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Implementation of influenza point-of-care testing and patient cohorting during a high-incidence season: a retrospective analysis of impact on infection prevention and control and clinical outcomes

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SUMMARY

Background: During high-incidence influenza seasons, a robust infection prevention and control policy is imperative to reduce nosocomial transmission of influenza.
Aim: To assess the impact of influenza point-of-care testing (POCT) in an emergency department (ED) and patient cohorting on an influenza ward on infection prevention and control and clinical outcomes.
Methods: Influenza POCT was operational in the study ED from 21st January 2018 and patient cohorting was operational on an influenza ward from 25th January 2018. A retrospective 'before–after' analysis was performed with pre-intervention defined as 1st November 2017 to 20th January 2018 and post-intervention defined as 21st January 2018 to 30th April 2018. The primary outcome was the rate of hospital-acquired influenza. Secondary outcomes included antiviral prescription and length of stay. The length of time that inpatients remained influenza-positive was estimated by polymerase chain reaction (PCR).
Findings: There were 654 inpatients with confirmed influenza during the 2017/18 influenza season: 223 pre- and 431 post-intervention. Post-intervention, there were fewer cases of hospital-acquired influenza per day (0.66 vs 0.95, $P < 0.0001$), median length of stay was shorter (5.5 vs 7.5 days, $P = 0.005$) and antiviral prescription was more frequent (80% vs 64.1%, $P < 0.0001$). Cohorting released 779 single rooms for use elsewhere in the trust. The fixed probability of being PCR-negative by the next day (P) was 0.14 [95% confidence interval (CI) 0.12–0.16] for immunocompetent patients. This implies that half of immunocompetent patients are PCR-negative by five days post-diagnosis (95% CI 5–6).
Conclusion: Influenza POCT in an ED and patient cohorting on an influenza ward were associated with reduced nosocomial transmission of influenza and improved patient flow.

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A policy of retesting immunocompetent patients five days post-diagnosis could allow half of these patients to come out of respiratory isolation earlier.
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Introduction

The case-fatality rate associated with influenza in hospitalized patients is 3.4–8.3% [1], and may be twice as high when influenza is hospital-acquired compared with community-acquired [2]. Nosocomial influenza outbreaks lead to increased bed occupancy and closed wards during winter months, with significant financial implications [3]. A robust infection prevention and control policy to reduce nosocomial transmission of influenza is therefore imperative, especially during years of high incidence (e.g. 2017/18 influenza season) [4,5]. The influenza strategy at the study hospital (a large tertiary teaching hospital) focused on five principles (Table I).

The Cobas Liat influenza A/B & respiratory syncytial virus (RSV) assay (Roche, Basel, Switzerland) (Liat) is an automated multiplex polymerase chain reaction (PCR) system with a rapid turnaround time of 20 min [6]. Previous studies have found its performance to be excellent, with sensitivity/specificity of 100%/97.1–100% for influenza A and 97.8–100/99.5–99.7% for influenza B [7,8].

Influenza A/B point-of-care testing (POCT) with Liat was implemented in the emergency department (ED), and patient cohorting was implemented in a designated influenza ward half-way through the influenza season. After the influenza season, a service evaluation was conducted to assess the impact of these new services on patient care and infection control. Outcomes included rates of hospital-acquired influenza, prescription of antiviral drugs and length of stay. Achievement of respiratory isolation, and an assessment of bed-days lost from influenza-related 'blocked beds' and single-room bed-days saved from patient cohorting was undertaken. The data also provided the opportunity to estimate the length of time that inpatients remained influenza-positive by PCR.

Methods

Design and study population

All inpatients with confirmed influenza at St. George's Hospital in South West London during the 2017/18 influenza season were included in this study. The influenza strategy (Table I) was facilitated and overseen through daily infection prevention and control meetings, and recording of all influenza cases in the hospital on the patient admission system (available to all relevant staff). The purpose of this service evaluation was to conduct a 'before–after' assessment of the impact of influenza POCT in an ED and patient cohorting on an influenza ward on infection prevention and control and clinical outcomes.

