COVID-19 Scientific Advisory Group
Rapid Evidence Report

Do the rapid COVID-19 tests on the market represent a feasible opportunity for Alberta?

1. **What are the reported performance characteristics of the rapid COVID-19 tests that have been approved for commercial (diagnostic) use in Canada?**
2. **What are the optimal strategies for deployment of rapid testing, to improve either clinical care or outbreak control in health care and community settings?**

Context

- It is unclear how the rapid (point-of-care) molecular and antigen tests for COVID-19 tests compare to each other.
- Five point-of-care testing devices/systems have been approved for diagnostic use by Health Canada:
    1) BD Veritor System for Rapid Detection of SARS-CoV-2 (Becton Dickinson and Company)
    2) BKit Virus Finder COVID-19 (Hyris Ltd.)
    3) ID NOW COVID-19 (Abbott Diagnostics Scarborough Inc.)
    4) Panbio COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostics)
    5) Xpert Xpress SARS-CoV-2 (Cepheid).
- The federal government has committed to distributing the consumables for the Abbott ID NOW and PanBio testing kits to each Canadian jurisdiction, however, the strategy for deploying the rapid test kits will be the responsibility of the public health leaders in the provincial/territorial governments.
- The implementation of rapid testing in other jurisdictions offers an opportunity to learn from their experiences in deploying rapid COVID-19 tests and avoid potential missteps. These implementation activities have included mass assessments, population-level testing to determine prevalence, returned traveler assessment, staff screening at long-term care facilities, and school testing.

Key Messages from the Evidence Summary

- The body of evidence for rapid testing platforms is poor – many of the studies are at high risk of bias. It is important to note that the evidence on this topic is rapidly evolving and meta-analytic findings should be considered carefully rather than accepted as truth. No high-quality evidence was identified regarding deployment of rapid tests.
- Studies validating rapid test platforms are generally at high risk of bias and often do not report the sensitivity and specificity of the platform. Instead, the reported results are framed as concordance with the reference standard (usually an NP swab tested on an RT-PCR platform). The applicability of these results may be limited in the Alberta context. The majority of the literature focused on the nucleic acid testing platforms (Abbott ID NOW, Cepheid Xpert Xpress) rather than the antigen testing platforms (BD Veritor, Panbio). No studies were identified that evaluated the BKit Virus Finder platform. The lack of studies for antigen-based rapid tests is likely related to their very recent introduction as diagnostic options.
- The manufacturers' specifications for testing kits are often higher than the characteristics seen under real-world conditions. According to the manufacturers: the Abbott ID NOW is 95% sensitive and 98% specific; the Cepheid Xpert Xpress 100% sensitive and specific; the BD Veritor platform is 84% sensitive and 100% specific; and the Panbio platform is 91% sensitive and 99.8% specific.

- In the literature, pooled meta-analytic estimates of the clinical testing characteristics of rapid nucleic acid tests suggest that the sensitivity of Abbott ID NOW is 77-80%, with a specificity of 99-100%. The literature for the Cepheid Xpert Xpress platform suggests the platform is approximately 99% sensitive and 97-100% specific.
- In the literature, estimates of testing characteristics suggest that the Panbio system is 73-98% sensitive and 100% specific, while estimates for the BD Veritor system range from a sensitivity of 84-96% and specificity of 99-100%.
- Guidelines from the World Health Organization, Health Canada, and the United States CDC suggest that rapid testing should be deployed in settings where repeat testing and/or rapid turnaround times are important. Situations where rapid tests could provide benefit include outbreak control, proactive monitoring in populations with high community prevalence, monitoring high-risk congregate living settings (eg. homeless shelters), or in communities where standard testing is not available, such as remote Indigenous communities.
- Beyond the clinical sensitivity and deployment strategy, there are practical implementation considerations to be made. The availability of the test kits are a major driver of which assays are implemented. The Public Health Agency of Canada (PHAC) is distributing a large number of Abbott ID NOW and Panbio kits and instruments at no cost to the province, while the technically superior Cepheid kit has relatively low availability and would need to be purchased by APL for implementation.
- Expert opinion on the deployment of rapid test platforms suggest that these tests can be used as a surveillance tool for lower-risk populations to conserve diagnostic testing capacity for populations where accuracy is paramount.

Committee Discussion

The committee reached consensus on the recommendations. There was a robust discussion among committee members about the possible uses of the testing platforms that will help to meet the public health goals of the COVID-19 response in Alberta. There was general agreement among committee members that rapid testing can potentially bolster a surveillance approach to monitor COVID-19 in key community settings (such as in schools or traveler screening) or in congregate living settings. It is still unclear how use of rapid tests should be prioritized but outreach testing in outbreak assessment and augmenting standard testing to improve laboratory workflow during capacity challenges were discussed. Committee members suggested further that these tests could have a significant role in improving outreach testing capacity in transient populations and for Indigenous populations, and in rural/remote settings. The lower sensitivity of the rapid testing platforms was noted, and it was discussed that using the rapid tests as “screening” is not the normal way that screening tests are conceptualized. The benefit to rapid tests are their speed rather than accuracy, as the risk of false negatives means that the individual will need to be tested with the more accurate RT-PCR method to ensure their SARS-COV-2 status if the individual has symptoms or has been exposed. As with any novel diagnostic test, it was noted that the rapid tests will need to be validated by Alberta Precision Laboratories prior to implementation.

Recommendations

1. Rapid testing platforms under consideration in Alberta must be evaluated in comparison to the molecular tests currently used by Alberta Precision Laboratories (the reference standard) for the diagnosis of COVID-19.
   Rationale: It is not expected for all these tests to be equivalent to the laboratory-based tests currently in use; however, understanding the diagnostic characteristics (eg, sensitivity, specificity, etc) will be key in understanding whether they should be deployed and, if so, in what settings.

2. A strategy for the deployment of rapid testing should take into account the following considerations: platform accuracy in special populations (eg. children, immunocompromised individuals, pregnant women, etc.); equity in distribution; tolerance of the collection method (ie. nasal vs. NP swab); and biosafety (ie. PPE requirements, specimen collection & handling, biohazard waste management).

Practical Considerations

- If the lower sensitivity of these tests is confirmed during AB validation, then repeat testing of negative samples with NP or OP swabs using an accepted APL test will be required. However, as the tests are reportedly highly specific and the likelihood of false positive tests is low, positive tests do not need followup validation which could reduce the number of samples sent to the APL diagnostic labs, if the test is used in higher pretest probability populations, which could substantially increase the efficiency of the laboratory workflows. Deployment of the rapid tests at existing assessment centres could also improve the turnaround time of tests for symptomatic individuals, thus reducing the number of contacts made by a SARS-CoV-2 positive individual and potentially supporting the contact tracing process.
- Repeat sampling can mitigate the lower sensitivity of rapid testing platforms. Portable rapid test systems (such as the antigen detection systems) could be used to identify disease transmission following a co-exposure event to "diagnose" outbreaks, which could facilitate early outbreak management. Possible settings for this application could include long-term care facilities, schools, or hospitals. However, this application requires an outreach strategy that supports testing personnel to go to the suspected outbreak site.
- Rapid testing may be used to expand proactive testing capacity for low-risk individuals. In these cases, there are fewer implications of a false negative test and screening of higher-risk populations could take place with appropriate follow-up if necessary. Neither Health Canada nor the Food and Drug Administration has approved point-of-care testing for asymptomatic individuals, but appropriate in-house validation may mitigate this barrier.
- In addition to the accuracy of the rapid testing platforms, the practical attributes and barriers/facilitators to implementation must be considered when planning the deployment of these systems. These are summarized for each platform in Table 1 below.

Table 1. Practical characteristics of each rapid testing platform approved for diagnostic use in Canada.

	Cepheid Xpert Xpress (Cepheid, 2020a)	**Abbott ID NOW (Abbott, 2020a)**	**BD Veritor (BD, 2020a)**	**Abbott Panbio (Abbott, 2020b)**	**BKit Virus Finder**
Analyte	RNA (*N2* & *E*)	RNA (*RdRp*)	Antigen (nucleocapsid)	Antigen (SARS-CoV-2 Ag)	RNA
Assay type	RT-PCR	Isothermal amplification	Chromatographic assay	Lateral flow assay	RT-PCR
Validated specimens	Nasal, Mid-turbinate, NP, OP swabs Nasal wash/aspirate	Nasal, throat, NP swabs	Nasal swab	NP swab	Unclear
Sensitivity (Literature)	99%	77-80%	84-96%	73-98%	Unknown
Specificity (Literature)	97-100%	99-100%	99-100%	100%	Unknown
Maximum time to result	45 minutes	13 minutes	15 minutes	15 minutes	Unclear
Kit availability	Low	High	None	High	None
Estimated cost (labor not included)	$40/test	$35/test (currently provided by PHAC at no cost)	Unclear	$5/test (currently provided by PHAC at no cost)	Unclear

Proprietary equipment	- Test cartridge - GeneXpert Instrument	- Proprietary lyophilized reagents - control swabs - test cartridge - ID NOW instrument	- Test strips - Control swabs - BD Veritor Analyzer	- Test devices - Control swabs - Sample extraction buffer	- Sampling materials and reagents (bKIT) - bCUBE analyser - bAPP results interpretation and display software
Healthcare provider	No limit	No limit	No limit	Must have scope of practice for NP swabs	Unclear
Processing time limit	Sample must be tested within 7 days (if stored cold)	Sample must be tested within 1 hr (if stored cold)	Samples must be tested immediately	Samples must be tested immediately	Unclear

Strength of Evidence

Overall, the body of evidence is of low-moderate quality. As with much of the evidence related to COVID-19, published work on test system validation appears to be opportunistic rather than carefully planned and the biases reflect this. The primary literature is at high risk of bias, however, the number of systematic reviews and meta-analyses on the topics at hand help to mitigate the biases of the individual studies but may quickly be outdated due to the rapidly evolving nature of the evidence. Specifically relating to research question 2, no rigorous evidence was identified that discussed the deployment of rapid testing. Articles from the peer-reviewed literature were commentary and thus subject to the author's personal bias on the subject, or were guidelines built upon expert consensus but not implemented anywhere

The results of the included studies are partially relevant to Alberta due to the differences in outbreak dynamics, sample collection logistics, and the in-house testing protocols. Studies comparing specimens or assays often published the concordance of the comparator to the reference standard, rather than the actual sensitivity and specificity of the method under scrutiny. This method offers some evidence as to the quality of the comparator test or specimen but is only independently useful if the standard used in Alberta is equivalent to that of the research group. The laboratories in Alberta use either a laboratory-developed real-time RT-PCR or any one of several Health Canada-authorized commercial tests. All tests have been evaluated for adequacy and, if implemented, have been found to be suitable for the diagnosis of COVID-19. Any novel specimens or test assays will need to be validated against one of the currently-used methods in Alberta (or equivalent commercial assay) to ensure appropriateness.

