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Effect of point-of-care influenza tests on antibiotic prescriptions by emergency physicians in a French hospital

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Influenza, point-of-care tests, emergency department, antibiotic prescriptions

SUMMARY

Background

Influenza is a public health issue worldwide. Although antibiotics should not be used to treat viral infections, they are often prescribed to patients with influenza-like illness (ILI). Such misuse promotes antibiotic resistance. The role of rapid point-of-care tests (POCT) in preventing antibiotic misuse in adults with ILI symptoms remains relatively unexplored.

Aim

To evaluate whether POCT implemented in 2018-2019 to detect influenza viruses lead to a decrease in antibiotic prescriptions compared to laboratory based influenza tests.

Methods

Adult patients with ILI in one emergency department (ED) were retrospectively enrolled over three epidemic seasons (from 2016-2017 to 2018-2019). The primary outcome was the rate of antibiotic prescriptions, which was compared between the three seasons in bivariate and multivariate analyses. Prescriptions for ancillary laboratory tests, chest X-rays and oseltamivir were also compared, along with hospitalisations and length of stay (LOS) at the ED.

Findings

Overall, 1849 patients were included. Median age was over 70 throughout all three seasons. The number of antibiotic prescriptions was significantly different between the three periods in bivariate analysis (48.3% in 2016/2017, 44% in

2017/2018 and 31.1% in 2018/2019; $p < 0,0001$) and in multivariate analysis (adjusted Odds Ratio [aOR]=0.48, 95%CI=0.30-0.76 for 2018/2019 and aOR=0.99, 95%CI=0.67-1.46 for 2017/2018, compared to 2016/2017). There were significantly fewer prescriptions of ancillary laboratory tests, X-rays, hospitalisations and more oseltamivir prescriptions in 2018/2019, compared to the previous seasons. LOS was significantly lower in 2018/2019 only for influenza-positive patients.

Conclusion

ED influenza POCT decreased antibiotic use and lead to less ancillary testing, X-rays and hospitalisations among patients with ILI. However, medico-economic studies are necessary before formulating definite recommendations.

INTRODUCTION

According to estimates by the World Health Organisation (WHO), every year up to 650,000 deaths are associated with respiratory illnesses caused by seasonal influenza [1]. In France, during the 2016/2017 influenza season, more than 1.9 million medical consultations involved patients with influenza symptoms, and more than 14,000 influenza related deaths were recorded, according to Santé publique France [2]. As these figures show, influenza represents a heavy burden. Hence, each year, preventive and active measures are put in place to contain the spread of the influenza virus, and to ensure that infected patients receive proper care.

Antibiotics should not be used in the treatment of viral infections. Yet they are often prescribed to patients with influenza-like illness (ILI) [3, 4]. Such prescriptions contribute to the emergence of multi-drug resistant bacteria [5, 6]. As a consequence, public health organisations and the WHO have issued guidelines calling for a rational use of antibiotics to fight the proliferation of resistant bacteria [7, 8]. Several studies demonstrated that the use of point-of-care tests (POCT) for influenza diagnosis could reduce antibiotic use among ILI patients [9-16]. Nonetheless, data on the impact of POCT compared to classic RT-PCR in adults remain limited [14-16].

RT-PCR POCT were deployed during the 2018/2019 influenza season in an Emergency Department (ED). The primary aim of this study was to evaluate whether the deployment of RT-PCR POCT for detection of influenza viruses A

and B, resulted in a decrease in the number of antibiotic prescriptions at the ED, among adult patients with ILI symptoms, in comparison to previous seasons when laboratory based influenza tests were used. Subsequently, we sought to evaluate whether there were less ancillary laboratory tests, less imaging exams, less hospitalisations, shorter length of stay (LOS) and more prescriptions of oseltamivir as a result of the roll-out of POCT.

METHODS

Patients and setting

A retrospective study was conducted in the ED of Grenoble Alpes University Hospital in France. About 60,000 people visit this ED every year. Patients were eligible for participation if they presented ILI, were admitted in the ED, and were at least 16 years old. The criteria for ILI included fever or feverishness and at least one of the following symptoms: sore throat, cough, myalgia or headache. These patients were all tested for influenza A and B. The study covered three influenza seasons: 2016/2017, 2017/2018 and 2018/2019. Patients who presented at the ED in January 2018 during the 11 days covered by a study [17] assessing the diagnostic accuracy of the POCT were excluded.

