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REVIEW

Point-of-care diagnostics for respiratory viral infections

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ABSTRACT

Introduction: Successful treatment outcomes for viral respiratory tract infections presenting from primary health care to quaternary hospitals will only be achieved with rapid, sensitive and specific identification of pathogens to allow effective pathogen-specific antiviral therapy and infection control measures.

Areas covered: This review aims to explore the different point-of-care tests currently available to diagnose viral respiratory tract infections, discuss the advantages and limitations of point-of-care testing, and provide insights into the future of point-of-care tests. The following databases were searched: Medline (January 1996 to 30 September 2017) and Embase (1988 to 30 September 2017), using the following keywords: 'point of care', 'respiratory virus', 'influenza', 'RSV', 'diagnostics', 'nucleic acid test' and 'PCR'.

Expert commentary: Viral respiratory tract infections cause significant morbidity and mortality worldwide, and point-of-care tests are facilitating the rapid identification of the pathogen responsible given the similarities in clinical presentation.

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1. Introduction

Worldwide, viral respiratory tract infections (vRTIs) are responsible for substantial morbidity and mortality. In the United Kingdom (UK), pneumonia and influenza ranked fourth and sixth as the underlying cause of death in 2011 for females and males, respectively [1]. Similarly, in the United States of America, pneumonia and influenza ranked sixth as the cause of hospitalization among Medicare beneficiaries [2]. These, however, are likely underestimates of the true burden of vRTIs as unrecognized infection may lead to other complications such as respiratory, cardiovascular or neurological, hospitalizations, and deaths [1,3,4].

As the clinical presentation of vRTIs can be similar, laboratory confirmation is important to determine the pathogen responsible for infection. Although viral culture remains the 'gold standard' for diagnosis in practice, virus isolation has been replaced by nucleic acid amplification testing (NAAT) in most reference laboratories given their increased sensitivity, specificity, breadth, and reduced turnaround times (TATs) to pathogen detection [5]. By contrast, point-of-care (POC) testing or near-patient testing which can be non-molecular- or molecular-based is increasingly being used to improve patient outcomes by providing faster TATs. POC testing is defined as the testing of a patient sample, performed in the surgery or clinic at or near the time of consultation. POC tests can also be used in the laboratory environment to provide more rapid testing than more traditional batched (e.g. multiplex NAAT) or slower (e.g. virus isolation) laboratory tests.

POC devices, especially the non-molecular-based assays, have the advantage of not requiring specialized laboratory equipment or expertise to operate, making them suitable for near patient deployment to provide rapid results in 'real-time' which translates to improved clinical decision-making and quality of care. In the management of vRTIs, POC testing facilitates the prescription of antivirals, guides infection control, and obviates unnecessary investigation and therapies.

The World Health Organization developed the ASSURED (affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable) [6] criteria that should be the paradigm for POC testing devices. As such, POC tests based on lateral flow immunochromatography (LFIC) remain the dominant method despite obvious limitations of limited sensitivity and the inability for multiplexing. Although 'lab on a chip' technologies have yet to be fully translated into clinical practice, they are likely to become more common in the future [7,8].

This review aims to explore the different POC tests currently available to diagnose vRTIs, discuss the advantages and limitations of POC testing, and provide insights into the future of POC tests.

2. Why use POC tests for vRTIs

The invention of polymerase chain reaction (PCR) in 1983 revolutionized modern microbiology laboratory diagnostics [9]. NAAT are typically performed in centralized laboratories due to the requirements for specialized equipment and

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technical expertise. Although NAAT is highly sensitive, specific, and quick in comparison with traditional methods such as viral culture, TATs may be delayed due to the requirements for specimen transport prior to testing and the use of batch testing [7].

Differentiating influenza from other respiratory viruses is vital as currently it is the only virus for which there is a safe, effective, and widely available treatment. The use of multiplex assays allows the simultaneous detection of more than one virus from the same sample. However, bacterial and/or viral co-infection in influenza virus infection are uncommon, with Blyth et al. reporting viral co-infection rates of approximately 3% in critically unwell adult and pediatric patients admitted during the 2009 flu season [10].

