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Cost evaluation of point-of-care testing for community-acquired influenza in adults presenting to the emergency department

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ABSTRACT

Background: Rapid molecular point-of-care tests (POCTs) for influenza have potential to produce cost savings in emergency departments (EDs) and acute care settings. To date, published projected savings have been based on estimated costs.

Objectives: This study aimed to describe the cost implications of a rapid influenza POCT using accurate real-world patient level costing data. 204 adult patients receiving point-of-care (POC) influenza testing in the ED as part of a routine clinical service were identified retrospectively, alongside a control cohort of 104 patients from the same influenza season. Costs for all were calculated at the individual patient level. Cost comparison was performed using an instrumental variable (IV) regression to overcome potential bias within the observational dataset.

Results: Patients who had a POCT on average cost 67 % less than those who did not (average cost reduction: £2066: 95 % CI: £624 and £2665). Moderate to high NEWS score at arrival, presence of ≥1 comorbidity, and age ≥70 years increased overall costs across both groups ($p < 0.05$).

Conclusions: Savings from POC testing can be attributed to more targeted treatments, fewer admissions and reduced lengths of stay. The IV regression results are supported by a second method (ordinary least square against baseline characteristics). They are also in line with existing work that use estimated costs but indicate greater savings than predicted previously. In conclusion, POC influenza testing in the emergency department produces significant cost savings, this is demonstrated here through an analysis using individual real-world patient level costing data.

1. Introduction

Influenza remains a major cause of morbidity and mortality in the United Kingdom, creating significant pressure on healthcare services. While cases can be identified upon clinical presentation, this approach is recognised to have poor sensitivity [1]. Accurate diagnosis is crucial to direct appropriate management and prevent nosocomial transmission.

Widely available molecular techniques, including polymerase chain reaction (PCR), are highly sensitive and specific in identifying influenza but traditionally required batched testing in specialist laboratories, creating delays. Recently, molecular point-of-care tests (POCTs) have become available which produce accurate results rapidly and require minimal training to operate.

Several groups have attempted to evaluate the impact of point-of-care (POC) influenza testing in emergency departments (EDs) and admissions units within the UK National Health Service (NHS) [2–6]. These groups estimate cost savings through reduced lengths of stay, reduced unnecessary isolation and increased targeted treatments. However, so far, the economic implications of POCTs have not been evaluated using real-world patient level data of costs incurred.

Building on existing literature, this study aims to accurately describe the cost implications of using a rapid influenza POCT (Roche cobas® Liat®) in adults presenting to the ED by retrospectively

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comparing an intervention and control group within the same influenza season and using real-world patient level costing data for each individual.

2. Materials and methods

2.1. Point of care testing

The Roche cobas® Liat® PCR system comprises an automated analyser and a single-use assay tube. We used a multiplex assay to detect influenza A and B, with a manufacturer reported sensitivity of 100 % for both species, and specificity of 96.8 % for influenza A, 94.1 % for influenza B [7]. Multiple study groups have reproduced similar sensitivity and specificity in controlled laboratory settings [8] and near-patient environments [9,10]. The sensitivity and specificity are comparable to other similar POC systems [11–14].

Respiratory samples were collected using a swab then placed into universal transport medium (UTM™). The manufacturer recommends nasopharyngeal sampling; however, we used pharyngeal samples as they were easier for staff to perform with minimal training and more acceptable to patients [15]. Approximately 200 µL of the inoculated UTM™ was transferred into the assay tube, sealed, then placed inside the analyser. Real-time RT-PCR occurs within the closed system, producing a result in 20 minutes. When possible, the remaining aliquot of UTM™ was sent for confirmatory laboratory testing. Frontline ED staff performed the testing; none had specialist laboratory skills.

