

CADTH Horizon Scan

An Overview of Emerging Point-of-Care Tests for Differentiating Bacterial and Viral Infections

Authors: Sinwan Basharat, Jennifer Horton

ISSN: 2563-6596

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein are those of CADTH and do not necessarily represent the views of Canada's federal, provincial, or territorial governments or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to Requests@CADTH.ca

Table of Contents

Key Messages	5
Purpose	5
Methods	5
Peer Review.....	6
Background	6
How They Work	7
Detecting Changes in Host Response Biomarkers	8
Detecting Specific Pathogens.....	8
Regulatory Availability	9
Summary of the Evidence	10
Diagnostic Accuracy.....	11
Antibiotic Prescribing	12
Cost-Effectiveness	14
Feasibility and Acceptability	15
Safety	15
Issues to Consider	16
Settings Where Technology Might Be Beneficial.....	16
POC Tests As Part of Antibiotic Stewardship Programs	17
Post-Pandemic Testing Landscape.....	17
Final Remarks	17
References	19

List of Tables

Table 1: Examples of Commercially Available POC Tests That Could be Used for Differentiating Viral and Bacterial Infections 10

Key Messages

- Antimicrobial resistance is an important health concern in Canada and around the world. Although resistance arises naturally, the overuse of antibiotics, among many other behavioural, social, and economic drivers, contributes to the emergence of resistance patterns. Within health care settings, diagnostic uncertainty, a situation in which it is uncertain whether a suspected infection is due to a bacterial, viral, or other microorganism, is regarded as a key driver that contributes to overuse of antibiotics. In these situations, antibiotics may be prescribed although the infection is viral.
- Emerging health technologies that can help reduce diagnostic uncertainty of acute infections at the point of care may help reduce the unnecessary use of antibiotics. If these point-of-care diagnostic devices demonstrate clinical benefit and cost-effectiveness for health systems, they may complement other interventions as part of antibiotic stewardship programs.
- This Horizon Scan provides an overview of new and emerging point-of-care tests that help differentiate bacterial and viral infections. Although rapid tests for identifying specific pathogens have existed for decades, these emerging tests aim to assess a wider range of possible pathogens and help inform treatment decisions.
- Different types of emerging devices, such as rapid molecular tests and immunoassays, are described including how they work and information about their capabilities that may influence their potential use. The report also describes the evidence about the diagnostic accuracy of certain tests and their effect on reducing antibiotic prescribing. Considerations are provided about where tests might be beneficial, such as primary care settings, and the emerging evidence base for their feasibility and acceptability.
- The emerging evidence suggests that point-of-care tests could be effective tools as part of antibiotic stewardship programs, but further studies assessing specific devices in randomized controlled trials are recommended by researchers and health technology assessment agencies. Monitoring the continued development of devices and the testing landscape, especially in post-pandemic health care, will be important for decision-makers.

Purpose

The purpose of this Horizon Scan is to present health care stakeholders in Canada with an overview of information related to point-of-care (POC) tests for differentiating bacterial and viral infections, a description of some of the published studies, and a summary of some important considerations related to the potential implementation of the technology, procedure, and intervention, should emerging evidence demonstrate value. This report is not a systematic review, does not involve critical appraisal, and does not include a detailed summary of study findings. It is not intended to provide recommendations for or against the use of the technology, procedure, and intervention technology.

Methods

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the devices were POC diagnostic tests that could help differentiate between bacterial and viral infections among people with suspected infectious disease and inform treatment decisions about whether antibiotics

should be used. Health technologies that aim to test for antibiotic susceptibility by identifying resistance profiles or other characteristics of suspected pathogens related to the use of specific antibiotics were not covered. Studies related to devices that primarily detect a specific bacterial or viral pathogen were not included unless they helped inform considerations about POC tests or were grouped together by systematic reviews. Conference abstracts and grey literature were included if they provided additional information to that available in the published studies.

Peer Review

A draft version of this bulletin was reviewed by 1 clinical expert with expertise in antibiotic stewardship interventions and improving health care quality within primary care settings.

Background

Antimicrobial resistance (AMR) refers to a phenomenon in which bacteria, viruses, and other microbial organisms acquire or develop biological defences against antimicrobial medicines, increasing the risk of disease spread and severe illness.¹ In Canada and across the world, AMR is an important health concern that has implications for health systems and poses a social and economic threat to society.¹⁻³ The Council of Canadian Academies' expert panel on AMR estimated that if resistance to first-line antimicrobials increased from 26% (2018 estimate) to 40% by 2050, this could lead to 140,000 preventable deaths and increase health care costs by \$6 billion to \$8 billion dollars.³

Although AMR occurs naturally, inappropriate prescribing of antibiotics is a key driver accelerating AMR.^{4,5} A number of factors contribute to inappropriate prescribing, including sociocultural factors, organizational systems, and practitioner-related training.² Diagnostic uncertainty is known to be an important driver of inappropriate prescribing, especially in primary care and emergency care settings.^{2,6,7} In situations when the cause of an infection is unknown, health care professionals may prescribe antibiotics despite the source of infection potentially being viral or another type of microbe. Unnecessary use of antibiotics is not only clinically ineffective, but may also be associated with treatment complications, adverse events, and increased emergence of antibiotic resistance.⁵

Particularly for respiratory tract infections, a symptoms-based assessment can provide some indication about the type of infection but it is often insufficient to determine the pathogen.⁸ Respiratory tract infections are also the leading illnesses associated with inappropriate prescribing.⁵ An analysis of electronic medical records from Ontario estimated that 15.4% of antibiotics prescribed in primary care were unnecessary; among acute respiratory illnesses, the rate of unnecessary prescribing was between 36.7% and 52.6%.⁹ A study from Manitoba reported that, within primary care, 15.9% of patients with viral infections received inappropriate prescribing of antibiotics.¹⁰ Similar estimates from the US suggest that half of the antibiotics prescribed for acute respiratory illnesses may be unnecessary.¹¹

Health technologies that can reduce diagnostic uncertainty in different health care settings, including community and primary care where more than 92% of antibiotics are prescribed, may help support antibiotic stewardship programs.^{2,8,12} Conventional testing methods of characterizing microbial pathogens (viruses, bacteria, or other microbes responsible

for causing disease) and identifying infectious diseases, such as microbial culturing and laboratory-based molecular tests, are highly accurate but resource-intensive and time-consuming.¹³ These tests may require people to make additional appointments, for example to blood testing laboratories, and results can often take 24 hours or longer, which may limit their practicality for guiding timely treatment decisions in many primary care settings and other health care settings where follow-up may be more challenging (e.g., emergency departments, urgent care centres, and walk-in clinics).¹⁴

Emerging POC tests aim to improve diagnostic certainty and potentially help reduce unnecessary use of antibiotics.¹⁵ Within Canada, POC tests that can specifically detect group A *Streptococcus* (GAS) in people presenting with acute pharyngitis (sore throat) are offered in limited settings.¹⁶ CADTH has previously reviewed the evidence about the clinical utility, safety, and cost-effectiveness of POC tests for detecting GAS.¹⁷ However, there are also emerging tests that aim to improve diagnostic certainty by either identifying the possible pathogen from a panel of viruses and bacteria, or providing information about whether the infection is likely bacterial or viral.¹⁵ Especially in the context of post-pandemic health care, where there may be greater interest to understand and test people with suspected infectious diseases, there is a need to understand the evidence base and issues around emerging POC tests. The purpose of this Horizon Scan is to provide an overview of emerging POC tests that may help differentiate between bacterial and viral infections and aid in reducing unnecessary antibiotic use as part of support antibiotic stewardship programs.