In influenza virus infection, it is recommended that antivirals such as neuraminidase inhibitors are commenced within 48 h of symptom onset [11]. Clinical judgment has been shown to have sensitivity of 29% when compared to PCR by Davis et al. when diagnosing influenza as symptoms often overlap, highlighting the need for rapid, sensitive, and specific identification of pathogens [12].

The main impact of POC testing is the rapidity of results, which is important to guide clinical management, infection control measures, and identify outbreaks of vRTIs. For influenza virus infection, immunochromatographic-based rapid influenza diagnostic tests (RIDTs) are most useful when the community prevalence of influenza is high, and the positive predictive value of the test is greatest [13]. Positive RIDTs in this context is highly suggestive of influenza infection. Patients with suspected influenza who have negative immunochromatographic-based RIDT results during the influenza season should undergo further testing with NAAT. However, RIDTs have good negative predictive values when the prevalence of influenza is high, despite their relative lack of sensitivity [14]. During periods of low influenza activity, RIDTs have low positive predictive values, and false positive results are more likely. These tests are therefore recommended only during periods of high influenza activity.

In outpatient pediatric settings, positive RIDTs increased the prescription of antiviral therapy and reduced antibiotic prescription [15]. Similarly, when clinicians treating children in an emergency department were aware of positive RIDT results, more patients received antivirals and less antibiotic therapies, had less ancillary investigations (such as complete blood counts, blood cultures, urinalysis, and chest X-rays), and were discharged faster [16].

A retrospective review of adults hospitalized with influenza virus infection by Falsey et al. in 2007 demonstrated that positive RIDTs resulted in the cessation of antibiotics and greater use of antiviral therapy; however, no significant differences in antibiotic days or hospital length of stay was noted [17]. A recent open-label randomized controlled trial that examined patients presenting to the emergency department or acute medical unit of a teaching hospital in the U.K. ascertained that there was no difference in the receipt of antibiotics in patients who were tested with molecular POC test compared to those who were not tested [13]. Similar to other data, this is likely to reflect local practices where antibiotics are routinely prescribed prior to the availability of the POC test result. However, the patients that were tested received more single doses or shorter courses of antibiotics. Furthermore, the mean length of stay was shorter and appropriate antiviral use was greater in patients who were tested. The mean TAT for POC testing versus routine laboratory testing was also significantly reduced from 37.1 h to 2.3 h.

POC tests may also guide infection control measures to optimize patient allocation and bed utilization within the hospital, reduce nosocomial transmission of respiratory viruses, and provide an earlier diagnosis of vRTIs [18–22]. In a prospective, multi-center study in the U.K., it was estimated that the cost savings for managing each subject with suspected influenza virus infection was £214 [12].

POC devices can also be deployed 'in the field,' such as in institutional outbreaks of vRTIs in long-term care facilities, retirement homes, day-care centers, camps, military barracks and schools, or in geographically remote locations. In these settings, identifying the etiology of an outbreak quickly to inform infection control and public health measures is important. The reduced sensitivity of POC tests in this setting may be overcome by testing multiple symptomatic subjects, although generally not all subjects are tested. An evaluation of RIDTs in influenza outbreaks determined that the overall sensitivity, specificity, positive predictive value, and negative predictive value compared to reverse transcriptase-PCR (RT-PCR) were 76.5%, 99.7%, 99.5%, and 85.3%, respectively [23].

2.1. Disadvantages of POC tests

The main limitation of non-molecular-based POC testing is reduced sensitivity and specificity compared to NAAT, as well as the expense and limited validated shelf-life (between 1–2 years) of the reagents [14,24,25]. However, these limitations do not necessarily preclude their use for the detection and management of vRTIs. Furthermore, the analytical sensitivity and specificity of POC tests will continue to improve and be comparable to current NAAT as newer methods and technologies that detect nucleic acid are incorporated into POC tests.

By its nature, POC tests are also not designed for high throughput applications as they do not have the capacity to test multiple specimens concurrently. In addition, earlier generations of POC tests used in the diagnosis of vRTIs only detected one pathogen such as influenza or respiratory syncytial virus (RSV). However, newer nucleic-acid-detection-based and non-nucleic-acid-detection-based multiplex POC tests that detect multiple respiratory viruses have been developed using bead-based or array-based technologies [26,27]. With the availability of pathogen-specific antiviral therapy, it is anticipated that there will be an increased requirement to identify the etiologic agent of the vRTI.