Limitations of this review

This review is subject to substantial limitations. There is a high risk of selection bias – samples for the validation studies were often obtained from populations with a high likelihood of COVID-19 (such as emergency departments or COVID-19 units), thus over-representing positive specimens. These strategies also systematically exclude asymptomatic individuals or those with mild symptoms that may not present to hospital or get tested for COVID-19. The artificial high prevalence of COVID-19 in these sample sets may have skewed the sensitivity and specificity results, as the false negative rate increases as the likelihood of test positivity increases.

Specifically related to research question 1, there were several studies that were poorly controlled and did not process their samples in equivalent ways. In several studies comparing testing platforms, the samples for the comparator methods were processed differently from the reference method (eg. on demand for the reference vs. frozen residual sample for the comparator). Viral ribonucleic acid (RNA) is highly susceptible to degradation and

the differences in specimen handling could influence the quality of RNA available for the tests to detect (in the case of nucleic acid amplification tests (NAAT)). Further, in many cases, those interpreting the test results for the sample or assay being validated were not blinded to the results obtained by the reference standard method for the correlated paired sample. This is more relevant to validation of the antigen testing platforms (BD Veritor and Panbio), where the result requires interpretation by the user (such as a band on a cartridge or test strip) rather than being displayed as a positive or negative result on a computer screen.

Summary of Evidence

Thirty articles (18 peer-reviewed) from the database search are included in the narrative summary below. Of these, 5 systematic reviews were included (3 were pre-review), 0 RCTs were included, 1 observational (prospective or cross-sectional) studies were included (5 were pre-review), 14 clinical validation studies were included (3 were pre-review), 5 commentaries were included, 3 guidelines from reputable sources were included, and 2 pieces of reputable grey literature were included. 2 articles were included *ad hoc*. Evidence extraction tables for each research question are included in the appendix of this report (Tables 4 & 5).

What are the reported performance characteristics of the rapid COVID-19 tests that have been approved for commercial (diagnostic) use in Canada?

Evidence from secondary and grey literature

Five systematic reviews with meta-analyses were identified in the literature search. The Abbott ID NOW and Cepheid Xpert Xpress systems are notably over-represented in the literature, and the studies included in the meta-analyses have a high degree of overlap. The pooled characteristics for the five approved test systems are shown in Table 2 below.

These meta-analyses show that for rapid nucleic acid testing systems, the Abbott ID NOW system has notably lower sensitivity than the Cepheid Xpert Xpress system (Axell-House et al., 2020; Dinnes et al., 2020; Van Walle et al., preprint). Pooled estimates of testing characteristics suggest that the sensitivity of Abbott ID NOW is 77-80%, although the specificity is 99-100% (Dinnes et al., 2020; Van Walle et al, preprint). The Cepheid Xpert Xpress platform is approximately 99% sensitive and 97-100% specific (Dinnes et al., 2020; Van Walle et al., preprint). No meta-analyses were available for the two antigen testing systems available in Canada (BD Veritor and Abbott Panbio), nor was the BKit Virus Finder system evaluated in any of the systematic reviews (or primary literature).

Systemic bias against Abbott systems is suggested by Mina et al. (2020), who rebuts the findings of Basu et al. (2020) (included in the meta-analyses). Mina (2020) comment that some factors that may have resulted in reports of lower sensitivities for the Abbott ID NOW are the type of sample handling procedures, populations skewed towards very low RNA concentrations, and different specimen collection; however, Mina (2020) itself is heavily biased towards Abbott and should be considered with a critical eye.

Table 2. Pooled performance characteristics of rapid COVID-19 tests from meta-analyses included in this review. Individual studies included in these meta-analyses are not included in the primary literature. Full details on each study are available in Table 4 in the appendix.

	Rapid Test System				
Reference	**Abbott ID NOW**	**Cepheid Xpert Xpress**	**BD Veritor**	**Panbio COVID-19 Ag**	**BKit Virus Finder**
Manufacturers Specifications	Sensitivity: 95.0% Specificity: 97.9% (Abbott Inc., 2020c)	PPA: 100% (88.7-100%) NPA: 100% (83.9-100%) (Cepheid, 2020b)	PPA: 84% (67-93%) NPA: 100% (98-100%) (BD, 2020b)	Sensitivity: 91.4% Specificity: 99.8% (Abbott Inc., 2020d)	Not publicly available

Axell-House et al., 2020	Sensitivity: 71.7-94% Specificity: 100%	Sensitivity: 96.1-100% Specificity: 100%	-	-	-
Dinnes et al., 2020	Sensitivity: 76.8%, (95% CI 72.9% to 80.3% Specificity: 99.6% (95% CI 98.4% to 99.9%)	Sensitivity: 99.4% (95% CI 98.0% to 99.8%) Specificity: 96.8% (95% CI 90.6% to 99.0%)	-	-	-
Subsoontorn, Lohitnaby & Konkaew, preprint	Sensitivity: < 80% (4/5 studies) Specificity: 100% (5/5 studies)	-	-	-	-
Van Walle et al., in preprint	Pooled positive agreement: 79.7 (75.9-83.1)	Pooled positive agreement: 98.8 (97.3-99.5) Specificity: 100.0 (82.4-100.0)	-	-	-
Yang et al., in preprint	-	Sensitivity: 0.99, 95%CI (0.98-1.00) Specificity: 0.97, 95%CI (0.95-0.98)	-	-	-

Evidence from the primary literature

Seventeen primary studies were identified that were not included in the meta-analyses above. As noted in the limitations of this review, most studies only published the agreement between the system being tested and the comparator, rather than the independent sensitivity and specificity of the tested system. This limits the applicability of the primary literature, as concordance data is only useful when the end user has the same reference standard as the study authors. More information about each study is available in Table 4 in the appendix.

Further, the risk of bias in many of these studies is high. In cases where samples were paired, there were often notably different protocols for specimen handling between the reference and the sample for the test platform. For example, in Serei et al., paired nasal swabs were collected for comparison between the Cepheid Xpert Xpress and Abbott ID NOW platforms. As the Cepheid was their diagnostic platform, swabs for this purpose were placed in viral transport media following collection and processed upon arrival at the laboratory (Serei et al., 2020). Conversely, although the swabs for the Abbott platform were collected and transported according to the manufacturers protocol, they were stored in the refrigerator upon arrival at the lab and not processed until several hours later (which is outside the recommended usage) (Serei et al., 2020). It is thus difficult to discern whether the published testing characteristics are inherent to the platform or due to the processing protocol.

Of the studies listed below in Table 3, the concordance values for the nucleic acid test platforms (Cepheid and Abbott) listed by Lephart et al. (2020), Chen et al. (2020), Dust et al. (2020), and Thwe & Ren (2020) offer a sufficiently unbiased reference standard or standard comparable to Alberta. These data suggest that the Abbott ID NOW platform is less accurate than standard RT-PCR diagnostic assays, although the degree of difference is unclear (Lephart et al., 2020; Thwe & Ren, 2020). Notably, Lephart (2020) is of poor quality and at high risk of bias – the Abbott platform was not used according to the manufacturer's recommendations and the authors used different swabbing methods for each platform. The Cepheid Xpert Xpress platform appears to be as accurate as standard RT-PCR diagnostic assays (Chen et al., 2020; Dust et al., 2020).

Few studies were identified that compared antigen testing platforms (BD Veritor and Panbio). The Panbio platform appears to be 100% specific and 73% sensitive overall, but this varies based on symptom status and the number of days after symptom onset (Linares et al., 2020; Gremmels et al., in preprint). The manufacturers of BD Veritor claim that the platform is 100% specific and 84% sensitive (CADTH, 2020); however, comparison against viral culture suggests better sensitivity than expected (96.4%), with some loss of specificity (98.7%) (Pekosz et al., preprint). When the sensitivity is calculated to compare to RT-PCR, the sensitivity of the BD Veritor platform is 78.9%.

No data was found for the Bkit Virus Finder platform.

Table 3. Clinical testing characteristics of rapid test systems approved for diagnostic use in Canada. Full details of each study are available in Table 4 in the appendix.

