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# **Incidence and characteristics of nosocomial influenza in a country with low vaccine coverage**

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**Running title:** Nosocomial influenza

## Summary

**Background:** Influenza vaccination coverage is low in France, in at-risk patients and in health-care workers.

**Aim:** We aimed to estimate the incidence of nosocomial influenza, its characteristics and outcome.

**Methods:** During one influenza season, we retrospectively evaluated all cases of documented influenza. Inpatients with symptoms onset  $\geq 48$  hours after admission were enrolled. Data were collected on a standardized questionnaire.

**Results:** From November 2017 to April 2018, 860 patients tested positive for influenza by PCR on a respiratory sample. Among them, 204 (23.7%) were diagnosed  $\geq 48$  hours after admission, of whom 57 (6.6% of all influenza cases) fulfilled inclusion criteria for nosocomial influenza: 26 women and 31 men, median age 82 years [interquartile range, 72.2-86.9]. Twenty patients (38.6%) had recently ( $< 6$  months) received the seasonal influenza vaccine. Median time between admission and symptoms onset, and between symptoms onset and diagnosis were, respectively, 11 days [7-19.5] and 29 hours [15.5-48]. Influenza was mostly acquired in a double-bed room ( $n=39$ , 68.4%), with documented exposure in 14 cases. Influenza B virus was more common in nosocomial (46/57, 80.7%), than in community-acquired cases (359/803, 44.6%),  $P<0.001$ . Mortality rate at three months was 15.8% ( $n=9$ ). Incidence of nosocomial influenza was estimated at 0.22 per 1000 hospital-days during the study period.

**Conclusion:** Nosocomial influenza is not rare in elderly inpatients, and may have severe consequences. Influenza B virus was over-represented, which suggests higher transmissibility and/or transmission clusters.

**Keywords** Nosocomial influenza, vaccine, outcome, incidence, elderly, influenza B virus

## Introduction

Influenza is a common cause of hospital admission during the influenza season, but it remains often undiagnosed. Failure to identify influenza cases, and to implement infection control measures, put contact patients and health care workers at risk of nosocomial influenza, especially in settings with low vaccination coverage, as in France [1][2]. Limited data are currently available on the burden of nosocomial influenza, although it may be life-threatening in patients with comorbidities, in pregnant women, or in elderly patients. In addition, its impact on health care workers absenteeism may be devastating, as workload is particularly high during influenza seasons in most hospitals.

Previous studies on nosocomial influenza contributed to estimate the burden and the characteristics of nosocomial influenza, in different settings [3][4]. These studies used various time thresholds, spanning from 48 to 96 hours between hospital admission and symptoms onset, to define nosocomial influenza [5]. The proportion of influenza classified as nosocomial in these hospital-based studies varied from 4 to 23%. The level of influenza vaccine coverage in health care workers may be a strong determinant of nosocomial influenza risk, for patients as well as for health care workers [6][7]. In France, immunization coverage against influenza in at-risk patients [2] and health care workers [8], has been dramatically low over recent years, due to vaccine hesitancy, fuelled by dissemination of fake news through various communication channels. We aimed to evaluate the incidence of nosocomial influenza in a tertiary care centre, its characteristics, and consequences.

## Methods

### *Study population*

Rennes University Hospital is a 1,500 bed-tertiary care hospital, which serves as a referral centre in Western France (population catchment area, one million inhabitants). We performed a retrospective study of all cases of nosocomial influenza documented during the 2017-2018 influenza season. Inpatients with influenza documented by PCR on respiratory samples were identified from the virology lab computerized database. Two different techniques of PCR were used during the study period: Seegene Allplex<sup>®</sup> respiratory panel 1 (Eurobio, Les Ulis, France), and GeneXpert<sup>®</sup> flu (Cepheid, Sunnyvale, CA, USA).

We reviewed the medical files of all patients who were tested positive  $\geq 48$  hours after hospital admission. Only patients who had no symptoms suggestive of influenza during the first 48 hours after admission (i.e. cough, fever, myalgia, rhinitis, pharyngitis, or headache) were finally included in this study. Data were collected with a standardized questionnaire, including demographics, comorbidities, recent ( $< 6$  months) influenza vaccination, symptoms reported by the time of influenza diagnosis, medical ward, type of room (single versus double), and 90-day outcome. When the latter data was not available from medical charts, the general practitioner was contacted by phone.

