CLINICAL AND SCIENTIFIC REVIEW OF THE SCOTTISH GOVERNMENT TESTING STRATEGY

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1. Introduction

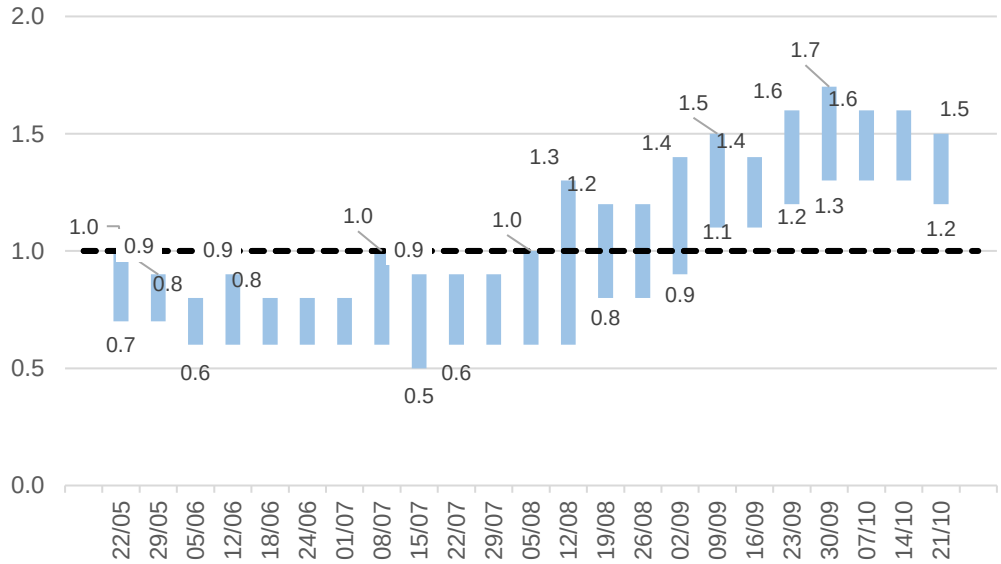
The most recent Scottish Government COVID-19 Testing Strategy was published on 17 August 2020. This note presents a clinical and scientific review of that strategy in the light of the latest evidence of the state of the epidemic in Scotland and the latest understanding of testing capacity and demand forecasts in the next three months.

It reviews the principles and priorities of the Testing Strategy, and presents the consensus clinical and scientific view of prioritisation for additional testing capacity that is currently being built. Finally, it considers innovations in testing on the near horizon, and how they may be deployed in addition to the range of policy interventions designed to reduce COVID-19 transmission.

2. The State of the Epidemic

The senior clinical advisers published an evidence paper on 7 October 2020 that set out the evidence at that point in time on the state of the epidemic in Scotland.[1] That paper noted the rate of growth in the epidemic was increasing, with R significantly above 1 since the middle of September. The reproduction rate R in Scotland was estimated on 21 October as being between 1.2 and 1.5. The estimated doubling time for infections in Scotland was between 10 and 15 days on 21 October.[2]

Figure 1: R Number in Scotland: May-October 2020, lower and upper bounds



[1] https://www.gov.scot/publications/coronavirus-covid-19-evidence-paper-october-2020/
[2] https://www.gov.scot/publications/coronavirus-covid-19-modelling-epidemic-issue-no-23/

Test positivity – on all measures – has been increasing since the beginning of September. The WHO epidemiological criteria[3] for considering whether the epidemic is controlled in a country include test positivity, specifically, that less than 5% of samples test positive for COVID-19, for at least the last two weeks. In Scotland, test positivity on this measure (positive tests as a proportion of all tests) rose above 5% on the 6th October, and remains above this level.

We know the total number of confirmed cases is lower than the total number of new COVID-19 infections, as some people don't have symptoms and some people with symptoms don't come forward for testing. Issue 23 of *Coronavirus (COVID-19) Modelling the Epidemic in Scotland* estimates new daily infections in Scotland between 154 and 330 per 100,000 people. This equates to between 8,400 and 18,000 people becoming infected each day in Scotland.