Influenza tests

Nasopharyngeal samples were collected according to the Centers for Disease Control and Prevention guidelines [18, 19]. Influenza viruses A and B were detected using laboratory based influenza tests {i.e RT-PCR Genexpert[®] (Cepheid, Sunnyvale, California, USA), RT-PCR R-DiaFlu[®] (Diagenode Diagnostics, Seraing, Liège, Belgium) and Respifinder[®] 2Smart (multiplex PCR) (Eurogentec, Seraing, Liège, Belgium)} and/or POCT {Cobas[®] Liat System (Roche Diagnostics, Rotkreuz, Switzerland)}. Laboratory based influenza tests were considered to have a long turnaround time (4 to 54 hours, versus 25 minutes for POCT). RT-PCR POCT were deployed during the 2018/2019 influenza season, whereas laboratory based influenza assays were used in 2016/2017, 2017/2018 and 2018/2019. The number of RT-PCR POCT being limited due to

financial constraints, their use started one week after the onset of the outbreak and was stopped three weeks after the peak in the 2018/2019 season.

Objectives and outcomes

The primary objective of this study was to evaluate if introducing RT-PCR POCT for detection of influenza viruses A and B led to a decrease in antibiotic prescriptions, among adult patients with ILI admitted to the ED of Grenoble Alpes University Hospital, compared to laboratory based influenza tests. The primary outcome was the rate of antibiotic prescriptions in each season. Only antibiotics prescribed for respiratory infections were considered: penicillins, cephalosporins, macrolides and related antibiotics, fluoroquinolones, aminoglycosides, glycopeptides, and anti-Pseudomonas beta-lactams. For the purpose of this study we only considered antibiotics prescribed at the ED. The secondary objectives were to examine whether ancillary laboratory tests (full blood count (FBC), blood chemistry, c-reactive protein (CRP), procalcitonin (PCT) and blood culture), imaging exams (chest X-rays) and hospitalisations were fewer when POCT were used. We also assessed the median LOS at the ED and the rate of oseltamivir prescriptions. Secondary outcomes were: ancillary laboratory tests (any versus none and mean number per visit), imaging exams (any versus none and mean number per visit), hospitalisations (i.e admissions after ED), oseltamivir prescriptions (any versus none) and median duration of visit at the ED.

Data collection

Data collection involved visits at the ED with an influenza test. Data regarding age, sex, prescriptions, hospitalisations and LOS were harvested from the ED

software, whereas data about influenza test results and ancillary laboratory tests were obtained from the laboratory database.

Analyses

Qualitative variables were described by their number and percentage, and quantitative variables by their mean and standard deviation (SD) or median and interquartile range (IQR). The 2018/2019 season (POCT and laboratory based influenza tests included) was compared to the 2016/2017 and 2017/2018 seasons (laboratory based influenza tests only) for all ED visits, and in subgroups (positive influenza test only and negative influenza test only). Groups were compared using the Kruskal–Wallis test, Pearson’s Chi-squared test or Fisher’s exact test as appropriate for continuous and categorical variables. A multivariate analysis on all ED visits was performed to assess the association between influenza seasons and antibiotic prescriptions, adjusting for age, sex, influenza test result and hospitalisation after ED stay. Given that patients may have several hospital visits with an influenza test, the assumption of independence was violated, thus we used a mixed effects logistic regression. Results are presented as adjusted odds ratios (aOR) and their 95% confidence interval (95%CI). The significance threshold was set at 0.05. Statistical analyses were performed with Stata software (Stata 12, StataCorp LP, College Station, Texas, USA).

Ethics

The study received ethics approval on the 3rd February 2021 (CECIC Rhône-Alpes-Auvergne, Clermont-Ferrand, IRB 5891).