### *Statistical analysis*

We compared nosocomial cases, and community-acquired cases, for the variables available in both categories (i.e. age, sex, influenza virus type, and date of diagnosis). Categorical variables were compared using Fisher's exact test. Continuous variables were compared using

Student's t-test. P-values  $<0.05$  were considered as significant. To estimate incidence, we divided the number of patients with nosocomial influenza as defined above, by the total number of hospital-days for all patients admitted during the study period, extracted from our hospital administrative system (Saphir). Statistical analyses were carried out using R-Studio 2015, Integrated Development for R (R-Studio, Boston, MA, USA).

### *Ethics*

The study was approved by the Ethics Committee of Rennes University Hospital (approval number: 20.17).

## Results

During the study period, 860 inpatients had influenza documented on respiratory samples, by Seegene Allplex<sup>®</sup> (n=504), or GeneXpert<sup>®</sup> (n=356). Of these, 204 were diagnosed on a respiratory sample obtained  $\geq 48$  hours after admission. Systematic review of the medical files of these 204 cases identified 57 cases who fulfilled our definition criteria for nosocomial influenza (Figure 1). Hence, the proportion of nosocomial cases among inpatients with documented influenza was 6.6% (57/860) during the study period. Characteristics of patients with nosocomial influenza are summarized in Table 1: They were 26 women and 31 men, with a median age of 82 years [interquartile range, 72-86.8]. Major comorbidities included diabetes (n=12, 21.1%), cardiopathy (n=11, 19.3%), and chronic respiratory disease (n=9, 15.8%). Twenty patients (35.1%) had received the seasonal influenza vaccine within the last six months. More than half of nosocomial influenza were acquired in the geriatric department (30/57), especially in middle- or long-term care facilities (28/57). Influenza was mostly acquired in a double-bed room (n=39, 68.4%), with documented exposure in 14 cases. The median time between admission and symptoms onset was 11 days [7-19.5], and the median time between symptoms onset and diagnosis was 29 hours [15.5-48]. The proportion of nosocomial influenza remained stable during the whole influenza season (Figure 3). The management and outcome of the 57 patients with nosocomial influenza are summarized in Table 2. Briefly, although most patients were treated with oseltamivir (42/57, 73.6%), and/or antibacterial agents (13/57, 22.8%), four patients were transferred to the intensive care unit, and nine patients (15.8%) died.

As compared to patients with community-acquired influenza admitted to the hospital during the study period, patients with nosocomial influenza were older (median, 82 vs. 47 years;

126  $P<0.00001$ ), and more likely to be infected by influenza virus type B: 46/57 (80.8%) vs.  
127 359/803 (44.7%),  $P<0.00001$  (Table I). Of note, patients with nosocomial influenza B were  
128 more likely to be vaccinated (19/46, 41.3%), than patients with nosocomial influenza A (1/11,  
129 9.1%),  $P<0.001$ . During the study period, the total number of hospital-days in our institution  
130 was 262,190. Hence, the incidence of nosocomial influenza in inpatients was estimated at  
131 0.22 per 1000 hospital-days.

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## Discussion

In this retrospective single-centre study, we found that nosocomial transmission of influenza is responsible for 6.6% of influenza cases managed in a tertiary care centre, that it disproportionately affects elderly patients, with 90-day mortality of 15.8%. Most cases of nosocomial influenza were caused by type B influenza virus: 46/57 (80.8%), as compared to 359/803 (44.7%) in community-acquired influenza,  $P < 0.00001$ . These findings are in line with previous series of nosocomial influenza cases, except that i) influenza A virus was the main cause of nosocomial influenza in all published studies to date [3][9][10]; ii) in-hospital mortality was usually lower (3.8-9%), despite higher proportion of immunocompromised patients (50-72%, but with heterogeneous definition) [9][4].