Reference	Test System	Sensitivity	Specificity	Concordance (Comparator)
CADTH, 2020	BD Veritor	84%	100%	-
Chen et al., 2020	Cepheid Xpert Xpress	-	-	100% (in-house RT-PCR)
Dust et al., 2020	Cepheid Xpert Xpress	-	-	100% (lab-developed RT-PCR)
Ghofrani et al. preprint	Abbott ID NOW	94.1% [CI 71.31-99.85%]	99.0% [CI 94.33-99.97%]	-
Gremmels et al., preprint	Panbio COVID-19 Ag	72.6% 95.2% (Ct < 32)	100%	-
Lephart et al., 2020	Abbott ID NOW	-	-	48% (NP swab vs. composite reference) 69% (POC vs. composite reference)
	Cepheid Xpert Xpress	-	-	100% (composite reference standard)
Linares et al., 2020	Panbio COVID-19 Ag Rapid Test Device (Nasopharyngeal)	Overall: 73.3% (95% IC: 62.2–83.8) Symptomatic <5 days: 85.3 % (95 % IC: 73.4–97.2 Symptomatic < 7 days: 86.5 % (95 % IC: 75.5–97.5) Symptomatic ≥ 7 days: 53.8 % (95 % IC: 26.7–80.9) Asymptomatic: 54.5 % (95 % IC: 0,25-0,84)	100%	-
Lowe et al., 2020	Cepheid Xpert Xpress	-	-	86.5% (Roche cobas or Lightmix RT-PCR assay)
McCormick-Baw et al., 2020	Cepheid Xpert Xpress (Saliva)	-	-	98%; 95% CI: 94.48% to 99.60%) (NP swab)
Pekosz et al., in preprint	BD Veritor	96.4% (95% CI: 82.3, 99.4)	98.7% (96.1, 99.7)	-

Reference	Test System	Sensitivity	Specificity	Concordance (Comparator)
		Calculated comparison to RT-PCR: 78.9%		
Procop et al., 2020	Cepheid Xpert Xpress	97.6%	-	-
	Abbott ID NOW	83.3%	-	-
Serei et al., 2020	Abbott ID NOW	-	-	60% (Xpert Xpress)
Smithgall et al., 2020	Cepheid Xpert Xpress	-	-	98.9% (Roche cobas RT-PCR)
	Abbott ID NOW	-	-	73.9% (Roche cobas RT-PCR)
SoRelle et al., preprint	Abbott ID NOW (Saliva)	-	-	78% PPA; 100% NPA (NP swab)
		-	-	83% PPA; 10% NPA (Cepheid)
Thwe & Ren, 2020	Abbott ID NOW	-	-	PPA: 53.3% (26.6-78.7%) NPA: 100% (97.8-100%) (multiple RT-PCR platforms
Wong et al., 2020	Cepheid Xpert Xpress (non-validated specimens)	-	-	99.2% PPA; 100% NPA (Lightmix RT-PCR)
Young et al., 2020	BD Veritor	-	-	96%-97.9%, Days 0-7 after symptom onset (Lyra)
				98.1 (95% CI: 96.1, 99.1), Days 0-5 after symptom onset (Sofia)

What are the optimal strategies for deployment of rapid testing, to improve either clinical care or outbreak control in health care and community settings?

No peer-reviewed evidence was identified that suggested an optimal strategy for implementing rapid COVID-19 testing. The included guidelines and expert commentary included in the synthesis below complement each other, but no literature was identified in the search to show that they have been implemented or evaluated in a real-world context. More details from the evidence for this question are available in Table 5 in the appendix.

Evidence from secondary and grey literature

Two sets of guidelines were identified (Health Canada, 2020; World Health Organization, 2020) and one information sheet (Health and Human Services, 2020) describing a model for rapid test distribution and implementation.

The Health Canada guidance and World Health Organization (WHO) both suggest using rapid testing as a way to monitor high-risk situations. These might include outbreak control, proactive monitoring in populations with high community prevalence, or use in remote/closed communities where standard testing is not available (Health Canada, 2020; World Health Organization, 2020). The guidance also suggests using rapid testing platforms to supplement capacity for asymptomatic testing (if there is sufficient sensitivity) (World Health Organization, 2020) or as a screening tool for symptomatic individuals following by confirmatory RT-PCR (Health Canada, 2020).

Both Health Canada and WHO note that antigen tests (such as BD Veritor and Panbio) should be used with caution where the decrease in sensitivity may result in missed cases, such as in areas with low prevalence (World Health Organization, 2020), where critical actions rest on the result (such as treatment decisions or individuals in high-risk settings) (Health Canada, 2020), or where the lower sensitivity can't be mitigated by repeated testing protocols (Health Canada, 2020).

The United States Centers for Disease Control and Prevention (CDC) (2020) are more specific with their guidance on rapid antigen tests. They suggest that the antigen tests should be used for screening in high-risk congregate settings where repeat testing may quickly identify SARS-CoV-2 positive individuals, and that RT-PCR be used to confirm the screening test when the antigen test result is inconsistent with the clinical context (CDC, 2020). The test results from an antigen test should be considered presumptive, however, may not need confirmation if there is a correlated pretest probability of disease (eg. high pretest probability prior to a positive test result) (CDC, 2020).

The United States Department of Health and Human Services has recently purchased 150 million Abbott BinaxNOW lateral flow colourimetric antigen tests and has published an overview of their distribution plan (Health and Human Services, 2020). The distribution pattern appears to balance clinical need with equity. The plan can be summarized as follows (Health and Human Services, 2020):

- States: 100 Million tests to be distributed at their discretion
- Nursing homes and assisted living: number based on degree of positivity in the county. Areas with >10% positivity will get tests for all staff 2X/week; Areas with 5-10% positivity will get tests for 50% of staff 1X/week
- Home Health and Hospice: Largest 100+ agencies will receive tests to allow for staff testing 1X/week
- Historically Black Colleges and Universities: Allocation based on number of staff and students. May be used at HBCU leaders' discretion.
- Indian Health Service: 300K tests distributed for eligible health programs; allocation at IHS discretion

Evidence from the primary literature

Four commentary articles were identified from thought leaders that may help to frame the deployment of rapid testing in Alberta. In general, they focus on using rapid testing to improve the speed of information flow for potentially infected individuals (Kost, 2020) and developing a COVID-19 screening model to conserve diagnostic testing capacity (eg. consumables, staff capacity) (Pulia et al., 2020; Wake et al., 2020; Pettit et al., 2020).

Pettit et al. (2020) describes a comprehensive framework for expanding testing capacity, in which rapid testing is a key element. They suggest a "4P" approach:

- **Prioritize** diagnostic testing for individuals and populations most at risk of infection or at risk of infecting others.
- **Propagate** testing capacity by expanding available test and sampling methods, as well as potentially expanding options for testing at non-traditional laboratory venues.
- **Partition** tests into screening vs. diagnostic applications to clearly delineate appropriate contexts of use.
- **Provide** evidence-based standards for characterizing test sensitivity, precision, and utility and apply them to available tests.

The model for using rapid testing (and other capacity expansion tools) is shown in Figure 1 (adapted from Pettit et al. (2020)). Briefly, diagnostic testing by RT-PCR should be designated for high-risk populations (to themselves or the public) or for confirming the results of screening tests (Pettit et al., 2020). Rapid tests with reasonable precision can be used to screen the proportion of the population that exceeds diagnostic capacity (eg. lower risk, asymptomatic, contacts, etc.), with diagnostic testing as a confirmatory step. The application of the 4P model is shown in Figure 1 below.

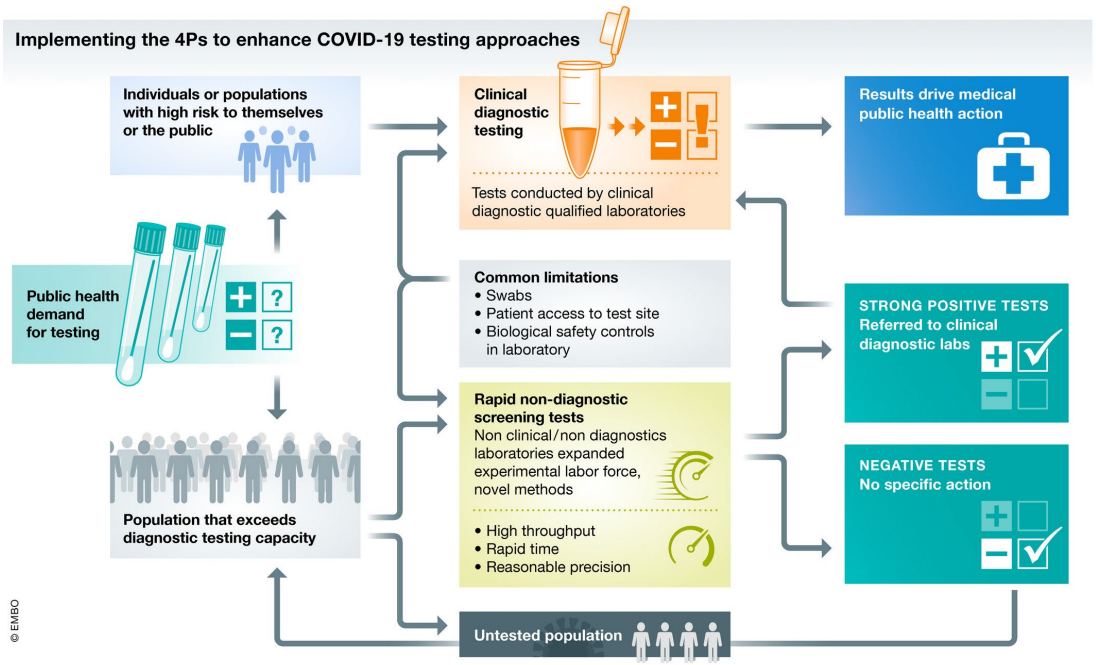

Figure 1. A potential model for expanding testing capacity in health systems by stratifying the population into high and low risk and utilizing novel test platforms, labour forces, and laboratories. Adapted from Pettit et al., 2020.

