


BMJ Open National Early Warning Score for predicting intensive care unit admission among elderly patients with influenza infections in the emergency department: an effective disposition tool during the influenza season

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To cite: Wang T-H, Jheng J-C, Tseng Y-T, *et al*. National Early Warning Score for predicting intensive care unit admission among elderly patients with influenza infections in the emergency department: an effective disposition tool during the influenza season. *BMJ Open* 2021;**11**:e044496. doi:10.1136/bmjopen-2020-044496

► Prepublication history and additional online supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2020-044496>).

Received 06 September 2020
Accepted 14 May 2021



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ABSTRACT

Objective During the influenza epidemic season, the fragile elderly are not only susceptible to influenza infections, but are also more likely to develop severe symptoms and syndromes. Such circumstances may pose a significant burden to the medical resources especially in the emergency department (ED). Disposition of the elderly patients with influenza infections to either the ward or intensive care unit (ICU) accurately is therefore a crucial issue.

Study design Retrospective cohort study.

Setting and participants Elderly patients (≥65 years) with influenza visiting the ED of a medical centre between 1 January 2010 and 31 December 2015.

Primary outcome measures Demographic data, vital signs, medical history, subtype of influenza, national early warning score (NEWS) and outcomes (mortality) were analysed. We investigated the ability of NEWS to predict ICU admission via logistic regression and the receiver operating characteristic (ROC) analysis.

Results We included 409 geriatric patients in the ED with a mean age of 79.5 years and approximately equal sex ratio. The mean NEWS ±SD was 3.4±2.9, and NEWS ≥8 was reported in 11.0% of the total patients. Logistic regression revealed that NEWS ≥8 predicted ICU admission with an OR of 5.37 (95% CI 2.61 to 11.04). The Hosmer-Lemeshow goodness-of-fit test was calculated as 0.95, and the adjusted area under the ROC was 0.72. An NEWS ≥8 is associated with ICU-admission and may help to triage elderly patients with influenza infections during the influenza epidemic season.

Conclusion The high specificity of NEWS ≥8 to predict ICU admission in elderly patients with influenza infection during the epidemic season may avoid unnecessary ICU admissions and ensure proper medical resource allocation.

INTRODUCTION

Seasonal influenza pandemic is a global public health issue that causes approximately 5 million cases of severe complicated

Strengths and limitations of this study

- This was the first study to evaluate the use of the National Early Warning Score (NEWS) in predicting intensive care unit (ICU) admission among elderly patients with influenza infections.
- The high specificity setting of NEWS ≥8 to predict ICU admission in elderly patients with influenza infection during the epidemic season, may avoid unnecessary ICU admissions and ensure proper medical resource utilisation.
- This is a single-centre retrospective cohort study.
- The subtypes of the influenza virus were not mentioned because different strains of the influenza virus may lead to different mortality rates.

influenza and 290 000–650 000 deaths worldwide each year.^{1 2} Of all the age groups, the elderly are at the highest risk of developing serious complications from influenza.³ It is estimated that 90% (approximately 186 000 cases) of influenza-related deaths⁴ and >60% (approximately 44 000 cases) of influenza-related hospitalisations in the USA were associated with the elderly.⁵ Meanwhile, up to over 30 000 excess hospitalisations per year was noted in Europe, including France, Germany, Italy, UK and Ukraine, during the seasonal influenza pandemics.⁶ Another study reported an estimated 18 000–96 000 influenza-related intensive care unit (ICU) admissions in the USA annually.⁷

Dispositioning (discharge, admission to ward or ICU) the influenza-infected elderly patients during the influenza epidemic season is challenging because the overwhelming number of patients with influenza in hospitals may heavily burden the limited

medical resources. Therefore, predicting ICU admission among elderly patients with influenza infections for the utilisation of medical resources appropriately is a crucial issue. There are several scoring systems in use to predict poor prognosis among elderly patients with influenza infections, for instance, the Geriatric Influenza Death (GID) score, which comprises five independent mortality predictors, including severe coma (Glasgow Coma Scale (GCS) score ≤ 8), histories of cancer and coronary artery disease (CAD), elevated C reactive protein (CRP) levels (>10 mg/dL) and bandaemia ($>10\%$ band cells). Patients scoring ≥ 3 points on this scale should be considered for ICU admission.⁸ However, the overcrowded emergency department (ED) during the influenza epidemic needs timely patient disposition (discharge, admission to ward or ICU), and it may take hours for the results of the laboratory variables for determination of the GID score to be revealed, which can lead to worsening the overcrowding.