To our knowledge, this study is the first to identify an association between influenza B virus and nosocomial influenza. Of note, the 2017-2018 influenza season (i.e., the study period) was remarkable for an unusually high proportion of influenza B virus, in outpatients as well as in inpatients, in a context of mismatch between the influenza B virus included in the recommended trivalent vaccine, and the main circulating strain in France that year: Indeed, the B/Yamagata strain was not included in the vaccine although it was responsible for 94% of all influenza B [11]. This sub-optimal vaccine effectiveness was particularly obvious in the population most affected by nosocomial influenza, the elderly [12][11]. However, these particularities are unlikely to explain why influenza B virus was disproportionately involved in nosocomial influenza that season, as it would similarly affect community-acquired influenza. Other hypotheses include higher transmissibility of influenza B virus in the nosocomial context, and/or cluster(s) of transmission. However, the latter would most likely be associated with heterogeneity over time, in the proportion of influenza B among

nosocomial cases during the study period, which we did not observe (Figure 3). In-depth epidemiological investigations assisted by phylogenetic analysis would contribute to decipher the mechanisms of influenza transmission in healthcare settings, but this could not be performed in our study, as isolates were not available for thorough molecular characterization [13].

Our estimates of the burden of nosocomial influenza must be interpreted with caution, given the very low vaccine coverage against influenza in France during the study period, i.e. 35.1% in at-risk patients targeted by official recommendations for yearly influenza vaccination, and 20-30% in health care workers [14]. In addition, around two thirds of nosocomial cases affected patients who were admitted in a double-bed room, although the proportion of double-bed rooms is gradually decreasing in France. Admission in a double-bed room is a risk factor for nosocomial influenza [15]. We found that nosocomial influenza disproportionately affects elderly patients in our hospital, as previously reported [9]. Only one paediatric case was identified, although Dionne et al. found that one third of nosocomial influenza occurs in children [10]. These discrepancies may be related to differences in case-mix, under-diagnosis of influenza in our paediatric units, or clusters of active transmission between children in Dionne et al's study.

The median time between symptoms onset and diagnosis was rather short in our study, around 29 hours [interquartile range, 15.5-48]. Others have found that time-to-diagnosis is reduced for nosocomial, as compared to community-acquired influenza [3]. This may be related to systematic monitoring of temperature and symptoms in inpatients. In addition, our institution has implemented extended working hours with rapid molecular testing assays and turn-

around-time <3 hours during the influenza season, which reduces the diagnosis delay [16] and allows earlier implementation of infection control measures, including patient isolation, use of masks for health care workers, and oseltamivir as curative and/or preventive treatment.

Of the 860 patients with documented influenza during the study period, 147 (17.1%) were retrospectively classified as community-acquired, as they presented ILI symptoms on admission, but they were tested more than 48 hours after admission. Delayed diagnosis of influenza is not uncommon due to the low specificity of ILI symptoms. This may contribute to the burden of nosocomial influenza, through delayed implementation of infection control measures. We found that droplet measures were implemented in most, but not all cases (82.5%), and that oseltamivir was prescribed for three quarters of patients. Systematic use of surgical masks was associated with a two-fold decline in the incidence of health care-associated influenza [17]. However, mandatory mask policy is difficult to maintain throughout the influenza seasons, and is considered as a motivation to promote influenza vaccine in health care workers, when imposed as the only alternative to vaccination [18].

One study found that the risk of nosocomial transmission is higher in case of contacts with contagious patients (relative risk, 17.96, 95%CI 10.1-32.0), as compared to health-care workers (relative risk 5.48, 95%CI 2.1-14.4) [19], although this was not confirmed by others [20]. In our study, 14 of 57 nosocomial influenza cases could be linked to contacts with another patient with influenza in a double-bed room, but the source remained unknown in 43/57 (75.4%) of cases. Health care workers may be involved in a substantial proportion of these nosocomial influenza with unknown source, given the dramatically low influenza vaccine coverage in health care workers in France during the study period, although we

cannot rule out transmission from other patients with undiagnosed influenza, or from relatives during hospital visits. High vaccination coverage decreases the risk of nosocomial influenza [21][22]. Different actions to promote influenza vaccine in health care workers have been implemented, including educational programs, and mandatory policy [7]. In our institution, education and communication efforts have been associated with a 50% increase in health care workers vaccination coverage, from 30% in 2018-2019 to 45% in 2019-2020 (manuscript in preparation). Timely electronic notifications of nosocomial influenza cases may also contribute to decreased in-hospital transmission [23]. Nosocomial influenza control is complex and may rely on a comprehensive package of prevention tools: influenza vaccine for patients and health care workers, barrier control measures, antiviral prophylaxis in selected cases, control of visits, and early exclusion of health care workers with ILI [24]. Antiviral prophylaxis with oseltamivir has been recommended as soon as two cases of documented influenza are identified within 72 hours in residents or patients of the same ward [25][26][27].

