Journal of Hospital Infection 103 (2019) 441–446

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

A service evaluation of simultaneous near-patient testing for influenza, respiratory syncytial virus, *Clostridium difficile* and norovirus in a UK district general hospital

J. Haigh [a,*], M.-T. Cutino-Moguel [b], M. Wilks [b], C.A. Welch [b], M. Melzer [a]

[a] Royal London and Whipps Cross University Hospital, Barts Health NHS Trust, London, UK
[b] Royal London Hospital, Barts Health NHS Trust, London, UK

ARTICLE INFO

Article history:
Received 25 June 2019
Accepted 29 August 2019
Available online 5 September 2019

Keywords:
Influenza
RSV
Norovirus
Clostridium difficile
Cepheid
GeneXpert
Infection prevention

SUMMARY

Background: The Cepheid® GeneXpert® (GXP) can simultaneously test for norovirus (NV), *Clostridium difficile* (CD), influenza A/B (IFA/B) and respiratory syncytial virus (RSV).
Aim: To compare centralized multiplex polymerase chain reaction (PCR) testing with localized GXP testing at a district general hospital.
Methods: From December 2017 to December 2018, samples received at Whipps Cross University Hospital (WCUH) were first tested at the local laboratory before transport centrally to the Royal London Hospital (RLH). At the RLH, a non-proprietary multiplex reverse transcriptase (RT) PCR assay was performed, which also tested for gastrointestinal or respiratory pathogens not tested for by the GXP.
Findings: A total of 1111 stool and respiratory samples were processed at both sites; 591 were respiratory and 520 were stool samples. Compared to centralized testing, the GXP gave sensitivity, specificity, and NPV all in excess of 97%, with the exception of RSV. The RSV assay had a sensitivity of 66.7% (95% confidence interval (CI) 24.1, 94.0) but an NPV of 99.7% (95% CI 98.6, 99.9). At the RLH, 65 (5.9%) additional respiratory or gastrointestinal viruses were detected, predominantly rhinovirus 35 (3.2%) and adenovirus 11 (1.0%). Compared to centralized testing, the median time saved for local respiratory and gastrointestinal sample testing was 19 h and 46 min and 17 h and 6 min, respectively.
Conclusions: Local GXP testing compared to centralized multiplex PCR testing for IF, NV and CD, demonstrated sensitivities, specificities and NPV between 95% and 100%. Turnaround times were faster, enabling quicker infection prevention and control decision making. In our local setting (WCUH), the GXP demonstrated the potential to reduce NV and IFA/B outbreaks.

Introduction

With the networking of UK National Health Service (NHS) laboratories, some hospitals have a reduced ability to provide virology results in a timely fashion. In these settings, near-

* Corresponding author. Address: Royal London and Whipps Cross University Hospital, Barts Health NHS Trust, 3rd floor Pathology and Pharmacy Building, 80 Newark St, London E1 2ES, UK. Tel.: +44 7791 127119; fax: +44 20 32460325.
E-mail address: john.haigh3@nhs.net (J. Haigh).

https://doi.org/10.1016/j.jhin.2019.08.022
0195-6701/

patient testing offers advantages both to patients and the Infection Prevention and Control Team (IPCT). Testing patients with symptoms at the first point of contact can identify infectious pathogens capable of causing outbreaks, improve patient management and mitigate the risk of infection transmission [1]. In particular, near-patient testing can quickly identify sporadic cases of norovirus (NV) that may cause hospital outbreaks [2] whilst negative results can offer reassurance that diarrhoeal outbreaks are not caused by NV.

Hospital outbreaks of NV-associated gastroenteritis are well described. Between July 2013 and June 2016, it is estimated that 290,000 bed days were lost, displacing 57,800 patients at a cost of almost £300 million to the UK health economy [3]. Whipps Cross University Hospital (WCUH) is a 730-bed district general hospital in East London, UK, and part of Barts Health (BH) NHS Trust. It serves an elderly, ethnically diverse population of approximately 275,500. Built in 1903, it has 54 isolation rooms and is mainly comprised of 'Nightingale' wards which facilitate the spread of infection. Between 8th January 2010 to the 20th February 2010, because of patient safety concerns, the hospital closed to all adult emergency admissions. During this busy six-week winter period, there were 92 new cases of NV, 31 primary and 61 secondary, and the hospital lost operational control and approximately £6 million of patient-related revenue.