2.2. Routine laboratory-based testing

Laboratory testing was performed at Leeds Teaching Hospitals molecular virology laboratory. An in-house multiplex PCR was used to detect influenza A, influenza B, sub-typing of influenza A for H1 (H1N1 pdm09) and H3 (H3N2), respiratory syncytical virus, metapneumovirus, adenovirus, rhinovirus, parainfluenza 1–4 and *Mycoplasma pneumoniae,* alongside an MS2 internal control. Further details are available in the supplementary materials.

2.3. Site selection

Work took place at St. James's University Hospital, part of Leeds Teaching Hospitals NHS Trust in Leeds, United Kingdom, where this POCT was being introduced for routine clinical service for the first time. The Trust has 2494 inpatient beds, of which 160 are critical care. It receives approximately 221,000 ED attendances per annum.

2.4. Selection of the intervention cohort

The intervention cohort were identified retrospectively and comprised the first 204 consecutive adult patients (> 16 years) presenting to the ED between 20th December 2017 and 5th January 2018 and receiving a POCT from the date of its introduction. This period immediately preceded the peak of the influenza season [16]. Decision to perform a POCT was made by the assessing clinician with support from a simple algorithm, which advised testing any patient with symptoms of influenza (fever, plus 2 or more of cough, sore throat, headache, rhinorrhoea, myalgia, vomiting and diarrhoea) or a clinical diagnosis of pneumonia, lower respiratory tract infection or infective exacerbation of chronic obstructive pulmonary disease (COPD). Of this cohort, 148 patients had confirmatory testing of their sample in the laboratory. There were 11 discrepant results (see supplementary material, Table S1) which we classified according to the final diagnosis decided upon by the treating physicians, as this reflected the actual management delivered.

2.5. Selection of the control cohort

A control cohort was identified retrospectively, opportunistically, and pragmatically. For logistical reasons, between 15th and 25th February 2018 no assay kits were available, so no POCTs were performed. Patients attending the ED during this period who were tested for respiratory viruses by laboratory-based PCR were therefore selected as controls. Controls were identified from a list of all samples collected between 15th February and 2nd March 2018 which received laboratory-based respiratory viral PCR testing. Although POCTs resumed on 26th February, a 5-day extension was incorporated to account for delays in decisions to test. The incubation period of influenza is 24–72 hours [17] so this period was limited to 5 days. After excluding patients < 16 years old and those who did not attend ED in the above time frame, 104 controls resulted.

2.6. Calculation of patient level costing

The costs assigned to all activity in the intervention and control cohorts were generated through the Leeds Teaching Hospitals patient level information costing system (PLICS). This uses electronic data to allocate a cost to each stage of a patient's treatment pathway. The total cost of each individual's ED attendance and, when applicable, the linked inpatient stay was calculated. This included variable costs (radiology, pathology, pharmacy) and fixed costs (staffing, facilities). It was not possible to find full costings for 13 individuals, possibly due to coding or data errors. Our primary analysis excluded these individuals. However, we assessed any potential impact of these missing data in a secondary analysis by imputing the missing costs via multiple imputation analysis assuming missing at random.

2.7. Cost comparison between the intervention and control cohort

Exploring the treatment effect of an intervention where only observational data are available is challenging. Observational data have not been randomised, therefore it is likely the average distribution of observed and unobserved characteristics among participants will be different. Consequently, an analysis via an ordinary least square (OLS) regression to adjust total incurred costs with co-variates known to be related to increased use of healthcare resources (e.g. length of stay, intensive care) could mask the true impact of the intervention. Several methods have been proposed to improve estimations of treatment effect in observational data. These methods seek to mimic randomisation or model directly the selection process to offer an unbiased treatment effect. Examples include OLS with baseline covariates, matching methods, inverse probability weighting or instrumental variables (IV) regression [18–20].

The IV method is the most common method to manage unobservable factors. An IV will mimic the effect of randomisation by identifying patients who should receive the intervention but will only affect the outcome via the specified treatment. This allows us to establish causality. Finding an adequate instrument, however, can be difficult [21]. Once an adequate instrumental variable is found, the IV regression analysis is performed in a 2-stage OLS model. The first evaluates the probability of being in the intervention arm: if the POCT was available, would the patient have been offered it? The predicted values of this regression analysis are then used to estimate the treatment effect.

