Published in final edited form as:
*J Hosp Med*. 2013 January ; 8(1): 20–24. doi:10.1002/jhm.1981.

# THE EFFECT OF FEVER ON HOSPITAL PRESENTATION, DIAGNOSIS AND TREATMENT IN PATIENTS WITH H1N1/09 INFLUENZA

**Madhuri M. Sopirala, MD, MPH**[1,2,3,*], **Douglas M Haas, MD**[4,6], **Naeem A. Ali, MD**[5,6], **Julie E. Mangino, MD**[4,6,8], **Xueliang Pan, PhD**[7], and **Abigail Norris Turner, PhD**[4,6]

[1] The Division of Infectious Diseases, University of Cincinnati Health System, Cincinnati, Ohio

[2] Department of Internal Medicine, University of Cincinnati Health System, Cincinnati, Ohio

[3] Department of Infection Control and Antimicrobial Stewardship, University of Cincinnati Health System, Cincinnati, Ohio

[4] The Division of Infectious Diseases, The Ohio State University Medical Center, Columbus, Ohio, USA

[5] The Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, The Ohio State University Medical Center, Columbus, Ohio, USA

[6] Department of Internal Medicine, The Ohio State University Medical Center, Columbus, Ohio, USA

[7] Center for Biostatistics, The Ohio State University Medical Center, Columbus, Ohio, USA

[8] Department of Clinical Epidemiology, The Ohio State University Medical Center, Columbus, Ohio, USA

## Abstract

**Objective—**Fever is typically considered part of the influenza-like illness in H1N1/09 influenza. We assessed the proportion of patients that did not have fever as part of their illness prior to hospital presentation. We assessed the role of fever on the delay in hospital presentation, diagnosis and treatment of these patients.

[*]**Address correspondence to:** Madhuri M. Sopirala, MD, MPH 234 Goodman Street 140 Mont Reid Cincinnati, OH 45219 Phone: 513-558-4704 Fax: 513-558-2089 madhuri.sopirala@uchealth.com.
Authors' Addresses
Douglas M. Haas, MD 2803 Kensington Place Columbus, OH 43202
Naeem A. Ali, MD 473 W 12th Ave 201 G DHLRI Columbus OH 43210
Julie E. Mangino, MD 410 W 10th Ave N1150 Doan Hall Columbus OH 43210
Xueliang Pan, PhD 2012 Kenny Road Columbus OH 43221
Abigail Norris Turner, PhD 410 W 10th Ave N1145 Doan Hall Columbus OH 43210

Financial Disclosures:
JEM: research grant to study ultraviolet disinfection from Medline Industries Inc. and honorarium for lectures at "Making a difference in Infectious Diseases Pharmacotherapy".
MMS: Royalties from UpToDate® for contribution to "Pathogenesis of osteomyelitis" and from Infectious Diseases Society of America for serving on the interactive panel for Clinical Interactive session.

**Methods—**We performed a retrospective analysis of all hospitalized adult patients with laboratory-confirmed pandemic H1N1/09 at a tertiary care center in the United States from June 1 to December 31, 2009.

**Results—**Fifty-six of 135 study patients (42%) had no fever; 31 (23%) required ICU admission and nine (7%) died. Those without fever had higher Charlson index (p=0.01), significantly longer time to hospital presentation (median four vs. two days, p<0.001), longer time to treatment since the onset of illness (median five vs. two days, p =0.001), and were more frequently in an ICU (p=0.01). After adjustment for age (<40 vs ≥40) and Charlson index (0, 1-2, ≥3), patients without fever had significantly increased likelihood of late hospital presentation (greater than two days from the onset of illness) (p=0.001) and also had increased likelihood of ICU stay (p=0.05).

**Conclusions—**Forty-two percent of patients with laboratory-confirmed H1N1/09 did not have fever as part of their illness prior to hospital presentation. Patients without fever had delayed presentation to the hospital and thus experienced delayed treatment.

### Keywords

Pandemic; H1N1/09; fever; diagnosis; treatment; influenza; hospital presentation

## INTRODUCTION

The Centers for Disease Control and Prevention (CDC) established a case definition during the 2009 influenza season for influenza-like illness (ILI): a temperature of ≥100.0°F (≥37.8°C), oral or equivalent, and cough or sore throat, in the absence of a known cause other than influenza [1]. Even though this definition is currently being revised, fever is still listed as a predominant symptom for influenza on the CDC website [2, 3].