How They Work

POC tests are diagnostic devices that can be administered at the point and place of care, which eliminates the need for additional trips to a testing location and can potentially provide results rapidly or within a short turnaround time.¹⁵ There is little consensus about what constitutes as rapid; generally, it refers to tests that can provide results within minutes to hours and can inform clinical decision-making.^{15,18} Studies have used “rapid” to indicate tests that can provide results in under 2 hours, with many tests able to provide results in under 15 minutes.^{19,20} There are also varied definitions of what is considered “point of care.” Generally, these tests are differentiated from conventional tests performed in dedicated laboratories by specialists; however, some POC tests may require some level of technical training.¹⁹

Conventional methods for microbial identification include tests that use microbial culturing, microscopy, biomarker identification, and/ or nucleic acid amplification techniques.^{13,21} These methods can provide high diagnostic accuracy but are often costly, resource-intensive, and time-consuming.¹⁵ Some conventional tests (e.g., certain molecular tests) can have run times of approximately 4 hours, but the additional time for sample collection and preparation and needing enough samples to complete a batch can lead to turnaround times for results to be 1 day or longer.¹⁴ Microbial culturing methods may take several days.¹³ Compared with conventional tests, POC tests may provide a faster alternative to diagnostic information and provide timely results to inform the use of antibiotics. Two types of POC tests that can help assess whether a person may have a viral or bacterial infection were identified. These tests either characterize host response biomarkers or identify specific viral and/or bacterial signals.

Detecting Changes in Host Response Biomarkers

One approach for differentiating between viral and bacterial infections is to examine host biomarkers that respond differently to both types of pathogens. Certain host biomarkers, including many immune response proteins, are known to either increase or decrease following a bacterial or viral infection and can be informative.^{15,22} Emerging POC tests aim to provide either quantitative (specific concentration level) or qualitative (whether the level is significant or not) assessment of different biomarkers. Tests measuring biomarkers such as C-reactive protein (CRP), procalcitonin, and pro-inflammatory cytokines are being developed and some are commercially available.^{22,23} The timing and intensity of each marker varies and influences different tests' usability and accuracy, for example:

- CRP is the most well-studied inflammation biomarker for predicting bacterial infections with POC testing.²¹ Plasma levels of CRP rise after 4 hours to 6 hours of bacterial infection and peak at 36 hours.^{22,24}
- Procalcitonin levels rise 3 hours after infection and peak within 24 hours.²³
- Cytokines, such as interleukin-6 and interleukin-8, have also been investigated as potential informative markers.²¹ However, cytokines have short half-lives, so levels rise and fall back to baseline relatively quickly (within 6 hours), and can have variable changes in response to different types of bacteria.²²

Other biomarkers are known to increase in response to viral infections. These include tumour necrosis factor-related apoptosis-inducing ligand (TRAIL), interferon (IFN) gamma-induced protein 10 (IP-10), and myxovirus resistance protein A (MxA).^{21,22} Emerging research suggests that tests which detect multiple biomarkers may provide higher diagnostic accuracy for assessing people with pneumonia than tests which detect a single biomarker.^{21,25}

Tests that examine host biomarkers rely on blood samples (either finger pricks or a greater volume for serum blood) and do not require extensive treatment of the samples. However, one of the challenges with these markers is that, without baseline information about specific individuals' biomarker levels, the test results may be incorrectly interpreted for some people.²⁶ This uncertainty in the results can occur because inflammation biomarkers are not exclusive to the infection response; therefore, other underlying health conditions or individual-level variation may be associated with higher levels and test results could be misinterpreted.²⁶ Authors of 2 systematic reviews have suggested that POC tests that use host biomarkers should consider the results as part of the entire clinical assessment and not stand-alone diagnostic tools.^{25,27} Other types of tests that detect changes in gene expression of host response genes after an infection are being developed,²⁸ but limited information about commercially available POC tests was identified.

Detecting Specific Pathogens

In a laboratory setting, identifying specific pathogens requires using microbial culturing methods or, more often, molecular information with real-time PCR tests.¹³ A second approach to differentiating between bacterial and viral infections, other than tests detecting host biomarkers, are emerging molecular tests that can detect a panel of various viruses and bacteria that aim to provide results more rapidly and near the POC. These tests are also based on PCR technology but 1 sample can be analyzed for multiple targets (referred to as *multiplex*) and can be operated without extensive laboratory training or equipment.^{29,30} The tests provide a trade-off between speed and comprehensive analysis of molecular information because tests are limited to identifying a pre-set list or panel of pathogens.²⁹ For

example, panel assays are able to identify viral pathogens such as influenza A/B, respiratory syncytial virus, human adenovirus, and bacterial pathogens such as *Chlamydomphila* and *Mycoplasma* within a single sample.²⁰ Some devices, such as influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) co-tests, are limited to detecting 2 viral pathogens.³¹ Most panel tests have been developed for respiratory infections and therefore use nasopharyngeal or sputum samples.²⁰

Antigen-based tests are also able to identify specific pathogens. They have been traditionally limited to detecting 1 or 2 specific pathogens, such as influenza A/B, GAS, and more recently SARS-CoV-2.³²⁻³⁴ However, an emerging antigen-based test, mariPOC, aims to detect multiple pathogens.³⁵ Antigen tests use lateral flow assays and because they rely on detecting viral or bacterial components, they are most effective during early stages of the infection when viral or bacterial load are often higher.³⁶ As these tests tend to have lower sensitivity, they may be limited in being able to diagnose illness, but may help rule out specific pathogens during clinical assessment.³⁶

Table 1 provides a list of emerging commercially available tests that could be used to help differentiate between viral and bacterial pathogens. However, not all tests may be available in Canada or are authorized specifically for differentiating between bacterial and viral infections because they may have been authorized for detecting infections. Tests produced by other manufacturers that assess the same biomarkers have not been listed. The list is not exhaustive and does not include tests that identify single or dual (co-tests) specific pathogens; rather, it includes examples of tests that can detect multiple targets or aid in detecting whether an infection may be bacterial or viral.

Regulatory Availability

Few POC tests that can aid in differentiating between viral and bacterial infections have been authorized for clinical use in Canada specifically for this purpose. [FebriDx](#) is single-use POC test that is authorized in Canada and Europe. It uses a finger prick blood sample to detect 2 biomarkers to provide a qualitative result about likely bacterial or viral infection within 15 minutes.³⁷ The test secured a Canadian distributor in March 2021.⁴⁵ POC tests that measure individual biomarkers, such as CRP and procalcitonin, have been authorized and are available in Canada for detecting infections (but not necessarily to aid in differentiating types of infections) from manufacturers such as [Abbott](#), [Radiometer](#), and [Roche](#). Immunoassay-based tests developed by these companies require a benchtop analyzer for different biomarkers and specific cartridges or sampling kits for individual biomarkers of interest.