After reviewing the dataset, we found that provisional diagnosis fulfilled IV criteria: predicting the probability of receiving the intervention (being offered a POCT if available); but not being directly correlated with the outcome (total cost of the hospital attendance). We tested provisional diagnosis as an instrumental variable via an OLS against total cost and found no correlation between the two, confirming its adequacy for use (supplementary material, Table S4). We also estimated the treatment effect via an OLS regression against baseline

Table 1
Baseline characteristics of intervention and control cohorts.

Variable	Controls n = 104	Intervention n = 204	*t*-test/ proportion test/ Wilcoxon rank-sum test as appropriate (Pr(|T| > |t|))
Demographics			
Age in years (CI)	64.19 (59.96–68.42)	65.50 (62.68–68.32)	−1.313 (0.601)
% Sex = female (SE)	62.5 (4.7)	60.3 (3.4)	2.2 (0.707)
National Early Warning Score (NEWS) on arrival to ED % NEWS > 5 (SE)	21.2 (4.0)	31.86 (3.3)	**−10.71 (0.048)**
Comorbidities			
% who had ≥ 1 comorbidity (SE)	88.46 (3.31)	90.19 (2.08)	−1.73 (0.637)
% with chronic lung disease (SE)	40.38 (4.81)	49.02 (3.50)	−8.63 (0.150)
Provisional diagnosis			
% Respiratory tract disease (SE)	33.65 (4.63)	61.27 (3.41)	**−27.62 (0.000)**
% Other (SE)	66.35 (4.63)	38.73 (3.41)	**27.62 (0.000)**

Pr(|T| > |t|) in bold represent significant at a 95 % level.
CI = confidence interval.
SE = standard error.

control characteristics only, to test the validity of our IV regression analysis. This method avoids potential contamination between the treatment and the outcome.

3. Results

Table 1 describes the baseline characteristics of the analysed population. Table 2 outlines the final diagnoses, alongside the proportion who were admitted for inpatient care, their length of stay, and the proportion who received antivirals.

In the initial OLS analysis, using well-known co-variates and provisional diagnosis to adjust for potential heterogeneity in our population showed a significant and positive relationship between total costs of the hospital attendance and length of stay, inpatient care, and intensive care admission (Table S4, supplementary materials). However, having the POCT (or being in the intervention group) was associated with an increase in total costs of hospital attendance by 34 % on average, despite a lower proportion of patients requiring inpatient care, intensive care and having shorter length of stays (Table 2). This indicates potential bias in these estimates.

The stage one IV regression analysis confirmed a strong relationship between the instrument (provisional diagnosis) and being offered a POCT (Table S5, supplementary materials). The second stage of the IV regression analysis (Table 3) shows the impact of the POCT on costs, and indicates that patients who had a POCT on average cost 67 % less than those who did not (average cost reduction: £2066: 95 % CI £624 - £2665). Other co-variates, including moderate to high NEWS at arrival, presence of ≥1 comorbidity, and age ≥70 years, increase overall costs across both cohorts ($p < 0.05$).

Table 3
Stage II IV regression analysis.

Effect on Cost for Different Covariates (IV regression) - Stage II			
	Value (Co-efficient)	Standard Error	P > |z|
POCT	−1.105	0.449	0.014
Age (40–70 years)	0.403	0.239	0.091
Age (over 70 years)	0.831	0.244	0.001
Sex	0.144	0.138	0.295
NEWS Score (> 4)	0.584	0.160	0.000
Comorbidity	0.567	0.278	0.041
Chronic Lung Disease	0.225	0.154	0.145
Intercept	6.593	0.420	0.000
Wald chi2(7) = 63.11 (Prob > chi2 = 0.0000)			

Total costs have been transformed to logarithmic form. Regression has been adjusted to produce robust SE estimations. Instrumented variable POCT; n = 291 (13 cases with missing inpatient care costs and 4 cases with missing arrival NEWS score).