The Cobas Liat POCT assay was used for the first time in the adult ED from 21st January to 14th April 2018. All patients admitted with possible influenza were tested by throat swab. Negative samples were routinely retested in the on-site diagnostic laboratory using Respiratory Pathogens 21 Multiplex Real-time PCR (Fast Track Diagnostics, Esch-sur-Alzette, Luxembourg) (rPCR) assay. Positive samples were not retested routinely, but many patients had subsequent samples taken soon after admission. These were tested by rPCR or the Cepheid Xpert Xpress Flu/RSV assay (Cepheid, Sunnyvale, CA, USA) (fPCR) where influenza was specifically queried or a rapid result was required.

An influenza ward was operational from 25th January to 6th April 2018. There were four, four-bedded bays (male influenza A, female influenza A, male influenza B and female influenza B) and seven single rooms. Bays had doors which remained closed. The ward (including staff, cleaners, equipment and toilets) was divided into separate influenza A and B sides. Staff shared common areas such as the staff room, sluice and clean utility rooms. Single rooms were used for those with mixed influenza A/B infection or those needing a single room for another reason. Patients considered appropriate for transfer on to the influenza ward included all adults with confirmed influenza. Transfer was avoided for unstable patients or where the patient required care from a speciality other than general medicine.

For the before–after analysis, the pre-intervention period is defined as patients admitted between 1st November 2017 and 20th January 2018, and the post-intervention period is defined as patients admitted between 21st January and 30th April 2018. Admission date, rather than date of influenza diagnosis, was used because the two interventions concerned identification of community-acquired influenza and patient flow following admission. Descriptive statistics of the 2016/17 season are provided for comparison.

Outcomes

The primary clinical outcome was the frequency of hospital-acquired influenza per day for patients admitted either pre- or post-intervention. Secondary clinical outcomes included rates of antiviral prescription, length of stay and 30-day all-cause mortality.

Secondary infection prevention and control outcomes included influenza-related blocked-bed-days per day, and an estimation of single-room bed-days saved by patients being in a bay on the influenza ward, rather than a single room elsewhere in the trust. A 'blocked-bed-day' describes an unoccupied bed that is closed to admissions for that day (e.g. because another patient in that bay has influenza).

Two subanalyses were performed to assess the impact of POCT in the ED and cohorting on the influenza ward on respiratory isolation for patients admitted with community-acquired influenza. All patients who underwent POCT in the ED known to be true-positives ($N = 76$) [26] were compared with 76 randomly-selected true-negative controls to assess if negative POCT results reduced single-room usage. This comparison could not be matched for age and sex because this information was not available for all POCT results. The 62/76 patients admitted following positive POCT were compared with 62 patients with community-acquired influenza (controls,

Table I
Five key principles of influenza strategy

Diagnosis	Isolation	Treatment and prophylaxis	Contacts	Outbreaks
Patients being admitted, inpatients and staff with possible influenza to be tested as soon as possible. Laboratory testing performed by rPCR and fPCR. Laboratory testing operational seven days per week with twice-daily rPCR runs and rapid fPCR testing for urgent cases. Liat point-of-care testing operational in emergency department from 21/1/18 to 14/4/18.	Inpatients with possible influenza transferred into a single room, and staff to refrain from working duties whilst awaiting test result. Inpatients with confirmed influenza transferred into respiratory isolation and staff with confirmed influenza to refrain from working duties. Respiratory isolation achieved by use of appropriate personal protective equipment by staff and transfer of patient into either: ■ a single room; or ■ a bed on the influenza ward if appropriate. Influenza ward fully operational from 25/1/18 to 6/4/18: divided into four four-bedded bays by sex/influenza strain alongside seven single rooms (see 'Methods'). Inpatients and staff with confirmed influenza retested five days after first swab by fPCR. Isolation lifted if immunocompetent and either: ■ symptom-free at seven days from symptom onset; or ■ influenza not detected by fPCR (whichever comes first). Isolation lifted if immunocompromised, and influenza no longer detected by fPCR on three sequential occasions.	Treatment with antivirals (oseltamivir/zanamivir) offered to all patients with confirmed influenza as per PHE guidelines. Treatment also offered to all staff with confirmed influenza. Prophylaxis offered to asymptomatic staff working on outbreak/cohort wards. Multi-faceted approach to encourage high uptake of vaccination (>90%) in patient-facing staff.	Inpatients in 'close proximity' to a case of confirmed influenza (e.g. same bay) for at least 4 h designated as a 'contact'. Contacts with symptoms/signs of possible influenza tested and managed as above. Bays containing contacts closed to further admissions. Contacts not to transfer into a new bay (only single room/discharge). Prophylaxis with oseltamivir offered to all contacts. Patients remain designated a 'contact' until either: ■ they are diagnosed with confirmed influenza (and managed as such); or ■ they have no symptoms/signs of possible influenza at 72 h since last contact with the case.	Where a patient in a bay is diagnosed with confirmed influenza: ■ they are transferred into respiratory isolation and managed as above; ■ other patients in the bay are designated contacts and managed as above; and ■ the bay is closed to further admissions until free of contacts as above. Where two bays on one ward are closed due to the same strain of influenza, the ward is closed to further admissions pending discussion at an outbreak meeting.