RESULTS

All patients

A total of 1849 patients were included over three influenza seasons from December 2016 to March 2019 (Figure 1, Table I). There was no significant difference in gender distribution among patients over the three seasons. However, age distribution was significantly different, with patients in the 2018/2019 season having the lowest median age (72 y.o. [49-85]), as opposed to 74 y.o. [55-85] in 2017/2018 and 81 y.o. [65-87] in 2016/2017, $p=0.0001$). Some patients had more than one ED stay, and more than one type of test for each ED visit (e.g. a POCT first, and then a laboratory based influenza test). Thus, over the three seasons the total number of influenza tests performed was 1941 for 1904 ED visits. In 2018/2019, 860 POCT and 127 laboratory based influenza tests were used, whereas in 2017/2018 and 2016/2017 the numbers of laboratory based influenza tests used were respectively 554 and 400 (no POCT during these two seasons). Antibiotic use among all patients was significantly different between the three seasons; with 31.1% (297/956) in 2018/2019, compared to 44% (241/548) in 2017/2018 and 48.3% (193/400) in 2016/2017 ($p<0.0001$). In multivariate analysis, the 2018/2019 season was associated with less antibiotic prescriptions (aOR=0.48, 95%CI=0.30-0.76) compared to the 2016/2017 season, but there was no significant difference between the 2017/2018 and 2016/2017 seasons (aOR=0.99, 95%CI=0.67-1.46) (Table II). Positive influenza test results (laboratory based influenza or POCT) were associated with fewer antibiotic prescriptions (aOR=0.56, 95%CI=0.39-0.81), while older age (aOR=1.02 per 1-

year increment, 95%CI=1.01-1.04) and being admitted after ED (aOR=4.65, 95%CI=2.44-8.86) increased the likelihood of being prescribed an antibiotic.

The prescription of complementary tests was significantly different between the three seasons; in 2018/2019, requests were lower for FBCs ($p<0.0001$), blood chemistry ($p<0.0001$), CRP ($p<0.0001$), blood cultures ($p<0.0001$) and X-rays ($p<0.0001$). The mean number of complementary tests and X-rays per visit followed the same trend except for PCT and blood cultures. For blood cultures, the mean number of exams was higher in 2018/2019 in comparison with 2017/2018 and 2016/2017. The number of hospital admissions after ED was significantly different between the three seasons; with 54% (516/956) in 2018/2019, compared to 61.7% (338/548) in 2017/2018 and 75.8% (303/400) in 2016/2017 ($p<0.0001$). The rate of oseltamivir prescriptions between the three seasons was significantly different, it was higher in 2018/2019 (12.9% (123/956), versus 2.7% (15/548) in 2017/2018 and 10% (40/400) in 2016/2017 ($p<0.0001$)). Considering all patients, LOS was not significantly different over the three seasons (660 minutes [472-1103] in 2018/2019 in comparison with 704 [450-1114] in 2017/2018 and 713 [421-1100] in 2016/2017).

Influenza positive patients

A total of 620 patients (32.6%) tested positive to influenza A/B (Table III).

Gender distribution was not significantly different between the three seasons for this group of patients. Nevertheless, age distribution was significantly different; in 2018/2019 the median age was 82 y.o. [67-87], in comparison to 69 y.o. [49-82] in 2017/2018 and 70 y.o. [41-83] in 2016/2017 ($p=0.0001$). In total, 641 tests

were performed, for 629 ED visits. In 2018/2019, 274 positive POCT and 20 positive laboratory based influenza tests were recorded, versus 190 and 157 positive laboratory based influenza tests in 2017/2018 and 2016/2017 respectively. Among positive patients only, the number of antibiotic prescriptions was also significantly different between the three seasons (18.9% (54/286) in 2018/2019, compared to 37.1% (69/186) in 2017/2018 and 48.4% (76/157) in 2016/2017, $p<0.0001$). The number of ancillary tests was also significantly lower in 2018/2019, compared to the previous seasons, for FBCs ($p<0.0001$), blood chemistry ($p<0.0001$), CRP ($p<0.0001$), blood cultures ($p=0.001$) and X-rays ($p<0.0001$). LOS (minutes) was significantly different between the three seasons (573 [407-943] in 2018/2019 in comparison with 736 [461-1186] in 2017/2018 and 691 [414-1081] in 2016/2017, $p=0.02$), as well as the number of hospitalisations (44.8% (128/286) in 2018/2019, versus 54.8% (102/186) in 2017/2018 and 73.3% (115/157) in 2016/2017, $p<0.0001$) and the number of oseltamivir prescriptions (42.7% (122/286) in 2018/2019 as opposed to 4.8% (9/186) in 2017/2018 and 15.3% (24/157) in 2016/2017, $p<0.0001$).

