Who and how to test in covid-19 – June 18th
[Redacted]

Testing in the context of SARS-CoV-2 detection and covid-19 disease serves a number of purposes. These include:

Diagnosis/case identification
Monitoring of disease activity in the population/communities (surveillance)
Assessments of health protection measures
Avoidance of transmission

The modalities of testing are:

- Virus detection
    - PCR-based detection
    - LAMP technology
    - Viral genome sequencing
    - Virus culture

- Antibody testing

Test results (with the exception of viral genome sequencing) are binary, either positive or negative and this result influences the purpose of performing the test. (A positive pcr-test will exclude someone from work but a negative test will allow return to work).

Principles for testing in the covid-19 epidemic.

At the current time there are some principles which guide selection of testing methodology and people tested. These have guided and should continue to guide policy as that evolves in response to where Scotland is in the epidemic cycle and the development of new innovative technologies. These include:

- A “test” is only part of a pathway which must include the “upstream” determinants of the success of the test and strategy as a whole. A test for diagnosis can only be helpful with a clear strategy for case identification. This will require ensuring the public’s understanding of the purpose of a test, clarity on who should be tested and ease of obtaining the test, the result and a management plan associated with that result.
- The speed with which the result is obtained for most viral detection and antibody tests will influence the policy and the public acceptance. Swift results and turnaround times are highly likely to be more effective in disease control and management.
- PCR-testing for SARS-Cov-19 is a good test for case identification but its precision and its utility in screening is more uncertain.
- No test is 100% accurate and the false sensitivity and false positivity will impact on the utility of testing at different levels of prevalence in the population. At the height of the epidemic the value of a test in either case

identification or screening will be different from at much lower levels of prevalence such as in the tail of the epidemic.

- Sensitivity of pcr-testing in asymptomatic individuals is an unresolved issue because of the gold standard (whether they get the disease) is not a universal outcome of a positive test (asymptomatic carriage and resolution)
- For diagnostic purposes a less than 100% accurate test will need to be interpreted in the light of the pre-test probability (which includes disease prevalence as well as patient specific factors).
- A positive antibody test at the time of writing does not confirm immunity from subsequent exposure to SARS-CoV-2. It does show that there has been recent previous infection.
- A test result will have an impact on the individual, those in their home and work place and the wider community.
- Where there is uncertainty testing should be conducted with rigour and in such a way as to generate new knowledge

Who to test?

1. Symptomatic testing for case identification

- Accurate and swift symptomatic testing with complete capture of all cases is an absolute priority as it triggers the main measure of control in the phases after release of lockdown – the test and protect programme. An increased focus on case finding must be encouraged so that more symptomatic people come forward for testing and trigger the in to Test & Protect pathway. Further data on uptake and follow-through is needed to understand the current gap. This overwhelming priority needs widespread communication as it is so different from the early messaging for those with symptoms.
- Extending testing to those with atypical symptoms or who are oligosymptomtaic/presymptomatic has the potential to identify more cases who may be shedding virus. These extended symptoms might include diarrhoea, thromboembolism etc.
- Selective use of viral genome sequencing to forensically identify transmission and spread should be integral to case identification when the disease is at low levels in order to be certain that transmission (or not) from an index case has occurred and that the T&P public health measures are working.
- Antibody testing may have utility in diagnosis/case identification where symptoms are compatible but presentation is after the virus shedding phase.

2. Asymptomatic testing for case identification

- Asymptomatic pcr-testing, can only be justified as a screening use of this testing modality where there is clear and certain gain from identifying a positive case. The clear gain is where identified individuals would expose high risk contacts either through work or home – patients with comorbidity, the elderly or where there is a closed community with a high likelihood of rapid transmission because of the difficulty of using PPE. The certainty of gain has to be assessed against the case prevalence rate. At low prevalence rate an

apparently low false positivity rate can have a significant effect on the utility of the test.

- Testing asymptomatic individuals stratified by characteristics that place them and those they live with or come in contact with could be extended to communities of particularly high risk (for example the homeless, those with high burden of comorbidities, BAME).

- The testing of asymptomatic “contacts” of proven index cases is a group that could be selectively considered. This is undertaken in some countries and it may be that this simply results in better engagement of the contact in the process of isolation. It is possible to see utility in managing clusters where early identification of a contact as positive (perhaps at the presymptomatic stage) would allow for additional contacts to be isolated (and tested). It maybe that contact PCR-testing could be coupled with serology testing.
- PCR Testing of asymptomatic HCW and carehome workers has been the subject of recommendations and policy elsewhere. It is suggested that the general principles outlined above should apply to the strategy for testing these groups. Care must be taken over the frequency of re-testing in such employment-specific cohorts. It is not clear how frequent this should be to be effective.

3. Surveillance testing

Surveillance testing in the main is undertaken by measuring antibodies to the SARS-CoV-2 virus. This shows prior infection and thus activity in the population if repeated over time. If and when immunity linked to an antibody test is proven it would show those who were able to work without danger in infected areas (immunity passports). The level of an immunity predicting antibody would also establish the level of immunity in the population and allow the establishment of “herd immunity” gained either through disease progression (not an aim) or in time through vaccination. At the current time there is no evidence of immunity from antibodies.

Antibody testing should at the moment aim to generate knowledge – of disease activity and whether antibodies provide immunity. The only potential advantage of knowing whether a group of a certain workforce have antibodies is if/when immunity is proven. This could arise from studies outside of Scotland/UK.

Antibody testing should be for surveillance and should be targeted at specific groups where knowledge will be useful. These are public health matters but could include schools, universities, and certain public sector workforce.

Within the HCW antibody testing should concentrate on the research study that will generate knowledge of immunity – the SIREN study.

PCR-Testing for under 5s has the potential to understand transmission and control in nursery school. There is the potential to do this by saliva testing rather than swab testing which is upsetting in this age group.

- Viral genome sequencing as surveillance has the potential to identify stable subtypes or new introductions in the population/community and should be expanded at times of management with lower disease prevalence

4. Additional considerations that will influence a successful covid-19 testing plan include:

- Public confidence in testing needs to be established and maintained. The importance of ensuring there is clear justification for the purpose of testing, how the data will be used, and confidence that results are acted on is key to this. A visible and repeated public communication strategy should be an integral part of plans.
- Clear communication of the evidence that underpins the decision making around testing is important. Consistency of strategic approach between groups will help compliance with, and confidence in, testing.
- Any decisions on how testing capacity is used must also take account of the impact beyond disease management on the people being tested. Thought has to be given to accessibility and design of testing services, and the demands placed on those who are tested.
- It will be important to prioritise groups for testing as outlined above. However, we must also evaluate the usefulness of the testing plans we are undertaking as we go, and be agile in how we adapt and direct our testing as a consequence. This may include patient/public feedback
- Any strategy for PCR testing must be mapped against our priorities for antibody and serological testing, to provide a full picture of coverage.
- Changes to the testing strategy has implications for the data flows and how these link into ECOSS. This must be taken account of in the decision making and service design.

5. Innovation in testing that may change testing strategy

Innovations in the way that tests can be undertaken are underway. These have the potential to give results much quicker and on a near-patient format

New Processes to allow work at Scale
Saliva-based testing
Guanidine viral inactivation
Pooling of Samples
“End-point” PCR
High Scale - Lower sensitivity at speed
LAMP technology.
High sensitivity - Low scale
Viral sequencing developments
Near patient testing
Expansion of cartridge based testing
LAMP technology
Multiplex testing
Testing for multiple respiratory pathogens