rPCR, Fast Track Diagnostics Respiratory Pathogens 21 multiplex polymerase chain reaction; fPCR, Cepheid Xpert Xpress Flu/respiratory syncytial virus assay; PHE, Public Health England.

Table II
Impact of influenza point-of-care testing in an emergency department and patient cohorting on an influenza ward on hospitalized patients with confirmed influenza

	2016/17 season (*N* = 154)	2017/18 season (*N* = 654)	*P*-value	2016/17 season (*N* = 154)	Pre-intervention (*N* = 223)	*P*-value	Pre-intervention (*N* = 223)	Post-intervention (*N* = 431)	*P* -value
Patient characteristics									
Age in years, median (IQR)	60 (29—79)	71 (50—82)	<0.0001	60 (29—79)	72 (50—83)	<0.0001	72 (50—83)	70 (50—82)	0.237
Male sex, *N* (%)	79 (51.3)	305 (46.6)	0.32	79 (51.3)	104 (46.6)	0.37	104 (46.6)	201 (46.6)	1.00
Severe immunosuppression, *N* (%)	23 (14.9)	71 (10.9)	0.16	23 (14.9)	23 (10.3)	0.18	23 (10.3)	48 (11.1)	0.75
Virus strain									
Influenza A, *N* (%)	143 (92.9)	343 (52.4)	<0.0001	143 (92.9)	107 (48.0)	<0.0001	107 (48.0)	236 (54.8)	0.1
Influenza B, *N* (%)	11 (7.1)	304 (46.5)	<0.0001	11 (7.1)	112 (50.2)	<0.0001	112 (50.2)	192 (44.5)	0.12
Influenza A&B, *N* (%)	0 (0)	7 (1.1)	0.20	0 (0)	4 (1.8)	0.10	4 (1.8)	3 (0.7)	0.20
Outcome measures									
Hospital-acquired influenza, *N* (%)	36 (23.4)	143 (21)	0.68	36 (23.4)	77 (34.5)	0.02	77 (34.5)	66 (15.3)	<0.0001
Hospital-acquired influenza per day, *N*	0.20	0.79	<0.0001	0.2	0.95	<0.0001	0.95	0.66	<0.0001
GP IFI consultations in England per 100,000, *N* — (A)	246	527.4		246	236.5		236.5	290.9	
Influenza-related blocked-bed-days, *N*	167	729		167	224		224	505	
Influenza-related blocked-bed-days per day, *N* — (B)	0.92	4.03	<0.0001	0.92	2.77	<0.0001	2.77	5.05	<0.0001
Influenza-related blocked-bed-days weighted by GP IFI rate — (B/A)*100, *N*	0.37	0.76	0.001	0.37	1.17	<0.0001	1.17	1.74	0.003
Antiviral drugs prescribed, *N* (%)	73 (47.4)[a]	488 (74.6)	<0.0001	73 (47.4)[a]	143 (64.1)	0.001	143 (64.1)	345 (80.0)	<0.0001
Length of admission in days, median (IQR)	4.5 (1.8—11.5)	5.5 (2.5—14.5)	0.019	4.5 (1.8—11.5)	7.5 (2.5—19.5)	0.001	7.5 (2.5—19.5)	5.5 (2.5—12.5)	0.005
30-day all-cause mortality, *N* (%)	9 (5.8)	52 (7.9)	0.37	9 (5.8)	23 (10.3)	0.13	23 (10.3)	29 (6.7)	0.11