Influenza negative patients

A total of 1229 patients tested negative to influenza A/B (Table IV). In this group of patients, trends were similar to the global population.

DISCUSSION

We observed a significant decrease in antibiotic prescriptions during the season in which influenza RT-PCR POCT were implemented, in comparison to the two previous seasons (31.1% of stays in 2018/2019 were associated with an antibiotic prescription, compared to 44% in 2017/2018 and 48.3% in 2016/2017). This decrease remained significant after adjusting for age, sex, influenza test result and admission after ED visit (aOR=0.48, 95%CI=0.30-0.76 in 2018/2019 compared to 2016/2017). In addition, we noted an increase in oseltamivir prescriptions; 12.9% of stays in 2018/2019 were associated with an oseltamivir prescription, in comparison to 2.7% in 2017/2018 and 10% in 2016/2017. The differences were even more significant when only patients with a positive influenza test were considered. We also found a decrease in the number of complementary exams, specifically FBCs, blood chemistry, CRP, blood cultures and X-rays after the rollout of POCT. Overall, more influenza detection tests were carried out in 2018/2019 alone (987, 50.9%) than in the previous two seasons combined; it is likely that since POCT (860 out of the 987 tests) were readily available at the ED in 2018/2019, physicians had less time or organisational barriers to their use.

Few data about the impact of using POCT in adult populations are available, the majority of studies focusing on children. We found three studies comparing POCT to classic RT-PCR for the diagnosis of influenza in adult patients. O'Connell *et al.* observed that the use of POCT was associated with lesser antibiotic consumption [16], while others found no reduction in antibiotic prescriptions [14, 15]. Four other studies demonstrated that influenza point-of-care (POC) testing leads to a

reduction in antibiotic use [9-11, 13]. However, they compared either patients with a positive influenza POCT to patients with a negative one, or patients tested with POCT to non-tested patients. One study comparing POCT to routine clinical care (without testing) found no significant difference in antibiotic prescriptions [12]. Regarding other outcomes, several studies demonstrated that POC testing was associated with a reduced LOS [12, 13, 15, 16, 20] and improved antiviral use [9, 12, 16, 21].

This study had a number of strengths that need consideration. The Cobas® Liat System used for POC testing in our study is highly accurate [17] in comparison to other POCT available [22-24]. Indeed, the Cobas® Liat System is an amplification-based test whereas many POCT used for influenza diagnosis are antigen-based tests. Moreover, this study is based on one of the largest series of patients [9-16, 20, 21]. It was conducted in real clinical conditions in an ED with high patient flow rather than a one-time study. The main limitations are inherent in the retrospective nature of the study, and factors other than the implementation of POCT could have an impact on our results. The larger and younger population tested in 2018/2019, or even a probable improvement in practices may have favored these results. Indeed, patient median age seems inferior in 2018/2019 compared to 2016/2017. But looking at season 2018/2019 versus 2017/2018, we see a decrease in antibiotic prescriptions despite similar patient age in both groups. This finding shows that lower patient median age was not the only factor explaining the decrease in antibiotic prescriptions. In addition, some of the tests used over the three influenza seasons can also diagnose respiratory syncytial virus (RSV), and some tests did come out positive to this pathogen (0.25% in 2016-

2017, 1.8% in 2017-2018, and 3.6% in 2018-2019). It is likely doctors behaved differently when treating RSV, which may have interfered with the outcomes for some patients. Nonetheless, when we analysed antibiotic prescription by multivariate analysis adjusting for age, sex, influenza test result and hospitalisation after ED stay, we still found a significant effect for the 2018/2019 season. It should be noted that there were no major changes in antibiotic prescription guidelines at Grenoble Alpes University Hospital during the three years covered by our study. Lastly, unlike some studies [14, 21] we were unable to evaluate time to result as the exact time of result was not available for POCT. We were also unable to determine time to antibiotic treatment for patients who received antibiotics. Medico-economic data on POCT compared to classic RT-PCR are scarce. While one study suggested favourable economic results with the use of POCT [25], another one found that the implementation of POCT was less cost-effective than treating all patients by oseltamivir without testing [26]. However, the latter was focusing on high-risk patients only.