This study has limitations. Firstly, as a single-centre study, our findings may not apply to other settings, especially given the low influenza vaccine coverage in France during the study period, for health care workers and for at-risk patients. The proportion of nosocomial cases among inpatients with influenza, and the incidence of nosocomial influenza, may be much lower in countries with better influenza vaccine coverage. Secondly, cases were identified through passive surveillance, when suspected by physicians in charge and documented. Hence, we probably underestimated the burden of nosocomial influenza in our institution, as the proportion of pauci-symptomatic influenza may be high [28]. In line with this hypothesis, only two cases of nosocomial influenza were documented in surgery departments during the study period, which may reflect lower awareness by surgical teams. Thirdly, cases classified as nosocomial may in fact be delayed diagnosis of community-acquired influenza, if early

symptoms of influenza have not been reported on admission. Finally, we defined nosocomial influenza as cases with no influenza symptoms during the first 48 hours after admission, in line with previous studies, and the natural course of influenza [5][29], although other used a larger time window (72-96 h). We performed a sensitivity analysis, extending the threshold to define nosocomial influenza at 72 hours, and 96 hours, between admission and symptom(s) onset. With a delay of 72, and 96 hours, the number of nosocomial influenza cases would be 55, and 52 respectively, as compared to 57 with the 48 hours threshold. The 5 patients that would not be enrolled with the longest threshold (96 hours) had no complication (i.e. ICU admission, pneumonia, or death).

## Conclusions

The burden of nosocomial influenza may be substantial in a country with low influenza vaccination coverage, accounting for 6.6% of all influenza cases managed in a tertiary care centre, with an estimated incidence of 0.22 per 1000 hospital-days and 90-day mortality of 15.8%. Influenza B virus was more common in nosocomial (46/57, 80.7%), than in community-acquired cases (359/803, 44.6%,  $P < 0.001$ ) in the absence of any identified cluster of transmission. This study advocates for increased influenza vaccine coverage for high-risk patients as well as for health care workers.

