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REVIEW

Point-of-care testing for respiratory viruses in adults: The current landscape and future potential

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Summary   Respiratory viruses are responsible for a large proportion of acute respiratory illness in adults as well as children, and are associated with a huge socio-economic burden worldwide. Development of accurate point-of-care tests (POCT) for respiratory viruses has been listed as a priority by the World Health Organisation and replacing the current paradigm of empirical antimicrobial use with directed use is a listed goal of the movement for reduction in antimicrobial resistance. POCTs for respiratory viruses have previously been limited by the poor sensitivity of antigen detection based tests and by a limited range of detectable viruses. Highly accurate molecular platforms are now able to test for a comprehensive range of viruses, can be operated by non-laboratory staff and can generate a result in approximately 1 h, making them potentially deployable as POCTs. The potential clinical benefits of POC testing for respiratory viruses in adults include a reduction in unnecessary antibiotic use, improved antiviral prescribing for influenza and rationalisation of isolation facilities. We review here the burden of disease, the currently available molecular platforms with potential for POCT use and the existing evidence for clinical and economic benefits of testing for respiratory viruses in adults.
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Introduction

Acute respiratory tract infections are responsible for an estimated 4.25 million deaths each year and are the third most common cause of death worldwide.[1] Although bacteria have previously been considered to be the principal aetiological agents of severe respiratory infection, the global importance of respiratory viruses in all age groups has been increasingly recognised in recent years.[2–4] Diagnostic technology for respiratory virus detection has evolved rapidly over the last two decades from viral culture and immunofluorescence to the current standard of molecular detection by polymerase chain reaction (PCR). This review focuses on the currently available molecular diagnostic platforms for respiratory virus detection with potential for use as point-of-care tests (POCT) and explores the current landscape for POCT in adults.

Respiratory viruses: clinical and economic burden of disease

Improvements in the sensitivity of diagnostic testing for respiratory viruses with the widespread use of nucleic amplification techniques such as PCR have helped to accurately define the burden of viral disease over the past two decades. In children respiratory viruses have been detected by molecular diagnostic techniques in 43–67% of cases of community acquired pneumonia (CAP),[5] over 90% of infants with bronchiolitis,[6] and approximately 85% of asthma exacerbations.[7] In adults approximately 20–40% of CAP cases,[8–12] 50–70% of asthma exacerbations[13] and 30–50% of chronic obstructive pulmonary disease exacerbations[14] are associated with respiratory virus detection. In hospitalised adults with acute respiratory illness, viruses are the most commonly detectable pathogen (being detected in around 50%) with bacterial detection being much less frequent, although antibiotic use is almost universal.[4] Furthermore, preceding viral infection is thought to be a key predisposing event to secondary bacterial infections in the lung and other sites in the respiratory tract.[15–17] Respiratory viruses including influenza have also been implicated in precipitating non-respiratory illnesses such as myocardial infarction, venous thromboembolism, stroke and loss of diabetic control.[18–22]

Infections with respiratory viruses are frequent events in all age groups and result in an enormous burden on health systems as well as the economic costs in direct medical expenses and indirect productivity losses. Direct medical expenses include outpatient clinic visits, emergency department visits, hospitalisations and treatment costs, including over-the-counter medication and drug prescriptions. Indirect productivity losses include missed workdays for adult patients and caregivers. In Europe direct costs attributed to pneumonia are estimated at approximately €10.1 billion annually and indirect costs of lost work days at €3.6 billion.[23]

Based on the 2003 population size, seasonal influenza epidemics resulted in an average of 610,660 life-years lost, 3.1 million hospital days and 31.4 million outpatient visits in the USA.[24] Direct medical costs averaged US$10.4 billion annually, and projected lost earnings due to illness and loss of life amounted to US$16.3 billion annually. The total economic burden of annual influenza epidemics using projected statistical life values amounted to US$87.1 billion.[25] The common cold also causes a significant economic burden with a US-based study estimating that non-influenza, viral respiratory tract illnesses (mostly common colds) cost around US$40 billion in 2001.[26]