With near-patient testing, to achieve optimal sensitivity, specificity, positive, and negative predictive values (PPVs and NPVs, respectively), the tested pathogen must be easily detectable within diagnostic samples and the infection must have a high prevalence in the target population. The cost of implementing near-patient testing can be justified when the disease has a high cost burden and creates great pressure on healthcare services. In addition to NV, respiratory infections caused by influenza A/B (IFA/B) and respiratory syncytial virus (RSV) all fit these criteria.

In 2013, within the four hospital sites comprising BH NHS Trust, all microbiology and virology sample analysis were centralized at the Royal London Hospital (RLH) site. Samples were transported by courier van for the eight-mile journey between WCUH and the RLH. Despite a regular dedicated courier service, there remained delays in receiving and processing patient samples. Consequently, positive and negative influenza (IF) and NV results were not acted upon in a timely manner, and there were delays in moving patients in and out of limited isolation facilities.

The Cepheid® GeneXpert® (GXP) is a random-access rapid, polymerase chain reaction (PCR) platform, capable of testing for NV, *Clostridium difficile* (CD), IFA/B and RSV. It has a small footprint and can easily be incorporated into a small local blood science laboratory. From December 2017 to December 2018, the aim of this study was to compare centralized multiplex PCR testing at the RLH to localized testing at WCUH for NV, CD, IFA/B and RSV using the GXP. The proportion of less pathogenic gastrointestinal (GI) and respiratory viruses, not detected by GXP testing, and transport and processing turnaround times (TATs) at both sites were also determined.

Methods

Sample capture

Testing was requested on the trust Cerner Millennium® (Cerner Ltd London, UK) electronic patient record (EPR) system and samples were sent to the WCUH pathology reception as per the local standard operating procedure (SOP). Medical Laboratory Assistant staff intercepted nasal, throat, and nasopharyngeal viral transport media (VTM) swabs for IFA/B and RSV from ambulatory care, the emergency department and ward-based patients. Stool and vomit samples were also intercepted from the same requesters and tested for NV and CD. The original samples were tested using the GXP and an aliquot made if it was not possible to test that sample immediately. Samples were then returned to the transport system so as not to delay arrival at the RLH for multiplex PCR testing, our gold-standard comparator.

Cepheid® GeneXpert® PCR method

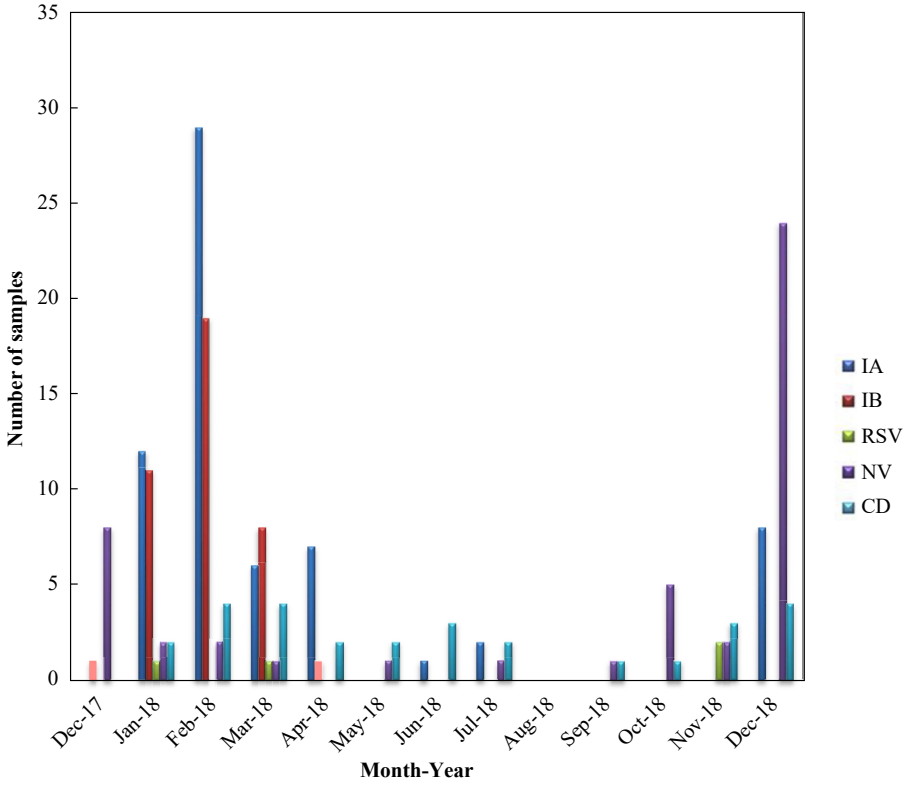
The GXP cartridge system uses reverse-transcription PCR (RT-PCR) for NV, IFA/B, RSV and standard PCR for CD. Inhibition of PCR was detected by transcription of a specimen control which reduced false-negative reporting.