Evolving Evidence

The evidence on this topic is rapidly evolving – research groups publish opportunistically as novel testing methods are adopted or considered. The evidence presented here is a useful starting point for the discussions regarding implementing novel specimen collection and rapid testing. The evidence should be revisited in the future (3-6 months) to address advances in the field.

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Authorship and Committee Members

This review was written by Rachael Erdmann and scientifically reviewed by Nathan Zelyas, Byron Berenger, Mathew Diggle, and David Walder. The full Scientific Advisory Group was involved in discussion and revisions of the document: Braden Manns (co-chair), Lynora Saxinger (co-chair, secondary reviewer), John Conly, Alexander Doroshenko, Shelley Duggan, Nelson Lee, Elizabeth MacKay, Andrew McRae, Melissa Potestio, James Talbot, Jeremy Slobodan, Brandie Walker, and Nathan Zelyas.

Appendix

Evidence Extraction Tables

Table 4. Evidence extraction table for research question 1 (Performance characteristics of tests approved in Canada)

Reference	Test Kit	Study description	Findings	Notes
Axell-House et al., 2020	Abbott ID NOW Cepheid Xpert Xpress	Systematic review of studies evaluating the testing characteristics of COVID-19 tests - 49 articles included	- Three studies evaluated Abbott ID NOW, an isothermal NAAT platform, with rPPA or rSN of 71.7% to 94%, and rNPA or rSP of 100% - Three studies evaluated Cepheid Xpert Xpress, with rPPA 96.1% to 100%, rNPA 74.3% to 100%, rOA 96.1% to 100%, and Cohen's Kappa of 0.92	
CADTH, 2020	BD Veritor	Horizon Scan of Antigen point-of-care testing	Manufacturer's reported sensitivity: 84% Manufacturer's reported specificity: 100%	October 2020
Chen et al., 2020	Cepheid Xpert Xpress	- Clinical validation study - 58 pairs of archived nasopharyngeal swab (NPS) and posterior oropharyngeal saliva specimens collected from 58 COVID-19 positive inpatients - NPS and saliva specimens were tested by the Xpert Xpress SARS-CoV-2 assay to manufacturer's instruction	- All 58 patients had either NPS or saliva tested positive by Xpert Xpress SARS-CoV-2 assay. Of these, 84.5% (49/58) tested positive in both NPS and saliva, 10.3% (6/58) tested positive in NPS only, and 5.2% (3/58) tested positive in saliva only. - No significant difference in the detection rate was observed between NPS and saliva for the Xpert assay (McNemar's test $p = 0.5078$) - The results from Xpert assay had 100% concordance with our in-house RdRp-Hel RT–PCR - No significant difference in *N2* or *E* gene target amplification	
Dinnes et al., 2020	Abbott ID NOW Cepheid Xpert Xpress	- Cochrane systematic review - 22 included publications (3198 unique samples) - Pooled results calculated for ID NOW and Xpert Xpress	- Summary sensitivity for the Xpert Xpress assay (99.4%, 95% CI 98.0% to 99.8%) was 22.6 (95% CI 18.8 to 26.3) percentage points higher than that of ID NOW (76.8%, (95% CI 72.9% to 80.3%) - Specificity of Xpert Xpress (96.8%, 95% CI 90.6% to 99.0%) was marginally lower than ID NOW (99.6%, 95% CI 98.4% to 99.9%; a difference of −2.8% (95% CI −6.4 to 0.8))	- More studies are urgently needed to be able to say if these tests are good enough to be used in practice - Authors suggest point-of-care tests may be used to replace lab-based RT-PCR if sufficiently accurate OR as triage to RT-PCR to

Reference	Test Kit	Study description	Findings	Notes
				allow earlier detection and rapid management
Dust et al., 2020	Cepheid Xpert Xpress	- Clinical validation of commercial assay compared to lab developed test (LDT) - Three test samples 1) A reference panel of simulated specimens derived from cultured SARS-CoV-2 virus that was inactivated by gamma irradiation and then added to viral transport medium (VTM) containing simulated respiratory secretion medium 2) a convenience set of clinical specimens submitted to CPL for routine viral diagnostic testing (i.e., nasopharyngeal swabs in VTM), and 3) AccuPlex™ SARS-CoV-2 Reference Material (SeraCare), which is recombinant viral RNA encapsulated in a replication-deficient mammalian virus. - Each assay was evaluated using at least 10 SARS-CoV-2-positive specimens, 10 SARS-CoV-2-negative specimens, and archived clinical specimens positive for other common respiratory viruses	- All methods demonstrated 100 % agreement with LDT-1 results - There were no false-negative or false-positive results, and no cross-reactivity with circulating respiratory viruses, including endemic coronaviruses. Ct values for the E gene target differed between assays. - Despite measurable differences in analytical sensitivity, the cobas® SARS-CoV-2 (Roche Diagnostics), Xpert® Xpress SARS-CoV-2 (Cepheid®) and three variations of a LDT performed equivalently and showed 100 % agreement when testing simulated and clinical specimens	
Ghofrani et al., in preprint	Abbott ID NOW	- Clinical evaluation of ID NOW test - Paired samples from 113 patients with suspected COVID-19 - PCR specimen used as reference standard	- 58 (51.3%) were nasal swabs, 33 (29.2%) were nasopharyngeal swabs, and in 22 cases (19.5%) the sample source had not been recorded - Assuming PCR to be the gold standard, 16 of the 17 PCR-positives were also positive by point of care test (POCT), while one was false negative - Calculated sensitivity = 94.1% [CI 71.31-99.85%] - Calculated specificity = 99.0% [CI 94.33-99.97%]	- Included in Subsoontorn but no pooled analysis
Gremmels et al., in preprint	Panbio Covid-19 Ag	- In both study sites, subjects were first sampled for routine RTqPCR testing, using a combined throat/nasopharyngeal swab. Study participants received an additional nasopharyngeal swab - After collection, swabs were transferred into 3 ml UTM until further processing. Nucleic acid extraction, RT-PCR and results interpretation were performed according the instructions of the manufacturer (Seegene) - Collected swabs were transferred into dedicated	- At the UMCU study site 1369 subjects were included, of which 139 tested positive for SARS-CoV-2 by RT-qPCR (prevalence: 10.2%) - At the Aruba study site 208 subjects were included, of which 63 tested positive for SARS-CoV2 (prevalence: 30.3%) - At the UMCU study site, 101 subjects tested positive by LFA yielding an overall sensitivity of 72.6% (95% CI: 64.5 – 79.9%). - Similar results were obtained at the Aruba study site, with an overall sensitivity of 81.0% (95% CI: 69.0 – 89.8%) and specificity of 100% (95% CI: 97.5 – 100%) - In our study cohorts specificity was 100%, overall sensitivity was	

Reference	Test Kit	Study description	Findings	Notes
		sample collection tubes containing a sampling buffer. Collected samples were subsequently processed in accordance with the manufacturer's protocol, within 2 hours of sample collection.	72.6% and 95.2% when using a Ct value of 32 as cut-off	
Lephart et al., 2020	Abbott ID NOW Cepheid Xpert Xpress	- Clinical evaluation study - NP and nasal swabs were collected from 88 patients, of which 75 were patients presenting in the ED and 13 were from a population of recovering COVID-positive inpatients (mean time from diagnosis = 26 days) - specimens transported in viral transport media and immediately tested as part of routine care - Residual NP specimen in VTM was stored at 4°C, transported to our offsite main laboratory, and within 24 h of collection, used for comparative study testing by m2000 and Xpert assays - Nasal swab collected in parallel and transported dry to lab, stored at 4C and tested with ID NOW within 24 hours - composite reference standard (CRS) as defined by result agreement of SARS-CoV-2 target in at least 2 of 4 NAAT results.	- Nasal swabs directly tested on the ID NOW assay had 48% positive agreement compared to the CRS, whereas Simplexa had 88%, m2000 had 96% and Xpert had 100% positive agreement - In point-of-care use, the PPA of ID NOW increased from 48% to 69%, whereas performance of the other assays was nearly identical	- Specimens not treated the same for ID NOW compared to Cepheid or RT-PCR systems
Linares et al., 2020	Panbio COVID-19 Ag Rapid Test Device (Nasopharyngeal)	- Clinical evaluation of test performance - ED: 135 symptomatic patients admitted with suspicion of COVID-19 and 17 asymptomatic patients with history of contact - Primary care: 50 symptomatic and 50 asymptomatic patients - 255 total swabs collected and tested; 23.5% positive by RT-qPCR - Two consecutive NP swabs from each patient (one for RT-PCR, one for rapid test)	- All symptomatic patients tested within 8 days of symptom onset - Overall sensitivity is 73.3% (95% IC: 62.2–83.8). Specificity is always 100%. - Considering only symptomatic patients with <5 days, <7 days or ≥7days since onset, the sensitivity was 85.3 % (95 % IC: 73.4–97.2) (Cohen's kappa = 0.897), 86.5 % (95 % IC: 75.5–97.5) (Cohen's kappa = 0.904) and 53.8 % (95 % IC: 26.7–80.9) (Cohen's kappa = 0.617) - Considering asymptomatic patients with close contact the overall sensitivity was 54.5 % (95 % IC: 0,25-0,84) (Cohen's kappa = 0.667)	- Sensitivity decreases as cycle threshold decreases
Lowe et al., 2020	Cepheid Xpert Xpress	- Evaluation of Xpert Xpress to conventional RT-PCR (cobas or Lightmix assays) based on NP swab - NP swabs previously confirmed positive with a Cycle threshold (Ct) ≥30 for SARS-CoV-2 by the cobas® (targets: Orf-1a and envelope (E) genes; FDA EUA) or the Lightmix® assay (target: E gene; research use	- Overall concordance on initial comparison was 86.5 % (32/37). There was 100 % concordance for samples with Ct values between 30−33.9. (= 0% discordance) - Among the samples with a Ct value ≥34 (lower viral load), 13 were initially detected by the Lightmix® assay and nine by the	- small sample size