The National Early Warning Score (NEWS) has the advantage of easy accessibility and prompt results because the variables of the scoring system consist of clinical vital signs, including respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness or altered mental status and body temperature. The NEWS allocates points in a weighted manner, and patients are classified into three categories according to their scores. According to Royal College of Physicians of London, patients with a low score (NEWS 1–4) should be evaluated by a competent registered nurse; those with a medium score (NEWS 5–6) should be reviewed by a ward-based doctor or an acute team nurse; and those with high scores (NEWS ≥ 7) should be assessed immediately by a clinical team with critical care competence and may be transferred to a higher-dependency care area.⁹

Although NEWS may be an effective and prompt tool for the dispositioning of patients in the influenza season, the optimal cut-off point to predict ICU admission among elderly patients with influenza infections may be different, because the physiological response to diseases may be different in the elderly as compared with adults. Moreover, a study showed that systemic inflammatory response syndrome (SIRS) criteria ≥ 3 among geriatric patients with influenza showed a greater accuracy for poor prognosis, which is different from the usual SIRS criteria cut-off point of 2 among non-geriatric patients.¹⁰ Therefore, we conducted this study to validate the utilisation of NEWS in predicting ICU admission among elderly patients with influenza infections.

METHODS

Study design, setting and participants

This study was conducted in the ED of Cathay General Hospital, a medical centre with 800 ward beds and 40 ED beds, located in Taipei, Taiwan. The number of patients visiting the ED was approximately 55 000 annually, with 33% of elderly adult patients.^{11 12} Elderly patients (age ≥ 65 years) who visited the ED between

1 January 2010 and 31 December 2015, fulfilling the following criteria, were included in the study: (1) tympanic membrane (TM) temperature $\geq 37.2^\circ\text{C}$ or an increase in baseline TM temperature $\geq 1.3^\circ\text{C}$ ^{11 12}; (2) influenza infections, defined as a positive influenza pharyngeal or throat swab test via de antigen detection¹³; (3) antiviral therapy with either oseltamivir or zanamivir within 24 hours of the diagnosis of influenza infections. We used BD Directigen Influenza A+B Kit for influenza test, and according to literature review, BD Directigen Influenza A & B kit had positive predictive rate of 85.7% and negative predictive rate of 89.8% for influenza A; positive predictive rate of 66.7% and negative predictive rate of 93.9% for influenza B¹⁴

Definition of variables and primary outcomes

There were no specific international guidelines to determine the need for ICU admission. Therefore, our critical care management committee established the ICU admission criteria as follows: (1) patients who require advanced respiratory support; (2) patients who suffer from shock or circulatory failure; (3) patients who require support for two or more of the organ systems and (4) physician's clinical judgement. The NEWS is a scoring system which comprises six simple physiological parameters including respiration rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness or new confusion and body temperature. Each parameter was allocated with a score according to their measurement, with the magnitude of the score reflecting to what extreme the parameter varies from the baseline. Further detailed information about the NEWS is listed in online supplemental file 1. The study endpoint was admission to the ICU.

Data collection, case assignments and control groups

A retrospective medical record review was performed on the patients who fulfilled the inclusion criteria. Demographic characteristics, patient's vital signs, influenza subtypes, laboratory data and details of past medical history, complications and mortality (table 1) were collected by an emergency physician. Required data that is not recorded in the patient's medical chart was considered negative, and the patient will be eventually excluded. The patients, who were included in the study, were categorised into the 'ICU' group and 'non-ICU' group. All variables were compared between the two groups.