Influenza

The influenza virus causes seasonal epidemics leading to excess hospitalisations and death mainly in the elderly and in patients with co-morbidity.[27,28] It causes severe illness in up to 5 million people and around half a million deaths per year worldwide.[29] Annual seasonal influenza vaccine is recommended in at risk groups[30] however vaccine uptake is sub-optimal[31,32] and high quality evidence for significant protection in the elderly is lacking.[33,34] The rate of hospitalisation in adults with influenza has been estimated at 5 to 20 per 100,000 overall[35,36] and may be as high as 1200 per 100,000 in those over 85 years old.[37] In adults hospitalised with laboratory confirmed influenza, 10–30% are admitted to critical care units and 3–15% die in hospital,[38,39] with outcomes being predicted by co-morbidity.[40] As noted above, in addition to acute respiratory presentations, influenza may precipitate decompensated cardiovascular disease, myocardial infarction, collapse or diabetic emergencies[20–22,41] and so many hospitalised cases of influenza are likely to remain undiagnosed. A recent Canadian study estimated that only around 1 in 14 emergency department visits due to influenza virus infection were correctly attributed to influenza.[42] It is likely, therefore, that the burden of influenza and its economic impact have been under-estimated.

Respiratory syncytial virus

RSV is the principle cause of bronchiolitis in infants but is now increasingly recognised as a major cause of severe respiratory illness in adults, with some studies suggesting a disease burden similar to that of influenza.[43,44] RSV affects all age groups and a study of hospitalised children and adults that calculated disability adjusted life years (DALYs) concluded that influenza and RSV were consistently the greatest causes of disease across all age groups.[45] Adults at high risk of severe RSV disease include the frail elderly, those with chronic cardio-respiratory disease and the immunocompromised. The mortality rate of RSV infection in adults and the elderly is similar to that of influenza (7–8%) but may reach 30–70% in the heavily immunocompromised[46] contrasting with the negligible RSV-related mortality in infected children.

Rhinovirus

Picornaviruses are responsible for the majority of common colds and adults typically suffer two to four symptomatic episodes per year.[47] They are also responsible for the majority of exacerbations of asthma in adults and a significant proportion of exacerbations of COPD.[13,14,48] Common colds cause an estimated 20 million lost workdays per year in the

US, with an estimated annual cost of around US$410 million for rhinovirus-related asthma exacerbations.[49]

Other respiratory viruses

Adenovirus infections are a common cause of mild acute respiratory illness in children, but also cause epidemics among adult military recruits and can cause serious infections in the immunocompromised and occasionally in immunocompetent adults.[50,51] The clinical impact of human coronaviruses 229E and OC43 infection has only recently been explored, with early data suggesting a prevalence in adults hospitalised with acute respiratory illnesses of between 3% and 11%.[4,52] A US multi-centre study showed that the prevalence of human metapneumovirus (hMPV) infection in hospitalised adults with respiratory symptoms was 2.6% and patients had similar clinical characteristics to those infected with RSV infection with increasing age being a risk factor for emergency department visit and hospitalisation.[44] Parainfluenza viruses seem to be of less importance in adults compared to paediatric populations, however they can cause influenza-like illness in adults and are detected in adults hospitalised with acute respiratory illness at low frequency.[4,45,53]

Diagnostic tests for respiratory viruses

Laboratory PCR

Nucleic acid amplification techniques such as PCR have now largely superseded cell culture and direct fluorescent antibody testing as the method of choice for routine diagnostic testing for respiratory viruses, due to their superior diagnostic accuracy and faster turnaround time. PCR is highly sensitive and specific but generally has a turnaround time of at least 24 h and requires specialist laboratory facilities and expertise.[54,55]

Rapid antigen detection tests for respiratory viruses

There are several commercially available FDA approved and CE marked, rapid diagnostic tests for respiratory viruses including influenza and RSV, which use antigen detection by either immune-chromatographic assay or immunofluorescence. Time to result is generally around fifteen minutes, they are easy to use and do not require laboratory support, and generally involve visual inspection of a test line (in addition to a control line). Unfortunately the clinical utility of rapid antigen based detection for respiratory viruses has been limited by their unacceptably poor sensitivity, especially in adults where it is around 50% for influenza[56] and lower for RSV,[57] meaning that they cannot be used to rule out infection. The Sofia Fluorescent Immunoassay Analyzer (Quidel, San Diego, CA, USA) is a benchtop analyser that combines lateral flow immunofluorescence-based antigen detection test kits with an optical sensor and provides a result in around 10 min. Test kits are available for influenza and RSV which are both FDA approved and CE marked. Sensitivity for detection of influenza is around 80%

compared to PCR and so may be higher than for some other rapid antigen tests.[58] Although it has not been evaluated in adults, in children the sensitivity for detection of RSV was around 70% compared to PCR but would be expected to be lower in adults.[59]