Traditional immunochromatographic RIDTs may not have been able to type/subtype influenza viruses. POC tests may not be available for the detection of novel respiratory viruses, avian influenza viruses, or novel influenza A reassortants when these first appear. The sensitivity of immunochromatographic RIDTs may also be reduced in the context of a newly circulating or avian influenza viruses, as evidenced by influenza A(H1N1)pdm09 and

A(H7N9) [28,29]. Other factors that may reduce the sensitivity of RIDTs include the type of respiratory tract specimen collected, time between symptom onset and specimen collection, poor specimen collection, suboptimal specimen transport, and misinterpretation of test results by inexperienced operators [30]. The use of objective readers to interpret results may, however, reduce the latter.

In countries with public universal health-care systems such as Australia, pathology testing done outside National Association of Testing Authorities accredited laboratories are not reimbursed. By contrast, the costs of performing POC tests are borne by the end-user in other countries without such health-care systems, which may limit their uptake. Although POC tests should be deployed near the patient, testing done outside accredited laboratories may impact on the quality of performing such tests.

Despite the likelihood of increased uptake of POC tests in the future, centralized and reference laboratory testing will still be required for the detection of other respiratory pathogens where POC tests are negative or not available; further characterization of the respiratory viruses detected (such as the typing/subtyping of influenza viruses) identify co-infections, antiviral susceptibility testing, and surveillance to inform public health authorities of impending or current outbreaks. Although accurate disease surveillance by relevant health authorities may be hampered using traditional stand-alone POC devices, this can be circumvented by new technologies that allow for wireless data transfer direct to public health departments.

3. Types of POC tests and their clinical performance

3.1. Non-nucleic acid amplification-based POC tests

Early generation POC tests were membrane-based non-nucleic acid amplification antigen detection tests. For influenza virus detection, these LFIC assays contain an antibody directed against influenza A and B virus nucleoprotein conjugated to colloidal gold on nitrocellulose strips affixed onto cards, cassettes, or cartridges [31]. Viral antigen present in the sample binds to the antibody-colloidal gold conjugate, and is trapped by the capture reagent which results in the appearance of a color band on the test strip. LFIC assays are also available for the detection of RSV. Antigen-based tests have lower sensitivity than NAAT-based POC tests, but have reasonable performance in pediatric populations with higher viral shedding and corresponding higher viral loads [32].

Although the mariPOC® (ArcDia International, Turku, Finland) multianalyte system can detect multiple respiratory viruses simultaneously (including influenza, RSV, parainfluenzaviruses, human metapneumovirus (hMPV), bocavirus, coronavirus, and adenovirus), it requires specialized equipment which is less portable and may not be always available.

As LFIC test strips are subject to reader interpretation, fluorescent immunoassays (FIAs) were developed to improve test interpretation. Using a similar principle to LFIC assays, FIAs such as the Sofia Influenza A + B (Quidel Corp., San Diego, CA) and Veritor (BD Diagnostics, Sparks, MD) systems use fluorescence readers and optical colorimetric devices to detect influenza nucleoproteins, respectively. The Sofia FIA uses specific antibody-coated beads coupled to a heat and light-stable europium chelate instead of colloidal gold in LFIC assays and results are read objectively [5,27,30,32–57]. Table 1 lists some examples and the performance of non-nucleic acid amplification-based POC tests that are currently available to detect respiratory viruses.

3.2. Nucleic acid amplification-based POC tests

Although nucleic acid amplification-based POC tests have been available for a few years now, their uptake has been limited by their slower TATs and costs. Despite their increased sensitivity and specificity and the potential for influenza virus typing/subtyping compared to non-nucleic acid amplification-based tests, TATs of over 60 min were generally considered too long for POC applications. More recently, TATs have substantially improved with improvements in RT-PCR methods and the use of loop-mediated isothermal amplification. Low cycle threshold values are a surrogate for high viral load [36,41]; however, this should be interpreted with caution given the non-uniformity in sample types and volumes (for example, nasal swabs (NS), nose and throat swabs (NTS), nasopharyngeal swabs (NPS), and nasopharyngeal aspirates (NPA)) [58].

