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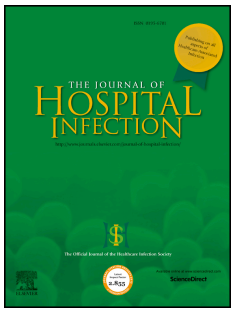

Implementation of influenza point-of-care-testing and patient-cohorting during a high-incidence season: a retrospective analysis of impact on infection prevention and control and clinical outcomes

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Title:

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 Emergency Department (ED) influenza point-of-care-testing (POCT) and influenza-ward patient-cohorting on infection prevention and control and clinical outcomes.

Methods
Influenza POCT was operational in our adult ED from 21st January 2018 and an influenza-ward from 25th January 2018. A retrospective 'before-after' analysis was performed with pre-intervention defined as 1st November 2017-20th January 2018 and post-intervention 21st January-30th April 2018. Primary outcome was rate of hospital-acquired influenza (HAI). Secondary outcomes included antiviral prescription and length of stay. The length of time inpatients remain influenza RNA detected by polymerase chain reaction (PCR) was also analysed.

Findings
There were 654 inpatients with confirmed influenza during the 2017/18 influenza season, 223 pre- and 431 post-intervention. Post-intervention, there was fewer HAI per day (0.66 v 0.95, $p<0.0001$), median length of stay in days was shorter (5.5 v 7.5, $p=0.005$) and antiviral prescription more frequent (80% v 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% CI, 0.12-0.16) for immunocompetent patients. This implies half of immunocompetent patients are PCR-negative by day 5 post-diagnosis (95% CI, 5-6).

Conclusion
ED influenza POCT and influenza-ward patient cohorting was associated with reduced nosocomial transmission of influenza and improved patient flow. A policy of retesting immunocompetent patients at day 5 post-diagnosis could allow half to come out of respiratory isolation earlier.

Introduction

The case fatality rate associated with influenza in hospitalised patients remains 3.4-8.3%[1] and may be twice as high when influenza is hospital-acquired (HAI) compared to community-acquired (CAI) [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 is therefore imperative, especially during years of high influenza incidence, such as the 2017/18 influenza season [4][5]. The influenza strategy at our large tertiary-centre teaching hospital focused around five principles (Table I).

The Roche Cobas® Liat® influenza A/B & RSV assay (Roche, Switzerland) (Liat) is an automated multiplex PCR system with a rapid turn-around time of 20 minutes [6]. Previous studies have found its performance excellent, with a sensitivity/specificity in the region 100%/97.1-100% for influenza A, and 97.8%-100/99.5-99.7% for influenza B [7][8].

We implemented influenza A/B point-of-care-testing (POCT) with Liat into the Emergency Department (ED) and patient-cohorting in a designated influenza-ward half-way through the influenza season. After the end of 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 HAI, prescription of antivirals 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 inpatients remained influenza positive by polymerase chain reaction (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. Our 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 into the impact of ED influenza POCT and influenza-ward patient-cohorting on infection prevention and control and clinical outcomes.

The Roche Cobas® Liat POCT assay (Roche, Switzerland) was used for the first time in the adult ED from 21st January to 14th April 2018. All patients being admitted with possible influenza were to be tested by throat swab. Negative samples were routinely re-tested in the on-site diagnostic laboratory by the Fast Track Diagnostics (FTD) Respiratory Pathogens 21 multiplex real time PCR (Fast-track Diagnotics, Luxembourg) (rPCR) assay. Positive samples were not routinely re-tested but many patients had subsequent samples taken soon after admission. These were tested either by rPCR, or the Cepheid Xpert® Xpress Flu/RSV assay (Cepheid, California, USA) (fPCR) where influenza was specifically queried or a rapid result required.