Multiple respiratory virus antigen detection

MariPOC (ArcDia Laboratories, Turku, Finland) is a CE marked, multi-analyte immunofluorescence-based antigen detection platform that can simultaneously detect 8 respiratory viruses (influenza A and B, RSV, adenovirus, hMPV, and parainfluenza types 1, 2, and 3) in addition to *Streptococcus pneumonia*. It has not been evaluated in adults but when compared to RT-PCT in children with acute respiratory illness diagnostic accuracy was generally moderate although sensitivity was as low as 12.5% for some viral targets.[60,61]

Molecular platforms with point-of-care testing potential

Alere i Influenza A&B

The Alere i Influenza A&B (Alere, San Diego, CA, USA) is an FDA approved and CE marked isothermal nucleic acid amplification-based system that uses a fluorescence-based molecular signal to detect influenza A and B. Results are generated within 15 min, with around 2 min of "hands on" time. The testing kits and analyser have been specifically designed to be used by non-laboratory clinical staff in an acute care environment and it is the only molecular platform that is FDA approved specifically as a POCT. In a study examining diagnostic accuracy involving 545 respiratory specimens from symptomatic patients (85% children and 15% adults), the sensitivity and specificity of the Alere i Influenza A&B assay was 99.3% and 98.1% for influenza A, and 97.6% and 100% for influenza B compared to viral culture and PCR.[62] However, a Swiss study of 436 participants (broadly two-thirds children and one-third adults) showed a lower pooled influenza A and B sensitivity of 82.3% (mostly influenza A rather than B) compared to PCR.[63] Another study using samples predominantly from adults, showed an even lower sensitivity for influenza A at 73.2%.[64] The high specificity demonstrated, simplicity of use and fast turnaround time make the Alere i Influenza A&B test an exciting prospect for point-of-care use however there have been no clinical trials evaluating clinical or health economic outcomes and the lower sensitivity in adults for influenza A and the limited range of pathogens detected limit its usefulness.

Biofire FilmArray Respiratory Panel

The FilmArray Respiratory Panel (BioFire Diagnostics, Salt Lake City, UT, USA) is and FDA approved and CE marked platform that uses nested real-time PCR to detect 20 respiratory pathogens (17 viral targets and 3 bacteria). The FilmArray requires 2 min of "hands on" time and produces a test result in one hour.[65] Several published

studies have evaluated the ease-of-use and turnaround time of the system and comparing the diagnostic accuracy to laboratory PCR. These studies have shown superiority of the FilmArray system in terms of ease-of-use and turnaround times compared to laboratory PCR.[66—68] Sensitivity and specificity compared to laboratory PCR (with confirmatory cell culture and sequencing) are excellent. Initial pooled sensitivity for viral targets was around 90% — principally due to poor sensitivity in adenovirus detection, however following improvements in the adenovirus assay this has risen to over 95%.[66,67,69,70] It is notable that these studies were all conducted within a laboratory rather at the point-of-care and a large proportion of these studies were conducted using samples from children rather than adults. A notable limitation of the system is the workflow as only a single specimen can be tested at any one time on the analyser.

A single study has examined clinical outcomes in children hospitalised with acute respiratory illness and tested with the FilmArray respiratory panel compared with standard laboratory PCR.[71] This was not a randomised controlled trial but examined outcomes pre and post intervention and the FilmArray respiratory panel was not used as a POCT but was housed within the existing laboratory. This study demonstrated that in patients tested with the FilmArray, the test result was available to clinicians after a mean time of 6 h versus around 24 h with standard laboratory PCR. The duration of antibiotics was shorter in those tested with the FilmArray although this was dependent on receiving the test results within 4 h. The duration of inpatient stay and the time in isolation facilities were shorter in those tested with the FilmArray if the results were positive for viruses. There have been no trials in adults and no randomised controlled trials to date examining the potential clinical benefits of using this system as a POCT.