The Alere™ i Influenza A & B utilizes isothermal nucleic acid amplification for qualitative detection of influenza A and B viruses. The assay involves real-time fluorescence-based detection of short amplicons following exponential isothermal amplification. Unlike other NAAT assays that require nucleic acid extraction following by thermal cycling using specialized equipment, this assay can be performed using a small benchtop instrument with TATs of 15 min [36,59].

The cobas® Liat® system (Roche Diagnostics, Basel, Switzerland) contains the reagents required for nucleic acid extraction, RT-PCR amplification, and detection of influenza A and B viruses in a single assay tube. The tube is then placed into a benchtop analyzer the size of a shoebox and results are available within 20 min. The RT-PCR cartridge-based Xpert® Xpress and Flu/RSV XC assays (Cepheid Inc., Sunnyvale, CA, U.S.A.) also has TAT of 30–70 min, respectively, for the detection of influenza A, B, and RSV.

The FilmArray® Respiratory Panel (Biofire Diagnostics, Salt Lake City, UT, U.S.A.) system detects up to 17 viruses and 3 bacteria using an automated multiplex PCR format that performs nucleic acid extraction and amplification in a bench top instrument. Although the TATs of the assay is 1 h, the instrument may be applied in specific situations given the range of pathogens that are tested simultaneously. Table 2 [36,60–79] details the types and performance of current nucleic acid amplification-based POC tests used to detect respiratory pathogens.

4. Specimen collection, transport, and pre-analytical issues

The performance of POC tests can be affected by a variety of factors, including the respiratory specimen type, age of the subject as well as the quality, handling, and timing of sample collection, with reported sensitivity between 53 and 100%

Table 1. Examples of non-nucleic acid amplification-based POC testing platforms for detecting respiratory viruses [5,27,30,32,35–54,56,57].

Assay type	Technology	Pathogens detected	Specimen	Specimen		Performance	
Alere BinaxNOW® Influenza A + B Card	LFIC	A/B	15	NW/NA/NS/NPS		Sens (%)	Spec (%)
(Alere Inc., Waltham, MA, U.S.A.)					A	44.4–83	93–100
					B	25–70.8	96–100
Alere BinaxNOW® RSV Card	LFIC	RSV	15	NW	RSV	Sens (%)	Spec (%)
(Alere Inc., Waltham, MA, U.S.A.)						41–93	82–100
Alere™ Influenza A + B	LFIC	A/B	10	NS		Sens (%)	Spec (%)
(Alere Inc., Waltham, MA, U.S.A.)					A	93.8	95.8
					B	77.4	98
QuickVue® Influenza A + B	LFIC	A/B	15	NS/NPS/NW/NPW		Sens (%)	Spec (%)
(Quidel Corporation, San Diego, CA, U.S.A.)					A	20–98	89–100
					B	21–87	90–100
QuickVue® RSV	LFIC	RSV	15	NPS/NW/NPW/NPA	RSV	Sens (%)	Spec (%)
(Quidel Corporation, San Diego, CA, U.S.A.)						58–92	90–100
Sofia®	LFIC	A/B	15	NS/NPS/NW/NPW		Sens (%)	Spec (%)
(Quidel Corporation, San Diego, CA, U.S.A.)					A	71.4–97	95–98.2
					B	33.3–96	96–99.5
					RSV	69–85	94–100
mariPOC®	PE	A/B, RSV	20–120	NA/NW/NS/NPS		Sens (%)	Spec (%)
Respi test		(hMPV);	(final results)		A	54.2–92	98.9–100
(ArcDia International Oy Ltd, Turku, Finland)		(PIV) types 1, 2 and 3;			B	88	99.5–100
		CoV,			RSV	50–92	98–100
		AdV, and *S. pneumoniae*					
BD Directigen™ EZ Flu A + B	LFIC	A/B,	15	NPS/NPA		Sens (%)	Spec (%)
(Becton Dickinson, Franklin Lakes, New Jersey, U.S.A.)					A/B	20.6–62.2	97.1–100
BD veritor™ Influenza A + B, BD veritor™ RSV	LFIC	A/B, RSV	10	NPS/NPA/NPW		Sens (%)	Spec (%)
(Becton Dickinson, Franklin Lakes, New Jersey, U.S.A.)					A	89.6–90.2	99.07
					B	87.5–98.8	100
					RSV	61.3–91.6	94.5–100
SD Bioline Influenza Ag (Standard Diagnostics Inc., Gyeonggi, Korea)	LFIC	A/B	15	TS/NS/NPS/NPA		Sens (%)	Spec (%)
					A/B	54.5–91.8	96.8–100
ESPLINE® Influenza A&B-N	EIA	A/B	15	TS/NPS/NPA		Sens (%)	Spec (%)
(Fujirebio, Inc., Japan)					A	86.8–91.2	95.8–97.1
					B	81.2–94.4	98–99.7

