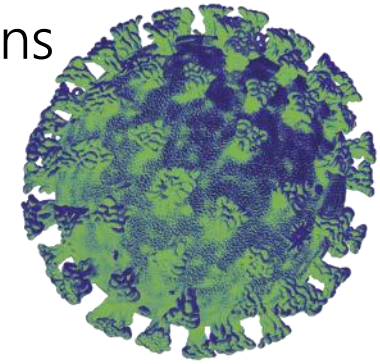
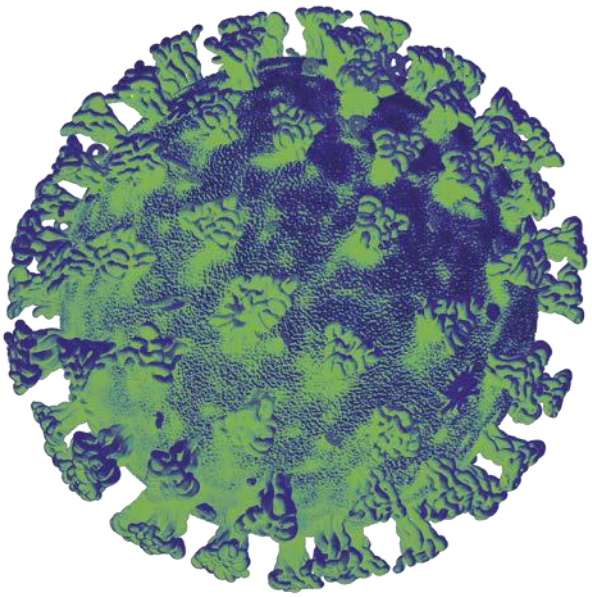
Llywodraeth Cymru
Welsh Government

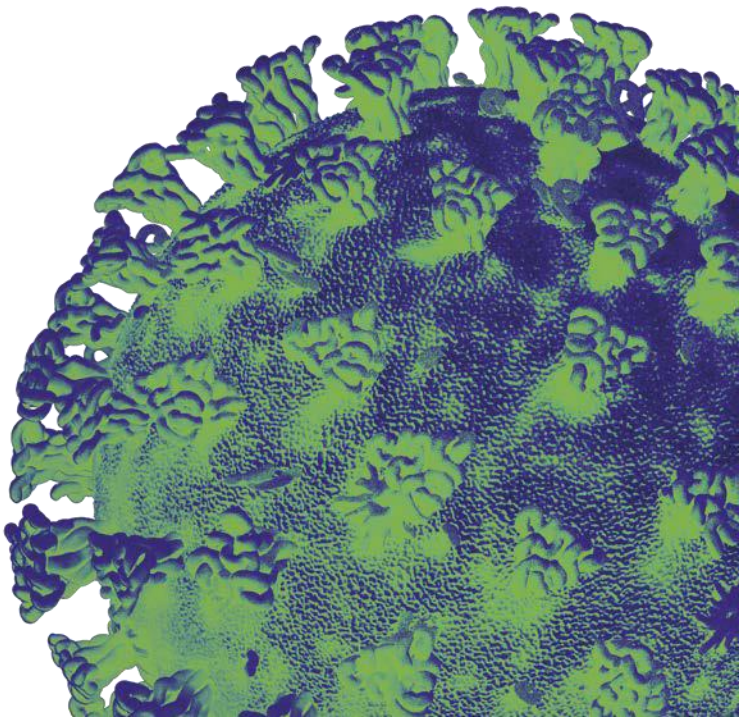
Technical Advisory Group

Consensus Statement on Use-Cases for Near Patient and Point-of-Care Tests for detecting SARS-CoV-2 viral RNA or Antigens

29 September 2020







Welsh Government COVID-19 Technical Advisory Group: Consensus Statement on Use-Cases for Near Patient and Point-of-Care Tests for detecting SARS-CoV-2 viral RNA or Antigens

Introduction

The acute diagnosis of COVID-19 has hitherto been based on the detection of viral RNA by RT-PCR performed on a number of laboratory platforms. New technological developments mean that there will soon be a number of new platforms to detect either viral RNA or antigens that may be deployable as Near Patient Tests (NPTs) or Point of Care Tests (POCTs).
The details of the tests and their performance characteristics are not yet available. However there is a need to assess potential use cases.

Key Elements for Consideration

Single Target vs Multiplex Testing

Currently the majority of samples are tested for SARS-CoV-2 alone. As we move into the winter season there will be a need, in some scenarios, to test for additional respiratory pathogen targets. Some of the proposed NPT/POCT can test for additional targets, including FluA, FluB, and RSV.
The scenarios where additional target testing would be useful include:

- When test results would determine the management of the individual patient. For example, if a symptomatic patient in primary or secondary care would be commenced on oseltamavir if positive for Flu.
- When test results would determine streaming within healthcare or similar situations. Currently patients are streamed according to COVID status. In the winter there will be a need to additionally stream taking account of Flu status.

For asymptomatic screening, specifically for COVID-19, multiplex testing would not be required.