The secondary analysis (OLS regression against baseline characteristics only) indicates similar but smaller cost reductions (average reduction 27 % or £830; 95 % CI 2 %–46 %, or £54 - £1409) (Table S6 supplementary materials). The results from a further analysis where costs were imputed for 13 patients with missing inpatient care costs showed no difference in our findings (analysis available on request).

Table 2
Final diagnoses, antiviral prescriptions, inpatient care and length of stay.

Variable	Controls (n = 104)	Intervention (n = 204)	*t*-test/ proportion test/ rank-sum as appropriate (Pr(|T| > |t|))
% Influenza	37.5 (39/104)	41.67 (85/204)*	−4.17 (0.481)
% Other respiratory virus	6.73 (7/104)	11.76 (24/204)	−5.03 (0.165)
% Negative respiratory sample	55.77 (58/104)	46.57 (95/204)	9.20 (0.127)
% Prescribed antiviral (oseltamivir)	37.5 (39/104)**	26 (53/204)***	**11.52 (0.037)**
% Inpatient care (SE)	91.3 (2.76)	74.5 (3.05)	**16.8 (0.000)**
% ICU (intensive care unit) stay (SE)	6.73 (2.46)	2.45 (1.08)	**4.28 (0.066)**
% HDU (high dependency unit) stay (SE)	5.77 (2.29)	5.39 (1.58)	0.38 (0.891)
Length of stay in days (CI)	11.49 (8.6–14.3)	6.49 (5.1–7.8)	**5.00 (0.000)**

Pr(|T| > |t|) in bold represent significant at a 95 or 90 % level.
CI = confidence interval.
SE = standard error.
* 76 patients tested positive for influenza by POCT, of which 56 were confirmed by secondary laboratory testing. The remaining 9 patients were assigned a diagnosis of influenza based on the final working diagnosis at discharge. A detailed description of how final diagnoses were assigned and the antiviral prescribing processes can be found in the supplementary materials.
** 30 had a confirmed diagnosis of influenza.
*** 51 had a confirmed diagnosis of influenza.

4. Discussion

POC testing allows physicians to rapidly and accurately identify influenza. This permits timely targeted treatments and implementation of infection control measures which might previously have been delayed or prolonged unnecessarily. Furthermore, rapid results should positively impact on length of stay. The introduction of influenza POC testing in an ED at Leeds Teaching Hospitals prompted this retrospective evaluation of its cost impact, using individual patient level costing data.

Our analysis demonstrates the provisional diagnosis variable is likely to influence the decision to offer a POCT. The POCT in turn is likely to influence the decision to discharge or admit a patient, and the related treatment choices. If influenza is detected and treated, the average length of stay is expected to be shorter, therefore overall costs are expected to reduce.

The initial OLS analysis indicated POCT use is linked to increased overall treatment costs. However, as highlighted, an OLS analysis against well-known co-variates would produce biased treatment effects driven by the lack of randomisation in this observational dataset. An IV analysis was able to estimate an unbiased treatment effect through using provisional diagnosis. This process allowed us to estimate a degree of causality between the POCT and the treatment pathway.

The magnitude of our results is relevant despite the potential uncertainty (average savings per patient between £600 and £2600). The wide confidence interval is likely related to the small sample size and single-centre based analysis. Despite this, we consider the results to be robust as they are supported by a second, alternative method (OLS against baseline characteristics) which also indicates cost savings, although smaller.