An influenza-ward was operational from 25th January to 6th April 2018. There were four, 4-bedded bays: male influenza A, female influenza A, male influenza B and female influenza B alongside seven single rooms. Bays had doors which remained closed. The ward (including staff, cleaners, equipment and toilets) were 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 another reason for single room. Patients considered appropriate for transfer onto 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 those patients admitted between 1st November 2017-20th January 2018 and post-intervention as 21st January-30th April 2018. Admission date, rather than date of influenza diagnosis, was used because the two interventions concerned identification of CAI 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 HAI 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 beds 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 sub-analyses were performed to assess the impact of ED POCT and influenza-ward cohorting on respiratory isolation for patients admitted with CAI. All patients with a ED POCT known to be a true-positive (n=76) were compared against 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 post positive POCT were then compared against 62 CAI controls (matched for age and sex) admitted pre-intervention to assess impact on the proportion of bed-days spent in respiratory isolation during the first 5 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 our policy to re-swab patients after 5 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 Hamilton primary sample handler and PCR set-up (PSU) system (Hamilton Company, USA) and Roche MagNA Pure 96 nucleic acid extraction system and Light Cycler 480 real time PCR system (Roche, 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 our Laboratory Information Management system, to create an excel spreadsheet 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 as per Public Health England (PHE) guidelines – i.e. including patients undergoing chemotherapy for malignancy, transplant recipients, HIV infected patients 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. CAI was defined as influenza confirmed by PCR <72 hours after admission, HAI ≥ 72 hours. This standard definition[10] is based upon the usual *in-vivo* incubation period for influenza being 1-3 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' ('RaTE) into which data was 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 IBM® SPSS® Statistics.

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 then plotted in a cumulative manner to display the proportion of patients PCR-negative per day post diagnosis

for the immunocompetent and severely-immunosuppressed separately. Our approach to those without both a t1 and t2, is discussed under Limitations 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 (AIC) favored 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

As a service evaluation of our influenza strategy, using only existing data collected during routine clinical practice, formal approval of the protocol by an ethics review board was not necessary.

Results

Influenza was detected in 268/975 (27.5%) of ED/inpatients tested pre-intervention and 555/ 1651 (33.6%) post-intervention. There were 654 inpatients with confirmed influenza during the 2017/18 influenza season compared to 154 the year before. Of these, 223 were admitted pre- and 431 post-intervention (Table II). The 2017/18 cohort was older than the previous year (median age 71 v 60 years, $p<0.0001$) with more influenza B (46.5% v 7.1%, $p < 0.0001$).

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

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

The sub-analysis shows single room usage within 48 hours of admission was lower in those admitted following a negative POCT in the ED (21.5% v. 74.8%, $p<0.0001$) (Table III). The number of admission bed-days within 48 hours of admission is less than 76x2(152) for both arms because some patients were discharged after one day. 74.8% of patients with known influenza were placed in single room because many were isolated on the cohort ward. Patients admitted with CAI with a positive POCT for influenza, spent a higher proportion of bed-days in respiratory isolation during the first five days of admission than those with CAI admitted pre-intervention (89.6% v 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 v 2.77, $P<0.0001$). Over its 71 days of being operational, the influenza-ward had 1000 potential bay bed-days. Over 46 days sampled, 143 bay beds were unoccupied. By this we can estimate 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 (1000-221) for use elsewhere in the trust at the cost of 221 lost bay bed-days.

During the 2017/18 season, 316(48.3%) of patients hospitalised 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. 161 patients had an initial rPCR and so CT value recorded. Figure 1 displays both the raw data and statistical model for those with severe immunosuppression and 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% 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 4 days for immunocompetent patients i.e. by day 5 post diagnosis 50% will be PCR negative (t50% = day 5, 95% CI, 5-6). For immunocompromised t50% = day 7 (95% CI 5-9). Initial CT value did not impact P (p=0.27).

Discussion

This is the first real-world evaluation into the impact of ED influenza POCT 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 was more influenza and a greater proportion of influenza B during the 2017/18 season than the year before (Table II).

Post-intervention, there were fewer cases of HAI (Table II), despite a greater number of reported CAI. Because of the vulnerable population involved, HAI is associated with a 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 the more influenza that is coming into the hospital (in the form of CAI admissions, but also staff and visitors)[10].