Diagnostic Sensitivity

The Diagnostic Sensitivity, along with the prevalence of disease in the test population, determines the likelihood of false negative results.
The table below shows the numbers of predicted false negative results if 1,000 people were tested at different disease prevalences for tests with sensitivities of 70, 80, or 90%. At low prevalences, such as the current background rate in the UK population of 0.05%, the number of false negative results would be zero even with a test sensitivity as low as 70%. However the number of false negatives becomes significant as the disease prevalence increases.
A higher test sensitivity is important in circumstances where the disease prevalence is higher, and the impact of a false negative result is high. For example, if the test is used for streaming symptomatic patients according to COVID-19 status, the prevalence in a symptomatic individual is likely to be higher, and the impact of a false negative result would be to stream the patient in a COVID ‘green’ area.
Lower test sensitivity may not be an issue if testing in low prevalence populations. For example, currently testing asymptomatic school children would give extremely few false negative results, even with a relatively poor test sensitivity. However, if

prevalence in the population increased, false negatives may become an issue.
It should be noted that the same issues around sensitivity need to be considered for any additional respiratory test targets.

Sensitivity (%)	Prevalence (%)	NPV	Negative results/1000 tests		
			Total negatives	True negatives	False negatives
70	0.05	1.0	980	980	0
	0.1	1.0	979	979	0
	0.5	1.0	977	975	2
	1	1.0	973	970	3
	5	1.0	946	931	15
	10	1.0	912	882	30
	20	0.9	844	784	60
80	0.05	1.0	980	980	0
	0.1	1.0	979	979	0
	0.5	1.0	976	975	1
	1	1.0	972	970	2
	5	1.0	941	931	10
	10	1.0	902	882	20
	20	1.0	824	784	40
90	0.05	1.0	980	980	0
	0.1	1.0	979	979	0
	0.5	1.0	976	975	1
	1	1.0	971	970	1
	5	1.0	936	931	5
	10	1.0	892	882	10
	20	1.0	804	784	20

Diagnostic Specificity

The Diagnostic Specificity of the test, along with the disease prevalence, determines the likelihood of false positive results.
The table below shows the predicted numbers of false positive results if a population of 1,000 people with different prevalences, were tested using a test with a specificity of 90, 95, or 98%. As can be seen, the number of false positives is relatively high, even with high specificity. When the prevalence is low, the proportion of false positives is extremely high.
A test would need to have a high specificity (and low false positive rate) when a positive result would have significant impacts. For example when:

- The result would be used to determine streaming of patients in healthcare or similar settings. False positives would be put at risk if streamed in a COVID-19 'red' area.
- The result would initiate 'closing' of a care home for 28 days
- The result would lead to exclusion of the patient from activities (e.g. school)
- The result would initiate isolation of the patient and contacts.

A low specificity can be mitigated by confirmatory testing. However, a rapid system would be required in order to resolve issues.
It should be noted that the same issues around specificity need to be considered for any additional respiratory test targets.

Specificity (%)	Prevalence (%)	PPV	Positive results/1000 tests		
			Total positives	True positives	False positives
90	0.05	0.0	100	0	100
	0.1	0.0	101	1	100
	0.5	0.0	104	4	100
	1	0.1	108	9	99
	5	0.3	138	43	95
	10	0.5	175	85	90
	20	0.7	250	170	80
95	0.05	0.0	50	0	50
	0.1	0.0	51	1	50
	0.5	0.1	54	4	50
	1	0.1	58	9	50
	5	0.5	90	43	48
	10	0.7	130	85	45
	20	0.8	210	170	40
98	0.05	0.0	20	0	20
	0.1	0.0	21	1	20
	0.5	0.2	24	4	20
	1	0.3	28	9	20
	5	0.7	62	43	19
	10	0.8	103	85	18
	20	0.9	186	170	16

Quality Assurance

There is good evidence that optimization of pathways using well designed use of POCT can be both clinically effective and cost efficient. There are clear benefits of using POCT especially where a fast turnaround time, accessibility or sample size is an issue. However, POCT is usually carried out in a busy environment with little or no 'thinking-time' before a change in patient management is instigated. The major risks arise from poor operator competency, lack of supervision, governance, failure to implement quality assurance processes, inappropriate testing by inexperienced personnel, lack of understanding on the limitations of use and uncertainty on how to act on the results. Adequate checks and balances must therefore be in place to prevent errors and reduce risks.

Users of POCT should have a sound understanding of the principles of quality assurance (QA). This is a systematic process of verifying that a product, or service is meeting the specific clinical requirements and includes, internal quality control (IQC), External quality assessment (EQA), Clinical audit and Risk Management. This includes the measures taken to ensure investigations are reliable and safe and includes:

- Having the right governance structure in place
- Correct identification of the patient
- Choosing the right test
- Obtaining the right sample (at the right time)
- Undertaking the right test procedure
- Undertaking IQC and EQA checks
- Recording results promptly and correctly
- Interpreting results accurately
- Taking appropriate action
- Documenting all procedures and actions
- Identifying and preventing errors
- Implementing quality improvements

Test Duration

The duration of the test will determine the required logistics and utility.