249     **Conflict of interest statement**

250     None

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## 257    **References**

- 258    [1]    Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, et al. The  
259    State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey.  
260    *EBioMedicine* 2016;12:295–301. <https://doi.org/10.1016/j.ebiom.2016.08.042>.
- 261    [2]    Robert J, Detournay B, Levant MC, Uhart M, Gourmelen J, Cohen JM. Flu vaccine  
262    coverage for recommended populations in France. *Médecine et Maladies Infectieuses* 2019.  
263    <https://doi.org/10.1016/j.medmal.2019.12.004>.
- 264    [3]    Macese N, Kotsimbos TC, Kelly P, Cheng AC. Hospital-acquired influenza in an  
265    Australian sentinel surveillance system. *The Medical Journal of Australia* 2013;198:370–2.  
266    <https://doi.org/10.5694/mja12.11687>.
- 267    [4]    Mitchell R, Taylor G, McGeer A, Frenette C, Suh KN, Wong A, et al. Understanding  
268    the burden of influenza infection among adults in Canadian hospitals: A comparison of the  
269    2009-2010 pandemic season with the prepandemic and postpandemic seasons. *American*  
270    *Journal of Infection Control* 2013;41:1032–7. <https://doi.org/10.1016/j.ajic.2013.06.008>.
- 271    [5]    Vanhems P, Bénet T, Munier-Marion E. Nosocomial influenza: encouraging insights  
272    and future challenges. *Current Opinion in Infectious Diseases* 2016;29:366–72.  
273    <https://doi.org/10.1097/QCO.0000000000000287>.
- 274    [6]    Talbot TR, Bradley SF, Cosgrove SE, Ruef C, Siegel JD, Weber DJ. Influenza  
275    Vaccination of Healthcare Workers and Vaccine Allocation for Healthcare Workers During  
276    Vaccine Shortages. *Infection Control & Hospital Epidemiology* 2005;26:882–90.  
277    <https://doi.org/10.1086/502512>.
- 278    [7]    Frenzel E, Chemaly RF, Ariza-Heredia E, Jiang Y, Shah DP, Thomas G, et al.  
279    Association of increased influenza vaccination in health care workers with a reduction in  
280    nosocomial influenza infections in cancer patients. *American Journal of Infection Control*  
281    2016;44:1016–21. <https://doi.org/10.1016/j.ajic.2016.03.024>.
- 282    [8]    Elias C, Fournier A, Vasiliu A, Beix N, Demillac R, Tillaut H, et al. Seasonal  
283    influenza vaccination coverage and its determinants among nursing homes personnel in  
284    western France. *BMC Public Health* 2017;17. <https://doi.org/10.1186/s12889-017-4556-5>.
- 285    [9]    Huzly D, Kurz S, Ebner W, Dettenkofer M, Panning M. Characterisation of  
286    nosocomial and community-acquired influenza in a large university hospital during two  
287    consecutive influenza seasons. *Journal of Clinical Virology* 2015;73:47–51.  
288    <https://doi.org/10.1016/j.jcv.2015.10.016>.
- 289    [10]    Dionne B, Brett M, Culbreath K, Mercier R-C. Potential Ceiling Effect of Healthcare  
290    Worker Influenza Vaccination on the Incidence of Nosocomial Influenza Infection. *Infection*  
291    *Control & Hospital Epidemiology* 2016;37:840–4. <https://doi.org/10.1017/ice.2016.77>.
- 292    [11]    Rondy M, Kissling E, Emborg H-D, Gherasim A, Pebody R, Trebbien R, et al. Interim  
293    2017/18 influenza seasonal vaccine effectiveness: combined results from five European  
294    studies. *Eurosurveillance* 2018;23. [https://doi.org/10.2807/1560-7917.ES.2018.23.9.18-](https://doi.org/10.2807/1560-7917.ES.2018.23.9.18-00086)  
295    00086.
- 296    [12]    Rolfes MA, Flannery B, Chung JR, O'Halloran A, Garg S, Belongia EA, et al. Effects  
297    of Influenza Vaccination in the United States During the 2017–2018 Influenza Season.  
298    *Clinical Infectious Diseases* 2019;69:1845–53. <https://doi.org/10.1093/cid/ciz075>.
- 299    [13]    Valley-Omar Z, Nindo F, Mudau M, Hsiao M, Martin DP. Phylogenetic Exploration  
300    of Nosocomial Transmission Chains of 2009 Influenza A/H1N1 among Children Admitted at  
301    Red Cross War Memorial Children's Hospital, Cape Town, South Africa in 2011. *PLoS ONE*  
302    2015;10:e0141744. <https://doi.org/10.1371/journal.pone.0141744>.
- 303    [14]    Jorgensen P, Mereckiene J, Cotter S, Johansen K, Tsovala S, Brown C. How close are  
304    countries of the WHO European Region to achieving the goal of vaccinating 75% of key risk

groups against influenza? Results from national surveys on seasonal influenza vaccination programmes, 2008/2009 to 2014/2015. *Vaccine* 2018;36:442–52. <https://doi.org/10.1016/j.vaccine.2017.12.019>.

[15] Munier-Marion E, Bénet T, Régis C, Lina B, Morfin F, Vanhems P. Hospitalization in double-occupancy rooms and the risk of hospital-acquired influenza: a prospective cohort study. *Clinical Microbiology and Infection* 2016;22:461.e7–461.e9. <https://doi.org/10.1016/j.cmi.2016.01.010>.

[16] Bouscambert M, Valette M, Lina B. Rapid bedside tests for diagnosis, management, and prevention of nosocomial influenza. *Journal of Hospital Infection* 2015;89:314–8. <https://doi.org/10.1016/j.jhin.2014.12.017>.

[17] Ambrosch A, Rockmann F. Effect of two-step hygiene management on the prevention of nosocomial influenza in a season with high influenza activity. *Journal of Hospital Infection* 2016;94:143–9. <https://doi.org/10.1016/j.jhin.2016.07.006>.

[18] Dorribo V, Lazor-Blanchet C, Hugli O, Zanetti G. Health care workers' influenza vaccination: motivations and mandatory mask policy. *Occupational Medicine* 2015;kqv116. <https://doi.org/10.1093/occmed/kqv116>.