Other authors have previously estimated cost savings where POCTs are used. Brooke-Pearce and Demertzi [4] retrospectively compared outcomes of patients presenting to the ED of a UK NHS hospital with flu-like symptoms in two consecutive seasons. Using estimated costs, they projected POCTs would save £16,632 - £33,264 per month through avoiding unnecessary isolation, and potentially £328,860 per month through reduced length of stay of POCT negative patients. Davis et al. [3] assessed the Alere™ I Influenza A/B POCT in 4 UK NHS hospitals. They projected POCTs would avoid a minimum of 1.1 days of incorrect isolation, saving £261,590 per 1000 patients. The test sensitivity in this analysis was only 77 % using throat swabs, therefore Allen et al. [22] developed a cost-consequence model for a hypothetical cohort to estimate cost impacts if more sensitive nasal swabs were used. Estimated savings were similar, at £242.73 per patient. Hansen et al. [23] considered the potential effect of POCTs on decision-making during ED visits in Minneapolis, United States. They compared physician management plans before and after testing, finding a change in 61 % of cases. Using a health economics model with costs derived from hospital billing and national databases, they projected POCTs could save $200.40/patient/ED visit.

Our estimates suggest average savings per patient of over £2,000, which is higher than other authors. These savings can be attributed to more targeted treatments, fewer admissions and reduced lengths of stay. Compared to existing work completed in the UK which use estimated costs [3,4,22] our results derive directly from individual patient level data. Although the cost of the POCTs have not been included (approximately £36 per POCT, versus approximately £25 per laboratory test) the use of POCTs would still produce significant savings.

5. Limitations

Testing took place prospectively in consecutive patients, but the cohorts and their data were identified retrospectively. Furthermore, controls were selected opportunistically and pragmatically through a 'natural experiment' resulting from difficulties with procurement. Although this allowed valid, real-world data to be used, there are limitations to this approach.

Whilst both groups derive from the same influenza season, they occurred 6 weeks apart. The intervention cohort is immediately prior to the peak of the season when transmission intensity was highest, meaning the groups are not fully comparable in terms of exposure. Despite this, both are within influenza season and occurred at times when influenza-confirmed secondary care admissions were similar [16]. We believe our approach is preferable to using a control group from a different influenza season.

The control group comprised largely of patients who were admitted and subsequently received laboratory-based testing. It is highly probable that patients were presenting to ED during the 'control period' with influenza-like symptoms, but were discharged without testing as they were not sufficiently unwell for admission. These patients would not have been identified and therefore not included in our analysis. This could potentially produce an overestimation in our analysis of the cost-savings.

We used pharyngeal samples instead of nasopharyngeal, which may have led to loss of sensitivity [24,25]. However, we felt this was outweighed by the benefits of pharyngeal sampling as discussed in the methods. Real-time PCR was our chosen gold standard for influenza detection due to its sensitivity and wide availability. However, we acknowledge this is a departure from viral culture or paired serum antibody titres which are traditionally used as gold standards.

Our analysis does not account for infection prevention and control (IPC) aspects, largely because this was difficult to accurately evaluate retrospectively. However, other groups have found POCTs to have a positive impact on nosocomial influenza rates and single-room bed days [3,5], so it could be assumed that our cost savings would only increase if IPC aspects were incorporated.

Finally, our retrospective observational analysis is based on a single-centre. Although we would expect similar results from other similar UK centres, a prospective randomised multi-centre analysis would be desirable to estimate the overall benefits to the NHS.

6. Conclusions

Point of care testing allows rapid and accurate influenza diagnosis, which has been shown to reduce lengths of stay, facilitate targeted treatments and promote correct isolation. These improvements would be expected to reduce overall costs, which is of key importance in healthcare settings. Our study using individual patient level costing data has confirmed the estimated work of previous authors that POC influenza testing in the ED would produce cost savings.

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CRediT authorship contribution statement

Anne Melhuish: Methodology, Data curation, Writing - original draft. **Armando Vargas-Palacios:** Methodology, Formal analysis, Writing - original draft. **Nahel Yaziji:** Methodology, Formal analysis, Writing - original draft. **Joe Selfridge:** Data curation, Writing - original draft. **Mitalee Pisavadia:** Data curation. **Gurdeep S. Sagoo:** Supervision, Writing - review & editing. **Jane Minton:** Supervision, Writing - review & editing.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2020.104533.

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