[BioFire's](#) FilmArray multiplex PCR assays can detect multiple pathogens and are authorized for clinical use in Canada. Different assays have a different set of viruses and bacteria that can be detected. The [ImmunoXpert](#) (MeMed) and [mariPOC](#) (ArcDia) tests are both authorized in Europe but are not authorized in Canada. A newer version of MeMed's immunoassay that can deliver results in 15 minutes received 510(k) or premarket clearance by the FDA in September 2021.⁴⁶

Summary of the Evidence

Specific devices have varied technical capabilities and have been tested in different settings and contexts; therefore, this Horizon Scan provides a general overview of the evidence base of emerging POC tests for differentiating viral and bacterial infections in clinical practice. Because of the complexity of comparing individual studies, the synthesis was limited to narrative and systematic reviews examining a range of devices; individual studies were referred to when limited information was found in reviews. There were 2 systematic reviews that described diagnostic accuracy and 2 systematic reviews that described the effect of POC tests on antibiotic prescribing rates; however, no systematic reviews described cost-effectiveness. Additional narrative reviews and other reports have also been included to provide further context.

The findings have not been critically appraised and are not intended to recommend for or against any specific device or health technology. Rather, the findings are intended to help inform considerations about settings and applications where POC tests may potentially help support antibiotic stewardship programs, should the tests demonstrate value.

Table 1: Examples of Commercially Available POC Tests That Could be Used for Differentiating Viral and Bacterial Infections

Test name and manufacturer	Type of assay (biomarkers)	Listed time to results	Pathogens detected	Sample type
FebriDx Lumos Diagnostics ³⁷	Immunoassay (CRP and MxA)	10 to 15 minutes	Nonspecific; viral or bacterial	Capillary blood
ImmunoXpert MeMed ³⁸	Immunoassay (CRP, TRAIL, and IP-10)	100 minutes (new version, MeMed BV may provide results in 15 minutes ³⁹)	Nonspecific; viral or bacterial	Serum blood
Afinion CRP Abbott ⁴⁰	Immunoassay (CRP)	4 minutes	Nonspecific; viral or bacterial	Capillary blood
AQT90 FLEX Radiometer ⁴¹	Immunoassay (procalcitonin)	Approximately 20 minutes	Nonspecific; viral or bacterial	Serum blood
FilmArray BioFire ⁴²	Multiplex PCR	45 minutes to 1 hour (varies by panel)	More than 20 viruses, bacteria, and parasites (varies by panel)	Nasopharyngeal swab for respiratory panels Stool sample for gastrointestinal panel
ePlex Respiratory Pathogen Panel GenMark Diagnostics ⁴³	Multiplex PCR	90 minutes	17 viruses and bacteria	Nasopharyngeal swab
mariPOC Respi+ ArcDia ⁴⁴	Immunoassay (multiple antigens)	20 minutes (preliminary); 2 hours (final results)	9 viruses and 1 bacterial pathogen	Nasopharyngeal swab

CRP = C-reactive protein; IP-10 = interferon gamma-induced protein 10; MxA = myxovirus resistance protein A; PCR = polymerase chain reaction; TRAIL = tumour necrosis factor-related apoptosis-inducing ligand.

Diagnostic Accuracy

Studies characterizing the diagnostic accuracy and clinical performance of POC tests report sensitivity, the ability of a test to correctly identify people who have been infected with a pathogen, and specificity, the ability of a test to correctly identify people who have not been infected with a pathogen.⁴⁷ Higher or lower sensitivity and specificity have implications about how a test may be used (i.e., for identifying a pathogen or ruling out a pathogen).⁴⁷ Findings were summarized from 2 systematic reviews,^{25,48} 3 narrative reviews,^{20,35,49} and 1 rapid assessment.²⁴

Tests With FDA or CE Approval

A narrative review provided an overview of more than 30 POC tests that can provide a result in under 2 hours and that have received FDA (US) or Conformité Européenne (Europe) authorization.²⁰ Of these, the majority of tests are able to test either 1 or 2 specific viral pathogens. Sensitivity and specificity of devices that use respiratory samples were reported to range between 80% to 100%.²⁰ The review did not calculate pooled estimates of diagnostic accuracies, but rather described and listed the diversity of different POC tests available, test characteristics (e.g., sample type, pathogens detected, and time to results), and the range of diagnostic accuracies reported by studies. The review was intended to help inform considerations about how tests may be integrated into clinical workflows based on test characteristics. For many POC tests, clinical validation studies had limited sample sizes; therefore, the authors indicated that measures of diagnostic performance should be interpreted with caution.²⁰

Immunoassay-Based POC Tests

One systematic review²⁵ pooled the results of studies that examined the diagnostic accuracy of ImmunoXpert and FebriDx in primary or secondary care settings.²⁵ The tests were compared with reference standards that included expert clinician panels or clinical decision-making tools that factored in data of clinical, laboratory, and PCR results of people being tested (note: reference standards may also be prone to some level of inaccuracy). Both tests are immunoassays that detect multiple host biomarkers that indicate whether a person may have a viral or bacterial infection but there are differences in sample collection and analysis platforms. One key difference between the tests is the time to results, which is 100 minutes for ImmunoXpert and 10 minutes to 15 minutes for FebriDx. The systematic review²⁵ reported that

- ImmunoXpert had a pooled:
 - sensitivity of 85% (95% CI, 75% to 91%) and specificity of 86% (95% CI, 73% to 93%) for bacterial infections
 - sensitivity of 90% (95% CI, 79% to 96%) and specificity of 92% (95% CI, 83% to 96%) for viral infections.
- FebriDx had a pooled:
 - sensitivity of 84% (95% CI, 75% to 90%) and specificity 93% (95% CI, 90% to 95%) for bacterial infections
 - sensitivity of 87% (95% CI, 72% to 95%) and specificity 82% (95% CI, 66% to 86%) for viral infections.

Additionally, the European Network for Health Technology Assessment conducted a rapid assessment of POC tests that measure CRP in primary care settings. Although diagnostic accuracies of different tests were reported, pooled estimates of sensitivity and specificity

were not provided.²⁴ The authors indicated that there was substantial heterogeneity among studies due to varied study designs, study populations, and uses of the POC CRP test results as part of clinical pathways, which made calculating pooled estimates challenging.²⁴ For example, in some settings, CRP POC testing was used alongside other clinical tools; studies also used different threshold criteria for determining what CRP levels suggest a bacterial infection.²⁴ Similar to findings by Health Technology Wales,⁵⁰ this Horizon Scan identified no systematic reviews reporting the diagnostic accuracy of POC tests that measure procalcitonin.