LFIC: lateral flow immunochromatography assay; A: influenza A; B: influenza B; RSV: respiratory syncytial virus; hMPV: human metapneumovirus; PIV: parainfluenzavirus; AdV: adenovirus; CoV: coronavirus; NW: nasal wash; NA: nasal aspirate; NS: nasal swab; NPS: nasopharyngeal swab; NPW: nasopharyngeal wash; TS: throat swab; NPA: negative percent agreement; Sens: sensitivity; Spec: specificity; EIA: enzymeimmunoassay.

Table 2. Examples of nucleic acid amplification-based POC testing platforms for detecting respiratory pathogens [36,60–79].

Assay type	Technology	Pathogens detected	Specimen	Specimen		Performance	
Alere™ i Influenza A & B	LAMP	A/B	15	NS/VTM		Sens (%)	Spec (%)
(Alere Inc., Waltham, MA, U.S.A.)	NEAR				A	77.8–97.9	62.5–100
					B	75–92.5	53.6–99
Alere™ i RSV	LAMP	RSV	13	NS/VTM		Sens (%)	Spec (%)
(Alere Inc., Waltham MA, U.S.A.)	NEAR				RSV	98.6–100	97–98
Xpert®Xpress Flu	rRT-PCR	A/B	20–30	NPS		PPA (%)	NPA (%)
(Cepheid Inc. Sunnyvale, CA, U.S.A.)					A	98.42	100
					B	98	98.6
Xpert®Xpress Flu/RSV	rRT-PCR	A/B & RSV	20–30	NPS		Sens (%)	Spec (%)
(Cepheid Inc. Sunnyvale, CA, U.S.A.)					A	97.8	100
					B	100	99.4
					RSV	90.6	99.4
						PPA (%)	NPA (%)
					A	100	95.2
					B	100	99.5
					RSV	97.1	99.6
Xpert® Flu	rRT-PCR	A/B & 2009 H1N1	75	NPS/NA/NW		Sens (%)	Spec (%)
(Cepheid Inc. Sunnyvale, CA, U.S.A.)					A	90–100	95.2–98.1
					B	100	99.1–99.6
					2009 H1N1	97.1–100	99.6
Xpert® Flu/RSV XC	rRT-PCR	A/B and RSV	40–63	NPS/NA/NW		PPA (%)	NPA (%)
(Cepheid Inc. Sunnyvale, CA, U.S.A.)					A	85.7–100	98.9–100
					B	92–100	100
					RSV	98.5–100	99.6–100
Cobas® Influenza A&B and RSV	rRT-PCR	A/B and RSV	20	NPS		PPA (%)	NPA (%)
(Roche Diagnostics, Basel, Switzerland)					A	98.4–99.6	96.5
					B	97.9–99.3	99.4
					RSV	96.8–97.8	98.4
Cobas® Influenza A/B	rRT-PCR	A/B	20	NPS		Sens (%)	Spec (%)
(Roche Diagnostics, Basel, Switzerland)					A	97.5–97.7	97.9–98.6
					B	96.9–99.2	97.9–99.4
FilmArray Respiratory Panel	End-point melt curve analysis	AdV; CoV (229E, HKU1, OC43, NL63); A (H1/2009, H1, H3);	60	NPS		Sens (%)	Spec (%)
(Biofire/Biomerieux)		B; hMPV; PIV1-4; RSV; RhV/EV			A	90–100	99.1–99.8
		Bordetella pertussis			B	100	100
		C.pneumoniae, M. pneumoniae			RSV	100	89.1–100
					AdV	88.9–100	99.2–100
					BocV	66.7–100	98.4–99.8
					RhV/EV	92.7–92.9	94.6–96.2
					PIV1	100	99.2–99.9
					PIV2	87.4–90	99.8–100
					PIV3	95.8–100	99.8–100
					PIV4	72.7–100	99.9–100
Simplexa™ Flu A/B + RSV	rRT-PCR	A/B, RSV	60	NPS/NTS/BAL		Sens (%)	Spec (%)
(Focus Diagnostics, Cypress, CA, U.S.A.)					A	91.7–100	100
					B	89.1–100	100
					RSV	80.7–90.1	100