Statistical analyses

The statistical priori power of this study was 0.80 calculated via G-power V.3.0, which indicate sufficient sample size to analyse this issue. Statistical analyses were performed via SPSS V.23.0 for Mac (SPSS). Continuous data that were normally distributed were presented as means \pm SDs, while continuous data that were not normally distributed were presented as

Table 1 Characteristics of geriatric patients with influenza in the emergency department

Characteristics	Total patients	ICU	Non-ICU	P value
	(n=409)	(n=46)	(n=363)	
Male sex	205 (50.1)	29 (63.0)	176 (48.5)	0.06
Age, years	79.5±8.3	79.3±7.8	79.6±8.5	0.81
Age subgroup				
Young elderly (65–74 years of age)	125 (30.6)	13 (28.3)	112 (30.9)	0.72
Moderately elderly (75–84 years of age)	174 (42.5)	22 (47.8)	152 (41.9)	0.44
Old elderly (≥85 years of age)	110 (26.9)	11 (23.9)	99 (27.3)	0.63
Vital signs				
Respiratory rate (per minute)	21.3±4.2	24.5±7.2	20.8±3.4	<0.01
Glasgow's Coma Scale	13.9±2.3	12.6±3.8	14.2±2.0	<0.01
SBP (mmHg)	146.1±30.5	150.5±45.0	145.6±28.2	0.47
Body temperature (°C)	38.18±0.93	37.9±1.1	38.2±0.9	0.13
Heart rate (beats/min)	98.8±20.5	105.5±27.0	98.0±19.5	0.02
Oxygen saturation (%)	96.8±7.9	91.5±12.2	97.5±7.0	<0.01
History				
Cancer	61 (14.9)	3 (6.5)	58 (16.0)	0.09
COPD	111 (27.1)	2 (4.3)	69 (19.0)	<0.01
Hypertension	263 (64.3)	35 (76.1)	228 (62.8)	0.07
Coronary artery disease	103 (25.1)	19 (41.3)	75 (20.4)	<0.01
Stroke	65 (15.9)	10 (21.7)	55 (15.2)	0.25
Diabetes	163 (39.8)	26 (56.5)	136 (37.5)	0.04
Laboratory data				
WCC (10 ⁹ /L)	10.6±5.8	12.8±6.4	10.3±5.7	<0.01
Bandaemia (band form >10%)	43 (10.2)	6 (13)	23 (6.3)	0.09
CRP (mg/dL)	8.2±10.1	12.5±10.8	7.7±10.0	0.01
Platelet (10 ⁹ /L)	186.2±158.8	199.8±85.6	184.5±166.1	0.54
NEWS	3.4±2.9	5.9±3.6	3.1±2.6	<0.01
NEWS ≥8	45 (11.0)	15 (32.6)	30 (8.3)	
Influenza subtypes				
Influenza A	278 (68.0)	32 (69.6)	246 (67.8)	0.87
Influenza B	120 (29.3)	11 (23.9)	109 (30.0)	0.39
Influenza A+B	11 (2.7)	3 (6.5)	8 (2.2)	0.09
Complications*				
Pneumonia	276 (67.5)	41 (89.1)	235 (64.7)	0.10
Urinary tract infection	74 (18.1)	8 (17.4)	66 (18.2)	0.47
Sepsis	34 (8.3)	7 (15.2)	27 (7.4)	0.07
Influenza vaccination	95 (23.2)	18 (39.1)	77 (21.2)	0.01
DNR	4 (0.98)	0 (0)	4 (1.1)	0.47
Mortality	20 (4.9)	10 (21.7)	10 (3.4)	<0.01

Data were presented as percentages or means ± SD.

*Not all the complications are listed in the table.

COPD, chronic obstructive pulmonary disease; CRP, C reactive protein; DNR, do-not-resuscitate; ICU, intensive care unit; NEWS, National Early Warning Score; SBP, systolic blood pressure; WCC, white cell count.

medians (IQRs). For independent samples, t-test or the Mann-Whitney-Wilcoxon test was used to compare continuous data. Pearson's χ^2 test or Fisher's exact test was used for categorical variables. The area under the receiver operating characteristic curve (AUROC) was

used to evaluate ICU admission discrimination ability. AUROCs were further adjusted for comorbidities that affect ICU admission. Furthermore, sensitivity, specificity, positive predictive value and negative predictive value (NPV) were also calculated.