Panel-Based POC Tests

One systematic review⁴⁸ examined the diagnostic accuracy of multiplex PCR assays capable of identifying a panel of different pathogens compared with reference standards, including RT-PCR, microbial culturing, and antibody assays. Of the different tests, FilmArray is capable of identifying a panel of both viral and bacterial pathogens. The systematic review, however, focused on the diagnostic accuracy of the test to identify common viral infections (e.g., influenza, adenovirus, and others). For detecting influenza A, FilmArray was reported to have a pooled sensitivity of 91.1% (95% CI, 84.8% to 94.9%) and a specificity of 99.5% (95% CI, 98.8% to 99.8%).⁴⁸ Diagnostic accuracy for detecting other viruses was similarly high (> 80%), except for adenovirus, which had a lower sensitivity (67.0%).⁴⁸

A narrative review described that tests using multiplex PCR can have higher levels of sensitivity and specificity than immunoassays and may provide information about specific antibiotic-resistant genes; however, they are reported to have longer run times and can be prone to test failure (10% to 30% failure rate).⁴⁹ Rapid antigen tests with multiple targets, such as the mariPOC test, can detect a panel of viruses and bacteria. They can have high test specificity but also lower sensitivity rates, which may affect their ability to rule out pathogens suspected of causing illness in clinical settings.^{20,35}

Antibiotic Prescribing

Antibiotic stewardship consists of a set of interventions and strategies used in a variety of health care settings, including general practice, emergency care, and inpatient care, to improve appropriate antibiotic use.⁵¹ Different outcomes are used to evaluate the effectiveness of interventions depending on the setting and the context.⁵² Outcomes, such as hospital length of stay, clinical outcomes, and antibiotic resistance patterns, are important measures, but can be affected by multiple factors and are difficult to assess between studies.^{52,53} For this Horizon Scan, the evidence specifically on antibiotic prescribing was reviewed.

Findings were summarized from 2 systematic reviews^{27,54} and 1 rapid assessment²⁴ assessing POC testing for CRP. There were a limited number of systematic reviews identified that assessed POC tests for other biomarkers for differentiating bacterial and viral infections; however, 1 randomized controlled trial (RCT)⁵⁵ for POC tests for procalcitonin was identified. Additional systematic reviews examined the effects of a combination of antibiotic stewardship interventions,⁵⁶ POC tests for detecting GAS,⁵⁷ and POC tests for influenza⁵⁸ on antibiotic prescribing. One narrative review,³⁰ but no systematic reviews, were identified that assessed POC tests able to detect a panel of pathogens.

Immunoassay-Based POC Tests

CRP and procalcitonin are the most well-studied immunological biomarkers that can differentiate between bacterial and viral infections.²¹ Most research on these biomarkers has focused on laboratory testing of both markers. However, 2 systematic reviews were identified that examined the effect of POC tests that measure CRP compared with usual care of no CRP testing and routine clinical assessment (may include diagnostic tools, scoring algorithms, or scans). In these 2 reviews, risk ratios were used to describe the change in antibiotic prescribing rates.

Evidence from these systematic reviews on immediate antibiotic prescribing showed that POC tests for CRP were associated with a risk ratio of 0.81 (95% CI, 0.71 to 0.92)²⁷ in ambulatory care settings (i.e., outpatient settings, walk-in clinics, or emergency departments) and a risk ratio of 0.79 (95% CI, 0.70 to 0.90)⁵⁴ in primary care settings more generally. Therefore, POC tests for CRP likely reduce antibiotic prescribing at the point where people seek care compared with usual care without a POC test. Both systematic reviews reported a stronger effect of lowering antibiotic prescribing rates when clinical guidance about interpreting CRP levels was provided alongside POC tests compared with the POC tests alone.^{27,54} The European Network of Health Technology Assessment similarly reported that POC testing for CRP was associated with a lower rate of antibiotic prescribing with a relative risk of 0.76 (95% CI, 0.67 to 0.86).²⁴ Overall, these evidence reviews report POC tests for CRP are associated with reducing antibiotic prescribing and may help guide antibiotic use in primary care setting. However, the study authors indicated a need for more RCTs to examine the effect of POC tests for CRP among children.^{24,27,54}

The 1 systematic review on procalcitonin research⁵⁹ reported that laboratory-based testing of this biomarker is associated with reduced antibiotic prescribing. Similar to findings from Health Technology Wales, no systematic reviews or health technology assessments were identified for POC testing for procalcitonin.⁵⁰ One RCT⁵⁵ from Switzerland examining a POC test for procalcitonin was identified. The study showed that POC testing for procalcitonin along with clinical guidance about interpreting the results was associated with a 26% (95% CI, 10% to 41%) reduction in antibiotic prescribing compared with usual care of no testing among adults attending primary care (visits to general practitioner) for suspected pneumonia.⁵⁵

One small retrospective study reported that the FebriDx test (which detects 2 immunological biomarkers) was associated with reduced antibiotic use.⁶⁰ However, authors of a systematic review that examined the diagnostic accuracy of immunoassay-based POC tests recommended that more research, particularly RCTs, is needed to assess the effectiveness of immunoassay-based POC tests.²⁵ The European Network of Health Technology Assessment, in the review of POC CRP tests, also recommended further research to understand the long-term effects of using POC tests on prescribing rates in different types of primary care settings.²⁴

POC Tests for Group A *Streptococcus* and Influenza

One systematic review included RCTs of multiple antibiotic stewardship interventions used in primary care to reduce antibiotic prescribing for people with respiratory tract infections.⁵⁶ The review identified 17 eligible studies, 6 of which showed clinically meaningful reductions (difference of 10% or greater) in prescribing rates among the intervention groups.⁵⁶ The review also reported that interventions that included communication skills training for health care professionals and rapid POC testing, either alone or in combination, reduced antibiotic

prescribing by 1.5% to 23.3%.⁵⁶ POC tests included in the studies were either tests that measured CRP or antigen tests for GAS.

A systematic review that focused on rapid antigen-based POC tests for GAS used in primary care settings reported that POC tests were associated with a 25% (95% CI, 18% to 31%) reduction in antibiotic prescribing compared with usual care.⁵⁷ Another systematic review that examined rapid POC tests for influenza viruses reported that 20 of 26 included studies showed POC tests used in emergency care, acute medical centre, or home visits for people presenting with suspected acute respiratory infections were associated with significantly decreased antibiotic prescribing.⁶¹ Eleven of these 20 studies also showed that a positive POC test result for influenza was associated with reduced antibiotic prescribing.⁶¹ Based on the evidence, the authors of the systematic review concluded that a positive result of influenza from POC tests may lead to a significant reduction of unnecessary antibiotic use.⁶¹

Panel-Based POC Tests

Research examining the effectiveness of POC tests that use multiplex PCR technology or tests that measure multiple targets is emerging. Although no systematic reviews were identified, 1 narrative review³⁰ describing the potential role of multiplex PCR panel assays (tests that can detect multiple viral and bacterial pathogens) for antibiotic stewardship was identified. The narrative review reported that studies in which panel assays were used in conjunction with tests for procalcitonin were more likely to observe significant reductions in antibiotic prescribing than studies that exclusively used panel assays.³⁰ Based on the available evidence, the authors concluded that panel assays on their own may increase rates of antiviral prescribing because the majority of panel targets are viral rather than bacterial, but they may be limited in significantly reducing rates of antibiotic prescribing.³⁰ It is uncertain what effect panel assays may have in influencing antiviral prescribing in Canadian health care settings because, according to clinical guidelines, antivirals for uncomplicated or mild flu-like illnesses are not prescribed for adults or children.^{62,63}

One of the POC tests identified in the narrative review was the FilmArray panel assay that can detect a combination of common viruses and bacteria. Additional studies published since the narrative review that specifically examined FilmArray, reported that the test may be associated with some level of reduced antibiotic use. These included 1 prospective cohort study⁶⁴ of children in critical care, 1 prospective cohort study⁶⁵ of people in emergency care, and 1 RCT⁶⁶ among people in a non-ICU hospital ward; all 3 studies reported that the test may have some influence on reducing antibiotic prescribing.