When planning for testing capacity, given the importance of people with symptoms coming forward for testing and ongoing efforts to increase the proportion of those with symptoms who do get tested, the view of the clinical and scientific advisers is that estimates for testing demand should take account of the order of magnitude of the potential total number of new daily infections as estimated by this modelling.

3. Current Testing Context – Latest Understanding of Capacity and Demand

Currently, approximately two thirds of laboratory capacity to process PCR tests in Scotland derives from the UK Government Testing Programme (the Lighthouse Laboratory Network) and one third from NHS Scotland laboratory capacity. Capacity can fluctuate on a day to day basis. The current seven day rolling average of laboratory capacity indicates available capacity of approximately 20,000 tests per day in the UK Government programme and approximately 10,000 tests per day through NHS Scotland laboratories.

The Testing Strategy published on 17 August outlined plans to build resilience and sustainability in NHS Scotland laboratory capacity on a regional basis. The current forecast for NHS Scotland laboratory development projects capacity to increase significantly by the end of December 2020. UK Government laboratory developments currently project Scotland's population share of Lighthouse processing capacity to also increase by the end of December, and we are taking a cautious approach to capacity projections reflecting the complexities involved in delivering significant laboratory capacity expansion..

The best understanding at this time, therefore, is that the planned expansion of overall testing capacity to 65,000 tests per day by winter is on track. The expansion of NHS Scotland capacity is also expected to rebalance the processing ratio towards a more equal split between UKG and NHS Scotland laboratories.

[3] https://apps.who.int/iris/bitstream/handle/10665/332073/WHO-2019-nCoV-Adjusting_PH_measures-Criteria-2020.1-eng.pdf?sequence=1&isAllowed=yMay

The latest understanding of demand for testing over the next three months is derived from SG Health and Social Care Analysis Testing Demand Modelling activity. The main component parts of demand are:

- symptomatic demand (both from estimated daily new infections derived from the SG Covid Modelling outlined above, and from people with cold/flu symptoms that are not caused by COVID-19);
- testing of hospital patients – for both clinical care of patients and to reduce the risk of in-hospital transmission;
- routine weekly testing of health and social care staff;
- additional testing for outbreaks (which can include testing asymptomatic people at the beginning of outbreaks in order to stop onward transmission as quickly as possible);
- surveillance testing.

One of the most challenging aspects of demand to estimate is symptomatic demand. The component that is required for estimated daily new infections is derived from the SG Covid Modelling estimates, published weekly. In order to derive estimates for non-Covid symptomatic demand (such as cold and flu in adults and children) a population survey was carried out in September 2020 to ask people what they would do given various symptoms and scenarios.

This approach was used because other approaches to estimating demand – for example, past trends in NHS 111 calls or GP appointments for respiratory conditions – are likely to underestimate the incentive to seek a test caused by the desire to rule out COVID this year. We know it can be challenging for individuals and households to self-isolate for the full time required, and can anticipate people being motivated to seek testing to rule out COVID and therefore the requirement to self-isolate for up to 14 days.

The results of this analysis produce estimates of symptomatic demand (caused by both COVID-19 and illnesses with similar symptoms) in the region of 35,000 tests per day. In addition, existing commitments for all the other categories of testing outlined above mean the best current understanding of demand is that around 54,000 tests per day are estimated to be required by December 2020.

This overview of total demand and capacity through NHS Scotland and the UK laboratory network indicates that on current assumptions there is sufficient capacity to meet modelled demand to end December 2020.

It is important to note that both capacity projections and modelled demand can and do change based on progress with laboratory expansion and new evidence on demand as prevalence changes. The clinical and scientific advisers' view is for close, continuous attention to be paid to both capacity and demand assumptions and their component parts, given the critical nature of ensuring sufficient capacity to meet symptomatic demand and for direct clinical care in particular.

Based on above, the understanding of clinical and scientific advisers is that there may be some additional capacity, over and above that required for the groups outlined in this document, in the order of 10,000- 15,000 tests per day by December

2020. Section four sets out the current principles and priorities of the Testing Strategy. The consensus clinical and scientific adviser view on prioritisation of any additional capacity is set out in section five.

