80% sensitivity and ≥97% specificity in the diagnosis of SARS-CoV-2 infections in a range of settings. This includes settings where NAAT is unavailable or where an excessive turnaround time would preclude clinical and public health utility of results. Additionally, ECDC advocates using tests with a performance closer to NAAT i.e. ≥90% sensitivity and >98% specificity, particularly in situations of lower COVID-19 prevalence, according to the HSC TWG recommendations. The ECDC also acknowledges that the tests need to be validated for the intended setting and situation.

The WHO advise that RADTs may be used in symptomatic individuals and recommend the application of clinical discretion to those with a negative result. This should include consideration of the epidemiological context and clinical history and presentation to determine whether confirmatory testing with NAAT or repeat testing with RADTs (within 48hrs), if NAAT is not readily available, is required. This guidance is similar to that of the CDC, with confirmatory testing with NAAT or serial antigen testing every 3–7 days for 14 days recommended, for symptomatic individuals with a negative antigen test, unless there is a low likelihood of SARS-CoV-2 infection. The ECDC also advises that RADTs may be considered in individuals with COVID-19-compatible symptoms. In settings with prevalence less than 10%, a second method for confirmation of positive samples is advised, such as RT-PCR or, if not available, a second RADT of a different brand. Furthermore, where the second test generates a negative result, symptomatic individuals are advised to stay at home until resolution of symptoms.

The HSE antigen validation project noted that well characterised RADTs may also have a role as a supplement to RT-PCR testing in the event of circumstances in which PCR capacity is not adequate to meet requirements. In such circumstances symptomatic people with a not-detected RADT would require further testing, either with PCR, or a second ADT 2-3 days later. Seven RADTs evaluated by this group in symptomatic individuals, met the minimum requirements set out by the WHO, noting that this evaluation was conducted prior to the emergence of the Delta variant in Ireland. Some variation in test performance and use of different sampling approaches was noted.

Antigen self-testing

The HSE antigen validation project reported that RADTs using nasopharyngeal collected swab samples were superior in terms of clinical sensitivity to nasal collected swabs. Additionally, collection by trained healthcare professionals was superior to self-testing. However, the use of antigen self-testing offers several advantages including the provision of rapid results could support the early detection and subsequent isolation of infectious cases, minimisation of exposure risk and potentially releasing testing capacity to ensure rapid access for vulnerable or high-risk individuals. However, the transfer of responsibility for reporting test results from laboratories and health professionals to individuals may lead to underreporting, reducing the opportunity to apply measures such as contract tracing, quarantine of contacts and monitoring of disease trends over time. Furthermore, in the context of a potential new variant, the opportunity to conduct genomic sequencing on those samples would be restricted. Additionally, while the current high incidence and high positivity lends itself to improved test performance, this would need to be kept under review.

2. Implementation of self-swabbing using PCR tests for symptomatic individuals

RT-PCR testing has remained the internationally recognised gold standard diagnostic test for SARS-CoV-2 throughout the pandemic based on their high sensitivity and specificity in detecting the virus. PCR testing amplifies viral ribonucleic acid (RNA), with samples typically processed in a laboratory and results typically available within 1 to 3 days. A limited selection of point-of-care tests are available with results available in about 15–45 minutes. A positive PCR may indicate current or recent disease. Due to prolonged presence of viral RNA, detection tests may not always indicate the presence of virus capable of replicating or being transmitted to others, however, such ‘positive’ cases still facilitate contact tracing and identification of other potential infectious individuals.

Advantages and disadvantages of PCR testing

The advantages of PCR testing include:
- High-sensitivity, high-specificity tests for diagnosing SARS-CoV-2 infection
- Tests can be used at the at home
- Repeat testing is not required
- High sensitivity and specificity
- Internal control for confirmation of appropriate sampling
- As specimens are transported to laboratories, they are suitable for further virus characterisation, including sequencing
- Laboratory processing facilitates monitoring of results and direct oversight and management by public health

The disadvantages associated with the use of PCR testing include:
- Longer turnaround time usually between 1 to 3 days potentially delaying the contact tracing process
- Sampling relies mostly on nasopharyngeal specimens, however, self-sampling is not currently clinically validated for PCR testing
- Self-sampling may be incorrectly conducted and may contribute to false negative results
- Costs of testing are higher than RADTs

Use of PCR testing

Due to the high specificity and sensitivity of PCR tests, this remains the recommended option for testing of symptomatic individuals, and confirmatory testing of symptomatic individuals with a negative antigen test. Owing to the high test performance repeat testing is not typically required or advised. Ct (cycle threshold) values represent the number of cycles of amplification elapsed before the test system signals detection of the target. In general terms, the higher the Ct value the lower the quantity of virus target (viral load) present in the sample. However, precise definition of a high
Ct value is difficult as the Ct value for a given sample will be different in different laboratories depending on the test platform and other factors. 

**Use of self-swabbing in PCR testing**

While the role of professionally administered testing is well established, more recently, the use of self-collection kits has emerged. Such tests involve self-swabbing conducted at home, with the sample transported to a laboratory for testing. Such kits form part of the testing pathway for symptomatic individuals in both the UK and US. Both the NHS and CDC have recently expanded use of self-collection PCR kits. When accessed through such testing pathways, the UK based tests are distributed through the postal service, whereas those in the US are available for collection from pharmacies and retail outlets. Instructional videos and guides have been made available to aid the specimen self-collection process. The NHS note that results are typically advised within 24 to 48 hours.

As with antigen self-testing, the use of specimen self-collection in the case of a COVID-19 positive individual reduces the risk of transmission to health care workers, and other individuals. Conversely, where the individual does not have COVID-19 the risk of exposure for the subject is also reduced. Furthermore, this pathway may reduce the use of personal protective equipment, improve access to testing, improve acceptability of testing, and expand current testing capacity. Additionally, as therapies emerge such as antiviral medications or monoclonal antibody treatments, use of specimen self-collection may free up capacity for prioritisation of individuals for testing that may potentially benefit from these therapies.

Many studies have demonstrated the utility of self-collected oropharyngeal or nasal specimens for respiratory viruses over the last decade. In relation to COVID-19, a number of studies have demonstrated a slight reduction in sensitivity with home swab use compared to professionally administered testing. A study of 185 participants comparing clinician-collected nasopharyngeal swabs to unsupervised home self-collected mid-nasal swabs and reported sensitivity and specificity of home swabs at 80.0% (95% CI, 63%-91%) and 97.9% (95% CI, 94%-99.5%), however analysis of swabs with a Ct value ≤32 demonstrated a sensitivity of home swabs of 95%. Another study of 501 subjects reported a 8.7% reduction in sensitivity when the test was self-collected, compared to professional collection (95%CI: 2.4% to 15.0%, p = 0.006). Conversely, a study on 43 paired samples for suspected SARS-CoV-2 cases noted higher detection by self-collected nasal specimens compared to clinician-collected nasopharyngeal specimens (85.1% vs 70%). Wehrhahn et al. also demonstrated the reliability of self-collection to healthcare worker collected testing in 236 patients, with 25/25 positive results detected by self-swabbing compared to 24/25 positive results detected in healthcare worker collected samples.

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8 https://www.nhs.uk/conditions/coronavirus-covid-19/testing/how-to-do-a-test-at-home-or-at-a-test-site/how-to-do-a-pcr-test/
For decision:
Based on the current epidemiological situation, current demands for PCR testing, and uncertainly relating to the impact of the Omicron variant, the Christmas period and the potential impact of these factors on short-term testing capacity, endorsement of the principle of expansion of testing capacity to self-testing and/or self-swabbing in symptomatic individuals.