GI sample processing

The GXP four-module system and the proprietary analysis kits were used throughout this study; Xpert® *C. difficile* BT (GXCDIFFBT-CE-10), Xpert® Norovirus (GXNOV-CE-10) and Xpress Xpert® Flu/RSV (XPRSFLU/RSV-CE-10, Cepheid UK Ltd Woburn Green, UK). The Cepheid SOP was adhered to, the only deviation being the use of dry rayon tipped swabs (Medical Wire, Bath, UK; MW118S) for processing faeces and vomit. Raw unformed stool specimens and vomit were collected in a sterile universal container, free from any additives. Specimens were stored at 2—8°C when necessary for up to 48 h. Stool samples were processed using a seasonal priority algorithm; between October and March they were processed for NV and then, if negative, for CD. From April to September the converse occurred, stool samples were analysed for CD and then, if negative, for NV. The only deviation from this was where samples were flagged as being part of a possible NV outbreak. This algorithm helped maximize module availability and speed of sample processing. A five-day testing service was operated, Monday to Friday from 09:00 to 17:00 h.

Respiratory sample processing

Xpress Xpert® Flu/RSV cartridges (Cat. No.XPRSFLU/RSV-CE-10) were used. The only deviations from the Cepheid's SOP were to use different specimen-collection equipment and additional sample types. The only sample type validated for the Xpress Flu/RSV is a nasopharyngeal swab. However, nose, throat, nasopharyngeal viral transport media swabs (Sigma Virocult® (Medical Wire, Bath, UK, Cat. No. MW951S) were processed instead of the Cepheid collection kit. Nasopharyngeal aspirates and bronchoalveolar lavage samples were also accepted. Specimens were transported at 2—8°C and stored at room temperature at 15—30°C for up to 24 h and refrigerated at 2—8°C for up to seven days before testing.



IA: influenza A; IB: influenza B; RSV: Respiratory Syncytical Virus; NV: norovirus; CD: Clostridium difficile.

Figure 1. Number of positive samples per month at Whipps Cross University Hospital.

Multiplex PCR testing for GI and respiratory viral pathogens at the RLH

The laboratory at RLH used QIAGEN® (Manchester, UK) equipment for the non-proprietary respiratory and GI PCR assays. Samples were extracted using QIAGEN® QIAsymphony® DSP DNA Mini Kit (cat. no. 937236) for the QiASymphony® SP/AS instrument (cat. no. 9020246). QuantiTect® Virus Kit (cat. no. 211031) along with Sigma® assay specific primers and probes, described previously [4–6], were used to create the master mix, this was then mixed with patient samples in individual reaction tubes using the QIAGEN® QIAgility® instrument. The sample reaction tubes were then loaded into a QIAGEN Rotor-Gene®. Analysis of melt curves took place via the Rotor-Gene® software and samples were deemed positive where there was a sufficient increase in fluorescence over a number of cycles. A respiratory sample testing service was offered seven days a week, Monday–Friday, 09:00–17:00 h and Saturday and Sunday, 09:00–13:00 h.

Reporting method and data analysis (GXP at WCUH)

There was no operator interpretation, the instrument had a specific programme for each cartridge and would signal whether the target pathogen was detected or not.