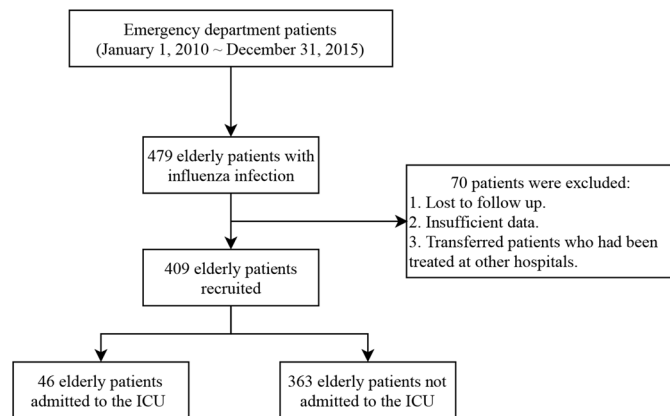


Figure 1 Flow chart of this study.

Patients and public involvement

This study did not involve patients and the public in the design or planning of the study.

RESULTS

Initially, a total of 479 geriatric patients in the ED were recruited into this study. After excluding 70 patients who were lost to follow-up, had insufficient data and transferred to be treated at other hospitals, 409 patients were eventually included (figure 1). The male to female ratio and the mean age \pm SD were approximately equal in both the groups. None of the patients signed the ‘do-not-resuscitate’ (DNR) agreement on admission.

Vital signs showed mean \pm SD of the respiratory rate and heart rate were significant higher in the ICU group (24.5 \pm 7.2/min and 105.5 \pm 27.0/min, respectively) than the non-ICU group (20.8 \pm 3.4/min and 98.0 \pm 19.5/min, respectively). Furthermore, consciousness level, GCS, was lower in the ICU group at 12.6 \pm 3.8 than the non-ICU group at 14.2 \pm 2.0, with a $p < 0.01$.

For medical histories, the prevalence of CAD and diabetes was significantly higher in the ICU group (41.3% and 20.4%) than in the non-ICU group (56.5% and 37.5%). While the laboratory data showed higher white blood cell count and CRP level in the ICU group, at 12.8 \pm 6.4 10^3 /mm³ and 12.5 \pm 10.8 mg/dL, than the non-ICU group, at 10.3 \pm 5.7 10^3 /mm³ and 7.7 \pm 10.0 mg/dL. The mean NEWS \pm SD was significantly higher in the ICU group (5.9 \pm 3.6) than in the non-ICU group (3.1 \pm 2.6). The percentage of NEWS \geq 8 was higher in the ICU group (32.6%) than in non-ICU group (8.3%).

The percentages of influenza A and influenza B infections showed no significant differences between the ICU and non-ICU groups. The patients were treated with either oseltamivir or zanamivir within 24 hours of the diagnosis of influenza infections being confirmed. Complications of influenza infections included pneumonia (67.5%), urinary tract infections (18.1%) and sepsis (8.3%). Influenza vaccination had shown no prominent difference between the ICU and non-ICU groups. The ICU group had a higher mortality percentage (21.7%) than the

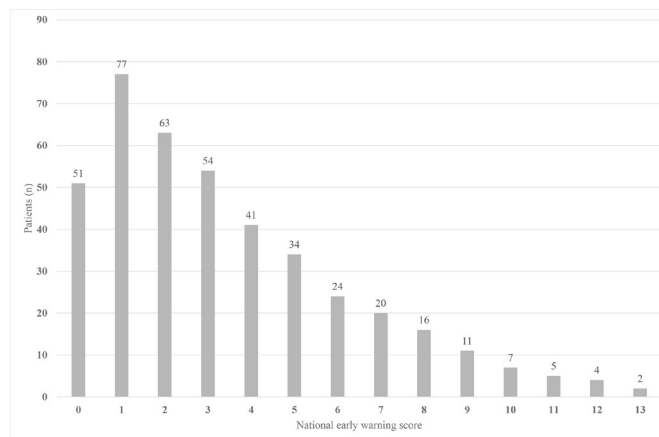


Figure 2 Distribution of patients by National Early Warning Score among elderly patients with influenza infections.

non-ICU group (3.4%). Causes of mortality among the 20 elderly patients were sepsis (14 patients), respiratory failure (three patients), and cardiovascular events (two patients with acute myocardial infarction and one with myocarditis). No statistical difference in DNR orders was observed between the ICU and the non-ICU groups.