LAMP: loop-mediated isothermal amplification; NEAR: nicking enzyme amplification reaction; rRT-PCR: real-time, reverse transcriptase polymerase chain reaction; A: influenza A; B: influenza B; RSV: respiratory syncytial virus; hMPV: human metapneumovirus; PIV: parainfluenzavirus; AdV: adenovirus; CoV: coronavirus; RhV/EV: rhino/enteroviruses; BocV: bocavirus; NW: nasal wash; NA: nasal aspirate; NS: nasal swab; NPS: nasopharyngeal swab; VTM: viral transport media; PPA: positive percent agreement; NPA: negative percent agreement; Sens: sensitivity; Spec: specificity.

[11,12,13,28,80]. Respiratory viruses are more likely to be detected when specimens are collected soon after symptom onset as viral loads are higher early in the illness, with viral shedding peaking in the first 48–72 h of illness in adults [24]. Children generally have higher viral loads and prolonged viral shedding compared to adults [11,36,81]. The optimal specimen type in young children is a NPA, and in adults paired NTS or NPS. Samples collected from the lower respiratory tract in hospitalized patients may improve the diagnostic yield.

In general, POC tests for vRTIs can be performed on upper respiratory tract samples including NTS, NPS, and NPA. However, nucleic acid amplification-based POC tests may be performed on lower respiratory tract samples such as tracheal aspirates and bronchoalveolar lavages. Whilst specimens are generally tested soon after collection at the POC, some are transported to the centralized laboratory for testing. POC testing can be performed at the bedside by clinicians or in the laboratory by trained laboratory staff. Although POC platforms are relatively simple to operate, training in both sample collection and platform use are essential to improve test performance.

The recovery of respiratory viruses is affected by the type of transport media used and the temperature under which specimens are transported [82]. For nasopharyngeal or oropharyngeal samples, detection is enhanced with the use of flocked swabs transported in universal or viral transport media promptly to the laboratory compared to Dacron polyester or rayon swabs [82]. It has been shown that flocked swabs have comparable sensitivity and specificity as NPA for the diagnosis of vRTIs and also has the advantages of being less invasive and not requiring a device for collection making it more widely accessible [83–87].

Sputum is not a preferred specimen due to its viscosity, but a recent study showed higher mean influenza A, RSV, and hMPV loads when testing sputa using the FilmArray® diagnostic assay that were processed using a 'dunk and swirl' method compared to NTS. This method involves dunking a sterile swab into sputum and swirling the swab into sterile water, which is subsequently processed [88]. In addition, Wolff et al. noted the improved detection of viral pathogens by testing high-quality sputa (defined as ≤10 epithelial cells/low power field and ≥25 white blood cells/low power field or a quality score of 2+) compared to nasopharyngeal or oropharyngeal swabs using the TaqMan® Array card (Thermo Fischer Scientific) [89]. Although saliva swab specimens are not preferred for the detection of respiratory viruses using POC tests, previous evaluations have demonstrated comparable detection rates when compared to NPS using NAAT [90]. By contrast, another study showed that testing of saliva samples can improve the detection of respiratory viruses where NPAs were negative [91].

The volume and method of nucleic acid extraction from submitted specimens can also affect NAAT performance; with different methods more suited to RNA, DNA, or total nucleic acids, there are commercial extraction methods [62,92]. Respiratory specimen type and the age of the subject tested also affects the performance of NAATs [11,93].