Cepheid GeneXpert Flu and Flu/RSV

The Xpert Flu (Cepheid, Sunnyvale, CA, USA) real-time PCR test cartridge is an FDA approved and CE marked test for use on the integrated, automated GeneXpert platform and detects influenza A and B with a turnaround time of about 75 min and reported "hands on" time of 2 min.[72,73] The modular multiple port system allows on-demand, random-access testing so that up to 16 tests can be run simultaneously (depending on the number of ports in the testing unit). The system has been evaluated in a prospective trial using samples from 300 adults with acute respiratory illness in emergency departments. In this group the sensitivity for detection of influenza was 95.3% (84.2%—99.4%) with a specificity of 99.2% (95% CI: 97.0%—99.9%) compared to laboratory PCR.[74] Although a comparatively easy to use test, there are currently no published trials evaluating its use as a point-of-care test or evaluating the potential clinical or health economic benefits of its use in emergency departments. The combined Xpert Flu/RSV cartridge has been evaluated in a retrospective study using adult and paediatric samples and demonstrated a sensitivity of 97% for influenza A, 100% for influenza B and 98% for RSV, with specificity 100% for all three viruses compared to laboratory PCR.[75] Although Xpert Flu and Xpert Flu/RSV have excellent sensitivity and clear point-of-care potential the restricted range of viruses currently detected is a limiting feature of this system.

This review focuses on platforms with a well established peer-reviewed evidence base incorporating clinical specimens however there are numerous other platforms in earlier stages of development and using a variety of sensing technologies, which are not included. Examples include the FDA cleared and CE marked Cobas Liat Influenza A/B (Roche Diagnostics, Indianapolis, IN, USA)[76] which uses PCR to detect influenza A and B in less than 20 min, and the GenMark eSensor Respiratory virus panel (GenMark Diagnostics, Inc., Carlsbad, CA) which uses cartridge based multiplexed PCR to detect a panel of respiratory viruses in 60—90 min.[77] A comparison of the reviewed molecular platforms for respiratory virus detection with POCT potential is shown in Table 1.

Respiratory virus point-of-care testing in the wider context

The UK Department of Health commissioned report into UK pathology services in 2006 noted the importance of developing clinically relevant point-of-care diagnostic tests to reduce turnaround times and improve patient pathways.[78] Despite this POCT for infectious diseases in the UK and globally have not advanced far beyond dipstick testing for urinary tract infection with in vitro diagnostic tests for infection remaining confined to large centralised laboratories. The associated slow turnaround times mean that

Table 1 Comparison of molecular platforms with point-of-care potential for detecting respiratory viruses.

System and panel	Benefits	Limitations	References
Alere i Influenza A&B	15 min run-time 2 min "hands on" time Simplicity	Moderate sensitivity for Influenza A Only influenza viruses detected	62—64
Biofire FilmArray Respiratory Panel	60 min run-time 2 min "hands on" time Wide range of viruses detected	Unable to process multiple samples simultaneously	65—71
Cepheid GeneXpert (Xpert Flu and Flu/RSV)	75 min run-time 2 min "hands on" time Modular system allows multiple simultaneous tests	Limited range of viruses detected	72—75

results are only available to clinicians many hours to several days after the patient has presented, and long after antimicrobial decisions have been made, perpetuating the current paradigm of empirical antimicrobial use rather than pathogen directed use. The Infectious Diseases Society of America policy paper 'Better Tests, Better Care: Improved Diagnostics for Infectious Diseases' acknowledges the ongoing culture of empirical antimicrobial use and the unmet need for rapid accurate tests for infectious diseases to allow appropriate pathogen directed therapy.[79]

The Wold Economic Forum has stated that antimicrobial resistance is the arguably the greatest threat to global human health and current high profile initiatives on combating resistance have focused attention on antimicrobial stewardship, which seeks to preserve existing antimicrobial agents and slow the development of resistance. One of the strategies to achieve this goal is the development of rapid diagnostic tests and biomarkers to ensure appropriate use of antimicrobials so that antimicrobial use is pathogen directed rather than empirical and only used in those where there is clear evidence of benefit.[80,81] In addition the increasing recognition of the huge global burden of respiratory viruses has led to the creation of the WHO's global Battle against Respiratory Viruses Initiative (BRaVe) initiative which aims to improve research into strategies to prevent, diagnose and manage respiratory virus infection. Priority areas include improved diagnostic tests for respiratory viruses including the creation and use of cheap, accurate and easy to use POCTs.[82]