GP, general practitioner; IFI, influenza-like illness; IQR, interquartile range.
2016/17 = 1st November 2016—30th April 2017 (181 days), 2017/18 = 1st November 2017—30th April 2018 (181 days), pre-intervention = 1st November 2017—20th January 2018 (81 days), post-intervention = 21st January 2018—30th April 2018 (100 days).
[a] Pharmacy data not available (figures from discharge summaries and To Take Out prescriptions only) so this is likely to be an underestimate.

Table III
Impact of point-of-care testing (POCT) result on respiratory isolation for those patients that were admitted

	POCT result		*P*-value
	Influenza detected ($N = 76$)[a]	No virus detected ($N = 76$)[b]	
Patient characteristics			
Age in years, median, (IQR)	61 (IQR 31–75)	54 (IQR 35–76)	0.732
Male sex, *N* (%)	37 (48.7)	38 (50.0)	0.87
Outcome			
Admitted *N* (%)	62 (81.6)	68 (89.5)	0.17
Admission bed-days within 48 h of admission, *N*	123	135	
Proportion of bed-days that were single rooms, *N* (%)	92 (74.8)	29 (21.5)	<0.0001

IQR, interquartile range.
[a] All cases of known true-positive POCT results.
[b] Randomly selected control group (matching for age/sex not possible as this information was not available for all POCT results).

matched for age and sex) admitted pre-intervention to assess the impact on the proportion of bed-days spent in respiratory isolation during the first five days of admission.

Data from patients with at least one subsequent swab were used within a post-hoc analysis to estimate time from initial PCR-positive sample to PCR negativity to assess the appropriateness of the policy to reswab patients after five days (and cease respiratory isolation early if negative; Table I).

Sample testing

Both rPCR and fPCR testing were performed by laboratory staff. rPCR testing was performed using the Roche Flow solution. This comprises a primary sample handler and PCR set-up system (Hamilton Company, Reno, NV, USA), and MagNA Pure 96 nucleic acid extraction system and Light Cycler 480 real time PCR system (Roche, Basel, Switzerland). fPCR is a cartridge-based molecular device capable of detecting influenza A/B and RSV.

Data collection

The infection prevention and control influenza database (kept for outbreak management) was cross-referenced against rPCR/fPCR data extracted from the laboratory information management system to create an Excel spreadsheet (Microsoft Corp., Redmond, WA, USA) of all patients hospitalized with confirmed influenza during the 2016/17 and 2017/18 seasons. Electronic patient records, discharge summaries/medications and pharmacy records were reviewed. 'Severely immunosuppressed' was defined in accordance with Public Health England (PHE) guidelines (i.e. including patients undergoing chemotherapy for malignancy, transplant recipients, patients infected with human immunodeficiency virus with CD4 <200/μL, and patients receiving high-dose systemic corticosteroids or other immunosuppressive therapies) [9]. POCT results were obtained from an ED log book. Community-acquired influenza was defined as influenza confirmed by PCR <72 h after admission, and hospital-acquired influenza was defined as influenza confirmed by PCR ≥72 h after admission. This standard definition [10] is based upon the usual in-vivo incubation period for influenza being one to three days [11], and a practical solution to the fact that information pertaining to symptom onset was not readily available. Data on influenza-related ward bay and bed closures was obtained from an electronic system 'Real-time Experience' into which data were entered regularly throughout the influenza season by the infection prevention and control nursing team.

Statistical analysis

For all comparisons between pre- and post-intervention periods, *P*-values were calculated using Chi-squared test for categorical data, and Mann–Whitney *U*-test for continuous data using SPSS (IBM Corp., Armonk, NY, USA).