During the spring of 2009 in New York City, 95% of patients with pandemic H1N1 influenza A met the case definition for ILI [4] whereas a report from Mexico [5] and another from China [6] reported that about one-third of patients presented without fever. A recent study found that the clinical features of H1N1/09 influenza and seasonal strains were similar in hospitalized patients [7]. Until recently, the CDC case definition for ILI included fever as a requisite symptom. Most clinicians still consider influenza a fever-based illness [8, 9]. Some studies have reported that seeking early medical care and early treatment for influenza resulted in reduced severity and duration of illness [10-13]. However, individuals without fever may not have sought early care because their illnesses did not meet all the criteria for ILI.

We hypothesized that significant number of our patients hospitalized during the H1N1/09 influenza pandemic did not have fever as part of the influenza-like illness prior to hospital presentation. We further hypothesized that this absence of fever was associated with delayed presentation to the hospital and delayed treatment. No prior studies have assessed the effect of fever on hospital presentation, diagnosis and treatment of H1N1/09 patients. We performed a retrospective cohort analysis comparing H1N1/09 patients with fever as part of their illness prior to hospital presentation to those without fever, to assess the influence of

fever on hospital presentation and on diagnosis and treatment in hospitalized patients with laboratory-confirmed H1N1/09 infection.

## METHODS

### Study Design and Setting

This retrospective cohort study was conducted at a tertiary care center with 1159 beds divided between two general hospitals (634 and 167 beds), a large cancer center (208 beds) and an inpatient cardiac hospital (150 beds).

### Selection of Participants

During the pandemic influenza season, clinicians throughout the tertiary care center were encouraged to obtain nasopharyngeal swabs to screen for influenza from all patients presenting to the hospital with respiratory illness, unexplained gastrointestinal symptoms, ILI, or any suspicion for influenza infection based on physician discretion. Patients were admitted through routine hospital admission procedures and triage. Physicians were encouraged to treat all patients in whom pandemic H1N1/09 was suspected empirically with an antiviral drug (oseltamivir). Patients with a positive H1N1/09 test were then continued on treatment. Obese patients, critically ill patients requiring intensive care unit (ICU) care, pregnant women and patients with chronic medical conditions such as chronic respiratory disease, chronic kidney disease, diabetes mellitus and immune compromising conditions were treated with a higher dose of oseltamivir (150 mg twice a day). Other patients were treated with the standard dose of oseltamivir (75 mg twice a day). The present analyses include all patients at least 18 years of age hospitalized with laboratory-confirmed pandemic H1N1/09 virus infection from 1 June 2009 through 31 December 2009. Subjects younger than 18 years and prisoners were excluded.

### Data Collection

Laboratory-confirmed pandemic H1N1/09 patients were identified from the hospital's infection control database. After identifying eligible patients, physician investigators accessed each electronic medical record to obtain health history, diagnosis, test results, disposition and clinical outcome information. We captured data on gender, race, age, comorbidities, symptoms and onset of illness, hospital presentation, diagnosis, treatment, ICU admission and death. Data abstraction was performed by an infectious disease physician using a standardized form and all data abstraction was validated by another infectious disease physician. The research was deemed exempt from further review by the Ohio State University Institutional Review Board review (2009E0979).

Subjects with laboratory-confirmed H1N1/09 virus infection were identified if nasal swab or respiratory secretions were positive for novel influenza A (H1N1) by specific rapid antigen or culture testing. Nasal swabs that were processed for confirmatory influenza testing by polymerase chain reaction were confirmed by panel (xTAG) or specific influenza A and B PCR (Luminex Molecular Diagnostics, Toronto, CA) [14]. Positive tests were confirmed using the Prodesse ProFlu-ST, Influenza A [2009] real-time PCR (H1N1 subtyping) assay (Focus Diagnostics, Cypress, CA).