Potential clinical benefits of point-of-care testing

Reduction in antibiotic use

The current culture of empirical antimicrobial use in patients with suspected infection is no longer considered sustainable due the emergence and proliferation of antibiotic resistance. Antibiotic use in hospitalised patients with acute respiratory illness is near universal despite the predominance of viruses and the low frequency of detectable bacteria in much of this patient group. Fig. 1 shows antibiotic use by detected pathogen in a large study of hospitalised adults from the UK.[4] Furthermore patients with acute respiratory illness syndromes that are known to be principally virally induced, such as exacerbations of asthma and acute bronchitis, are often treated with antibiotics despite the lack of evidence for benefit, and in the case of asthma, national guidelines discouraging their use.[83–85] In the study from the UK referenced above almost 60% of patients hospitalised with an exacerbation of asthma received at least one dose of antibiotic whilst in hospital.[4] The use of respiratory virus POCT could potentially reduce unnecessary antibiotic use in patients with acute respiratory illness especially in those conditions known to be principally viral and where antibiotic use has not shown benefit, by demonstrating to clinicians that the patient's illness and fever are explained by the presence of a virus. Patients with uncomplicated Influenza-like illness caused by respiratory viruses including influenza, are often treated with antibiotics due to diagnostic confusion with bacterial infection. In these patients the early detection of a
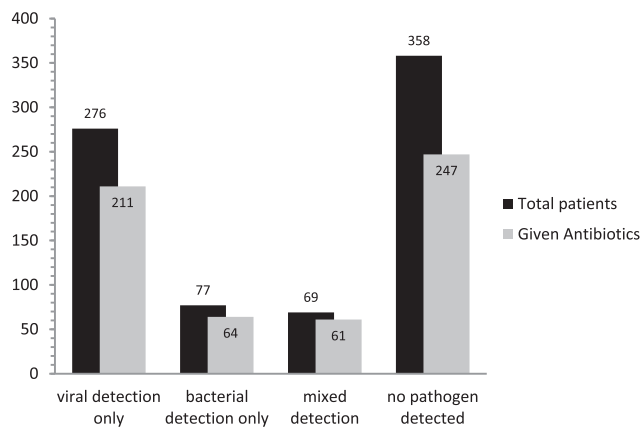

Figure 1 Antibiotic use in patients by detected aetiology from a study of hospitalised adults with acute respiratory illness (n = 758). Mixed detection refers to the concurrent detection of viruses and bacteria in the same patient. [Reproduced from: Clark TW, et al. Adults hospitalised with acute respiratory illness rarely have detectable bacteria in the absence of COPD or pneumonia; viral infection predominates in a large prospective UK sample. J Infect 2014;69(5):507–15].

respiratory virus in the absence of evidence of concomitant bacterial infection may prevent unnecessary antibiotic use.

The evidence base for respiratory virus testing reducing unnecessary antibiotic use is limited and mainly consists of trials using rapid antigen based testing for influenza. A large randomised control trial evaluating the clinical and health economic benefits of rapid antigen testing for influenza in hospitalised adults did not demonstrate any improvement in antibiotic use or other clinical or health economic benefits in those tested with rapid antigen tests compared to laboratory testing.[86] In a small non-randomised study of hospitalised adults rapid diagnostic testing for influenza using antigen detection demonstrated small reductions in antibiotic use (74% vs 99%) with no increase in adverse events in those where antibiotics were withheld.[87] Studies in children including several small randomised controlled trials have evaluated the impact of routine rapid antigen testing for influenza on antibiotic use, with inconsistent results.[88–92] For molecular tests the evidence base is even more limited with trials using molecular testing platform within the laboratory rather than as POCT, with the associated prolonged turnaround times. The impact of respiratory virus testing in adult outpatients with acute respiratory illness was assessed in a small randomised controlled trial using laboratory-based PCR. Results were available the next day in those randomised to viral PCR testing and even with this delay antibiotic prescribing was significantly reduced compared to those treated with standard care (5% vs 12%).[93] As noted above the FilmArray respiratory platform has been clinically evaluated in a single centre paediatric study where the platform was not used as a POCT but was housed within the central laboratory. Although not a randomised controlled trial it demonstrated reductions in antibiotic use in those testing positive for viruses with the FilmArray versus standard laboratory PCR, although only when results were available within 4 h, underscoring the importance of rapid results

and suggesting possible further reductions if the platform was used as a POCT.[71]