For stool and respiratory samples, sensitivity, specificity, PPV and NPV were calculated to assess the performance of the Cepheid® instrument at WCUH compared to the gold standard of multiplex PCR testing at the RLH. Less significant viral respiratory or GI pathogens missed due to selective testing were also recorded. When results were discordant, samples were sent for third-party testing. Third party assays used were the BD MAX™ CDifficile (BD Wokingham, UK), the *High*-Plex® Upper Respiratory Pathogens MT-PCR (AusDiagnostics UK Ltd) and a non-proprietary influenza triplex PCR (Public Health England VRD, Colindale, London, UK). The Laboratory Information System (LIS) was interrogated to determine the date and time of sample request, date and time sample received, processing time and date and time a final report was released from both laboratories. Collated project data was matched to the RLH analysis via the laboratory-assigned number. Samples were matched using a database giving the results from both labs and whether the results agreed or disagreed. Results TATs were calculated for both sets of data by subtracting the sampling time and date from the receipt time and date, giving the time taken for the sample to reach the laboratory. In the same way the sample receipt in the laboratory time and date was subtracted from the final report time and date, to give the time from receipt to the issue of the final report. These were expressed as median times with interquartile ranges (IQRs).

Patient pathways

If a patient tested NV positive (either test) they were immediately isolated or, depending upon bed availability,

Table I
Samples tested locally at Whipps Cross University Hospital (WCUH) confirmed as true or false at Royal London Hospital (RLH)[a]

	True positive	True negative	False positive	False negative	Total
Influenza A	65	511	14	1	591
Influenza B	40	540	10	1	591
RSV	4	574	11	2	591
Clostridium difficile	28	420	7	0	455
Norovirus	47	438	3	2	490

[a] Data from 1111 samples processed at both Whipps Cross University Hospital and the Royal London Hospital between December 2017 and December 2018. RSV, respiratory syncytial virus.

cohorted. If a patient tested IFA/B positive (either test) a clinical decision was made on hospital admission based upon age, co-morbidities and severity assessment. If admitted to hospital, patients were isolated or cohorted and treated with an antiviral agent. If the decision was not to admit, the patient may have been prescribed an antiviral agent, based on clinical assessment.

Results

From December 2017 to December 2018, 1111 stool and respiratory samples were processed at both RLH and WCUH. 591 (53.2%) were respiratory samples and 520 (46.8%) were stool samples. Due to the seasonal testing algorithm, not all 520 stool samples were tested for both CD toxin genes and NV. Four-hundred and fifty-five were tested for CD and 490 tested for NV. The number of samples received and the positivity rate demonstrated seasonality, with most samples and positives received in the winter months. From January to February (2017/18 winter months), more IF was detected than NV, although in December 2018, substantially more NV was detected than influenza (Figure 1). There was also variation in the types of wards or areas where patients with IFA/B (105) and NV (47) were detected. For IFA/B, patients were in the following areas at time of diagnosis: Accident and Emergency (A&E), 10 (9.5%); acute assessment or clinical decision unit, 36 (34.3%); ambulatory care, six (5.7%); medical wards 37 (35.2%); high-dependency unit (HTU)/intensive therapy unit (ITU), 6 (5.7%); surgical wards, five (4.8%); and paediatric wards, five (4.8%). For NV, most patients were: on medical wards, 37 (78.7%); acute assessment unit (AAU), six (12.8%); and on paediatric wards, four (8.5%). None were diagnosed in A&E, Ambulatory Care, HDU/ITU or on surgical wards.

Of the respiratory samples tested locally at WCUH, 109 (18.4%) tested positive for IFA, IFB or RSV and, of the stool samples, 47 (9.6%) and 28 (6.2%) were positive for NV and CD, respectively. Compared to testing at the RLH, there were 45 false-positive results and six false-negative results (Table I). Using RLH testing as our gold standard, the sensitivity, specificity, PPV and NPV for the five major pathogens, with the exception of RSV, demonstrated excellent sensitivity, >95%, and all assays had an NPV of >99%. In nearly all cases, a negative result ruled out suspected infection (Table II).

Table III
Third-party analysis of non-concordant samples

	RLH result confirmed by third-party laboratory	WCUH (GXP) result confirmed by third-party laboratory
Influenza A	7	6
Influenza B	7	0
RSV	1	3
Clostridium difficile	3	1
Total	18	10

GXP, GeneXpert®; RLH, Royal London Hospital; RSV, respiratory syncytial virus; WCUH, Whipps Cross University Hospital.