Table IV
Impact of point-of-care testing (POCT) and patient cohorting on the influenza ward on respiratory isolation for patients admitted with community-acquired influenza

	Admitted patients		*P*-value
	Post-intervention ($N = 62$)[a]	Pre-intervention ($N = 62$)[b]	
Patient characteristics			
Age in years, median (IQR)	64 (44–82)	68 (38–79)	0.842
Male sex, *N* (%)	28 (45.2)	28 (45.2)	1
Length of stay in days, (IQR)	4 (3–10)	4 (2–7)	0.468
Admission bed-days within five days of admission, *N*	251	233	
Proportion of bed-days that were single rooms, *N* (%)	225 (89.6)	186 (79.8)	0.003

IQR, interquartile range.
[a] All cases of patients admitted after positive POCT, where result known to be true-positive.
[b] Sixty-two community-acquired influenza controls (matched for age and sex) admitted pre-intervention.

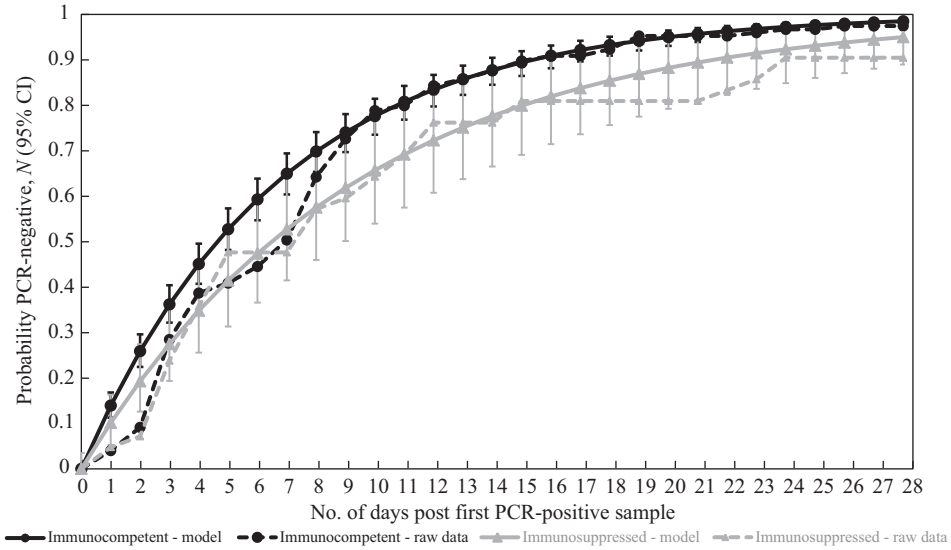

Figure 1. Time until influenza polymerase chain reaction (PCR)-negativity from first PCR-positive sample. CI, confidence interval.

For the time until PCR negativity analysis, time from first PCR-positive swab (t0) until last positive swab (t1) informed the minimum possible time of possible PCR positivity (lower bound). Time from t0 until first PCR-negative swab (t2) informed the maximum time of PCR positivity (upper bound). For the raw data analysis, the midpoint between t1 and t2 provided an estimate of the duration of PCR positivity for each patient. This was plotted in a cumulative manner to display the proportion of PCR-negative patients per day post-diagnosis separately for immunocompetent and severely immunosuppressed patients. The approach towards patients without both t1 and t2 is discussed below.

For the statistical model, the probability of being PCR-negative by the next day '*P*' was estimated by maximum likelihood using R's 'optim' function. Akaike information criterion favoured a geometric model, whereby *P* was of a fixed value, over a mixed effects model that allowed *P* to vary for each patient, and a semi-parametric approach whereby *P* was allowed to vary over time.

Ethics

Formal approval of the protocol by an ethics review board was not required as this was a service evaluation of the influenza strategy, using only existing data collected during routine clinical practice. A medical research council (MRC), NHS Health Research Authority decision tool indicated "you do not need NHS REC approval for sites in England."

Results

Influenza was detected in 268/975 (27.5%) ED inpatients tested pre-intervention and 555/1,651 (33.6%) ED inpatients tested post-intervention. There were 654 inpatients with confirmed influenza during the 2017/18 influenza season, compared with 154 during the 2016/17 season. Of these, 223 were admitted pre-intervention and 431 were admitted post-intervention (Table II). The 2017/18 cohort was older than the 2016/17 cohort (median age 71 vs 60 years, $P < 0.0001$), with more cases of influenza B (46.5% vs 7.1%, $P < 0.0001$).