[19] Vanhems P, Voirin N, Roche S, Escuret V, Régis C, Gorain C, et al. Risk of Influenza-Like Illness in an Acute Health Care Setting During Community Influenza Epidemics in 2004–2005, 2005–2006, and 2006–2007: A Prospective Study. *Archives of Internal Medicine* 2011;171. <https://doi.org/10.1001/archinternmed.2010.500>.

[20] Pagani L, Thomas Y, Huttner B, Sauvan V, Notaridis G, Kaiser L, et al. Transmission and Effect of Multiple Clusters of Seasonal Influenza in a Swiss Geriatric Hospital. *Journal of the American Geriatrics Society* 2015;63:739–44. <https://doi.org/10.1111/jgs.13339>.

[21] Potter J, Stott DJ, Roberts MA, Elder AG, O'Donnell B, Knight PV, et al. Influenza Vaccination of Health Care Workers in Long-Term-Care Hospitals Reduces the Mortality of Elderly Patients. *Journal of Infectious Diseases* 1997;175:1–6. <https://doi.org/10.1093/infdis/175.1.1>.

[22] Carman WF, Elder AG, Wallace LA, McAulay K, Walker A, Murray GD, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *The Lancet* 2000;355:93–7. [https://doi.org/10.1016/S0140-6736\(99\)05190-9](https://doi.org/10.1016/S0140-6736(99)05190-9).

[23] Munier-Marion E, Bénet T, Dananché C, Soing-Altach S, Maugat S, Vaux S, et al. Outbreaks of health care-associated influenza-like illness in France: Impact of electronic notification. *American Journal of Infection Control* 2017;45:1249–53. <https://doi.org/10.1016/j.ajic.2017.05.012>.

[24] O'Reilly F, Dolan GP, Nguyen-Van-Tam J, Noone P. Practical prevention of nosocomial influenza transmission, “a hierarchical control” issue. *Occup Med (Lond)* 2015;65:696–700. <https://doi.org/10.1093/occmed/kqv155>.

[25] Uyeki TM, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis* 2019;68:e1–47. <https://doi.org/10.1093/cid/ciy866>.

[26] Jefferson T, Jones M, Doshi P, Spencer EA, Onakpoya I, Heneghan CJ. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. *BMJ* 2014;348:g2545. <https://doi.org/10.1136/bmj.g2545>.

[27] Okoli GN, Otete HE, Beck CR, Nguyen-Van-Tam JS. Use of neuraminidase inhibitors for rapid containment of influenza: a systematic review and meta-analysis of individual and household transmission studies. *PLoS ONE* 2014;9:e113633. <https://doi.org/10.1371/journal.pone.0113633>.

[28] Ridgway JP, Bartlett AH, Garcia-Houchins S, Cariño S, Enriquez A, Marrs R, et al.



355 Influenza Among Afebrile and Vaccinated Healthcare Workers. *Clinical Infectious Diseases*  
356 2015;60:1591–5. <https://doi.org/10.1093/cid/civ163>.  
357 [29] Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE, Cummings DA. Incubation  
358 periods of acute respiratory viral infections: a systematic review. *The Lancet Infectious*  
359 *Diseases* 2009;9:291–300. [https://doi.org/10.1016/S1473-3099\(09\)70069-6](https://doi.org/10.1016/S1473-3099(09)70069-6).  
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363 **Table I.** Baseline characteristics of inpatients with influenza

	Nosocomial cases (n=57)	Community- acquired cases (n=803)	<i>P</i> value
Age, years	82 [72-86.8]	47 [4.7-76.4]	<0.001
Male	31 (54.4)	392 (48.9)	0.64
Influenza virus type			<0.001
Influenza A	11 (19.2)	444 (55.3)	
Influenza B	46 (80.8)	359 (44.7)	
Comorbidities			
Diabetes	12 (21.1)		
Cardiopathy	11 (19.3)		
Chronic respiratory disease	7 (12.3)		
Ward			
Medical, acute care	21 (36.7)		
Surgery	2 (3.5)		
Middle-term care facility	18 (31.6)		
Long-term care facility	10 (17.6)		
Other	6 (10.5)		
Geriatric department	30 (52.6)		
Time from admission to symptoms onset, days	12 [7-19.5]		
Time from symptoms onset to diagnosis, hours	29 [15.5-48]		
Influenza vaccine status			
Vaccinated	20 (35.1)		
Not vaccinated	16 (28.1)		
Unknown	21 (36.8)		
Type of room			
Double bed-room	39 (68.4)		
Single bed-room	10 (17.5)		
Unknown	8 (14.0)		