A recent Cochrane review evaluating the use of rapid viral diagnostics for acute febrile respiratory illness in children in the emergency department concluded that there is currently insufficient evidence to support rapid viral testing to reduce antibiotic use in this setting. The authors have suggested an adequately powered trial with antibiotic use as the primary outcome measure.[94]

Directed antiviral agent use

Influenza

The neuraminidase inhibitors (NAI) Oseltamivir and Zanamivir are licensed antivirals for the treatment and prevention of influenza and are recommend by UK Public Health England for the treatment of hospitalised adults with suspected and confined influenza A and B.[95] Although there has been controversy regarding the evidence for their efficacy from the original pharma sponsored trials, there is now a large body of evidence from observational studies suggesting a significant reduction in mortality in hospitalised adults with confirmed influenza.[96] Although the degree of benefit from NAIs is probably greatest when they are started with 48 h of symptom onset there is evidence in adults to suggest ongoing benefit when started beyond this time and up to 5 days of symptoms.[96,97] This is particularly pertinent as patients infected with influenza often present to hospital after 48 h of symptom duration.[4] In current UK practise patients with suspected influenza are generally treated empirically with NAI whilst awaiting the results of laboratory PCR testing.[95] This strategy leads to unnecessary NAI exposure with the associated risk of side effects in patients who are subsequently found not to have influenza. Following the recent publication of the independent meta-analysis of oseltamivir trials,[98] an editorial letter (published in the *Lancet*) suggested that, in view of the modest efficacy and moderate risk of nausea and vomiting with oseltamivir, the administration of this drug should ideally be directed with the use of diagnostic tests rather than used empirically.[99] The use of a molecular point-of-care test has the potential to allow implementation of directed rather than empirical NAI treatment thus maximising clinical benefit for those with influenza infection and minimising unnecessary antiviral exposure and drug related adverse events in those without.

As noted above several studies in children and a single study in adults have suggested improved use of NAIs using rapid antigen testing for influenza versus routine clinical care[87−92] although there have been no studies evaluating molecular platform POCTs with this outcome measure. In addition to NAIs there are several promising novel and re-purposed anti-influenza agents currently in late stages of clinical development including nitazoxanide, favipiravir (T-705) and anti-m2e monoclonal antibody.[100−102]

Respiratory syncytial virus

There are currently no specific antiviral agents licensed for RSV infection. The broad spectrum antiviral agent ribavirin is sometimes used in immunocompromised adults with severe RSV infection but its use is limited by safety concerns and difficulties with administering the nebulised solution[103,104] and there have been no randomised controlled trials to evaluate its efficacy. Several small molecule anti-RSV agents are in the late stages of clinical development including Gilead's GS-5806, a RSV fusion protein inhibitor which has demonstrated a reduction in symptoms and viral load[105] in a challenge study of healthy adults and is currently being trialled in hospitalised adults.[106]

Rhinovirus

There are currently no specific antiviral agents licensed for the prevention or treatment of rhinovirus infection. The rhinovirus capsid binding agent pleconaril[107] showed promise in clinical trials of naturally occurring colds but was rejected by the US Food and Drug Administration due to the relatively high frequency of side effects, drug interactions and concerns over resistance.[108] Phase 2 trials of the human rhinovirus capsid binder vapendavir (BTA798) are currently underway in adult asthmatics with naturally acquired rhinovirus infection.[109] A single centre randomised controlled trial of inhaled beta interferon has demonstrated reduced severity of rhinovirus induced asthma exacerbation in severe asthmatics[110] and larger confirmatory trials are ongoing.

Promising candidate antiviral agents in late stages of development are listed in Table 2.

Infection control

Respiratory viruses are known to be highly infectious and to cause nosocomial outbreaks and so testing and isolation of suspected cases is a central tenet of infection control practices in hospitals. Currently cases are isolated based on clinical suspicion with laboratory testing providing definitive results in 24−48 h. This leads to patients without

Table 2 Examples of promising candidate antiviral agents currently in late stage development.