CONCLUSION

The introduction of influenza RT-PCR POCT in the ED could reduce antibiotic use and the number of ancillary tests among adult patients with ILI symptoms in comparison with classic RT-PCR tests. A reduced number of hospitalisations and shorter visits at the ED, as well as an increase in the use of oseltamivir among patients with a positive flu result are likewise observed. Further studies are needed on the medico-economic front, focusing on amplification-based POCT, to

complement current knowledge of the impact of these tests, and to be able to formulate recommendations.

AUTHORS' CONTRIBUTIONS

All authors have carefully read the manuscript, provided a critical review and approved the final version. AB, MG and CL designed the study, analysed and interpreted the data, and drafted the manuscript. SL and DV were involved in the implementation of the strategy, data collection and interpretation for virological aspects. JF and JLB were involved in the implementation of the strategy, data analysis and interpretation.

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DECLARATION OF INTEREST

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Table I - Characteristics of all patients tested for influenza

	2016/2017	2017/2018	2018/2019	<i>P</i> value
	N*= 400	N*= 548	N*= 956	
Age, years, median [IQR]	n*= 391	n*= 531	n*= 927	
	81 [65-87]	74 [55-85]	72 [49-85]	0.0001
Male	n*= 391	n*= 531	n*= 927	
	176 (45)	268 (50.5)	476 (51.4)	0.10
Influenza test results:				
- Flu A	157 (39.3)	69 (12.6)	286 (29.9)	-
- Flu B	0 (0)	117 (21.4)	0 (0)	-
- Negative	243 (60.8)	362 (66.1)	670 (70.1)	-
Tests:	N= 400	N= 554	N= 987	
- Genexpert	49 (12.3)	126 (22.7)	46 (4.7)	-
- R-DiaFlu	350 (87.5)	428 (77.3)	81 (8.2)	-
- Multiplex	1 (0.3)	0 (0)	0 (0)	-
- Cobas Liat	0 (0)	0 (0)	860 (87.1)	-
Antibiotic prescriptions	193 (48.3)	241 (44)	297 (31.1)	< 0.0001
Ancillary laboratory tests:				
- FBC, n (%)	388 (97)	534 (97.5)	861 (90.1)	< 0.0001
- FBC, mean (SD)	1.10 (0.39)	1.07 (0.37)	0.98 (0.43)	0.0041
- Blood chemistry, n (%)	389 (97.3)	533 (97.3)	860 (90)	< 0.0001
- Blood chemistry, mean (SD)	1.15 (0.49)	1.11 (0.48)	1.01 (0.52)	0.0006
- CRP, n (%)	390 (97.5)	532 (97.1)	852 (89.1)	< 0.0001
- CRP, mean (SD)	1.10 (0.38)	1.05 (0.34)	0.96 (0.42)	< 0.0001
- PCT, n (%)	23 (5.8)	48 (8.8)	68 (7.1)	0.20
- PCT, mean (SD)	0.06 (0.23)	0.09 (0.28)	0.07 (0.26)	0.72
- Blood culture, n (%)	252 (63)	364 (66.4)	526 (55)	< 0.0001
- Blood culture, mean (SD)	0.69 (0.59)	0.85 (0.74)	1.01 (1.01)	< 0.0001
Chest X-rays, n (%)	329 (82.3)	435 (79.4)	631 (66)	< 0.0001

Chest X-rays, mean (SD)	0.84 (0.40)	0.81 (0.44)	0.67 (0.49)	< 0.0001
Hospital admission after ED	303 (75.8)	338 (61.7)	516 (54)	< 0.0001
Length of stay, minutes, median [IQR]	<i>n</i> *= 332 712.5 [421-1100]	<i>n</i> *= 392 704.5 [449.5-1113.5]	<i>n</i> *= 574 660 [472-1103]	0.95
Oseltamivir prescriptions	40 (10)	15 (2.7)	123 (12.9)	< 0.0001

Data are presented as n (%) or median [interquartile] or mean number [standard deviation]. N*: number of influenza specimens collected. *n**: number of patients. N: number of influenza tests. ***n****: number of patients after exclusion of outpatients. IQR = interquartile range; SD = standard deviation; FBC = full blood count; CRP = c-reactive protein; PCT = procalcitonin.