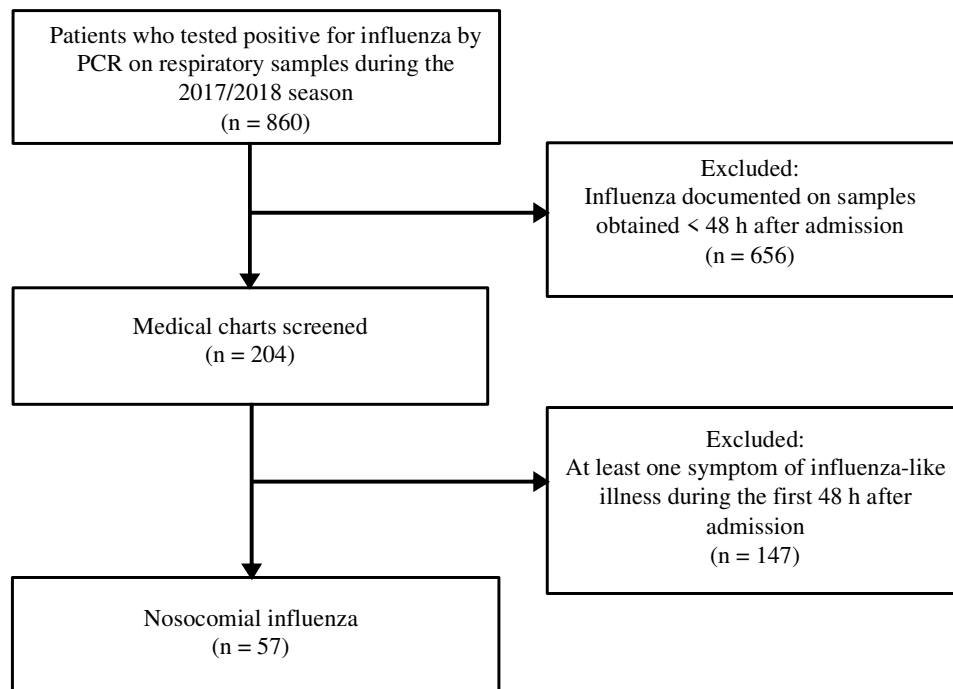
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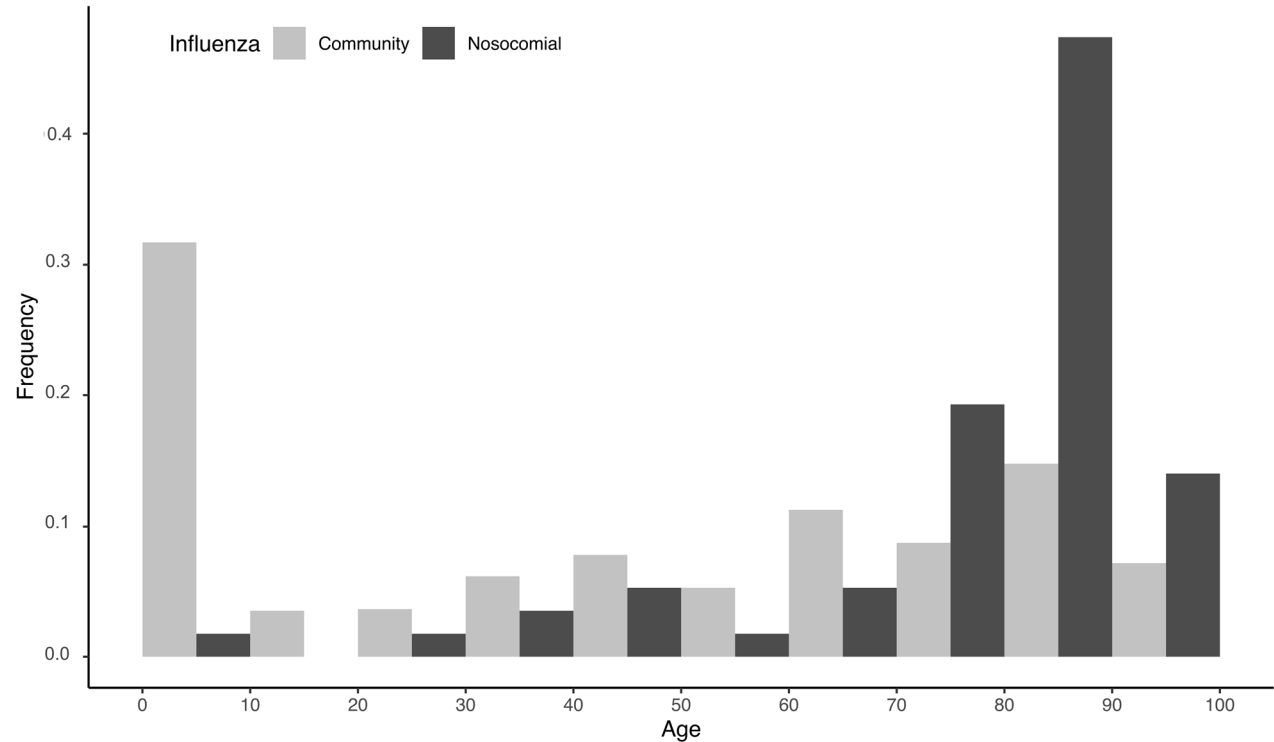
**Table II.** Management and outcome of patients with nosocomial influenza (n=57)