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

Reduction in HAI 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 preventing both droplet and short-range airborne transmission remains the goal of most guidelines [14][15]. 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 hours after 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. Our policy involved re-swabbing 5 days from diagnosis and lifting respiratory isolation early if PCR-negative (Table I). The 'time until PCR-negativity analysis' suggests this was not unreasonable because half of patients were PCR-negative by this time (Figure 1). These results align with previous studies showing that by day seven of *illness* (rather than post-diagnosis) half of inpatients are PCR-negative [18]. Our decision to treat those with severe immunosuppression differently is because these patients have elsewhere been shown to shed virus for longer [10]. In our data t50% was day seven for immunocompromised patients but this difference was not statistically significant (p=0.052). The deviations of the model from the raw data curve at days 3 and 8 most likely stem from the five-day testing policy (i.e. if someone tested negative on day five then the t1-t2 midpoint would be day 3). Given that the raw data is probably heavily distorted by the testing policy the geometric model may more accurately estimate true 'time until PCR-negativity' in our 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 *over*-estimate, not underestimate, infectivity. This means our policy to lift isolation early in those that are PCR-negative is reasonable (whereas a policy requiring PCR-negativity may not be).

This policy did not apply to the severely immunocompromised who were required to have three PCR-negative swabs, and would ideally stay in a single room even if non-infectious. Our re-swab 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 case of co-infection.

In agreement with prior studies[20][21], we found that prescription of neuraminidase inhibitors (NAI) increased post-introduction of an influenza POCT (Table II). Whilst no randomized control trials (RCTs) have examined the effectiveness of NAI in inpatients, a large meta-analysis of cohort data from the H1N1 pandemic suggested that NAI use within 48H of symptoms may reduce mortality by as much as 50% - adjusted odds ratio (aOR) 0.50 (95% CI, 0.37-0.67%, $p< 0.0001$) [22]. No benefit was found for treatment started after 48H, except in a subgroup of adults admitted to critical care. A Spanish study analyzing data across 6 influenza seasons also found NAI had greatest impact if given within 48H, but benefit for administration up to five days post symptoms onset was observed[23]. ED influenza POCT may have increased antiviral prescriptions for those with confirmed influenza by enabling diagnosis within 48H of symptom onset [20].

Increased antiviral prescription may have contributed towards reduction in HAI by reducing ongoing transmission. NAIs reduce duration of symptoms by around a day[24] and a study of adults hospitalised with influenza found the proportion still PCR-positive by day 7 fell from 57.1% to 14.3% when NAIs were given within 48H ($p=0.004$) [18]. Perhaps also because of the use of antivirals, we found reduction in length of stay comparable to a previous RCT [21] but this may also reflect the greater proportion of CAI 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 ED POCT testing, patients with possible influenza are often placed in a single room for 24-48 hours until laboratory testing confirms or refutes the diagnosis. In our study, patients with negative POCT results were isolated in single rooms less often than those with positive POCT results (21.5% v. 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]. Our 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 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 there were 28 patients that were diagnosed with HAI post-intervention but admitted pre-intervention and so are counted under the pre-intervention arm. However, those diagnosed with HAI in the pre-intervention period but admitted prior to November 1st were similarly not included under the pre-intervention arm. It is important to consider that the perceived lower rates of HAI in the post-intervention period may reflect diminishing incidence of influenza in April. However, the absolute number of HAI was lower post-intervention and there were more GP (IFI) consultations in this period.

There are important limitations of the 'time until PCR-negativity analysis' because data was not collected through re-swabbing at regular intervals but rather a post-hoc analysis of swabs taken in clinical practice. There were patients with both a t1 and t2 (n=94), t1 but no t2 (88), t2 but no t1 (n=134) and neither t1 nor t2 (n=338).

Patients with neither t1 nor t2 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 will therefore represent the 'sicker' patients – who may remain PCR-positive for longer. This means the results are highly applicable for use in guiding hospital infection prevention and control policies which are only concerned with inpatients.