Post-intervention, 226/317 (71.3%) adults admitted with community-acquired influenza received POCT, of which 208 (92%) were positive. There were no significant differences in age, sex, rates of severe immunosuppression, or influenza strain between patients admitted pre- and post-intervention (Table II).

The rate of hospital-acquired influenza per day was lower post-intervention (0.66 vs 0.95, $P < 0.0001$). This was despite there being a higher reported rate of influenza in the community in the post-intervention period [290.9 vs 236.5 general practitioner (GP) influenza-like-illness (IFI) consultations in England per 100,000 in each period] [4,5] (Table II). Comparing pre-with post-intervention for all inpatients with influenza, the median length of stay was shorter (5.5 vs 7.5 days, $P < 0.0001$) and the proportion of patients prescribed antiviral drugs was greater (80% vs 64.1%, $P < 0.0001$). There was no significant difference in 30-day all-cause mortality (6.7 vs 10.3%, $P = 0.11$).

The subanalysis shows that single-room usage within 48 h of admission was lower in patients admitted following a negative POCT in the ED (21.5% vs 74.8%, $P < 0.0001$) (Table III). The number of admission bed-days within 48 h of admission is less than 76 × 2 (152) for both arms because some patients were discharged after one day. In total, 74.8% of patients with known influenza were placed in single rooms because many were isolated on the cohort ward. Patients admitted with community-acquired influenza with a positive POCT for influenza spent a higher proportion of bed-days in respiratory isolation during the first five days of admission than patients with community-acquired influenza admitted pre-intervention (89.6% vs 79.8%, $P = 0.003$) (Table IV).

There were more influenza-related blocked-bed-days per day post-intervention, partly because of the cohort ward (5.05 vs 2.77, $P < 0.0001$). Over its 71 days of operation, the influenza ward had 1,000 potential bay-bed-days. Over 46 days sampled, 143 bay beds were unoccupied. From this, it can be estimated that over the 71 days, 221 bay beds were unoccupied [(143/46)x71 = 221]. Therefore, the influenza ward released

approximately 779 single-room bed-days (1,000–221) for use elsewhere in the trust at the cost of 221 lost bay-bed-days.

During the 2017/18 season, 316 (48.3%) patients hospitalized with influenza had at least one subsequent swab, and so were included in the time until PCR negativity analysis. Of these, 42 (13.3%) had severe immunosuppression. One hundred and sixty-one patients had an initial rPCR, so the cycle threshold (Ct) value was recorded. Figure 1 displays both the raw data and statistical model for those with severe immunosuppression and those without.

The fixed-probability value of being PCR-negative by the next day (*P*) was not significantly lower for those with severe immunosuppression [0.10, 95% confidence interval (CI) 0.07–0.14] than those without (0.14, 95% CI 0.12–0.16) ($P = 0.052$). This implies a median duration of PCR positivity of four days for immunocompetent patients [i.e. by day five post-diagnosis, 50% will be PCR negative (t50% = day five, 95% CI 5–6)]. For immunocompromised patients, t50% = day seven (95% CI 5–9). The initial Ct value did not impact *P* ($P = 0.27$).

Discussion

To the authors' knowledge, this is the first real-world evaluation of the impact of influenza POCT in an ED and patient cohorting on both clinical and infection prevention and control outcomes in a high-incidence setting. In agreement with PHE data [4,5], there were more cases of influenza and a greater proportion of influenza B during the 2017/18 season compared with the 2016/17 season (Table II). An evaluation of the POCT performance is provided in an accompanying paper [26].

Post-intervention, there were fewer cases of hospital-acquired influenza (Table II), despite a greater number of reported cases of community-acquired influenza. Due to the vulnerable population involved, hospital-acquired influenza is associated with substantial morbidity and mortality, so this is a significant finding [12]. It is made even more impressive by the fact that nosocomial outbreaks are more likely when more cases of influenza are coming into the hospital (in the form of community-acquired influenza admissions, but also staff and visitors) [10].

Interestingly, the rate of hospital-acquired influenza per day was greater in the 2017/18 pre-intervention period compared with the 2016/17 season (0.95 vs 0.2, $P < 0.0001$), which may indicate the potential impact that the high incidence of influenza would have made had it not been for the interventions.