During this service evaluation, the GXP assays gave 51 (4.6%) of 1111 non-concordant results. When results were discordant, some of these were sent for third-party testing where 18 (35.3%) RLH results were confirmed, 10 (19.6%) GXP results were confirmed. Thirteen samples ((a) IFA, (b) IFB, (c) RSV and (d) *C. difficile*) were 'true-false positives' or samples that tested GXP positive but tested negative at the RLH. Twenty-three (45.1%) were not retested due to insufficient remaining specimen (Table III).

Because local testing at WCUH was limited to five major pathogens, 65 (5.9%) other less pathogenic viruses were detected at the RLH site. Most commonly, these included rhinovirus, adenovirus, and metapneumovirus. The aetiology and proportion of other viral pathogens isolated are summarized in Table IV.

The median time taken for a stool or respiratory sample to reach the WCUH laboratory was 3:55 (h:min) (IQR 1:02–18:39) and 2:26 (IQR 0:46–12:42) respectively, compared to 17:51 (IQR 7:59–22:31) and 18.50 (IQR 10:09–24:19) at the RLH Virology Department. The median time to process a stool or respiratory sample at the WCUH laboratory was 2:53 (IQR 2:25–3.30) and 1:08 (IQR 0:52–1:42) respectively, compared to 6:06 (IQR 4.44–21:48) and 4:30 (IQR 3:52–5:46) at RLH. Therefore, when the combined transit and processing times are compared, the median difference was approximately a 19-h delay for a respiratory sample and a 17-h delay for a GI sample.

Table II
Sensitivity and specificity analysis of Whipps Cross University Hospital testing compared with the Royal London Hospital

	Influenza A	Influenza B	RSV	*Clostridium difficile*	Norovirus
Sensitivity, % (95% CI)	98.5 (90.7, 99.9)	97.6 (85.6, 99.9)	66.7 (24.1, 94.0)	100.0 (85.0, 100.0)	95.9 (84.9, 99.3))
Specificity, % (95% CI)	97.3 (95.5, 98.5)	98.2 (96.6, 99.1)	98.1 (96.6, 99.0)	98.4 (96.5, 99.3)	99.3 (97.8, 99.8)
PPV, % (95% CI)	82.3 (71.7, 89.6)	80.0 (65.9, 89.5)	26.7 (8.9, 55.2)	80.0 (62.5, 90.9)	94.0 (82.5, 98.4)
NPV, % (95% CI)	99.8 (98.7, 99.9)	99.8 (98.8, 99.9)	99.7 (98.6, 99.9)	100.0 (98.8, 100.0)	99.5 (98.1, 99.9)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; RSV, respiratory syncytial virus.

Table IV
Other viral pathogens detected from the sample group by multiplex polymerase chain reaction at Royal London Hospital ($N = 1111$)

Pathogens	Number of samples
Adenovirus	11 (0.99%)
Astrovirus	2 (0.18%)
Enterovirus	3 (0.27%)
Metapneumovirus	8 (0.72%)
Para-influenza 3	2 (0.18%)
Rhinovirus	35 (3.15%)
Rotavirus	1 (0.09%)
Sapovirus	3 (0.27%)
Total	65 (5.85%)

Discussion

GXP testing for NV, CD and IFA/B proved similar to multiplex PCR testing at the RLH. Sensitivity and specificity, compared to RLH testing, were all >95% with only the RSV assay significantly less sensitive. GXP missed seven IFBs (Table III) so may be less sensitive than centralized testing for IFB detection. A small number of false-positive samples for IFA/B and RSV (compared to centralized testing) probably meant that some patients were unnecessarily isolated and treated with antivirals, although another explanation is that the GXP was more sensitive for IFA and RSV testing. For the five major pathogens NV, CD, IFA/B and RSV, the NPVs were all >99%, indicative of a high level of certainty in ruling out suspected infection. This was a valuable aid in keeping open wards with suspected diarrhoeal or IF outbreaks which, ordinarily, may have been closed. A significant number of less pathogenic viruses were detected (e.g. rhinovirus) but none of these was deemed to be of significant infection-control importance in immunocompetent patients. Taking this into account, it was concluded that the viral targets covered by the GXP were sufficient, without the need for full-panel PCR testing at the RLH, unless patients were aged <16 years or immunocompromised.

TAT for receipt and reporting of samples at WCUH was considerably shorter compared to centralized testing at the RLH. This meant that the infection prevention and control team could immediately act on results; keeping wards open following negative results but also isolating infectious patients with positive results in a more timely fashion.