Cost-Effectiveness

A narrative cost-effectiveness review comparing rapid POC tests to conventional laboratory-based PCR tests reported that many studies have examined cost differences of individual tests, but the evidence base about their cost-effectiveness in clinical practice was mixed.⁶⁷ The review reported variable cost-effectiveness results based on how tests are used to inform clinical decision-making, study settings (e.g., emergency care or inpatient care), and study designs. The authors concluded that there is a need for more RCTs to assess their added value.⁶⁷ Similarly, another review of POC tests used in emergency care reported that there was limited health economic outcomes reported by studies and randomized trials are needed to assess the effect of POC tests on clinical workflow, clinical management, and patient outcomes.²⁰ In particular, the review highlighted the need to contextualize cost-effectiveness studies based on who performs the POC tests, time to results, interpretation of results, and

how results influence treatment decisions, which all will vary based on the health care setting and geography.²⁰

One cost-modelling study from the UK estimated that implementing POC testing within general practices and emergency care settings could provide cost-savings to the national health system.⁶⁸ The study considered the hypothetical implementation of the FebriDx test or a similar test that can provide results within 15 minutes for diagnosing acute respiratory infections. The study estimated that the cost-savings from potentially reduced prescriptions, adverse events of antibiotics, and health care use could be between £3.6 million to £17.9 million annually for the National Health Service.⁶⁸ However, the authors of the study cautioned that their modelling had simplified both costs and benefits so it may not reflect the true cost-effectiveness of POC tests and their impact on the health system.⁶⁸ Another economic modelling study that focused specifically on CRP POC testing reported that cost-effectiveness of tests was unclear because there was substantial variation in how tests were used and implemented in clinical practice.⁶⁹

Feasibility and Acceptability

Feasibility and acceptability assessments, as part of clinical validation studies, have described the views of people receiving test results and health care professionals administering POC tests. For example, a mixed-methods evaluation from the UK that examined POC testing in primary care reported that clinicians and other health care staff felt enthusiastic about such tests and their potential to help reduce diagnostic uncertainty.⁷⁰ However, staff also expressed concerns about tests that take longer than 1 hour, and clinicians stated a need for more rigorous research to assess the added value of POC tests on patient care and outcomes.⁷⁰ Another clinical feasibility study assessing the views of patients and practitioners in general practices in the Netherlands also reported increased patient satisfaction and concerns about time to results.³⁵

A pilot study from Australia offered POC CRP testing in community pharmacies and reported that nearly all people suspected of having respiratory tract infections who received the testing service rated it as excellent (88.9%) or good (10.3%) in a follow-up questionnaire.⁷¹ Half the participants (50.9%) also reported that the test results changed their perception about needing antibiotics.⁷¹

There is a large body of evidence on the acceptability of POC tests used for influenza and GAS, which could be applicable to emerging POC as well. For example, a retrospective study of 7,050 people across 3 Canadian provinces who received POC tests for GAS reported that tests can be effective in appropriately guiding antibiotics use and may be acceptable for people seeking treatment.⁷²

Safety

The primary safety concern with all diagnostic tests is whether a test can accurately and reliably make a correct diagnosis and how that diagnostic information influences treatment decisions.⁷³ For POC tests that may aid in differentiating bacterial and viral infections, the result may insinuate that an antibiotic treatment course be withheld.¹² In different health care settings, the implications of withholding antibiotics will vary. For example, in otherwise healthy people with mild or less severe illnesses who present at primary care, restricting antibiotics may not be associated with significant safety concerns because the condition may be self-limiting.⁷⁴

At a systems level, reducing antibiotic use within primary care is shown to be associated with a small increase in cases of pneumonia (1.1 more cases per year in an average practice of 7,000 patients), but not an increase in cases of severe illness.⁷⁵ However, treatment guidelines recommend increased caution when making treatment decisions among subgroups of people at higher risk of developing severe illness.^{16,74,75} Similarly, people with more severe illness who are admitted to hospital general or intensive care wards may require greater diagnostic certainty offered by conventional testing methods to better inform treatment decisions.^{12,18} Reviews have reported a need to further assess the safety concerns of POC tests for both individual patients and the public health implications related to their potential effect on antimicrobial resistance patterns.^{12,25}

Issues to Consider

Settings Where Technology Might Be Beneficial

In addition to test performance and usability for different types of pathogens, characteristics about operating POC tests, infrastructure set up, and integration into clinical workflow will inform if and where POC might provide benefit to patients and health systems.¹⁵ POC tests are not intended to be stand-alone diagnostic devices, but rather a part of a wider clinical assessment that takes into account patient characteristics and symptoms.^{18,25,26} The sensitivity and specificity of different tests can be high (> 80%), but many studies have reported there can be substantial variability in these estimates depending on the context of where and how tests are implemented.^{20,24,25} Health care systems determining whether to incorporate POC tests should contextualize study findings to their specific settings to understand their potential impact to clinical work flow.

Before the COVID-19 pandemic, guidelines from the National Institute for Health and Care Excellence (NICE) recommended that POC testing for the CRP biomarker among people suspected of pneumonia could be used to inform treatment decisions within primary care.⁷⁶ Similarly, a NICE innovation briefing about the FebriDx device suggested that the intended place of the device could be primary care or settings such as emergency care or outpatient clinics (not requiring hospital admission) should the device demonstrate value in more rigorous research studies.⁷⁷ Within these settings, patient volumes are higher, there may be limited time to perform time-consuming diagnostics assays, and the rates of inappropriate prescribing of antibiotics are known to be higher.^{2,6,78} Community pharmacies have also been recommended as potential places where this technology may be further evaluated.^{71,79}

Tests that can be performed easily with minimal training by health care professionals or other health care staff and can provide results within a short time might be beneficial. Two systematic reviews examining emerging POC tests that can differentiate between viral and bacterial infections indicated that tests that require table top analyzers and additional technical training, albeit not to the extent of a laboratory specialist, may not be suitable for primary care settings.^{25,30} This might include multiplex PCR tests or immunoassays that require longer run times of approximately 1 hour or more and some level of sample treatment and preparation.¹⁹ One study also reported that although tests that require longer run times are quicker than conventional testing methods, additional staff are often required to run the tests which can add additional time to workflows and limit their ability to inform treatment

decisions quickly.^{70,80} These types of tests may be more suitable in settings where there is a dedicated testing facility or additional staff to operate the tests.