A reduction in hospital-acquired influenza may result from improvements in respiratory isolation. POCT and availability of beds on the influenza ward increased the rates of respiratory isolation in the first five days of admission when patients are most infectious (Table IV). Influenza transmission routes remain controversial [11,13], but respiratory isolation focusing on the prevention on both droplet and short-range airborne transmission remains the goal of most guidelines [14,15]. The ideal duration of isolation is more contested. PHE guidelines advise that inpatients with risk factors for prolonged viral shedding (e.g. old age, significant co-morbidity, immunosuppression, pneumonia) should remain in isolation until 24 h after the resolution of symptoms, rather than rely on any five-day rule [16,17]. Inpatients may have cough or fever for reasons other than influenza, leading to unnecessary isolation. The policy at the study hospital involved reswabbing five days after diagnosis, and lifting respiratory isolation early if the patient is PCR-negative (Table I). The time until PCR negativity analysis suggests that this was not unreasonable because half of the patients were PCR-negative by this time (Figure 1). These results align with previous studies showing that half of inpatients are PCR-negative by day seven of illness (rather than post-diagnosis) [18]. The authors' decision to treat those with severe immunosuppression differently was because these patients have previously been shown to shed virus for longer [10]. In the study data, t50% was day seven for immunocompromised patients, but this difference was not significant ($P = 0.052$). The deviations of the model from the raw data curve at days three and eight most likely stem from the five-day testing policy (i.e. if someone tested negative on day five, the t1–t2 midpoint would be day three). Given that the raw data are probably heavily distorted by the testing policy, the geometric model may more accurately estimate true time until PCR negativity in the study population.

The link between PCR negativity and end of infectiousness is not well established, but non-infective influenza nucleic acids remain detectable by PCR after viral culture becomes negative, and animal models suggest that it is viral culture that correlates best with the presence of infective virions [19]. PCR negativity is therefore likely to overestimate, not underestimate, infectivity. This means that the hospital policy to lift isolation early in patients who are PCR-negative is reasonable, whereas a policy requiring PCR negativity may not be.

This policy did not apply to severely immunocompromised patients who were required to have three PCR-negative swabs, and would ideally stay in a single room even if they were non-infectious. The reswab policy generally utilized fPCR, so all patients were known to be RSV PCR-negative before de-isolation. For symptomatic patients, it may be prudent to utilize a panel such as rPCR that detects a range of respiratory pathogens in cases of co-infection.

In agreement with previous studies [20,21], this study found that prescription of neuraminidase inhibitors (NAIs) increased after the introduction of influenza POCT (Table II). Whilst no randomized controlled trials have examined the effectiveness of NAIs in inpatients, a large meta-analysis of cohort data from the H1N1 pandemic suggested that NAI use within 48 h of symptoms may reduce mortality by as much as 50% (adjusted odds ratio 0.50, 95% CI 0.37–0.67%, $P < 0.0001$) [22]. No benefit was found for treatment started after 48 h, except in a subgroup of adults admitted to critical care. A Spanish study analysing data across six influenza seasons also found that NAIs had greatest impact if given within 48 h, but benefit for administration up to five days after symptom onset was observed [23]. Influenza POCT in the ED may have increased antiviral prescriptions for those with confirmed influenza by enabling diagnosis within 48 h of symptom onset [20].

Increased antiviral prescription may have contributed towards the reduction in hospital-acquired influenza by reducing ongoing transmission. NAIs reduce the duration of symptoms by approximately one day [24], and a study of adults hospitalized with influenza found that the proportion who were still PCR-positive by day seven fell from 57.1% to 14.3% when NAIs were given within 48 h ($P = 0.004$) [18]. Perhaps also because of the use of antiviral drugs, a reduction in length of stay was found compared with a previous randomized controlled trial [21], but this may also reflect the greater proportion of cases of

community-acquired influenza in the post-intervention group. Studies failing to show an effect on length of stay have generally had delays between presentation and the POCT result [25], and this is why POCT may be best situated in the ED.