Day of onset of illness was defined as the day when the patient started developing one or more symptoms of influenza-like illness. Day of hospital presentation was defined as the day when the patient either presented to the emergency department or a physician's office and was subsequently admitted or was directly admitted to the hospital. Fever was defined as a temperature of 100° Fahrenheit (F) or greater at presentation or reported subjective fever upon presentation and reported antipyretic use (nonsteroidal anti-inflammatory drugs or acetaminophen) prior to admission. When multiple temperature readings were present in the emergency department record, any recorded temperature of 100° Fahrenheit (F) or greater was considered a fever. The Charlson co-morbidity index predicts the ten-year mortality for a patient with a range of co-morbid conditions such as heart disease, AIDS, or cancer. The Charlson comorbidity index was calculated according to previously described methods [15-17]. Diabetes, chronic respiratory disease (asthma, chronic obstructive pulmonary disease), and chronic kidney disease with hemodialysis were recorded as comorbidities if these diagnoses were documented in the patient notes. Immunosuppression was defined as oral steroid use or other immunosuppressive medication, organ transplantation, HIV infection or cancer chemotherapy. Empiric antibiotic treatment was defined as treatment with antibiotics regardless of the evidence of bacterial infection. Proven bacterial co-infection was defined as infection with bacterial pathogens documented by a positive bacterial culture from any site that was obtained in response to clinical suspicion of bacterial infection.

### Data analysis

Demographic and clinical characteristics were summarized for all patients and for those patients with or without fever as part of their illness prior to hospital presentation. Continuous variables were summarized as mean (± standard deviation) or median values. For categorical variables, the percentage of patients in each category was calculated. For comparison between patients with fever and those with no fever, for continuous variables the two-sample t-test for normally-distributed data or the Wilcoxon rank-sum test for non-normal data was used. The Pearson chi-square test was used for categorical data. We performed a logistic regression analysis to examine the association between fever and time to presentation and ICU admission, adjusting for patient age and Charlson index. All analyses were carried out using SAS® 9.2 software (SAS, Cary, NC).

## RESULTS

We identified 135 hospitalized patients with laboratory-confirmed pandemic H1N1 virus infection during the study period. A substantial number of patients (n=56, 42%) had no fever as part of their illness prior to hospital presentation. Thirty-one patients (23%) required treatment in an ICU during hospitalization and nine (7%) died. While we observed no differences between patients with fever and those without fever prior to hospital presentation in gender, race or age (Table 1), patients without fever had higher Charlson index compared to those with fever (p=0.01, Wilcoxon rank-sum test). Patients without fever also had significantly longer time to presentation to the hospital since the onset of illness, compared to those with fever (median of four vs. two days, p<0.001). Patients without fever also had

significantly longer time to initiation of proper treatment since the onset of illness compared to those with fever (median of five vs. two days, p=0.001).

Patients were rapidly diagnosed and treated after presentation to the hospital with no significant difference by fever status at presentation (p=0.17 and 0.07 for differences in time from hospital presentation to diagnosis and treatment, respectively). While 82% (65/79) of patients with fever received empiric antibiotic treatment, only 59% (33/56) of those with no fever received empiric antibiotic treatment (p=0.003). Prevalence of bacterial co-infection was similar between the two groups (5% in the fever group vs. 9% in the group without fever; p=0.067). Patients without fever were more frequently in an ICU than those with fever (p=0.01), but we observed no significant differences in mortality by fever status at presentation in the small number of deaths during the study period (p=0.61). Compared to patients with no fever, after adjustment for age (<40 vs ≥40) and Charlson index (0, 1-2, ≥3), patients with fever had significantly decreased likelihood of late hospital presentation (greater than two days from the onset of illness) (adjusted odds ratio (OR): 0.27, p=0.001). Patients with fever also had decreased likelihood of ICU stay compared to patients with no fever, after adjustment for age and Charlson index (adjusted OR: 0.42, p=0.05) (Table 2).

Patients who presented to the hospital more than two days after the onset of illness were significantly more likely to be treated in an ICU during their hospitalization (p<0.001). Among 71 patients who presented to the hospital more than two days after the onset of illness, 27 patients were treated in an ICU and 44 patients did not require ICU care.

Among 64 patients who presented to the hospital within two days of the onset of illness, four patients were treated in an ICU and 60 patients did not require ICU care. Those who presented to the hospital more than two days after the onset of illness also had a non-significantly higher death rate: seven of 71 (10%) versus two of 64 (3%). Among the comorbidities tested, patients with no fever were significantly more likely to have diabetes mellitus (p=0.03).

ICU patients had a slightly higher median Charlson index than those who did not receive ICU care (median score 1 vs. score 0 for ICU patients vs. non-ICU patients, respectively; p=0.052). We observed no difference in median Charlson index between patients with late hospital presentation (>two days from onset of illness) and those with early hospital presentation (≤ two days from onset of illness) (p=0.51).