Reference	Test Kit	Study description	Findings	Notes
		only) were selected for comparison with the Xpert® (targets: nucleocapsid (N2) and E genes; FDA EUA). - 37 samples re-evaluated	cobas® assay. Discordance within this subgroup was 23 % (5/22).	
McCormick-Baw et al., 2020	Cepheid Xpert Xpress	- Validation of saliva samples on Xpert Xpress system - A total of 156 paired NPS and saliva specimens were tested; NP samples tested on demand and saliva samples tested within 12 hours (stored at 4C)	- 153/156 (98%; 95% confidence interval [CI], 94.48% to 99.60%) samples were in overall agreement - 47/49 samples were positive in saliva compared with the NPS, resulting in a positive percent agreement of 96% (95% CI, 86.02% to 99.5%). A total of 105/106 samples had a negative saliva and NPS result	
Mina et al., 2020	Abbott ID NOW	- Commentary / Rebuttal of Basu et al. (2020) - ID NOW test has consistently demonstrated a high level of performance against a gold standard (nasopharyngeal (NP) swab, ranging from 83.3% - 95.0% positive agreement (sensitivity) and 96.5% - 100.0% negative agreement (specificity) - Basu et al. (2020) raise questions about the accuracy of ID NOW - Here we describe three problems that can explain essentially all of the loss in sensitivity measured by Basu et al. to explain this important anomalous finding	- In the study, investigators compared results from the ID NOW and Cepheid Gene Xpert Xpress POC tests, using the Cepheid GeneXpert Dx laboratory instrument as their comparator reference method - In a number of key comparisons, specimens were diluted into VTM rather than direct inoculation of the swab into the ID-NOW test reagent, suggested by the manufacturer. - In all populations tested, the specimens used in the study represent an extra-ordinarily skewed distribution of samples with very low RNA concentrations. All (100%) specimens missed by the ID-NOW in the study represent such low RNA concentrations that they likely reflect non-culturable or non-viable virus RNA remaining after infectious virions have been cleared - When direct inoculation of the swab into the ID NOW assay reagent was performed, a useful assessment of the assay was obscured by the choice to compare anterior nasal swabs on the ID-NOW to nasopharyngeal swabs on the Xpert Xpress	- Some funding received from Abbott for the ID NOW validation study
Pekosz et al., in preprint	BD Veritor	- Prospective paired NP swabs collected from 76 participants - Specimens for the RT-PCR assay consisted of 71 NP swabs (37 and 34 positive and negative, respectively) and five OP swabs (1 and 4 positive and negative swabs, respectively) - Both the antigen test and RT-PCR were performed in accordance with manufacturers instructions - BD Veritor compared against viral culture and RT-PCR reference standard	- The 38 RT-PCR positive specimens were tested for the presence of SARS-CoV-2 using infection of VeroE6TMPRSS2 cell cultures (SARS-CoV-2 TMPRSS2 culture). Overall, 28 RT-PCR positive specimens were also positive by SARS-CoV-2 TMPRSS2 culture and 10 of 38 RT-PCR-positive specimens were negative by SARS-CoV-2 TMPRSS2 culture - Of the 38 RT-PCR-positive results utilized for these analyses, nine were antigen test negative. - The antigen test demonstrated a sensitivity and specificity of 96.4% (95% CI: 82.3, 99.4) and 98.7% (96.1, 99.7), respectively	

Reference	Test Kit	Study description	Findings	Notes
			- The positive predictive value (PPV) for the antigen test was 90.0% (76.3, 97.6), while the PPV for the RT-PCR assay was only 73.7% (60.8, 85.3) (Based on study prevalence of 11.2%)	
Procop et al., 2020	Cepheid Xpert Xpress Abbott ID NOW	- Clinical validation study - Nasopharyngeal (NP) or nasal swabs were collected by a trained medical practitioner, and were submitted in transport medium and never frozen - 239 specimens collected; 168 contained SARS-CoV-2 and 71 were negative - Each specimen tested on all five systems; specimen was considered to contain the SARS-CoV-2 virus if the results of two or more of the five tests studied were positive according to the standard operating procedure	- 238 specimen results were available for assessment of the Xpert Xpress SARS-CoV-2 (Cepheid) assay. There were four false negatives and five false positives when this assay was assessed against a composite standard. - 239 specimen results were available for assessment of the ID Now COVID-19 (Abbott) assay. There were 28 false negatives and two false positives when this assay was assessed against a composite standard. - ID NOW sensitivity: 83.3% - Cepheid sensitivity: 97.6% - For the ID Now COVID-19 (Abbott) assay, both log10 viral load (OR, 0.32; 95% CI, 0.18-0.50; P < .001) and swab/transport medium (OR, 4.95; 95% CI, 1.30-25.30; P = .018) were significantly associated with false-negative results in a multivariable analysis	- False-negative results for the Simplexa COVID-19 Direct Kit (DiaSorin) and ID Now COVID-19 (Abbott) assays tended to occur more frequently as time from onset of symptoms increased and Ct values increased
Serei et al., 2020	Cepheid Xpert Xpress Abbott ID NOW	- Paired nasal swabs from 105 adults presenting to ED - Swab in viral transport media used for testing on Xpert Xpress RT-PCR system - “Dry” swab collected without VTM, stored at 4C for up to 12 hours before testing with ID NOW system	- all samples run on the Cepheid were valid - 96 samples (91.4%) produced a valid result and 9 (8.57%) were invalid on the ID NOW - The overall positivity rate, as detected by Cepheid, was 20.8% (20/96), while the ID NOW detected just 12.5% (12/96) positive specimens. The overall positive agreement between Cepheid and ID now was 60%. - Specimens positive using the Cepheid assay, but negative in the ID NOW assay had N2 gene detected in 8/8 (100%) samples, with an average Ct value of 38.4 (range: 34.1–41.3), and 6/8 (80%) of samples had E gene detected with an average Ct of 33.7 (range: 28.2–37.7).	- Clear differences in sample handling
Smithgall et al., 2020	Cepheid Xpert Xpress Abbott ID NOW	- Clinical validation study - Deidentified remnant patient samples used for routine clinical testing with the cobas SARS-CoV-2 assay on the 6800 platform were used to evaluate the Xpert and ID Now assays - 113 NP swabs collected in 3 mL of viral transport media or universal transport media were included. The specimens were collected from 111 adult and 2	- Overall positive agreement with ID Now was 73.9% (95% CI: 63.2 – 82.3%) - Overall positive agreement with Xpert was 98.9% (95% CI 92.9 – 100%). - Negative agreement was 100% (95% CI 83.4 – 100%) and 92.0% (95% CI 72.4 – 98.6%) for ID Now and Xpert, respectively. - Both ID Now and Xpert showed 100% positive agreement for medium and high viral concentrations, defined as Ct value <30	- Accuracy of both Xpert and ID NOW decreases with low viral load - Included in Subsootorn et al. but not pooled

Reference	Test Kit	Study description	Findings	Notes
		pediatric patients who were all seen in inpatient or emergency room locations. - cobas 6800 used as reference standard		
SoRelle et al., in preprint	Abbott ID NOW	- Clinical validation study - We tested a total of 96 patient saliva samples on the ID NOW. Sixty-seven specimens were paired collections with NPS in VTM. - We first compared ID-NOW saliva results with results from paired NPS specimens tested by either the Xpert® Xpress SARS-CoV-2 or Real-Time SARS-CoV-2 RT-PCR assays.	- 78% (18/23) positive percent agreement (PPA) and 100% (43/43) negative percent agreement (NPA) for saliva tested by ID NOW compared with NPS in VTM - False-negative (FN) saliva samples were associated with elevated NPS CN (Abbott, N2: 30.44 or Ct values - Comparing saliva tested by Cepheid system vs. ID NOW: we observed 83% (19/23) PPA and 100% NPA (25/25). FN samples by ID NOW again exhibited elevated Ct values (E: 36.4, 36.5, 42.7, 43.3; N2: 36.1, 37.6, 39, 41.2)	
Subsoontorn, Lohitnaby & Konkaew, in preprint	Abbott ID NOW	Systematic review and meta-analysis; 43 studies included (5204 patient samples) - 33 of 43 studies at high risk of selection bias - 31 of 43 studies at high risk of index test bias (interpreted with knowledge of reference standard results) - Reference standard tests of nearly all studies are RT-qPCR, a gold standard for RNA virus detection	- 5 studies testing Abbott ID NOW (Basu, Ghofrani, Smithgall, SoRelle, Moore) - ID Now reported low sensitivity, specificity and pooled ln(DOR) - four out of five ID NOW studies included in our review reported less than 80% sensitivity (only Ghofrani (2020) reports sensitivity above 90%) - 5/5 ID NOW studies report ~100% specificity	- Results are not pooled; individual studies included in this review
Thwe & Ren, 2020	Abbott ID NOW	- Retrospective data review of test results from 182 paired NP swabs (dry NPS for ID NOW and NPS-VTM for RT-PCR platforms) - Swabs collected from symptomatic inpatients and ED patients - Collective data set from all RT-PCR platforms against ID NOW	- Overall agreement was 96.2% (95% CI: 92.2–98.4%) - The positive percent agreement (PPA) was 53.3% (95% CI: 26.6–78.7%) - Negative percent agreement (NPA) was 100% (95% CI: 97.8–100%) - Overall false-negative rate by ID NOW was 47% (7/15)	- Authors note in the discussion that there has been an FDA recall of NPS-VTM for ID NOW due to potential for high number of false negative results
Wong et al., 2020	Cepheid Xpert Xpress	- Clinical evaluation study - 162 samples (119 positive, 42 negative) collected from 158 patients with suspected COVID-19; 120 deep throat saliva and 42 lower respiratory tract (not paired) - 74/162 were archived samples stored at -70C, 88/162 were prospective samples - Samples screened with standard of care (TIB-Molbiol LightMix® SarbecoV E-gene assay) prior to testing with Xpert Xpress	- The overall performance on both non-validated specimen types has weighted Kappa value 0.98, PPA of 99.16 % and NPA of 100% - Xpert Xpress assay can be used with non-validated specimens with results comparable to standard of care NAAT	- Samples not paired with NP swab; can't be compared to gold standard reference