In the absence of POCT testing in the ED, patients with possible influenza are often placed in a single room for 24–48 h until laboratory testing confirms or refutes the diagnosis. In this study, patients with negative POCT results were isolated in single rooms less often than those with positive POCT results (21.5% vs 74.8%, $P < 0.0001$) (Table III). Furthermore, the influenza ward admitted 168 patients over its duration, releasing 779 single-room bed-days for use elsewhere in the trust. Hospital single rooms are a precious resource in winter months, so measures to prevent influenza POCT increasing single-room usage are essential [21].

The benefits of an influenza ward may not be as great during years of lower influenza prevalence, or when there is less pressure on hospital beds. Patient cohorting is unlikely to be appropriate if isolating all cases in single rooms remains feasible [15]. Diligence was required during the periods when the influenza ward was transitioning in and out of operation to prevent nosocomial transmission of influenza [10]. The present results may not be reproducible without rapid diagnostics for influenza, or the constant supervision of an experienced and dedicated infection prevention and control team.

Limitations

This study supports the effectiveness of a comprehensive influenza strategy 'as a whole'; however, being an observational and uncontrolled analysis, it cannot demonstrate that the two interventions caused the outcomes measured, either individually or together. There remains the possibility of a time bias whereby staff were more familiar and organized at implementing other elements of the influenza strategy (such as prescribing antivirals) as time went on, independent of the two interventions. This could, however, be seen as testament to the impact of the strategy as a whole.

Another caveat is that 28 patients were diagnosed with hospital-acquired influenza post-intervention but were admitted pre-intervention, and so are counted under the pre-intervention arm. However, patients diagnosed with hospital-acquired influenza in the pre-intervention period but admitted prior to 1st November were not included under the pre-intervention arm. It is important to consider that the perceived lower rates of hospital-acquired influenza in the post-intervention period may reflect diminishing incidence of influenza in April. However, the absolute number of cases of hospital-acquired influenza was lower post-intervention, and there were more GP IFI consultations in this period.

The time until PCR negativity analysis has important limitations because data were not collected through reswabbing at regular intervals, but rather through a post-hoc analysis of swabs taken in clinical practice. There were patients with both t1 and t2 ($N = 94$), t1 but no t2 ($N = 88$), t2 but no t1 ($N = 134$), and neither t1 nor t2 ($N = 338$).

Patients with neither t1 nor t2 values were excluded as they contribute little information to the model, and largely represent those discharged from hospital before five days. Those remaining in the analysis represent the 'sicker' patients, who may remain PCR-positive for longer. This means that the results are highly applicable for use in guiding hospital infection prevention and control policies which are only concerned with inpatients.

Patients with t1 but no t2 values were included to inform the lower bound (exclusion of those whose second/last swab was positive would overestimate P). For these patients, t2 was taken as t1+5 days. This assumes that the lack of further swabbing is because the patient recovered, and had they been reswabbed five days later, they would have been PCR-negative. The alternative of taking t2 as infinite would underestimate P. Those with t2 but no t1 values were included to inform the upper bound (exclusion of those whose second/last swab was negative would underestimate P). For these patients, t1 was taken as t0.

A sensitivity analysis was performed to assess the impact of these assumptions. Focusing on the immunocompetent patients, if patients with t1 but no t2 values are excluded, $P = 0.16$ (95% CI 0.14–0.18) and t50% = day four (95% CI 4–5). If they are included but t2 is taken as infinite, $P = 0.11$ (95% CI 0.09–0.12) and t50% = day seven (95% CI 6–8). If patients with t2 but no t1 values are excluded, $P = 0.10$ (95% CI 0.08–0.11) and t50% = day seven (95% CI 6–8), and if only patients with both t1 and t2 values are included, $P = 0.09$ (95% CI 0.07–0.11) and t50% = day eight (95% CI 6–10).

Ultimately any inclusion/exclusion will bias the model in one direction or another, but the rationale is described above. These limitations mean that this model should not be relied upon to drive policy change, but, accompanied by prior research [18], it provides support for a five-day retesting policy.

In conclusion, during a season with high rates of both influenza A and B, influenza POCT in an ED and patient cohorting on an influenza ward were associated with a significant reduction in nosocomial transmission of influenza, and released 779 single rooms for use elsewhere in the trust. A policy of retesting immunocompetent patients at five days after diagnosis could allow as many as half of the patients to come out of respiratory isolation early.

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Conflict of interest statement
None declared.

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