The distribution of elderly patients with influenza infections according to the NEWS was as follows: 51 (12.5%) patients, 0 points; 77 (18.8%), 1; 63 (15.4%), 2; and, 218 (53.3%), \geq 3 points (figures 2 and 3). The Youden’s index of NEWS was 0.32, and the optimal cut-off point for NEWS to predict ICU admission among elderly patients with influenza infections was calculated as \geq 8 points. Univariate logistic regression showed that a NEWS \geq 8 predicts ICU admission with an OR of 5.37 (95% CI 2.61 to 11.04). The Hosmer-Lemeshow goodness-of-fit score was 0.95 for NEWS \geq 8 (table 2).

The AUROC was adjusted for CAD ($p = 0.01$) and diabetes ($p = 0.04$). The adjusted AUROC for predicting ICU admission showed that NEWS \geq 8 (0.72; 95% CI 0.66 to 0.81) had an acceptable ICU admission discrimination ability (figure 4, table 3). The performance of NEWS

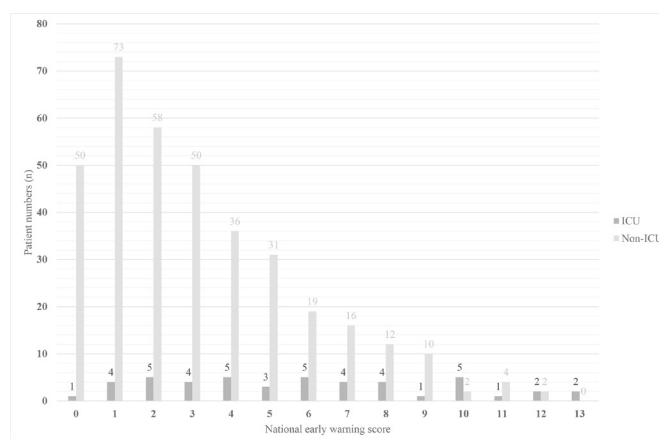


Figure 3 Distribution of patients admitted to the intensive care unit (ICU) and patients not admitted to the ICU by National Early Warning Score among elderly patients with influenza infection.

Table 2 Predicting ICU admission among geriatric patients with influenza infections by using news score ≥ 8 , identified by univariate logistic regression

Score	B	OR	95% CI	P value	Hosmer-Lemeshow goodness of fit
NEWS ≥ 8	1.68	5.37	2.61 to 11.04	<0.01	0.95

ICU, intensive care unit; NEWS, National Early Warning Score.; .

≥ 8 in predicting ICU admission among elderly patients with influenza infections showed a high specificity of 0.92 (95% CI 0.88 to 0.94) and a high NPV of 0.91 (95% CI 0.90 to 0.93) (table 4).

DISCUSSION

We consider NEWS instead of NEWS2 to identify ICU admission among elderly patients with influenza infections in the ED because several studies showed NEWS2 non-superior to NEWS in discriminating patients with adverse outcomes.^{15 16} NEWS2 was originally designed to improve safety for patients with hypercapnic respiratory failure, with oxyhemoglobin saturation by pulse oximetry (SpO₂) adjustments. However, a multicentre retrospective observational study, conducted in the UK, which identified 48 898 patients, showed that NEWS2 do not improve discrimination of adverse outcomes in patients with type 2 respiratory failure, while compared with the original NEWS.¹⁵ Furthermore, a Danish study also showed similar