Reference	Test Kit	Study description	Findings	Notes
Van Walle et al., in preprint	Abbott ID NOW Cepheid Xpert Xpress	Systematic review and meta-analysis; 157 studies included	- Limited data were available for five POC antigen tests and five POC nucleic acid tests. Large variability in positive agreement was observed. - ID NOW: Pooled positive agreement = 79.7 (75.9-83.1); n=483. No data on specificity. - Xpert Xpress: Pooled positive agreement = 98.8 (97.3-99.5); n=427. Specificity = 100.0 (82.4-100.0); n=18	- Evidence available for point of care tests is scarce - Authors recommend further test validation and inclusion as part of a testing algorithm
Yang, et al., in preprint	Cepheid Xpert Xpress	Systematic review and meta-analysis; 18 studies included	- Pooled sensitivity was 0.99, 95%CI (0.98-1.00) (I^2=0%, P=0.7132) - Pooled specificity was 0.97, 95%CI (0.95-0.98) (I^2=42%, P=0.1417)	
Young et al., 2020	BD Veritor	- Clinical validation study - Veritor/Lyra comparison: nasal specimens and either nasopharyngeal or oropharyngeal specimens from 251 participants with COVID -19 symptoms (≤7 days from symptom onset [DSO]), ≥18 years of age) - Veritor/Sofia comparison: nasal specimens from 361 participants with COVID-19 symptoms (≤5 DSO), ≥18 years of age) - Swabs were shipped for testing on dry ice (-70°C); nasal swabs were shipped dry and OP/NP swabs were shipped in universal viral transport medium. Samples processed the same way regardless of testing model	Veritor vs. Lyra: - The 0-5 DSO range was the shortest range tested to have a PPA value above 80% and include at least 30 reference positive results (PPA ranges from 81.8% to 87.5% within 5 DSO) - The 0-6 DSO range also met PPA value acceptance criteria (PPA 82.4% at 6 DSO) - PPA = 76.3 at 7 DSO - The NPA for the Veritor test was 100% for the 0 -1 to 0-5 DSO ranges; however, the NPA value for the 0-6 and 0-7 DSO ranges was 99.5% (95% CI: 97.4, 99.9) - Overall percent agreement over 7 DSO ranges from 96.0% to 97.9% Veritor vs. Sofia: - The PPA, NPA, and OPA for the Veritor test compared to the Sofia 2 test using specimens at the 0-5 DSO range were 97.4 (95% CI: 86.5, 99.5), 98.1 (95% CI: 96.0, 99.1), and 98.1 (95% CI: 96.1, 99.1)	- Veritor test was required to achieve ≥80% PPA relative to the laboratory reference standard (with at least 30 positive specimens by reference) in order to be considered acceptable for FDA -EUA

Table 5. Evidence extraction for research question 2 (Deployment of rapid testing)

Reference	Study Type	Study description	Findings/Recommendations	Notes
United States Centers for Disease Control and Prevention, 2020	Guidance	- Interim guidance on the use of rapid antigen tests - Rapid antigen tests perform best when the person is tested in the early stages of infection with SARS-CoV-2 when viral load is generally highest - Rapid antigen tests can be used for screening testing in high-risk congregate settings in which repeat testing could quickly identify persons with a SARS-CoV-2 infection to inform infection prevention and control measures, thus preventing transmission. There may be value in providing immediate results with antigen tests even though they may have lower sensitivity than RT-PCR tests, especially in settings where a rapid turnaround time is required. - The “gold standard” for clinical diagnostic detection of SARS-CoV-2 remains RT-PCR. Thus, it may be necessary to confirm a rapid antigen test result with a nucleic acid test, especially if the result of the antigen test is inconsistent with the clinical context - The evaluation of a diagnostic antigen test result should consider the length of time the patient has experienced symptoms. Generally, clinicians can rely upon a positive diagnostic antigen test result because the specificity of current FDA-authorized antigen tests is high in a person who has COVID-19 symptoms. - Ideally, confirmatory RT-PCR testing should take place within two days of the initial antigen testing. If RT-PCR testing is not available, clinical discretion can be used in whether to recommend the patient isolate. - When used for screening testing in congregate settings, test results for SARS-CoV-2 should be considered presumptive. Confirmatory nucleic acid testing following a positive antigen test may not be necessary when the pretest probability is high, especially if the person is symptomatic or has a known exposure. - Confirmatory nucleic acid testing following a negative antigen test used for screening testing may not be necessary if the pretest probability is low, the person is asymptomatic, or has no known exposures, or is part of a cohort that will receive rapid antigen tests on a recurring basis		
Health and Human Services, 2020	Distribution Information	- Distribution plan of Abbott BinaxNOW COVID-19 test (lateral flow immunoassay for nucleocapsid protein) 150 Million tests to be distributed between: - States (100M) to be distributed at their discretion - Nursing homes and assisted living; number based on degree of positivity in the county. Areas with >10% positivity will get tests for all staff 2X/week; Areas with 5-10% positivity will get tests for 50% of staff 1X/week - Home Health and Hospice: Largest 100+ agencies will receive tests to allow for staff testing 1X/week - Historically Black Colleges and Universities: Allocation based on number of staff and students. May be used at HBCU leaders’ discretion. - Indian Health Service: 300K tests distributed for eligible health programs; allocation at IHS discretion - FDA statement: If healthcare providers are using SARS-CoV-2 diagnostic tests for screening asymptomatic individuals, and highly sensitive tests are not feasible, or if turnaround times are prolonged, healthcare providers may consider the use of a less sensitive POC test, even if they are not specifically authorized for this indication - For congregate care settings – like nursing homes or similar settings – repeated use of rapid POC testing may be superior for overall infection control compared to less frequent, highly sensitive tests with prolonged turnaround times.		

Reference	Study Type	Study description	Findings/Recommendations	Notes
Health Canada, 2020	Guidance	- Interim guidance on use of rapid antigen detection tests - In scenarios where critical decisions and actions rest on a test result (e.g., a symptomatic resident in a long-term care home, a patient in the ICU who needs remdesivir), the recommended test would be the most accurate test - it is important to identify scenarios where Rapid Antigen Diagnostic Tests (RADT) can be used effectively to increase access to testing in a manner that accounts for the lower sensitivity parameters - testing protocols that mitigate the decrease in sensitivity, such as through the use of repeated testing, can define the scenarios where RADT offer added value - A second broad category for use includes situations that involve the prospective monitoring of asymptomatic individuals for introduction of SARS-CoV-2 into high risk settings Proposed use cases: - Testing in selected, symptomatic individuals within 5 days of symptom onset (followed by confirmatory testing if positive). - Repeated testing of workers in remote work areas to prevent introduction or minimize the chance of spread within a work site. - Prospective testing of workers in high risk settings including those in large processing plants (e.g., meat plant workers), long-term care (LTC) facility workers, offshore/marine workers. - In an outbreak situation where multiple symptomatic patients can be tested rapidly on site if faster presumptive results will help inform public health action. - Repeated testing of inmates entering a correctional facility who have been out on visits or who are new to the facility.		
Kost (2020)	Other	- Narrative review / Commentary on the geospatial "hotspots" of disease outbreaks and the need for point of care testing to bridge the knowledge gap - Delta t_{Dx} is the time the diagnosis is confirmed minus the time the patient is infected, or, $\Delta t_{Dx} = [t_{confirmed}] - [t_{infected}]$. The goal of POC strategies is to minimize Δt_{Dx}. - the time delay from infection to symptoms, $\Delta t_{Sx} = [t_{symptoms}] - [t_{infected}]$, tells us how quickly the patient responds pathophysiologically -Subtracting the two deltas, $\Delta t_{Dx} - \Delta t_{Sx} = [t_{confirmed}] - [t_{symptoms}]$, an interval of maximum risk during which safe spacing and sheltering are crucial - proactive POC diagnosis results in $\Delta t_{Dx} < \Delta t_{Sx}$	- Testing must transition away from the delays and mistakes of distant reference laboratories to accurate POC and rapid tests that are highly accessible. - Until multiplex testing is available, affordable, timely, and deliverable at points of need, one should use the POC or rapid COVID-19 testing method with the best proof of high sensitivity and high specificity, both at least 97.5% - POCT will help facilitate rapid identification of COVID-19 carriers and their contacts; rational safe spacing and sheltering; protection of vulnerable groups; smart deployment of resources, healthcare workers, and isolation facilities; certification within 72 hours of noncarrier state before clearing immigration in other countries; workforce testing before returning to work; and importantly, alleviation of fear, panic, layoffs, and economic fallout. - People have a right to know. They should be able to self-test at will or have free access to provider testing and follow-up to assure the virus has been cleared, to lessen stealth transmission in the community.	- Commentary article – recommendations have not been implemented/tested