Those with t1 but no t2 were included to inform the lower bound (to exclude 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 swab is because the patient recovered, and had they been re-swabbed 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 were included to inform the upper bound (to exclude 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, if patients with a t1 but no t2 are excluded, P=0.16 (95% CI, 0.14-0.18), t50% day 4 (95% CI, 4-5). If they are included but t2 taken as infinite P=0.11 (95% CI, 0.09-0.12), t50% day 7 (95% CI, 6-8). If those with t2 but no t1 are excluded P=0.10 (95% CI, 0.08-0.11), t50% day 7 (95% CI, 6-8) and if only those with both t1 and t2 are included P=0.09 (95% CI, 0.07-0.11) t50% day 8 (95% CI, 6-10).

Ultimately any inclusion/exclusion will bias the model in one direction or another, our rational is described above. These limitations mean this model should not be relied upon to drive policy change, but accompanied by prior research[18] it provides support for a 5 day re-testing policy.

Conclusions

During a season with high rates of both influenza A and B, ED influenza POCT and influenza-ward patient cohorting was associated with 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 day 5 post-diagnosis could allow as many as half to come out of respiratory isolation early.

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Table I Five key principals of influenza strategy

Diagnosis	Isolation	Treatment & Prophylaxis	Contacts	Outbreaks
Patients being admitted, inpatients and staff with possible influenza to be tested as soon as possible. Laboratory testing performed by Fast Track Diagnostics (FTD) Respiratory Pathogens 21 multiplex PCR (henceforth rPCR) and Cepheid Xpert Xpress Flu/RSV assay (henceforth fPCR). Laboratory testing operational seven days a week with twice daily rPCR runs and rapid fPCR testing for urgent cases. **Liat POC testing operational in ED from 21/1/18-14/1/17.**	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 (PPE) by staff and transfer of patient into either: ▪ A single room ▪ A bed on the influenza-ward if appropriate **Influenza-ward fully operational from 25/1/18-6/4/18**: divided into 4x4 bedded bays by gender/influenza strain alongside seven single rooms (see 'Methods'). Inpatients and staff with confirmed influenza re-tested five days after first swab by fPCR. Isolation lifted if immunocompetent and either: ▪ Symptom free at seven days from diagnosis *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 four hours 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) ▪ They have no symptoms/signs of possible influenza at 72 hours since last contact with the case *or* ▪ They have no symptoms/signs of possible influenza at 48 hours since last contact with the case *and they are taking oseltamivir prophylaxis*.	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 ▪ The bay 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.

Table II Impact of ED influenza POCT and flu-ward patient cohorting on hospitalised 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									
Median age in years, (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									
HAI, n (%)	36 (23.4)	143 (21)	0.68	36 (23.4)	77 (34.5)	0.02	77 (34.5)	66 (15.3)	< 0.0001
HAI per day, n	0.20	0.79	<0.0001	0.2	0.95	<0.0001	0.95	0.66	<0.0001
GP influenza-like-illness (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
Antivirals prescribed, n (%)	73 (47.4)*	488 (74.6)	<0.0001	73 (47.4)*	143 (64.1)	0.001	143 (64.1)	345 (80.0)	< 0.0001
Median length of admission in days, (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

2016/17 = 1st Ovember 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 20118 (100 days)

* Pharmacy data not available (figures from discharge summaries and TTOs only) so this is likely to be an under-estimate

Table III Impact of POCT result on respiratory isolation for those patients that were admitted

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

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)

Table IV Impact of POCT and flu-ward cohorting on respiratory isolation for patients admitted with CAI

	Admitted patients		
	Post-intervention (n = 62)[a]	Pre-intervention (n = 62)[b]	*P* value
Patient characteristics			
Median age in years, (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 5 days of admission, n	251	233	
Proportion of bed-days that were single rooms, n (%)	225 (89.6)	186 (79.8)	0.003

a) All cases of patients admitted post positive-POCT, where POC known true positive
b) 62 CAI controls (matched for age and sex) admitted pre-intervention

Figure 1 Time until influenza PCR-negativity from first PCR-positive sample