POC Tests As Part of Antibiotic Stewardship Programs

A broader consideration about different POC tests is their potential role as part of antibiotic stewardship programs. Fundamentally, POC tests are intended to inform treatment decisions and lead to changes for both health care professionals and people seeking care for a suspected infection who may be uncertain about the need for antibiotics.¹⁸ Although diagnostic uncertainty is an important factor related to inappropriate prescribing, health care professionals' tolerance for uncertainty and the clinical guidelines adopted to deal with uncertainty are also important implications in primary care settings.⁶ A systematic review identified 80 different factors discussed in studies that may be associated with inappropriate prescribing of antibiotics, which highlights the complexity of the issue.⁵³

In different settings, a combination of interventions can be effective to reduce unnecessary use of antibiotics, including communication training for health care professionals, adoption of delayed prescriptions, feedback on prescribing data, or educational material for the public.^{56,81} Interventions, including POC tests, to reduce antibiotic prescribing are also shown to be more effective in contexts where rates of prescribing are higher.⁵⁶ In places where there are higher levels of antibiotics prescribing, system-level interventions that address clinical decision-making and improve public health messaging may lead to broader quality improvements in health care.⁸¹ More research about POC tests and how they are integrated into a system of other antibiotic stewardship programs can help to better assess their potential benefit.^{12,81}

Post-Pandemic Testing Landscape

Due to the COVID-19 pandemic and heightened awareness of testing, particularly for respiratory tract infections, there may be increased interest in testing and greater diagnostic certainty for other illnesses.⁷⁶ The proliferation of emerging POC testing technologies that can accurately and quickly provide diagnostic information near the place of care will likely continue for several years.⁸² Increased investment into research and development of health technologies along with increased expectations of diagnostic information about suspected illness may continue to influence the testing and POC testing landscape.

Final Remarks

Emerging POC tests that may aid in differentiating between bacterial and viral infections may be 1 tool in a wider set of interventions aimed at reducing the unnecessary use of antibiotics. Although single-pathogen tests have existed for decades, emerging tests that can detect multiple pathogens or help provide information about whether an infection is likely caused by a bacterial or viral pathogen may help reduce diagnostic uncertainty. POC tests may support other antibiotic stewardship interventions in certain health care settings associated with higher rates of unnecessary antibiotic use, and where it may be feasible to use tests.² However, more rigorous research evaluating emerging devices in RCTs, cost-effectiveness studies, and studies assessing safety outcomes are needed to demonstrate value.^{12,24,25,76} There was limited information identified about emerging POC tests for differentiating bacterial and viral infections in conditions other than suspected respiratory illness, such as urinary

tract infections; this may be an area of future development. If POC tests are shown to provide benefit, understanding the role these tests could play among a broader set of interventions for antibiotic stewardship may help health systems in Canada and across the world address the threat of AMR.

References

1. World Health Organization. Antimicrobial resistance. *Fact Sheets* 2021; <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>. Accessed 2021 Nov 29.
2. Public Health Agency of Canada. Preserving Antibiotics Now and Into the Future - Chief Public Health Officer of Canada's 2019 Spotlight Report. 2019; <https://www.canada.ca/en/public-health/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/preserving-antibiotics/message.html>. Accessed 2021 Nov 29.
3. When Antibiotics Fail. *The Expert Panel on the Potential Socio-Economic Impacts of Antimicrobial Resistance in Canada*. Ottawa, ON: Council of Canadian Academies; 2019: <https://cca-reports.ca/wp-content/uploads/2018/10/When-Antibiotics-Fail-1.pdf>. Accessed 2021 Nov 29.
4. Holmes AH, Moore LSP, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *The Lancet*. 2016;387(10014):176-187. [PubMed](#)
5. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014;5(6):229-241. [PubMed](#)
6. Wang D, Liu C, Zhang X, Liu C. Does diagnostic uncertainty increase antibiotic prescribing in primary care? *NPJ Prim Care Respir Med*. 2021;31(1):17. [PubMed](#)
7. Shallcross LJ, Rockenschaub P, McNulty D, Freemantle N, Hayward A, Gill MJ. Diagnostic uncertainty and urinary tract infection in the emergency department: a cohort study from a UK hospital. *BMC Emerg Med*. 2020;20(1):40. [PubMed](#)
8. Shah SN, Bachur RG, Simel DL, Neuman MI. Does This Child Have Pneumonia?: The Rational Clinical Examination Systematic Review. *JAMA*. 2017;318(5):462-471. [PubMed](#)
9. Schwartz KL, Langford BJ, Daneman N, et al. Unnecessary antibiotic prescribing in a Canadian primary care setting: a descriptive analysis using routinely collected electronic medical record data. *CMAJ Open*. 2020;8(2):E360-E369. [PubMed](#)
10. Singer A, Fanella S, Kosowan L, et al. Informing antimicrobial stewardship: factors associated with inappropriate antimicrobial prescribing in primary care. *Fam Pract*. 2018;35(4):455-460. [PubMed](#)
11. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA*. 2016;315(17):1864-1873. [PubMed](#)
12. Vos LM, Oosterheert JJ. Testing for viral infections in severe lower respiratory tract infections; the unpredictable effects of diagnostic certainty. *Clin Microbiol Infect*. 2019;25(11):1302-1303. [PubMed](#)
13. Franco-Duarte R, Cernakova L, Kadam S, et al. Advances in Chemical and Biological Methods to Identify Microorganisms-From Past to Present. *Microorganisms*. 2019;7(5). [PubMed](#)
14. Beal SG, Assarzagdegan N, Rand KH. Sample-to-result molecular infectious disease assays: clinical implications, limitations and potential. *Expert Rev Mol Diagn*. 2016;16(3):323-341. [PubMed](#)
15. Kozel TR, Burnham-Marusch AR. Point-of-Care Testing for Infectious Diseases: Past, Present, and Future. *J Clin Microbiol*. 2017;55(8):2313-2320. [PubMed](#)
16. Sauve L, Forrester AM, Top KA. Group A streptococcal pharyngitis: A practical guide to diagnosis and treatment. *Paediatr Child Health*. 2021;26(5):319-320. [PubMed](#)
17. Rapid Tests for the Diagnosis of Group A Streptococcal Infection: A Review of Diagnostic Test Accuracy, Clinical Utility, Safety, and Cost Effectiveness. *Rapid response report: peer-reviewed summary with critical appraisal*. Ottawa (ON): CADTH; 2018: <https://www.cadth.ca/rapid-tests-diagnosis-group-streptococcal-infection-review-diagnostic-test-accuracy-clinical>. Accessed 2021 Nov 29.
18. Dhesi Z, Enne VI, O'Grady J, Gant V, Livermore DM. Rapid and Point-of-Care Testing in Respiratory Tract Infections: An Antibiotic Guardian? *ACS Pharmacol Transl Sci*. 2020;3(3):401-417. [PubMed](#)
19. Lisby JG, Schneider UV. Point of care testing for infectious disease: ownership and quality. *J Antimicrob Chemother*. 2021;76(3 Suppl):iii28-iii32. [PubMed](#)
20. Bouzid D, Zanella MC, Kerneis S, et al. Rapid diagnostic tests for infectious diseases in the emergency department. *Clin Microbiol Infect*. 2021;27(2):182-191. [PubMed](#)
21. Tsao YT, Tsai YH, Liao WT, Shen CJ, Shen CF, Cheng CM. Differential Markers of Bacterial and Viral Infections in Children for Point-of-Care Testing. *Trends Mol Med*. 2020;26(12):1118-1132. [PubMed](#)
22. Kapasi AJ, Dittrich S, Gonzalez IJ, Rodwell TC. Host Biomarkers for Distinguishing Bacterial from Non-Bacterial Causes of Acute Febrile Illness: A Comprehensive Review. *PLoS One*. 2016;11(8):e0160278. [PubMed](#)
23. Niehues T. C-reactive protein and other biomarkers—the sense and non-sense of using inflammation biomarkers for the diagnosis of severe bacterial infection. *LymphoSign Journal*. 2018;5(2):35-47.
24. O'Brien K, Gloeckner L, Jordan K, et al. C-reactive protein point-of-care testing (CRP POCT) to guide antibiotic prescribing in primary care settings for acute respiratory tract infections (RTIs). *Rapid assessment on other health technologies using the HTA Core Model for Rapid Relative Effectiveness Assessment*: European Network For Health Technology Assessment; 2019: <https://www.eunetha.eu/the-collaborative-assessment-otca12-on-c-reactive-protein-point-of-care-testing-crp-poct-to-guide-antibiotic-prescribing-in-primary-care-settings-for-acute-respiratory-tract-infections-r/>. Accessed 2021 Nov 29.
25. Carlton HC, Savovic J, Dawson S, Mitchelmore PJ, Elwenspoek MMC. Novel point-of-care biomarker combination tests to differentiate acute bacterial from viral respiratory tract infections to guide antibiotic prescribing: a systematic review. *Clin Microbiol Infect*. 2021;27(8):1096-1108. [PubMed](#)