Antiviral agent	Target	Mechanism	Developmental stage	Reference
Nitazoxanide	Influenza	Multiple	Phase 2/3	100
Favipiravir (T-705)	Influenza and other viruses	Inhibition of RNA polymerase	Phase 3	101
Anti-M2e monoclonal antibodies	Influenza	Binding to M2e epitope	Phase 2	102
GS-5806	RSV	Fusion inhibitor	Phase 2	105
Vapendavir (BTA798)	Rhinovirus	Capsid binder	Phase 2	109
Inhaled beta-interferon	Rhinovirus and other viruses	Restored antiviral response in asthmatics	Phase 2/3	110

infection occupying valuable isolation facilities unnecessarily for several days and reducing patient flow through the hospital. Although intuitively POCTs for respiratory viruses performed in emergency departments should improve isolation facility use and patient flow there is a paucity of quality evidence for the effects of POCTs in this setting. A systematic review of published literature on the subject of POCTs for the diagnosis of infectious diseases concluded that although POCTs may have a role in infection control the lack of good, consistent clinical data surrounding their use outside of the laboratory is a limiting factor in their implementation.[111] A single centre non-randomised paediatric study from the UK suggested significant improvement in isolation facility use and patient flow with rapid antigen based POCT for RSV during the winter months.[112] The previously mentioned non-randomised pre and post intervention paediatric study using the FilmArray respiratory panel as a POCT demonstrated a reduction in the time spent in isolation facilities in patients tested with POCT versus standards laboratory PCR testing.[71]

Other benefits

Several studies evaluating the use of antigen detection based POCTs for influenza in children have shown a decrease in the number of investigations performed on influenza positive patients compared with those tested with standard of care.[89–92,113] One of these also suggested a reduction in the duration of hospitalisation for those testing positive for influenza[89] as did the previously mentioned study using the FilmArray in children.[71] The potential clinical benefits listed above could translate in to an overall economic benefit for health care organisations. A study using decision analytic modelling to ascertain the most cost effective testing strategy in children presenting to the emergency department with influenza-like illness suggested that rapid PCR using the FilmArray respiratory panel was superior to standard laboratory PCR or rapid antigen testing. However the incremental costs per QALY were high and many questionable assumptions about the effects of diagnosing a respiratory virus infection on investigations, antibiotic and antiviral use were made.[114] Another study using health economic modelling evaluated the cost effectiveness of PCR based rapid diagnostics (Cepheid Xpert Flu assay) for the diagnosis of influenza in high risk adults

presenting to the emergency department. They concluded that PCR based rapid testing was the most cost effective strategy although this depended on the prevalence of influenza and again was based on strong assumptions of antiviral use and efficacy.[115]

The potential benefits of POC testing for respiratory viruses in adults are listed in Table 3.

Conclusion

The current global priority of replacing empirical antimicrobial use with pathogen directed therapy to help combat resistance, coupled with the recent development of rapid, accurate and easy-to-use molecular test platforms for respiratory viruses, sets the scene for rolling out a point-of-care testing strategy in patients presenting with acute respiratory illness. The potential benefits of such a strategy include a reduction in unnecessary antibiotic use, improved use of directed antiviral therapy for influenza, improved use of isolation facilities in secondary care, a reduction in the number of investigations performed and a reduction in the duration of hospitalisation in some situations. These effects could be associated with an overall health economic benefit. There is a substantial evidence gap and high quality randomised controlled trials evaluating molecular POCTs in adults and using clinically relevant outcomes such as antibiotic use, directed antiviral use and infection control facility use are urgently needed. In addition to the existing agents active against influenza there may soon also be available a range of clinically effective antiviral agents active against other respiratory viruses such as RSV and rhinovirus. For these agents to be utilised effectively, especially in hospitalised patients with severe disease, routine early testing for the presence of viruses with molecular POCTs will be necessary to allow targeted treatment.

Author contributions

NJB, HFS and TWC were all involved in the design, literature search and writing the manuscript, including the final version submitted.

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None declared for all authors.

Table 3 Summary of potential benefits of POCT for respiratory viruses along with complicating factors.

Potential benefit of POCT	Complicating factors
Reduced unnecessary antibiotic use	Co-infection with bacteria is common
Improved antiviral use[a]	Ongoing controversy over efficacy of neuraminidase inhibitors
Improved isolation facility use	Increased detection of viruses may stretch limited resources
Reduced economic cost	Health economic modelling assumption are largely speculative

[a] Currently only neuraminidase inhibitors for influenza.

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