## DISCUSSION

We present the first study to assess the influence of presence of fever as part of the illness prior to hospital presentation on time to presentation and treatment for H1N1/09 patients. By comparing patients who had fever with those who did not, we showed that patients with fever tended to seek medical care sooner and thus received treatment sooner. Those without fever may not have realized they needed to seek medical care until much later in the course of disease compared to those with fever. Given that ICU stay was significantly more likely in patients with late presentation and no fever, these findings have important medical and economic consequences for individual patients and health care systems. Our findings, in

conjunction with previous studies indicating reduced disease severity with early treatment of influenza (10-13), can be used to educate the public to seek medical care for influenza early, even in the absence of fever.

Our study confirms previous observations that a significant number of patients with H1N1/09 did not have fever (5, 6). Nevertheless, fever appeared to trigger initiation of empiric antibiotic treatment. Empiric antibiotic use was significantly higher in the fever group. There was no difference in the median Charlson index among those who received antibiotic treatment and those who did not, suggesting that comorbidities are unlikely to explain the observed association. Empiric antibiotic treatment appeared not to affect whether or not a patient required ICU care during the hospitalization, though this association is difficult to measure because the majority of ICU patients (84%) were admitted to an ICU on the same day as hospital admission. We saw no difference in laboratory-confirmed bacterial co-infection between patients presenting with and without fever. We did not observe a significant effect of late presentation or fever on mortality, though the small number of deaths in the study likely limited our ability to detect any association.

Recent studies have shown that clinical signs cannot reliably differentiate H1N1/09-positive and H1N1/09-negative patients [18, 19]. In our study, patients in the fever and non-fever groups received prompt diagnosis and treatment once they presented to the hospital. This may be because clinicians were encouraged to test patients based on any suspicion for influenza infection and to treat for influenza while waiting for the result of testing. This may explain the similar timeframes for diagnosis and treatment between the fever and non-fever groups.

## Limitations

Our study took place in a single medical center, and our findings may not be generalizable to other clinical settings. However, this large tertiary care center admits 25% of patients in central Ohio. Our study focused on hospitalized patients only and excluded patients who may have presented to the emergency department with H1N1/09 but were not hospitalized. Thus, our findings can be applied to patients with severe enough disease to warrant hospitalization. It is possible that patients without fever presented early (within two days of onset of illness) and were treated as outpatients; these individuals would not have been captured in the current analysis. However, our primary goal was to assess the effect of fever on the overall course of H1N1/09 presentation, diagnosis and management in hospitalized patients. Provider bias may have played a role in the decision to admit patients to the hospital, but clinicians were encouraged to use a standardized protocol to drive decisions to test and admit. We studied H1N1/09 patients only, and our findings may not be generalizable to patients infected with other influenza types. However, H1N1/09 influenza symptoms are similar to other types of influenza. We also did not collect data on insurance status which may play a role in patients' choice to seek hospital care.

## Strengths

Our study also has substantial strengths. Because clinicians tested all patients with symptoms of respiratory illness and unexplained gastrointestinal symptoms irrespective of

the presence of fever, we were able to assess the proportion of H1N1/09 patients without fever as part of their illness and to determine that the most common presenting symptoms were respiratory. Our analysis includes only patients with laboratory-confirmed H1N1/09 infection. Our surveillance was strengthened by the availability of real time PCR confirmatory testing performed in our own molecular microbiology laboratory.

### Conclusions

In this study, nearly half of patients with H1N1/09 requiring hospitalization did not have fever as part of their illness. Patients with fever tended to seek medical care sooner and thus received treatment sooner. Patients with late presentation and no fever were more likely to need ICU admission. Our findings reinforce previous studies that indicate better outcomes with early treatment of influenza (10-13). These findings can be used to prompt clinicians to consider treating hospitalized patients with influenza and to educate the public to seek medical care soon after the onset of illness, despite absence of fever, if symptoms of respiratory illness and unexplained gastrointestinal symptoms are present during the influenza season.