4. Testing Strategy Principles and Priorities

The Testing Strategy published on 17 August contained the set of principles below.

TESTING STRATEGY – PRINCIPLES

1. Testing is part of our overall public health approach designed to minimise transmission of the virus, in line with our overall strategy of driving the number of cases of COVID-19 in Scotland to the lowest levels possible.

2. Our priorities for testing are guided by scientific, clinical and public health advice from our expert advisory structures.

3. Our approach to testing, including prioritisation, is flexible and adaptable to the prevailing conditions of the pandemic at any time.

4. Our approach to testing takes full recognition of the limitations of testing (particularly at low levels of disease prevalence) as well as the opportunities of testing.

5. Our overall priority at this stage of the management of the disease is rapid identification and testing of people with symptoms.

6. Asymptomatic testing will increasingly be used on a risk based approach to both minimise transmission through active case finding and to reduce harm to individuals at high risk.

7. The deliverability of any new testing priorities and pathways will be considered at an early stage to maximise successful implementation.

8. The capacity to accurately and efficiently record, report, interpret and respond to every test in a timely manner is critical.

The collective view of the clinical and scientific advisers is that this set of principles remains appropriate for guiding the testing strategy going forward. In addition, it is recommended that an additional principle is added to reflect the importance of ensuring sufficient *access* to testing. The view of advisers is that there is a risk of focussing on processing capacity overshadowing the importance of sample collection – the ease with which people who have symptoms can access a test, or those groups who are routinely tested can access their test, and the speed of obtaining results.

The five priorities for testing in the current strategy are set out below:

TESTING PRIORITIES – NEXT PHASE

1. Whole Population Testing of anyone with symptoms (Test & Protect).

2. Proactive Case Finding by testing contacts and testing in outbreaks.

3. Protecting the vulnerable and preventing outbreaks in high risk settings by routine testing.

4. Testing for direct patient care, to diagnose and to treat, and to support safe patient care as NHS services restart.

5. Surveillance to understand the disease, track prevalence, understand transmission and monitor key sectors.

The view of clinical and scientific adviser is that these remain appropriate overall general priorities for testing, given the prevailing conditions of the pandemic in Scotland and the likely timescales for treatments and vaccines that will impact on the epidemiology of the pandemic.

In particular, it is the unanimous view of clinical and scientific advisers that the overriding priorities for testing capacity in Scotland are symptomatic demand and clinical care of patients.

5. Priorities for additional capacity in PCR Testing

The current plans to build additional capacity in both NHS Scotland laboratories and UK Government programme are intended to build sufficient capacity to both meet the demand as set out above, and to enable some extension of testing to priority groups. Clinical and scientific advisers note the statement on population case detection produced by SPI-M, updated on 11th September, that:

> *"SPI-M-O agree that the top priority should be to rapidly test symptomatic people and isolating their contacts. Testing symptomatic people is an order of magnitude more likely to identify someone infected with SARS-COV-2 than testing asymptomatic people in an outbreak area. However testing alone will not reduce transmission if people cannot or will not self-isolate, following the receipt of a positive test".*[4]

As set out in section four above, we are in agreement that the overall priority for testing is to meet symptomatic demand, and that this will be more challenging in winter when other respiratory viruses will be circulating.

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4 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/926953/S0743_SPI-M-O_Statement_on_population_case_detection.pdf

Our consensus view of the prioritisation of capacity, over and above that required to meet symptomatic demand, clinical care requirements and existing commitments, is that the focus in any extension of routine regular asymptomatic testing should be on protecting those most vulnerable to severe harm.

Severe harm in this context includes those groups at higher risk of mortality from contracting COVID-19 – for which there is now overwhelming evidence that the highest risk factor, by orders of magnitude, is age.

In the past week (15- 21th October) there have been 81 deaths where someone has died within 28 days of their first positive test result for Covid-19 in Scotland, which is over double the number of deaths over the week 8-14th October .