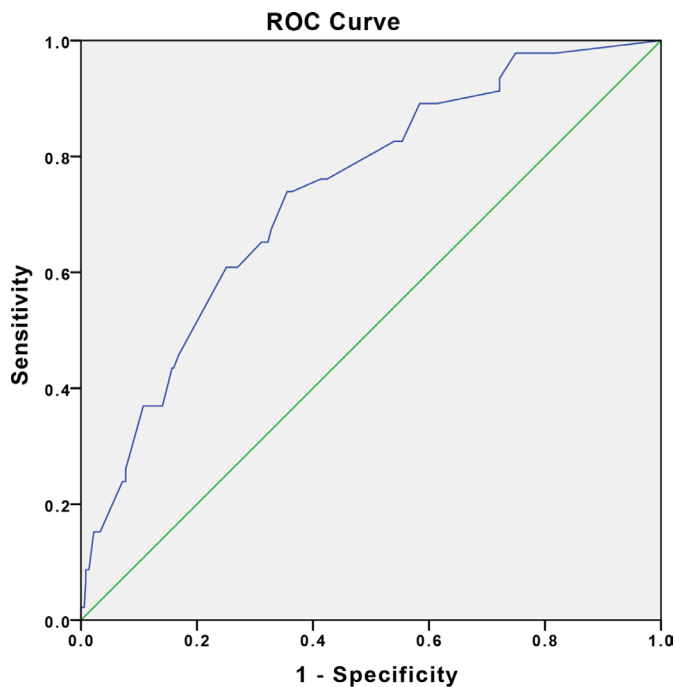


Figure 4 Area under the curve of National Early Warning Score ≥ 8 to predict intensive care unit admission among elderly patients with influenza infection.

Table 3 Adjusted AUROC for ICU admission discrimination of NEWS score ≥ 8 among geriatric patients with influenza infections

NEWS ≥ 8	AUROC	95% CI	P value
Adjusted	0.72	0.66 to 0.81	<0.01
Unadjusted	0.69	0.62 to 0.74	<0.01

AUROC, area under the receiver operating characteristic; ICU, intensive care unit; NEWS, National Early Warning Score.; .

result with decreased sensitivity for 48-hour mortality and ICU admission while evaluating patients via the modified NEWS than the unmodified NEWS, and concluded that the identification of deterioration may be compromised by modifications.¹⁶

The NEWS is an early warning scoring (EWS) system developed by a multiprofessional working group by reviewing and modifying numbers of the EWS systems, especially the Vitalpac Early Warning Score (ViEWS). Adjustments were made according to clinical and professional recommendations.¹⁷ Furthermore, three points were added to every extreme value in the physiological parameters of the NEWS to overcome the paucity of extreme values in the ViEWS database.¹⁸ NEWS has also been used to identify early cardiac arrest, unanticipated ICU admission,¹⁹ acute medical admissions²⁰ and non-elective surgical admissions²¹ even in prehospital settings.²²

NEWS was also capable of predicting the deterioration of patients in the ED with sepsis because Goulden *et al* discovered that NEWS had an equivalent or even superior value for quick sequential organ failure assessment and SIRS criteria in predicting mortality and ICU admission among patients in the ED with sepsis.²³ Among patients at risk of adverse clinical outcomes, the NEWS had an equivalent performance in identifying patients similar to the Medical Emergency Team Criteria.²⁴ A literature review conducted by Nannan Panday *et al* showed that ICU admission among ED patients was best predicted by NEWS.²⁵ However, NEWS has never been validated for use in predicting ICU admission among elderly patients with influenza infections.

This study discovered that the optimal cut-off point for NEWS to predict ICU admission among influenza-infected elderly patients was 8 points, as identified by the

Table 4 Performance of NEWS score ≥ 8 in predicting ICU admission among geriatric patients with influenza infections

NEWS ≥ 8	
Sensitivity	0.33 (0.19–0.48)
Specificity	0.92 (0.88–0.94)
Positive predictive value	0.33 (0.23–0.46)
Negative predictive value	0.91 (0.90–0.93)

NEWS, National Early Warning Score; ICU, intensive care unit.



Youden's index. The sensitivity, specificity, positive predictive value and NPV were 33%, 92%, 33% and 91%, respectively. The high specificity of 92% and NPV of 91% may be useful in ruling out poor prognosis and ICU admission among elderly patients with influenza infection.⁸ A test with a high sensitivity but low specificity may result in admitting patients who are not actually severely ill to the ICU.²⁶ In contrast, a test with high specificity and low sensitivity, similar to the performance of NEWS ≥ 8 in the present study, may possess the advantage of a low false-positive rate, which may avoid unnecessary ICU admissions. As medical resources are usually deficient during the influenza epidemic season, it is crucial to avoid unnecessary ICU admissions and ensure proper medical resource utilisation.