26. Binnie A, Lage J, Dos Santos CC. How can biomarkers be used to differentiate between infection and non-infectious causes of inflammation? *Evidence-Based Practice of Critical Care*. 2020;319-324.e311.
27. Verbakel JY, Lee JJ, Goyder C, et al. Impact of point-of-care C reactive protein in ambulatory care: a systematic review and meta-analysis. *BMJ Open*. 2019;9(1):e025036. [PubMed](#)
28. Tsalik EL, Henao R, Montgomery JL, et al. Discriminating Bacterial and Viral Infection Using a Rapid Host Gene Expression Test. *Crit Care Med*. 2021;49(10):1651-1663. [PubMed](#)
29. Hogan C, Caya C, Papenburg J. Rapid and simple molecular tests for the detection of respiratory syncytial virus: a review. *Expert Rev Mol Diagn*. 2018;18(7):617-629. [PubMed](#)
30. Covert K, Bashore E, Edds M, Lewis PO. Utility of the respiratory viral panel as an antimicrobial stewardship tool. *J Clin Pharm Ther*. 2021;46(2):277-285. [PubMed](#)
31. Combined Testing for Severe Acute Respiratory Syndrome Coronavirus 2 and Influenza. *CADTH Horizon Scan*. Ottawa (ON): CADTH; 2021: <https://covid.cadth.ca/screening/combined-testing-for-severe-acute-respiratory-syndrome-coronavirus-2-and-influenza/>. Accessed 2021 Nov 29.
32. Green DA, StGeorge K. Rapid Antigen Tests for Influenza: Rationale and Significance of the FDA Reclassification. *J Clin Microbiol*. 2018;56(10). [PubMed](#)
33. Cohen JF, Bertille N, Cohen R, Chalumeau M. Rapid antigen detection test for group A streptococcus in children with pharyngitis. *Cochrane Database Syst Rev*. 2016;7:CD010502. [PubMed](#)
34. Health Canada Medical Devices Directorate. Testing devices for COVID-19: Antigen testing devices. 2021; <https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/medical-devices/testing/antigen-devices.html>. Accessed 2021 Oct 1.
35. Bruning AHL, de Kruijf WB, van Weert H, et al. Diagnostic performance and clinical feasibility of a point-of-care test for respiratory viral infections in primary health care. *Fam Pract*. 2017;34(5):558-563. [PubMed](#)
36. Azar MM, Landry ML. Detection of Influenza A and B Viruses and Respiratory Syncytial Virus by Use of Clinical Laboratory Improvement Amendments of 1988 (CLIA)-Waived Point-of-Care Assays: a Paradigm Shift to Molecular Tests. *J Clin Microbiol*. 2018;56(7). [PubMed](#)
37. FebrIDx. The Science Behind the Accuracy. 2021; <https://www.febridx.com/the-science>. Accessed 2021 Nov 25.
38. MeMed. MeMed. 2021; <https://www.me-med.com/memed-bv>. Accessed 2021 Nov 25.
39. MeMed. What is MeMed BV? <https://www.me-med.com/copy-of-memed-bv>. Accessed 2021 Oct 1.
40. Abbott. Afinion CRP. 2021; <https://www.globalpointofcare.abbott/en/product-details/afinion-crp.html>. Accessed 2021 Nov 25.
41. Radiometer. Rapid procalcitonin (PCT) test. 2021; <https://www.radiometer.ca/en-ca/products/immunoassay-testing/aqt90-flex-immunoassay-analyzer/pct-on-the-aqt90-flex-immunoassay-analyzer>. Accessed 2021 Nov 25.
42. BioFire. The BioFire FilmArray System. 2021; <https://www.biofire.com/products/filmarray/>. Accessed 2021 Nov 25.
43. GenMark Diagnostics. Respiratory Pathogen Panel. 2021; <https://genmarkdx.com/panels/eplx-panels/respiratory-pathogen-panel/>. Accessed 2021 Nov 25.
44. mariPOC. mariPOC Respi+ test for COVID-19 and influenza-like illnesses. 2021; <https://www.arcadia.com/maripoc/tests/respi-tests/>. Accessed 2021 Nov 25.
45. Business Wire. Lumos Diagnostics Announces Northern Diagnostics as Official Canadian Distribution Partner. *Financial Post*. 2021 Mar 3, 2021.
46. Kent C. US approves MeMed test to distinguish bacterial from viral infections. 2021; <https://www.medicaldevice-network.com/news/memed-bacteria-virus-test/>. Accessed 2021 Oct 1.
47. Swift A, Heale R, Twycross A. What are sensitivity and specificity? *Evid Based Nurs*. 2020;23(1):2-4. [PubMed](#)
48. Huang HS, Tsai CL, Chang J, Hsu TC, Lin S, Lee CC. Multiplex PCR system for the rapid diagnosis of respiratory virus infection: systematic review and meta-analysis. *Clin Microbiol Infect*. 2018;24(10):1055-1063. [PubMed](#)
49. Millot G, Voisin B, Loiez C, Wallet F, Nseir S. The next generation of rapid point-of-care testing identification tools for ventilator-associated pneumonia. *Ann Transl Med*. 2017;5(22):451. [PubMed](#)
50. Procalcitonin point-of-care testing for initial assessment of suspected sepsis *Evidence Appraisal Report*. Cardiff (UK): Health Technology Wales; 2019: <https://www.healthtechnology.wales/wp-content/uploads/2019/02/EAR006-Point-of-care-procalcitonin-testing.pdf>. Accessed 2021 Nov 29.
51. McGregor JC, Fitzpatrick MA, Suda KJ. Expanding Antimicrobial Stewardship Through Quality Improvement. *JAMA Netw Open*. 2021;4(2):e211072. [PubMed](#)
52. Dik JW, Hendrix R, Poelman R, et al. Measuring the impact of antimicrobial stewardship programs. *Expert Rev Anti Infect Ther*. 2016;14(6):569-575. [PubMed](#)
53. McKay R, Mah A, Law MR, McGrail K, Patrick DM. Systematic Review of Factors Associated with Antibiotic Prescribing for Respiratory Tract Infections. *Antimicrob Agents Chemother*. 2016;60(7):4106-4118. [PubMed](#)
54. Martinez-Gonzalez NA, Keizer E, Plate A, et al. Point-of-Care C-Reactive Protein Testing to Reduce Antibiotic Prescribing for Respiratory Tract Infections in Primary Care: Systematic Review and Meta-Analysis of Randomised Controlled Trials. *Antibiotics (Basel)*. 2020;9(9). [PubMed](#)
55. Lhopitalier L, Kronenberg A, Meuwly JY, et al. Procalcitonin and lung ultrasonography point-of-care testing to determine antibiotic prescription in patients with lower respiratory tract infection in primary care: pragmatic cluster randomised trial. *BMJ*. 2021;374:n2132. [PubMed](#)