There are three other comparable instruments to the GXP; bioMérieux® Biofire® FilmArray®, QIA GEN® QiaStat® and GenMark® ePlex®. All of these are random-access bench-top analysers which offer simultaneous NV and IFA/B testing. The complexity of operation is low for all platforms, although cost per test for the GXP is cheaper, making it, at present, our platform of choice.

The GXP also demonstrated versatility in processing different types of samples although results were not analysed according to respiratory tract sample types. As there were sometimes delays in collecting stool samples, it would have been advantageous to process rectal swabs, particularly in an outbreak situation, but this was not possible and should be the subject of a further study.

Our service evaluation was unique in that no other near-patient platforms that tested simultaneously for IFA/B and NV were found. There have been two studies of NV using the GXP, both in laboratory settings, one using the CDC NV reference method [7], and one using an in-house NV PCR assay [8]. This group was the only one to investigate TAT. Regarding IF, there have been three GXP IFA/B evaluations, one compared the Hologic® Prodesse® ProFlu +® and cell culture [9]. The second evaluated the impact of rapid PCR on patient length of stay (LOS) and, finally, a point of care evaluation which also used Hologic® Prodesse® ProFlu +® as their comparator [11]. These publications varied in sample size, comparative methods and settings, with only one study comparing localized with centralized testing [10]. Overall, like our study, the sensitivity of the GXP for IFA/B and NV was between 93% and 100% and the NPV between 99% and 100%. The speed of the GXP proved to be advantageous in making quicker patient-care decisions and offering infection prevention and control advice when compared with batch non-random-access PCR platforms. One study proved that there was a significant reduction in patient LOS and microbiology test requests for patients with a positive GXP result [10].

Our study demonstrated that the high sensitivities and NPVs for IFA, IFB and NV were, again, reproducible. The value of simultaneous testing for IF and NV was also demonstrated with high numbers of IFA and IFB detected in the 2017/18 winter season compared to far higher numbers of NV detected in the 2018/19 winter season. The impact on patient flow and initial management, which was also experienced, has been demonstrated in other studies [12,13]. Although this study emphasized the utility of rapid IF and NV results, the RSV results also had an impact on patient flow in paediatric wards. As previously described, availability of a positive RSV result in a symptomatic child can allow for cohorting of patients that is reflected in better utilization of isolation facilities [14].

There were some limitations to this study. Automated results were taken at face value. Ct values in discordant samples that may have been false positives were not taken into consideration, nor were verification data available to provide evidence that the automated result was valid for this population. Data was not collected according to patient clinical speciality (including paediatrics) and results were not compared and contrasted. This study was unable to accurately calculate bed days lost, although, anecdotally, at least 300 bed days were saved over a 12-month period. Based on non-tariff prices, the GXP costs £30 for Xpert® Flu/RSV compared to £21 for multiplex in-house respiratory panel. A cost effectiveness argument for localized testing can therefore be made on the basis of a reduction in bed days lost and reduced cleaning costs, despite our lack of precise data.

In the UK, following the Carter report [15], there has been an emphasis on centralization and formation of pathology networks. The efficiency of networks relies upon good transport and IT links which can be difficult to organize, particularly for hospitals in different NHS Trusts. A competing model is the Lord Darzi vision [16] which can be summarized as 'localize where possible, centralize where necessary'. Our service evaluation demonstrated the utility of a localized random-access real-time PCR platform incorporated into a blood science laboratory. The advantages were faster turnaround times and comparable performance when testing for IFA/B, CD and NV. Clearly, this is a local testing innovation which aligns well with the Darzi vision.

Acknowledgements

The authors would like to thank Lindiwe Mangena, Aminur Miah, Kathir Mahadevan, Ritesh Mistry, Ikra Mohammad, Vinosaan Muthurajah, Marcus Nunes, Sarah Whitney & IPC colleagues at WCUH, and Melvyn Eydmann and the managers of Microbiology/Virology at RLH.

Conflict of interest statement
None declared.

Funding sources
This project was funded by a grant award from Barts Charity, grant number MGU0362. Barts Charity is a charity registered in England and Wales No. 212563, and a company registered in England and Wales, No. 7168381.