Cases in older people remain significantly lower numbers than in younger age groups, but the proportion of cases in the 60+ age groups has been increasing in recent weeks. Case numbers in the 0-19 age range have declined slightly over the past week, in the 20-39 age range this has remained relatively static with only minimal increases for other age groups of around 10%, this week saw an increase in 30% for cases in the over 80s.

It is clear from these data that Scotland is following the pattern evident in other countries: infections starting in younger age groups steadily progressing through the population to reach older age groups at significantly higher risk of adverse outcomes.

Figure 3: Number of new cases per 100,000 people by age

Cases over 7 days per 100,000	16 October 2020	17 October 2020	18 October 2020	19 October 2020	20 October 2020	21 October 2020	22 October 2020
0 - 19 yrs	106	104	93	92	93	93	96
20 - 39	202	204	189	189	191	196	205
40 - 59	172	178	164	166	171	179	185
60 - 79	108	111	105	106	109	116	121
80+	112	120	117	114	115	136	148

We also know from evidence and experience that care homes are particularly high risk settings. There has been a recent increase in cases associated with care homes. As of the 21st of October 11% of care homes had a current case of suspected COVID-19.

Given this evidence, the consensus view of clinical and scientific advisers is that prioritising additional testing capacity to protect those most vulnerable to severe harm should focus on additional routine testing to mitigate the risk of asymptomatic transmission within care homes. This could include extending routine testing to visiting staff in care homes, stratified by risk – focussing first, for example, on those delivering close contact personal care to care home residents - to designated care home visitors, and to staff who provide care at home for those most vulnerable to harm.

We also recommend expanding testing of healthcare workers – with a focus on those caring for the more vulnerable patient groups and potentially too in areas where we are seeing higher community prevalence. Testing for surveillance – at a population level and in key population groups including healthcare workers – should

also be prioritised. This is important for early warning and to inform strategic decisions.

In addition to protecting the most vulnerable, other priorities include: extending asymptomatic testing to more groups of close contacts of confirmed positive cases, when recommended by local health protection teams, and more intensive use of asymptomatic testing in outbreaks. This would help shut down outbreaks as quickly as possible, reducing their contribution to overall community transmission.

This clinical prioritisation has been carried out on the basis of PCR testing capacity, rather than new technology which may or may not come on stream, and may or may not offer a similar level of test sensitivity and specificity.

6. Innovations in testing and potential developments

The current gold standard test for the COVID-19 virus is PCR testing. The above sections of this note are based on our current understanding of the context for PCR testing capacity and demand in the next three months in Scotland.

PCR testing has been very effective in the management of symptomatic disease to diagnose COVID-19 as it detects the presence of the causative agent in the context of symptoms that indicate possible infection. It is sensitive (it has a low false negative rate) and specific (a low false positive rate).

The standard PCR-based test, as with all tests, has some limitations. Among the most significant of these is that detection of virus RNA does not always equate with infectivity – for example, the test may remain positive after the patient has become non-infectious and remnant RNA is being amplified. In the presence of relevant symptoms this is seldom an issue but this feature of the test can limit is accuracy in the context of asymptomatic individuals and when a symptomatic individual has recovered.

Additional limitations of standard PCR-based testing are that results are not rapid as samples require extraction, the PCR reaction takes a finite time, and scaling up the numbers of tests conducted requires a linear expansion in physical and human resource.

New innovations in testing may bring more rapid results and significant expansions in capacity, which may play a role in management of the pandemic. The increasing evidence that cases can be asymptomatic requires tests that can be conducted at scale and repeated amongst asymptomatic but at-risk groups. This approach would lead to an increase in isolation of infective, asymptomatic cases and it is essential that as capacity to test for COVID-19 using new innovations are expanded the capacities that support isolation also increase. There is no point identifying cases without being able to support isolation and ensure compliance with this.

In addition, on occasions, it is essential to be able to test rapidly to allow individuals to enter high-risk environments where an unidentified infected case would have

serious consequences because of new introduction of COVID-19 into an environment of highly vulnerable individuals.