Reference	Study Type	Study description	Findings/Recommendations	Notes
			- The recent pattern of COVID-19 stealth transmission demonstrates people must be tested irrespective of symptoms and isolated if confirmed. - POC diagnostics for COVID-19 must be environmentally robust, certified for the conditions encountered, and monitored.	
Pettit et al., 2020	Other	- Authors describe a novel, geographically agnostic framework (the 4Ps framework) to guide multidisciplinary, scalable, resource-efficient, and achievable efforts toward enhanced testing capacity. - 4P framework: Prioritize, Propagate, Partition, Provide **Prioritize** diagnostic testing for individuals and populations most at risk of infection or at risk of infecting others. **Propagate** testing capacity by expanding available test and sampling methods, as well as potentially expanding options for testing at non-traditional laboratory venues. **Partition** tests into screening vs. diagnostic applications to clearly delineate appropriate contexts of use. **Provide** evidence-based standards for characterizing test sensitivity, precision, and utility and apply them to available tests.	- Figure 3 included in text - Authors describe a model for expanding testing capacity while conserving resources by stratifying diagnostic testing and screening testing. - Diagnostic testing by RT-PCR should be designated for high-risk populations (to themselves or the public) or for confirming the results of screening tests - Screening test capacity can be built by using rapid tests (that have reasonable accuracy) and expanding lab capacity to academic or industry labs with appropriate clinical oversight	- This is a proposed framework only; it is conceptually supported with evidence but has not been implemented anywhere
Pulia et al., 2020	Other / Commentary	- Commentary on multi-tiered testing approaches for COVID-19 - Ideally, any patient requiring evaluation can be (i) quickly triaged as having either viral, bacterial or absent immune response to an infection and then (ii) receive rapid confirmatory testing - A multi-tiered, rapid diagnostic strategy incorporating (i) a rapid host immune response assay as an initial triage test, (ii) confirmatory molecular testing and (iii) a rapid IgM/IgG serology test for assessing which patients would benefit from quarantine, further testing, or therapeutics targeting COVID-19 - As a first step, the host immune response assay can differentiate the cause of the infection as viral or bacterial. Patients with a viral positive host response would receive pathogen-specific molecular testing. - Second step: Patients identified as bacterial infection could undergo additional evaluation (e.g. chest imaging) and be started on appropriate antibacterial therapy. - Third step: Patients with a negative bacterial and viral host response test and less than 7 days of symptoms would be referred for confirmatory molecular testing if defined as high-risk or home quarantine if they do not meet the high-risk criterion		- Commentary, has not been implemented in any jurisdiction
Wake et al., 2020	Other	Description of implementation of rapid POC tests to complement clinical assessment of COVID-19 symptoms to reduce the risk of transmission to susceptible patients (thorough COVID-19 triage and cohorting)	- Clinical assessment tool relies on clinical history and findings, laboratory results and radiology to categorize patients according to clinical likelihood of COVID-19	

Reference	Study Type	Study description	Findings/Recommendations	Notes
			- Universal screening of all hospital admissions identifies asymptomatic and pre-symptomatic patients with potential to transmit infection - Patients are triaged to separate wards; patients with no symptoms or signs of COVID-19 (likelihood score 0) are separated from those with low grade suspicion of COVID-19 (score 1); those with high grade suspicion (score 2) or confirmed COVID-19 (score 3) are cohorted together on a separate ward. - Patients with low-grade suspicion (score 1) are cared for in isolation rooms when possible and prioritised for rapid SARS-CoV-2 PCR testing to establish their appropriate clinical area	
World Health Organization, 2020	Guidance	Recommendations for the use of rapid antigen testing: - To respond to suspected outbreaks of COVID-19 in remote settings, institutions and semi-closed communities where nucleic acid testing is not immediately available - To support outbreak investigations (e.g. in closed or semi-closed groups including schools, care-homes, cruise ships, prisons, work-places and dormitories, etc.). Antigen testing can be used to screen at-risk individuals and prioritize sample collection from RDT-negative individuals - To monitor trends in disease incidence in communities, and particularly among essential workers and health workers during outbreaks or in regions of widespread community transmission - Where there is widespread community transmission, RDTs may be used for early detection and isolation of positive cases in health facilities, COVID-19 testing centres/sites, care homes, prisons, schools, front-line and health-care workers and for contact tracing. Requires safe management practices of RDT-negative individuals - Testing of asymptomatic contacts of cases may be considered even if the Ag-RDT is not specifically authorized for this use, since asymptomatic cases have been demonstrated to have viral loads similar to symptomatic cases - Use of Ag-RDTs is not recommended in settings or populations with low expected prevalence of disease (e.g. screening at points of entry, blood donation, elective surgery), especially where confirmatory testing by NAAT is not readily available		

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List of Abbreviations

AHS: Alberta Health Services

AQ: Airport Quarantine

CI: Confidence interval

COVID-19: Coronavirus Disease-2019

CRS: Composite Reference Standard

CT: Contact Tracing

Ct: Cycle threshold

DSO: Days from Symptom Onset

DTS: Deep-throat secretions

ED: Emergency department

EUA: Emergency Use Authorization

FDA: Food and Drug Administration

HIQA: Health Information and Quality Authority

KRS: Knowledge Resource Services

LDT: Lab-developed test

LTC: Long-term Care

NAAT: Nucleic Acid Amplification Technology

NP: Nasopharyngeal

NPA: Negative Percent Agreement

NPS: Nasopharyngeal Swab

NPV: Negative Predictive Value

NS: nasal swab

OA: Overall Agreement

OP: Oropharyngeal

OPA: Overall Percent Agreement

POC: Point of Care

POCT: Point of Care Test

PPA: Positive Percent Agreement

PPV: Positive Predictive Value

RADT: Rapid Antigen Diagnostic Test

RDT: Rapid Diagnostic Test

RNA: ribonucleic acid

RT-PCR: Reverse transcriptase polymerase chain reaction

SAG: Scientific Advisory Group

UTM: Universal Transport Media

VTM: Viral Transport Media

WHO: World Health Organization

Methods

Literature Search

A literature search was conducted by Lauren Seal and Rachel Zhao from Knowledge Resources Services (KRS) within the Knowledge Management Department of Alberta Health Services. KRS searched databases for articles published in 2020 and included: Medline, CINAHL, PubMed/LitCOVID, Trip Pro, Google Scholar, medRxiv/BioRxiv, and grey literature from CEBM, CADTH, CDC, and WHO. A separate search was conducted for each research question; the full search strategy is included in this appendix.

Articles identified by KRS in their search were initially screened by the librarian for obvious irrelevance. Articles were then screened by title and abstract against the inclusion/exclusion criteria listed in Table 6 below. In total, 271 articles were identified by KRS with references and abstracts provided for further review. Duplicates that were retrieved from different search strategies were not removed. 147 articles were excluded following title and abstract review, and an additional 104 articles were excluded following full-text screening and evidence extraction in accordance with the inclusion/exclusion criteria stated below. 50 articles were included in the final narrative synthesis.

Table 6. Inclusion and exclusion criteria for results of the literature search

Inclusion Criteria	Exclusion Criteria
- Any test population - COVID-19 - Includes sensitivity, specificity and/or predictive values - Q1 only: Compares saliva samples with conventional sampling (NP, throat, nasal) - Q2 only: compares tests from symptomatic and asymptomatic cases - BKit Virus Finder COVID-19 (Hyris Ltd) - BD Veritor System for Rapid Detection of SARS-CoV-2 (BD & Company) - Abbott ID NOW COVID-19 (Abbott Diagnostics Scarborough) - Panbio COIVD-19 Ag Rapid Test Device (Abbott Rapid Diagnostics) - Xpert Xpress SARS-CoV-2 (Cepheid) - Human study - English language - Any jurisdiction - Meta-analysis, Systematic review, guidelines, controlled trial, observational study, grey literature, preprint	- Article is not from a credible source - Article does not have a clear research question or issue - Presented data/evidence is not sufficient to address the research questions - Viruses other than COVID-19 - Blood sample testing - Test characteristic of samples alone (no comparison) - Serological study - Infectivity study - Analytical sensitivity - Sample pooling advice - Q1 only: Compares aspects of testing protocol OTHER than sample site or symptoms (eg. collection method, PCR type, extraction methods, etc.) - Q2 only: does not compare tests from symptomatic and asymptomatic cases - Spartan Cube COVID-19 System (Spartan Bioscience Inc.)

- Q4 only: commentary, narrative review - Published in 2020	- Commentary, opinion, editorial, narrative review; modelling study

Critical Evaluation of the Evidence

Exclusion criteria for study quality were adapted from the Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018). Potential articles were evaluated on three criteria: 1) Peer reviewed or from a reputable source; 2) Clear research question or issue; 3) Whether the presented data/evidence is appropriate to address the research question. Preprints and non peer-reviewed literature (such as commentaries and letters from credible journals) are not excluded out of hand due to the novelty of COVID-19 and the speed with which new evidence is available.

Table 7 below is a narrative summary of the body of evidence included in this review. The categories, format, and suggested information for inclusion were adapted from the Oxford Centre for Evidence-Based Medicine, the Cochrane Library, and the AGREE Trust (Urwin, Gavinder & Graziadio, 2020; Viswanathan et al, 2012; Wynants et al., 2020; Brouwers et al., 2010).

Table 7. Narrative overview of the literature included in this review.