5. Quality assurance

As POC tests are not usually performed in a laboratory, they are not subject to the quality assurance requirements imposed on laboratories for accreditation purposes. The tests are generally registered and approved by governing bodies such as the US FDA, Europe's Conformité Européene, and Australia's Therapeutic Goods Administration. However, manufacturers are not under any obligations to monitor and/or improve the performance of their diagnostic assays, which may decline over time due to antigenic or genotypic divergence of established viruses. It is therefore important that reference laboratories continually assess the performance of POC tests and notify the relevant manufacturers and governing bodies when a decline in performance is detected.

Several guidelines and policy documents are available to guide implementation and specify key requirements of POC testing. The international standard ISO 22870:2006 (POC testing – Requirements for quality and competence) outlines the requirements that need to be applied when performing POC testing [94]. Internal quality control and external quality assessments are required to ensure reliable results. Where no quality control material is available, patient specimens should be substituted, and results compared to those from another accredited laboratory. Other important issues that need to be considered include pre-implementation validation of the POC device, oversight of the clinical governance, and maintaining good laboratory practice and operation of the devices.

6. Conclusions

There has been greater awareness of respiratory viruses as a cause or precipitant of upper and lower respiratory tract infections in primary care and hospital settings. Worldwide, respiratory tract infection causes substantial morbidity and mortality [95–97]. As the clinical presentation of vRTIs can be similar, laboratory confirmation is important. Traditional testing methods have substantially improved, and pathogen-specific antivirals will require the identification of the underlying etiologic agent in a timely fashion. Future technological advances will no doubt improve the performance of POC tests and further data from randomized controlled trials are awaited on the clinical and financial impact of POC tests in the management of patients with acute respiratory illness.

7. Expert commentary

vRTIs cause significant morbidity and mortality worldwide, and similarities in clinical presentation make it challenging to identify the pathogen responsible without microbiological confirmation.

The increasing availability of therapies directed against specific pathogens and host responses places greater importance on making an accurate and rapid diagnosis in the management of vRTIs, and novel point of care technologies will facilitate this.

Although near patient testing is useful for individual patient management, samples should also be referred to the diagnostic laboratory for more specialized testing including antiviral resistance testing, epidemiological purposes, and/or vaccine development when indicated.

8. Five-year view

There is increasing pressure on laboratories to aid in the diagnosis of vRTIs within a clinically relevant time frame to benefit patient treatment, guide infection control practices, obviate unnecessary investigations and therapies, and improve public health surveillance. This may be achieved with the use of POC devices at the bedside, in both resource-rich and poor settings. Several platforms are being calibrated for self-testing by patients. Improvements in technologies including miniaturization of testing platforms, advances in battery capacity to enhance portability, expansion of test menus, and data transmission will further revolutionize POC testing. This is likely to shift testing away from the traditional centralized diagnostic laboratory. Clinicians, pathology providers, and public health professionals should be prepared for this inevitable and impending paradigm shift.

Key issues

- There is greater awareness of viruses being the cause or precipitant of upper and lower respiratory tract infections, with vRTIs responsible for substantial morbidity and mortality worldwide.
- The clinical presentation of vRTIs is often similar, making laboratory confirmation paramount both for treatment of the individual and also public health.
- Although viral culture remains the 'gold standard' for diagnosis in practice, virus isolation has been replaced by NAAT in most reference laboratories given their increased sensitivity, specificity, breadth, and reduced TATs to pathogen detection.
- Point-of-care testing is defined as the testing of a patient sample, performed in the surgery or clinic at or near the time of consultation.
- Point-of-care testing can be non-molecular (LFIC, FIA) or molecular based.
- The performance of POC tests can be affected by a variety of factors including the type of respiratory sample, age of the subject as well as quality, handling and timing of sample collection.
- Advantages of POC testing include improved clinical decision-making and quality of care including a reduction in unnecessary investigation and therapies, prescription of antivirals, as well as guiding infection control practices all of which can reduce costs.
- Disadvantages of POC testing including reduced sensitivity and specificity for non-molecular based assays as well as the expense and limited validated shelf life.
- As the WHO developed the ASSURED criteria as the paradigm for POC testing devices, those based on lateral flow immunochromatography remain the dominant method despite obvious limitations of limited sensitivity and the inability for multiplexing.

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Declaration of Interest

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