The current gold-standard PCR technique does not fulfil the dual, but separate, challenges of very large-scale testing or of rapid results. There are emerging technologies that address these limitations. These technologies are developmental but disruptive for our management of COVID-19. They will come with different profiles of techniques, speed and volume and when assessed against PCR-based testing and will have different sensitivity and specificity.

Testing at scale

There are broadly three methods to increase scale:

1. technological developments that allow scale but require prior sample processing (and, therefore, are no quicker that current PCR) (eg endpoint PCR, LAMPORE);
2. technological developments that do not require prior sample processing and therefore are quicker (eg lateral flow antigen devices);
3. Sample pooling, using standard PCR.

The balance of benefit from volume of tests completed versus accuracy is at the heart of the global debate on the usefulness of these novel tests. The reduced sensitivity may be mitigated in part by repeat, frequent testing. A potentially infectious case can be identified with a less sensitive test repeated more frequently than a fully sensitive test that cannot be performed so frequently. Lateral flow antigen devices are likely to be the first available of these technologies. Sample pooling is another potentially available technique in the short term may offer increases in testing capacity..

The clinical and scientific advisers also note and concur with the consensus statement for SAGE on mass testing published on 31 August 2020.[5] That consensus statement notes testing should be driven by public health considerations and priorities, and states:

“mass testing is most likely to be beneficial and feasible in cluster outbreak scenarios and well defined higher risk settings (eg health and care settings, higher risk occupations such as food processing facilities, universities) where it can help detect and prevent large outbreaks early, and compliance can be measured and moderated. …Finding the right combination of tests is not trivial and will require careful pilot studies”.

New technology and rapid frequent testing are potentially significant new interventions to enhance our overall pandemic response strategy. The testing programme will need to engage with these techniques as they emerge. It is critical to acknowledge that the evidence base for these new technologies – especially in

5 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/914931/s0712-tfms-consensus-statement-sage.pdf#:~:text=Multidisciplinary%20Task%20and%20Finish%20Group%20on%20Mass%20Testing,a%20multidisciplinary%20group%20established%20to%20examine%2C%20from%20technological%2C

real world applications in specific population groups – is small but growing. Given this, the view of clinical and scientific advisers is that the testing programme should engage in these new technologies in the form of pilots in the first instance, to develop better understanding of how each technology may operate in specific contexts. Hand in hand with this, the testing system needs to be prepared for rapid change to adopt these techniques should their value be demonstrated following pilot evaluation.

7. Conclusion

In summary, in our review of the current Testing Strategy, advisers note the considerable uncertainty around the likely prevailing pandemic conditions in Scotland in the next three months. It is too early to detect any impact on transmission from the restrictions introduced on 9th October. We note the findings published on 15th October in Issue 22 of *Coronavirus (COVID-19) : Modelling the epidemic in Scotland*[6] that indicate the number of contacts per person has fallen since 22 September, and the reduction in the numbers of people visiting other locations, in particular other homes, in recent weeks. This suggests the rule of six and restrictions on households meeting are having some effect which it is hoped will feed through to confirmed cases.

We note that forecasts of projected capacity and demand for PCR testing are subject to much uncertainty. Our considered view is that ensuring there is sufficient capacity for testing all those with symptoms and testing for clinical patient care are the overriding clinical and scientific priorities for the next three months. In addition, in considering the principles of the Testing Strategy, our advice is there should be greater focus on the importance of fast turnaround times, so that testing achieves its intended purpose of reducing transmission by enabling prompt contact tracing and isolation of potentially infectious close contacts. A greater focus on enabling ease of access to testing for all communities is also recommended.

We note the current efforts to build capacity in both NHS Scotland and UK Government laboratory programmes are forecast to produce additional capacity by December 2020. The clinical and scientific view is that this should be prioritised for:

- more intensive asymptomatic testing where that is most likely to find positive cases and thereby contribution to reducing transmission (by testing close contacts and more intensive asymptomatic testing early in outbreaks); and
- extensions of routine testing to protect the vulnerable.

Applications of new testing technologies should be carefully piloted to build the evidence on the extent to which they achieve their intended outcomes.

[6] https://www.gov.scot/publications/coronavirus-covid-19-modelling-epidemic-issue-no-22/