References

[1] Moore C. Point-of-care tests for infection control: should rapid testing be in the laboratory or at the front line? J Hosp Infect 2013;85:1—7.
[2] Beersma MF, Sukhrie FH, Bogerman J, Verhoef L, Mde Melo M, Vonk AG, et al. Unrecognized norovirus infections in health care institutions and their clinical impact. J Clin Microbiol 2012;50:3040—5.
[3] Sandmann FG, Shallcross L, Adams N, Allen DJ, Coen PG, Jeanes A, et al. Estimating the hospital burden of norovirus-associated gastroenteritis in England and its opportunity costs for non-admitted patients. Clin Infect Dis 2018;67(5):693—700.
[4] Bibby DF, McElarney I, Breuer J, Clark D. Comparative evaluation of the Seegene Seeplex RV15 and real time PCR for respiratory virus detection. J Med Virol 2011;83:1469—75.
[5] Van Elden LJR, Van Loon AM, Van der Beek A, Hendriksen AW, Hoepelman AIM, Van Kraaij MGJ, et al. Applicability of a real-time quantitative PCR assay for diagnosis of respiratory syncytial virus infection in immunocompromised adults. J Clin Microbiol 2003;41:4378—81.
[6] Kageyama T, Kojima S, Shinohara M, Uchida K, Fukushi S, Hoshino FB, et al. Broadly reactive and highly sensitive assay for Norwalk-like viruses based on real-time quantitative reverse transcription-PCR. J Clin Microbiol 2003;41(4):1548—57.
[7] Gonzalez MD, Langley LC, Buchan BW, Faron ML, Maer M, Templeton K, et al. Multicentre evaluation of the Xpert norovirus assay for detection of norovirus genogroups I and II in fecal specimens. J Clin Microbiol 2016;54(1):142—7.
[8] Henningsson AJ, Bowers AN, Nordgren J, Quttineh M, Matussek A, Haghunds S, et al. Rapid diagnosis of acute norovirus-associated gastroenteritis: evaluation of the Xpert Norovirus assay and its implementation as a 24/7 service in three hospitals in Jonkoping County, Sweden. Eur J Clin Infect Dis 2017;36(10):1867—71.
[9] Novak-Weekley SM, Marlowe EM, Poulter M, Dywer D, Speers D, Rawlinson W, et al. Evaluation of the Cepheid Xpert Flu assay for rapid identification and differentiation of influenza A, influenza A 2009 H1N1, and influenza B viruses. J Clin Microbiol 2012;50(5):1704—10.
[10] Wabe N, Li L, Lindeman R, Yimsung R, Dahm MR, Clezy K, et al. Impact of rapid molecular diagnostic testing of respiratory viruses on outcomes of adults hospitalized with respiratory illness: a multicenter quasiexperimental study. J Clin Microbiol 2019;57. e01727-18.
[11] Cohen DM, Kline J, May LS, Harnett GE, Gibson J, Liang SY, et al. Accurate PCR detection of influenza A/B and respiratory syncytial viruses by use of Cepheid Xpert Flu+RSV Xpress assay in point-of-care settings: comparison to Prodesse ProFlu+. J Clin Microbiol 2018;56(2):e01237—43.
[12] Cohen-Bacrie S, Ninove L, Nougairede A, Charrel R, Richet H, Minodier P, et al. Revolutionizing clinical microbiology laboratory organisation in hospitals with in situ point-of care. PLoS One 2011;6:e22403.
[13] Lee-Lewandrowski E, Corboy D, Lewandrowski K, Sinclair J, McDermott S, Benzer TI, et al. Implementation of a point-of-care satellite laboratory in the emergency department of an academic medical centre. Impact on test turnaround time and patient emergency department length of stay. Arch Pathol Lab Med 2003;127:456—60.
[14] Mills JM, Harper J, Broomfield D, Templeton KE. Rapid testing for respiratory syncytial virus in a paediatric emergency department: benefits for infection control and bed management. J Hosp Infect 2011;77:248—51.
[15] Lord Carter of Coles. Report of the review of NHS pathology services in England. 2006. Available at: https://www.networks.nhs.uk/nhs-networks/peninsula-pathology-network/documents/CarterReviewPathologyReport.pdf [last accessed April 2019].
[16] Professor the Lord Darzi of Denham KBE. High quality care for all: NHS Next Stage Review final report. 2008. Available at: https://webarchive.nationalarchives.gov.uk/20130105053023/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085825 [last accessed April 2019].