	Description
Volume	5 systematic reviews were included (3 were pre-review), 0 RCTs were included, 1 observational (prospective or cross-sectional) studies were included (5 were pre-review), 14 clinical validation studies were included (3 were pre-review), 5 commentaries were included, 3 guidelines from reputable sources were included, and 2 pieces of reputable grey literature were included.
Quality	The body of evidence included in this review is of moderate quality overall. As with much of the evidence related to COVID-19, published work on test validation appears to be opportunistic rather than carefully planned and the risk of bias reflects this. There is a high risk of selection bias – in the observational studies, specimens were often obtained from emergency departments or COVID-19 units rather than from community testing sites. Specimens were taken from those with clinical suspicion of or confirmed COVID-19, thus ensuring an over-representation of positive specimens in the sample set. This sample collection strategy used in many studies heavily biases towards symptomatic patients, as it systematically excludes asymptomatic or paucisymptomatic individuals that may not present to hospital or get tested for COVID-19. The artificial high prevalence of COVID-19 in these sample sets may have skewed the sensitivity and specificity results, as the false negative rate increases as the likelihood of positivity increases. In many cases, those interpreting the test results for the sample or assay being validated were not blinded to the results obtained by the reference standard method for the correlated paired sample. In studies where concordance or agreement was measured, this has the potential to skew the results towards higher concordance than the true value.

	Specifically related to research questions 1 (saliva) and 3 (rapid testing), there were several studies that were poorly controlled and did not process their samples in equivalent ways. For example, in many studies comparing saliva with nasopharyngeal swabs, the swab would be processed immediately for diagnostic purposes while the saliva sample would be refrigerated or frozen for several hours prior to processing. In several studies comparing rapid testing methods, the sample collection and storage methods were different (eg. nasopharyngeal swabs stored in transport media, vs. collected and stored dry) or the samples for the comparator methods were processed differently from the reference method (eg. on demand for the reference vs. frozen residual sample for the comparator). Viral RNA is highly susceptible to degradation and the differences in specimen handling could influence the quality of RNA available for the tests to detect. For research question 4, no rigorous evidence was identified that discussed the deployment of rapid testing. Articles from the peer-reviewed literature were commentary and thus subject to the author's personal bias on the subject, or were guidelines built upon expert consensus but not implemented anywhere.
Applicability	The results of the included studies are somewhat applicable to Alberta. Studies comparing specimens or assays often published the concordance of the comparator to the reference standard, rather than the actual sensitivity and specificity of the method under scrutiny. This method offers some evidence as to the quality of the comparator test or specimen, but is only independently useful if the standard used in Alberta is the same as that of the research group. Since Alberta uses a lab-developed RT-PCR assay to test for COVID-19, any novel specimens or test assays will need to be validated against the in-house method to ensure appropriateness.
Consistency	The evidence appears to be consistent across studies.

Search Strategy

Strategy for Research Question 1

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to October 12, 2020

#	Searches	Results
1	exp Coronavirus/ or Coronavirus Infections/ or coronaviru*.mp. or corona viru*.mp. or ncov*.mp. or n-cov*.mp. or novel cov*.mp. or COVID-19.mp. or COVID19.mp. or COVID-2019.mp. or COVID2019.mp. or SARS-CoV-2.mp. or SARSCoV-2.mp. or SARSCoV2.mp. or SARSCoV19.mp. or SARS-Cov-19.mp. or SARSCov-19.mp. or SARSCoV2019.mp. or SARS-Cov-2019.mp. or SARSCov-2019.mp. or severe acute respiratory syndrome coronaviru*.mp. or severe acute respiratory syndrome cov 2.mp. or 2019 ncov.mp. or 2019ncov.mp.	69356
2	(BKit or Bd Veritor or ID Now or PanBio or (Xpert and Xpress)).mp.	121
3	1 and 2	39

TRIP Database Pro

(BKit or Bd Veritor or ID Now or PanBio or (Xpert and Xpress) AND (coronaviru* OR "corona virus" OR ncov* OR n cov* OR COVID-19 OR COVID19 OR COVID-2019 OR COVID2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV2 OR SARSCOV19 OR SARS-COV-19 OR SARSCOV-19 OR SARSCOV2019 OR SARS-COV-2019 OR SARSCOV-2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2020

PubMed
((BKit or Bd Veritor or ID Now or PanBio or (Xpert and Xpress)) AND (((wuhan[tw] AND (coronavirus[tw] OR corona virus[tw])) OR coronavirus*[ti] OR COVID*[tw] OR nCov[tw] OR 2019 ncov[tw] OR novel coronavirus[tw] OR novel corona virus[tw] OR covid-19[tw] OR SARS-COV-2[tw] OR Severe Acute Respiratory Syndrome Coronavirus 2[tw] OR coronavirus disease 2019[tw] OR corona virus disease 2019[tw] OR new coronavirus[tw] OR new corona virus[tw] OR new coronaviruses[all] OR novel coronaviruses[all] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[nm] OR 2019 ncov[tw] OR nCov 2019[tw] OR SARS Coronavirus 2[all]) AND (2019/12[dp]:2020[dp]))) AND (("2000/01/01"[Date - Publication] : "3000"[Date - Publication]))

WHO Covid-19 Database
BKit or Bd Veritor or ID Now or PanBio or Xpert Xpress

medRxiv & bioRxiv
Search 1: Bkit and posted between "01 Jan, 2020 and 14 Oct, 2020"
Search 2: “Bd Veritor” and posted between "01 Jan, 2020 and 14 Oct, 2020"
Search 3: "id now" and posted between "01 Jan, 2020 and 14 Oct, 2020"
Search 4: PanBio and posted between "01 Jan, 2020 and 14 Oct, 2020"
Search 5: "Xpert Xpress" and posted between "01 Jan, 2020 and 14 Oct, 2020"

Google/Google Scholar
covid-19 BKit or Bd Veritor or ID Now or PanBio or Xpert Xpress

Strategy for Research Question 2

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to October 13, 2020

#	Searches	Results
1	exp Coronavirus/ or Coronavirus Infections/ or coronaviru*.mp. or corona viru*.mp. or ncov*.mp. or n-cov*.mp. or novel cov*.mp. or COVID-19.mp. or COVID19.mp. or COVID-2019.mp. or COVID2019.mp. or SARS-CoV-2.mp. or SARSCoV-2.mp. or SARSCoV2.mp. or SARSCoV19.mp. or SARS-Cov-19.mp. or SARSCov-19.mp. or SARSCoV2019.mp. or SARS-Cov-2019.mp. or SARSCov-2019.mp. or severe acute respiratory syndrome coronaviru*.mp. or severe acute respiratory syndrome cov 2.mp. or 2019 ncov.mp. or 2019ncov.mp.	88912
2	Point-of-Care Testing/	1968
3	((point of care or point-of-care or sample-to-answer or sample to answer or rapid* or fast* or automat* or commercial* or real time or real-time) adj3 (test or tests or testing or assay*)).kf,tw.	78670
4	2 or 3	79594
5	exp Guidelines as Topic/	163323
6	(strateg* or guideline*).kf,tw.	1551746
7	5 or 6	1636418
8	1 and 4 and 7	145

TRIP Database Pro
(point of care test* or point of care assay* or point-of-care test* or point-of-care assay* or sample-to-answer test* or sample-to-answer assay* or sample to answer test* or sample to answer assay* or rapid* test* or rapid assay* or fast* test* or fast* assay* or automat* test* or automat* assay* or commercial* test* or commercial* assay* or real time test* or real time assay* or real-time test* or real-time assay*) AND (coronaviru* OR "corona virus" OR ncov* OR n cov* OR COVID-19 OR COVID19 OR COVID-2019 OR COVID2019 OR SARS-COV-2 OR SARSCOV-2 OR SARSCOV2 OR SARSCOV19 OR SARS-COV-19 OR SARSCOV-19 OR SARSCOV2019 OR SARS-COV-2019 OR SARSCOV-2019 OR "severe acute respiratory syndrome cov 2" OR "severe acute respiratory syndrome coronavirus*" OR "2019 ncov" OR 2019ncov OR Hcov*) from:2020
Filter: All Secondary Evidence

PubMed
((point of care test* or point of care assay* or point-of-care test* or point-of-care assay* or sample-to-answer test* or sample-to-answer assay* or sample to answer test* or sample to answer assay* or rapid* test* or rapid assay* or fast* test* or fast* assay* or automat* test* or automat* assay* or commercial* test* or commercial* assay* or real time test* or real time assay* or real-time test* or real-time assay*)) AND (strategy* or guidline*) AND (((wuhan[tw] AND (coronavirus[tw] OR corona virus[tw])) OR coronavirus*[ti] OR COVID*[tw] OR nCov[tw] OR 2019 ncov[tw] OR novel coronavirus[tw] OR novel corona virus[tw] OR covid-19[tw] OR SARS-COV-2[tw] OR Severe Acute Respiratory Syndrome Coronavirus 2[tw] OR coronavirus disease 2019[tw] OR corona virus disease 2019[tw] OR new coronavirus[tw] OR new corona virus[tw] OR new coronaviruses[all] OR novel coronaviruses[all] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[nm] OR 2019 ncov[tw] OR nCov 2019[tw] OR SARS Coronavirus 2[all]) AND (2019/12[dp]:2020[dp]))) AND (("2000/01/01"[Date - Publication] : "3000"[Date - Publication]))

WHO Covid-19 Database
Point-of-Care Testing

medRxiv & bioRxiv
"covid-19 rapid tests deployment strategy " and posted between "01 Jan, 2020 and 15 Oct, 2020"

Google/Google Scholar
Search string 1: covid rapid tests deployment strategy
Search string 2: covid point-of-care tests deployment strategy

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