<b>Management of nosocomial influenza</b>	<b>n (%)</b>
Oseltamivir	42 (73.6)
Antibacterial treatment for pneumonia	13 (22.8)
Droplet precaution	47 (82.5)
<b>Outcome</b>	
30-day mortality	7 (12.3)
90-day mortality	9 (15.8)
Intensive care unit admission	4 (7.0)

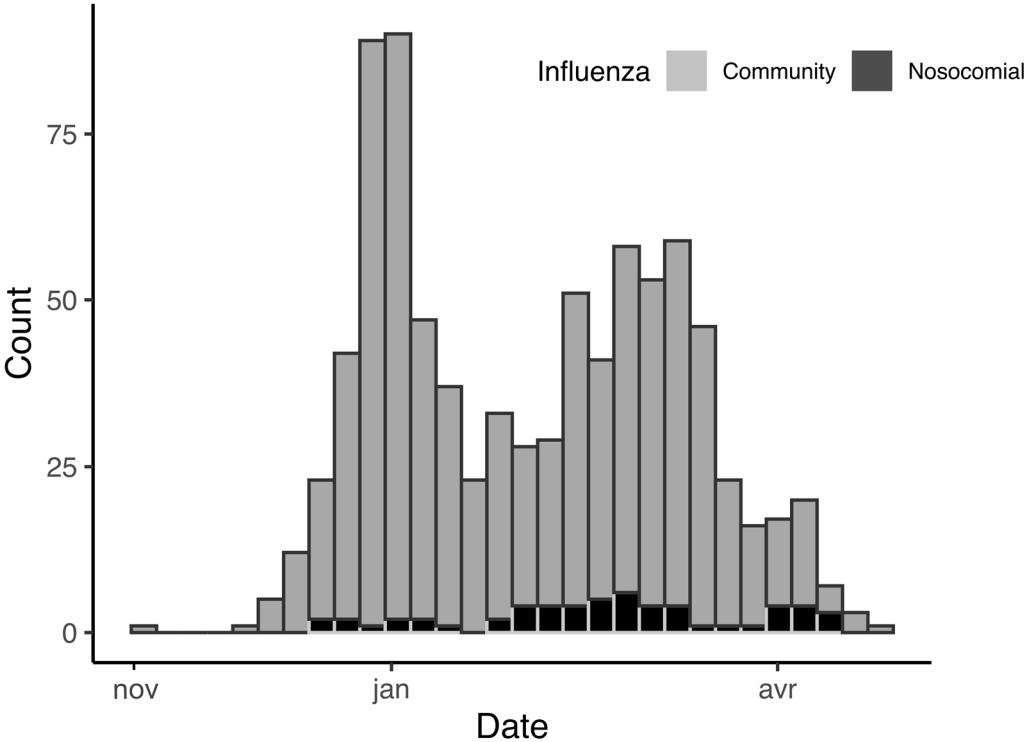
**Figure 1.** Flowchart of the study



**Figure 2.** Age of patients with nosocomial and community-acquired influenza.



380 **Figure 3.** Nosocomial and community-acquired influenza, date of diagnosis



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