## ACKNOWLEDGEMENTS

None

FUNDING SOURCE

None

## REFERENCES

1. CDC. Update: Infections with a swine-origin influenza A (H1N1) virus - United States and other countries, April 28, 2009. MMWR. 2009; 58:433–4. [PubMed: 19407738]
2. United States Centers for Disease Control and Prevention. [June 11, 2012] Clinical Signs and Symptoms of Influenza. http://www.cdc.gov/flu/professionals/acip/clinical.htm#signs.
3. United States Centers for Disease Control and Prevention. [June 11, 2012] Cold Versus Flu. http://www.cdc.gov/flu/about/qa/coldflu.htm.
4. CDC. Swine-origin influenza A (H1N1) virus infections in a school – New York City, April 30, 2009. MMWR. 2009; 58(Dispatch):1–3.
5. The New York Times. [May 13, 2009] Many swine flu cases have no fever. http://www.nytimes.com/2009/05/13/health/13fever.html?_r=1&ref=health.
6. Cao B, Li XW, Mao Y, Wang J, Lu HZ, Chen YS, et al. National Influenza A Pandemic (H1N1) 2009 Clinical Investigation Group of China: Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in China. N Engl J Med 2009. 361(26):2507–17.
7. Cheng AC, Kotsimbos T, Reynolds A, et al. Clinical and epidemiological profile of patients with severe H1N1/09 pandemic influenza in Australia and New Zealand: an observational cohort study. BMJ Open. Jan 1.2011 1
8. [June 11, 2012] Colds and the Flu. http://familydoctor.org/familydoctor/en/diseases-conditions/colds-and-the-flu/symptoms.html.
9. [June 11, 2012] Flu or Cold Symptoms?. http://www.webmd.com/cold-and-flu/cold-guide/flu-cold-symptoms.
10. Moscona A. Neuraminidase inhibitors for influenza. N Engl J Med. 2005; 353:1363–1373. [PubMed: 16192481]

11. Aoki FY, Macleod MD, Paggiaro P, Carewicz O, El Sawy A, Wat C, et al. Early administration of oral oseltamivir increases the benefits of influenza treatment. J Antimicrob Chemother. 2003; 51:123–129. [PubMed: 12493796]
12. Kawai N, Ikematsu H, Iwaki N, Satoh I, Kawashima T, Maeda T, et al. Factors influencing the effectiveness of oseltamivir and amantadine for the treatment of influenza: a multicenter study from Japan of the 2002-2003 influenza season. Clin Infect Dis. 2005; 40:1309–1316. [PubMed: 15825034]
13. Bowles SK, Lee W, Simor AE, Vearncombe M, Loeb M, Tamblyn S, et al. Use of oseltamivir during influenza outbreaks in Ontario nursing homes, 1999-2000. J Am Geriatr Soc. 2002; 50:608–616. [PubMed: 11982659]
14. Ginocchio CC, St George K. Likelihood that an unsubtypeable influenza A virus result obtained with the Luminex xTAG respiratory virus panel is indicative of infection with novel A/H1N1 (swine-like) influenza virus. J Clin Microbiol. 2009; 47:2347–2348. [PubMed: 19494066]
15. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373–383. [PubMed: 3558716]
16. Needham DM, Scales DC, Laupacis A, Pronovost PJ. A systematic review of the Charlson comorbidity index using Canadian administrative databases: a perspective on risk adjustment in critical care research. J Crit Care. 2005; 20(1):12–19. doi.10. 1016/j.jcrc.2004.09.007. [PubMed: 16015512]
17. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992; 45(6):613–619. doi: 10.1016/0895-4356(92)90133-8. [PubMed: 1607900]
18. Park KS, Park TS, Suh JT, Nam YS, Lee MS, Lee HJ. Characteristics of outpatients with pandemic H1N1/09 influenza in a tertiary care university hospital in Korea. Yonsei Med J. Jan; 2012 53(1): 213–20. [PubMed: 22187255]
19. Crisinel PA, Barazzone C, Kaiser L, et al. Comparison of clinical presentation of respiratory tract infections in H1N1/09-positive and H1N1/09-negative patients. Eur J Pediatr. Jan; 2012 171(1): 159–66. [PubMed: 21674140]

*J Hosp Med*. Author manuscript; available in PMC 2014 December 19.