Table II - Multivariate analysis of the association between seasons and antibiotic prescriptions for all patients

Adjustment variable	Adjusted OR* [95%CI]
Period	
- 2016-17	reference
- 2017-18	0,99 [0,67 – 1,46]
- 2018-19	0,48 [0,30 – 0,76]
Age (by year)	1,02 [1,01 – 1,04]
Male gender	1,33 [0,99 – 1,80]
Positive Influenza test result	0,56 [0,39 – 0,81]
Hospital admission after ED (Yes)	4,65 [2,44 – 8,86]

*Adjusted for age, sex, influenza test result and hospital admission after ED stay

Table III - Characteristics only for patients with a positive influenza test result

	2016/2017	2017/2018	2018/2019	<i>P</i> value
	N*= 157	N*= 186	N*= 286	
Age, years, median [IQR]	n*= 154	n*= 183	n*= 283	
	82 [67-87]	69 [49-82]	70 [41-83]	0.0001
Male	n*= 154	n*= 183	n*= 283	
	66 (42.9)	95 (51.9)	142 (50.2)	0.21
Tests:	N= 157	N= 190	N= 294	
- Genexpert	17 (10.8)	41 (21.6)	6 (2)	-
- R-DiaFlu	140 (89.2)	149 (78.4)	14 (4.8)	-
- Multiplex	0 (0)	0 (0)	0 (0)	-
- Cobas Liat	0 (0)	0 (0)	274 (93.2)	-
Antibiotic prescriptions	76 (48.4)	69 (37.1)	54 (18.9)	< 0.0001
Ancillary laboratory tests:				
- FBC	152 (96.8)	181 (97.3)	234 (81.8)	< 0.0001
- Blood chemistry	153 (97.5)	183 (98.4)	236 (82.5)	< 0.0001
- CRP	154 (98.1)	182 (97.9)	230 (80.4)	< 0.0001
- PCT	3 (1.9)	15 (8.1)	18 (6.3)	0.04
- Blood culture	97 (61.8)	128 (68.8)	148 (51.8)	0.001
Chest X-rays	135 (86)	150 (80.7)	178 (62.2)	< 0.0001
Hospital admission after ED	115 (73.3)	102 (54.8)	128 (44.8)	< 0.0001
Length of stay, minutes, median [IQR]	n *= 127	n *= 125	n *= 143	
	691 [414-1081]	736 [461-1186]	573 [407-943]	0.02
Oseltamivir prescriptions	24 (15.3)	9 (4.8)	122 (42.7)	< 0.0001

Data are presented as n (%) or median [interquartile]. N*: number of influenza specimens collected. n*: number of patients. N: number of influenza tests. **n***: number of patients after exclusion of outpatients. IQR = interquartile range; FBC = full blood count; CRP = c-reactive protein; PCT = procalcitonin.

Table IV - Characteristics only for patients with a negative influenza test result

	2016/2017	2017/2018	2018/2019	<i>P</i> value
	N*= 243	N*= 362	N*= 670	
Age, years, median [IQR]	n*= 237 80 [62-87]	n*= 348 75 [61-86]	n*= 644 73 [52-86]	0.004
Male	n*= 237 110 (46.4)	n*= 348 173 (49.7)	n*= 644 334 (51.9)	0.35
Antibiotic prescriptions	117 (48.2)	172 (47.5)	243 (36.3)	< 0.0001
Ancillary laboratory tests:				
- FBC	236 (97.1)	353 (97.5)	627 (93.6)	0.006
- Blood chemistry	236 (97.1)	350 (96.7)	624 (93.1)	0.01
- CRP	236 (97.1)	350 (96.7)	622 (92.8)	0.006
- PCT	20 (8.2)	33 (9.1)	50 (7.5)	0.65
- Blood culture	155 (63.8)	236 (65.2)	378 (56.4)	0.01
Chest X-rays	194 (79.8)	285 (78.7)	453 (67.6)	< 0.0001
Hospital admission after ED	188 (77.4)	236 (65.2)	388 (57.9)	< 0.0001
Length of stay, minutes, median [IQR]	n*= 205 736 [424-1147]	n*= 267 696 [447-1035]	n*= 431 702 [487-1128]	0.42
Oseltamivir prescriptions	16 (6.6)	6 (1.7)	1 (0.2)	< 0.0001

Data are presented as n (%) or median [interquartile]. N*: number of influenza specimens collected. n*: number of patients. *n**: number of patients after exclusion of outpatients. IQR = interquartile range; FBC = full blood count; CRP = c-reactive protein; PCT = procalcitonin.

Figure 1 - Flow chart