56. Kochling A, Loffler C, Reinsch S, et al. Reduction of antibiotic prescriptions for acute respiratory tract infections in primary care: a systematic review. *Implement Sci*. 2018;13(1):47. [PubMed](#)
57. Cohen JF, Pauchard JY, Hjelm N, Cohen R, Chalumeau M. Efficacy and safety of rapid tests to guide antibiotic prescriptions for sore throat. *Cochrane Database Syst Rev*. 2020;6:CD012431. [PubMed](#)
58. Aabenhus R, Jensen JU, Jorgensen KJ, Hrobjartsson A, Bjerrum L. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. *Cochrane Database Syst Rev*. 2014(11):CD010130. [PubMed](#)
59. Schuetz P, Wirz Y, Sager R, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. *The Lancet Infectious Diseases*. 2018;18(1):95-107. [PubMed](#)
60. Davidson M. FebriDx Point-of-Care Testing to Guide Antibiotic Therapy for Acute Respiratory Tract Infection in UK Primary Care: A Retrospective Outcome Analysis. *Journal of Ancient Diseases & Preventive Remedies*. 2017;05(03).
61. Egilmez E, Walker GJ, Bakthavathsalam P, et al. Systematic review of the impact of point-of-care testing for influenza on the outcomes of patients with acute respiratory tract infection. *Rev Med Virol*. 2018;28(5):e1995. [PubMed](#)
62. Allen UD. The use of antiviral drugs for influenza: Guidance for practitioners. *Paediatr Child Health*. 2018;23(8):563-564. [PubMed](#)
63. Mubareka S, Aoki FY, Allen UD, Hatchette TF, Papenburg J, Evans GA. 2020–2021 AMMI Canada guidance on the use of antiviral drugs for influenza in the setting of co-circulation of seasonal influenza and SARS-CoV-2 viruses in Canada. *JAMMI*. 2020;5(4):214-222.
64. Brotons P, Villaronga M, Henares D, et al. Clinical impact of rapid viral respiratory panel testing on pediatric critical care of patients with acute lower respiratory infection. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2020;Oct:S0213-0005X(0220)30285-30288.
65. Yang S, Li H, Tang Y, et al. Multiplex Tests for Respiratory Tract Infections: The Direct Utility of the FilmArray Respiratory Panel in Emergency Department. *Can Respir J*. 2020;2020:6014563. [PubMed](#)
66. Shengchen D, Gu X, Fan G, et al. Evaluation of a molecular point-of-care testing for viral and atypical pathogens on intravenous antibiotic duration in hospitalized adults with lower respiratory tract infection: a randomized clinical trial. *Clin Microbiol Infect*. 2019;25(11):1415-1421. [PubMed](#)
67. Pinsky BA, Hayden RT. Cost-Effective Respiratory Virus Testing. *J Clin Microbiol*. 2019;57(9). [PubMed](#)
68. Schneider JE, Boehme C, Borisch B, Dittrich S. Application of a simple point-of-care test to reduce UK healthcare costs and adverse events in outpatient acute respiratory infections. *J Med Econ*. 2020;23(7):673-682. [PubMed](#)
69. Holmes E, Harris S, Hughes A, Craine N, Hughes D. Cost-Effectiveness Analysis of the Use of Point-of-Care C-Reactive Protein Testing to Reduce Antibiotic Prescribing in Primary Care. *Antibiotics*. 2018;7(4). [PubMed](#)
70. Khalid TY, Duncan LJ, Thornton HV, et al. Novel multi-virus rapid respiratory microbiological point-of-care testing in primary care: a mixed-methods feasibility evaluation. *Fam Pract*. 2021;38(5):598-605. [PubMed](#)
71. Sim TF, Chalmers L, Czarniak P, et al. Point-of-care C-reactive protein testing to support the management of respiratory tract infections in community pharmacy: A feasibility study. *Res Social Adm Pharm*. 2021;17(10):1719-1726. [PubMed](#)
72. Papastergiou J, Trieu CR, Saltmarche D, Diamantourous A. Community pharmacist-directed point-of-care group A Streptococcus testing: Evaluation of a Canadian program. *J Am Pharm Assoc (2003)*. 2018;58(4):450-456.
73. Singh H, Schiff GD, Graber ML, Onakpoya I, Thompson MJ. The global burden of diagnostic errors in primary care. *BMJ Qual Saf*. 2017;26(6):484-494. [PubMed](#)
74. Rapid tests for group A streptococcal infections in people with a sore throat. *Diagnostic guidance 38*. London (UK): National Institute for Health and Care Excellence; 2019: <https://www.nice.org.uk/guidance/dg38>. Accessed 2021 Nov 29.
75. Gulliford MC, Moore MV, Little P, et al. Safety of reduced antibiotic prescribing for self limiting respiratory tract infections in primary care: cohort study using electronic health records. *BMJ*. 2016;354:i3410. [PubMed](#)
76. Thornton HV, Khalid T, Hay AD. Point-of-care testing for respiratory infections during and after COVID-19. *Br J Gen Pract*. 2020;70(701):574-575. [PubMed](#)
77. FebriDx for C-reactive protein and myxovirus resistance protein A testing. *Medtech innovation briefing 224*. London (UK): National Institute for Health and Care Excellence 2020: www.nice.org.uk/guidance/mib224. Accessed 2021 Nov 29.
78. Brink AJ, Van Wyk J, Moodley VM, et al. The role of appropriate diagnostic testing in acute respiratory tract infections: An antibiotic stewardship strategy to minimise diagnostic uncertainty in primary care. *S Afr Med J*. 2016;106(6):30-37. [PubMed](#)
79. Essack S, Bell J, Burgoyne D, et al. Point-of-Care Testing for Pharyngitis in the Pharmacy. *Antibiotics (Basel)*. 2020;9(11). [PubMed](#)
80. Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *The Lancet Respiratory Medicine*. 2017;5(5):401-411. [PubMed](#)
81. Patel SV, Pulcini C, Demirjian A, van Hecke O. Rapid diagnostic tests for common infection syndromes: less haste, more speed. *J Antimicrob Chemother*. 2020;75(8):2028-2030. [PubMed](#)
82. Sachdeva S, Davis RW, Saha AK. Microfluidic Point-of-Care Testing: Commercial Landscape and Future Directions. *Front Bioeng Biotechnol*. 2021;8:602659. [PubMed](#)