A test that takes 10 minutes may be practical in non-healthcare or primary –care settings for individuals to wait for results. However a test that takes 60 minutes would be less practical.

A test that takes 60 minutes may be practical in a secondary healthcare setting as part of a patient assessment, and may improve turnaround times as a NPT. However, rapid tests (1 hour turnaround) will be available at all acute hospitals.

For testing of symptomatic individuals, there will be an issue of segregation while waiting for the test, and then result. A longer turnaround will cause increased challenges while patients await results.

Daily Throughput

The number of tests that can be performed in a working day on each platform will be a factor in determining the utility of the platform. Higher throughput would require multiple platforms.
Some platforms can perform 1 test per hour, while others can deliver more.
Examples of use cases include:

- In an average Welsh GP Practice of 7812 patients, there will be an average of 23 consultations due to seasonal respiratory infection per week over winter (ranging from of 9 to 69 consultations per week over winter). So demand in an average practice for symptomatic testing would increase from 2 tests per day to a peak of 14, with an average of 5 tests per working day. It follows that it is very likely that more than one platform would be needed in an average practice[1].
- A Cluster-based primary care respiratory centre, covering a typical population of 50,000, would perform a mean of 29 tests a day (with a range from 15 tests to a peak of 89 per day over the winter). This assumes all in-hours cases are diverted to this cluster respiratory hub. Again multiple platforms would be needed.[1]
- In Urgent Primary Care (GP-Out of Hours), the proportion of consultations coded with acute respiratory infection over winter ranges from 9% to 56% of all consultations. [1] In the last four winters in ABMUHB/SBUHB GPOOH, consultations are a mean of 257 per day November to March (range 187 to 359) with 50% being face to face over three sites. Thus a single GP OOH base could expect between 3 and 60 tests per day.
- For testing in a closed setting, such as a care home, the number of individuals to be tested would be a factor. For a care home with 50 residents, a capacity of 50 tests in a working day would be needed to test all residents in a day.

Complexity/Ease of Use

The test should ideally be easy and simple to use. This will determine the type of staff who can use the test and the level of training required.

Training

There should be training available for the platform which should be straightforward. Ideally the training would be delivered through ‘Train-the-Trainer’.

IT/Data Issues

There should be a mechanism of recording results electronically. Ideally the test should have the ability interface into WLIMS to record results plus quality metadata.

[1] Morbey RA, Elliot AJ, Harcourt S, Smith S, de Lusignan S, Pebody R, Yeates A, Zambon M, Smith GE (2018). Estimating the burden on general practitioner services in England from increases in respiratory disease associated with seasonal respiratory pathogen activity. Epidemiology and Infection 146, 1389–1396. https://doi.org/ 10.1017/S0950268818000262

Estates Requirements

The estate requirements will determine the setting where the test can be used. These will include:

- Space. Testing should ideally be performed in a designated area. Platforms will have different footprints
- Electricity supply may be required.
- Water supply may be required.
- Handwashing facilities would be required

Waste disposal

Consideration should be given to waste disposal. SARS-CoV-2 is a Category 3 organism and waste disposal should take account of whether the virus is inactivated in the testing process, and any chemical disposal needs.

Potential Use Cases

The following potential use cases could be considered. All would need assessment against the criteria above to establish whether they are practical, and, if so, how a service should be configured.

SETTING		**USE**
Primary Care	General Practice	Differential Diagnosis of patients presenting with symptoms of possible COVID, Influenza, Pneumonia, COPD & Asthma
	"Cluster" Respiratory Centres	Differential Diagnosis of patients presenting with symptoms of possible COVID, Influenza, Pneumonia, COPD & Asthma
	Urgent Primary Care (GP-OOH)	Differential Diagnosis of patients presenting with symptoms of possible COVID, Influenza, Pneumonia, COPD & Asthma
Secondary Care	ED	Diagnosis of symptomatic patients
		Screening of all admissions
	AMU/ASU	Screening of all admissions
	Testing Unit	Pre-screening prior to surgery
		Pre-screening prior to invasive intervention
		Pre-screening prior to chemotherapy
		Staff screening at beginning of shift (specified areas)
Care Home	Care Home	Diagnostic testing of symptomatic patients
		Outbreak testing
		Screening of all admissions
		Screening of all visitors

		Staff screening at beginning of shift
Prisons	Reception	Reception of all new admissions (Day 0 , 8)
	Hospital	Diagnostic testing of symptomatic prisoners
		Staff screening at beginning of shift
Schools		Diagnostic testing of symptomatic children
		Outbreak testing
		Staff screening at beginning of shift
		Pupil screening at beginning of day
Universities	Student Health	Diagnostic testing of symptomatic students
	?	Student screening at beginning of day
Community	Drop-in centre	
	Pharmacy	Diagnostic testing of symptomatic patients
MTU	Care Home	Outbreak testing
	Workplace	Outbreak testing

Guidance Documents

Medicines and Healthcare Products Regulatory Agency (MHRA) guidance:
Management and Use of IVD Point of Care Test Devices.

Welsh Government Policy and procedure on the Management of Point of Care Testing:
What, when and how? WHC (2017) 034