The vital signs were acquired at the triage, which could more clearly reflect the patients' primitive physiological response to the disease, because vital signs retrieved after treatments such as antipyretic therapy or fluid supplementation may affect the primitive physiological response. A possible reason for the extreme vital signs observed at the ED may be associated with the delayed seeking of medical attention by the elderly patients⁸ because the mean duration between onset of initial symptoms to the time of arrival in the ED was 3.56 days in this study. Patients admitted to the ICU were more likely to present with initial extreme vital signs, with a mean respiratory rate of 24.5/mi, mean GCS score of 12.6, mean heart rate of 105.5/min and a mean oxygen saturation level of 91.5%. While incorporating each vital sign into the NEWS system, a sum of 8 points was calculated (individual score for each clinical vital sign: 2 points, 3 points, 1 point, and 2 points), which is compatible with our calculated cut-off of 8 points.

Influenza-infected elderly patients who were admitted to the ICU had a significantly higher percentage of a history of diabetes and CAD. A previous study showed that CAD may affect prognosis in elderly patients with influenza infections¹⁰ because influenza infections may exaggerate underlying cardiac disease and increase the chances of myocardial infarction among patients with a history of CAD.²⁷ Meanwhile, patients with a history of diabetes may be more susceptible to sepsis because of the impairment of innate immune response caused by poor glycaemic control.²⁸ The high prevalence of chronic obstructive pulmonary disease (COPD) in this study, compared with the overall geriatric population, was probable due to the impaired pulmonary function of the elderly patients with COPD, which makes them more susceptible to influenza infection.²⁹

Although influenza vaccination plays an important role in attempts to reduce the mortality burden of influenza, the mortality benefits of influenza vaccination in elderly people is still controversial. Several studies, since 1980, were unable to proof significant decrease in influenza-related mortality, even as vaccination coverage increased from 15% to 65%. In addition, the effectiveness of the influenza vaccine also varies from season to

season.³⁰ Further researches are needed to clarify this issue.

The strength of this study is that this is the first study to evaluate the use of the NEWS in predicting ICU admission among elderly patients with influenza infections. However, there were some limitations to this study. First, the severity of influenza infections may be higher because the study was conducted in a tertiary medical centre. Second, because of a retrospective chart review study setting, certain patient-related data or information may have been missed. Third, the subtypes of the influenza virus were not mentioned because different strains of the influenza virus may lead to different mortality rates.³¹ Fourth, the diagnosis of influenza was based on the rapid antigen test, which may have yielded false-positive or false-negative results. Advanced examinations, such as reverse transcription PCR, immunofluorescence assay, or viral culture should be performed to confirm the diagnosis of influenza infection. However, advanced examinations are expensive and time-consuming; therefore, it is more practical to use rapid antigen test instead for its simplicity and prompt results. Fifth, this was a single-centre study, and the results of this study may not be generalisable to other countries; further external validation is needed to prove the findings of this study.

CONCLUSION

In conclusion, NEWS ≥ 8 had the advantage of both high specificity and NPV to predict ICU admission among elderly patients with influenza infections in the ED. This suggest lower false-positive rate of ICU admission during the influenza pandemic season, and consequence in reserving medical resources for the actual critical patients.

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Acknowledgements We thank Editage for English language editing.

Authors contributions T-HW, J-CJ, Y-TT, L-FC and J-YC designed and conceived this study, T-HW and J-CJ wrote the manuscript. J-YC performed the statistical analysis. J-YC and L-FC provided professional suggestions. All authors read and approved the final manuscript.

Funding The authors received no specific funding for this work. The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests All authors denied any conflict of interest.

Patient consent for publication Not required.

Ethics approval This study was approved by the institutional Review Board of the Cathay General Hospital and was conducted according to the Declaration of Helsinki. Due to the retrospective setting of this study, the need for informed consent from the patients was waived.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data available within the article or its supplementary materials

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