**Table 1**

Comparison of baseline characteristics among patients with fever and those with no fever as part of their illness prior to hospitalization

| | | Fever N=79 (59%) | No Fever N=56 (42%) | Unadjusted Odds Ratio | *p*-value* |
|---|---|---|---|---|---|
| Gender | Female [n (%)] | 41 (52%) | 34 (61%) | 0.7 | 0.31[1] |
| Race | White [n (%)] | 45 (57%) | 29 (52%) | 1.03 | 0.30[3] |
| | Black [n (%)] | 30 (38%) | 20 (36%) | | |
| | Other [n (%)] | 4 (5%) | 7 (13%) | | |
| Age | Mean ± SD (range) | 43 ±15 (18-89) | 48 ± 17(19-89) | | 0.060[2] |
| Charlson index | Median (range) | 0 (0,13) | 1 (0, 13) | | 0.010[2] |
| Co-morbidities | | | | | |
| Obese (BMI ≥30) | [n (%)] | 37 (50%) | 29 (54%) | 0.82 | 0.571[3] |
| Chronic respiratory illness (asthma, COPD) | [n (%)] | 19 (24%) | 13 (23%) | 1.05 | 0.910[3] |
| Diabetes | [n (%)] | 14 (18%) | 19 (34%) | 0.419 | 0.031[3] |
| CKD with hemodialysis | [n (%)] | 12 (15%) | 6 (11%) | 1.49 | 0.451[3] |
| Immunocompromised | [n (%)] | 29 (38%) | 13 (23%) | 1.92 | 0.095[3] |
| Days from onset to hospital presentation | Median (range) | 2 (0-10) | 4 (1-21) | | 0.0001[2] |
| # with days >2 | n (%) | 31 (39%) | 40 (71%) | 0.26 | <0.001[3] |
| Days to diagnosis from hospital presentation | Median (range) | 0 (0-3) | 0 (0-5) | | 0.166[2] |
| # with days >2 | n (%) | 1 (1%) | 3 (5%) | 0.24 | 0.170[3] |
| Days to Oseltamivir since admission | Median (range) | 0 (0-13) | 1 (0-14) | | 0.07[2] |
| Days to Oseltamivir since onset of illness | Median (range) | 2 (0-13) | 5 (1-19) | | 0.0003[2] |
| # with days >2 | n (%) | 35 (44%) | 39 (70%) | 0.24 | 0.001[3] |
| Need for ICU care | n (%) | 12 (15%) | 19 (34%) | 0.35 | 0.010[3] |
| Death | n (%) | 6 (8%) | 3 (5%) | 1.45 | 0.061[3] |
| Bacterial co-infection | n (%) | 5 (n=79; 6%) | 9 (15%) | 0.35 | 0.067[3] |

| | | Fever N=79 (59%) | No Fever N=56 (42%) | Unadjusted Odds Ratio | *p*-value* |
|---|---|---|---|---|---|
| Empiric antibiotics | | 65 (n= 77; 84%) | 33 (59%) | 3.24 | 0.003[3] |
| Lower Respiratory symptoms | n (%) | 72 (91%) | 50 (91%) | 1.03 | 0.963[3] |
| Cough | n (%) | 58 (73%) | 38 (69%) | 1.24 | 0.585[3] |
| Shortness of breath | n (%) | 34 (43%) | 25 (46%) | 0.91 | 0.782[3] |
| Respiratory failure | n (%) | 7 (9%) | 7 (13%) | 0.67 | 0.472[3] |
| Sore throat/congestion/rhinorrhea | n (%) | 21 (27%) | 10 (18%) | 1.63 | 0.257[3] |
| Gastrointestinal symptoms (nausea, vomiting, diarrhea) | n (%) | 30 (38%) | 13 (24%) | 1.98 | 0.080[3] |

SD = Standard deviation; BMI = Body mass index; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; ICU = Intensive care unit

*$p$-values calculated using two-sample t test[1] (normally-distributed data) or Wilcoxon rank sum test[2] (non-normal data) for continuous variables and Pearson $\chi^2$ test[3] for categorical data between the patients with fever and those with no fever.

## Table 2

Effect of fever on late (>2 days from onset of illness) hospital presentation or ICU admission, after adjusting for age and Charlson index using multivariate logistic regression.

| | Adjusted odds ratio | *p*-value |
|---|---|---|
| *Late hospital presentation (>2 days from onset of illness)* | | |
| Fever (vs. no fever) | 0.27 | 0.001 |
| Age (≥40 years) | 2.06 | 0.071 |
| Charlson Index | | |
| 1-2 | 0.69 | 0.38 |
| ≥3 | 1.01 | 0.99 |
| *ICU admission* | | |
| Fever (vs. no fever) | 0.42 | 0.05 |
| Age (≥40 years) | 1.21 | 0.701 |
| Charlson Index | | |
| 1-2 | 0.66 | 0.448 |
| ≥3 | 4.02 | 0.016 |