JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
WILEY

ORIGINAL ARTICLE

Infectious Disease

Predicting severe disease in patients diagnosed with seasonal influenza in the emergency department

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Abstract

Objectives: We sought to develop an evidence-based tool to risk stratify patients diagnosed with seasonal influenza in the emergency department (ED).

Methods: We performed a single-center retrospective cohort study of all adult patients diagnosed with influenza in a large tertiary care ED between 2008 and 2018. We evaluated demographics, triage vital signs, chest x-ray and laboratory results obtained in the ED. We used univariate and multivariate statistics to examine the composite primary outcome of death or need for intubation. We validated our findings in patients diagnosed between 2018 and 2020.

Results: We collected data from 3128 subjects; 2196 in the derivation cohort and 932 in the validation cohort. Medical comorbidities, multifocal opacities or pleural effusion on chest radiography, older age, elevated respiratory rate, hypoxia, elevated blood urea nitrogen, blood glucose, blood lactate, and red blood cell distribution width were factors associated with intubation or death. We developed the Predicting Intubation in seasonal Influenza Patients diagnosed in the ED (PIIPED) risk-stratification tool from these factors. The PIIPED tool predicted intubation or death with an area under the receiver operating characteristic curve (AUC) of 0.899 in the derivation cohort and 0.895 in the validation cohort. A version of the tool including only factors available at ED triage, before laboratory or radiographic evaluation, exhibited AUC of 0.852 in the derivation cohort and 0.823 in the validation cohort.

Conclusion: Clinical findings during an ED visit predict severe outcomes in patients with seasonal influenza. The PIIPED risk stratification tool shows promise but requires prospective validation.

KEYWORDS
emergency department, illness severity, risk stratification, seasonal influenza

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1 | INTRODUCTION

1.1 | Background

Seasonal influenza carries a heavy annual burden of morbidity and mortality. The US Centers for Disease Control and Prevention (CDC) reported that influenza contributed to 35 million illnesses, 16 million medical visits, 380,000 hospitalizations, and 20,000 deaths in the United States during the prototypical 2019–2020 influenza season.[1] A recent estimate of worldwide influenza disease found that seasonal influenza is responsible for around half a million deaths each year.[2] This translates into a significant economic burden, with lost worker productivity costing the United States economy an average of $11.2 billion annually and increased health care use contributing $3.2 billion in direct medical costs each year.[3] These public health and economic impacts of influenza highlight the need for rapid and appropriate risk stratification of patients diagnosed with symptomatic disease in acute care settings to optimize the use of limited health care resources.

There are no widely used or validated risk stratification tools for patients with laboratory-confirmed seasonal influenza. Established risk stratification tools for community acquired pneumonia, such as the CURB-65 (confusion, uremia, respiratory rate, blood pressure, age ≥ 65 years) score and the Pneumonia Severity Index score, do not have acceptable sensitivity for detecting severe disease in patients infected with influenza.[4–8] Several risk stratification tools, including the Pandemic Medical Early Warning Score and CURB-65, were assessed in the 2009 H1N1 influenza pandemic and demonstrated limited sensitivity to appropriately identify patients at risk for severe disease.[4,6,7] Other developed scoring systems exhibit poor ability to identify seasonal influenza patients at high risk for severe disease in the acute care setting.[8,9] Promising findings from ED patients in Taiwan[10] require validation and evaluation in US EDs.

1.2 | Importance

A validated risk stratification tool with high sensitivity and specificity for severe disease in patients diagnosed with seasonal influenza in the ED would substantially benefit patients and the broader health care system. Successful implementation of an effective risk stratification tool could potentially decrease unnecessary laboratory and radiographic testing in very low risk patients and limit hospital admissions in lower risk patients while helping identify those most at risk for severe outcomes.

1.3 | Goals of this investigation

In the present work, we sought to characterize a large cohort of patients diagnosed with seasonal influenza in an urban, academic medical center ED. We then worked to derive and validate a risk stratification tool that can predict severe disease resulting in intubation or death.

The Bottom Line

Seasonal influenza is a major public health concern that requires early identification and management of patients at risk of severe outcomes. In this single-center retrospective study, the authors developed a novel risk stratification tool, Predicting Intubation in seasonal Influenza Patients diagnosed in the ED (PIIPED) to predict the need for intubation or death among patients diagnosed with seasonal influenza in the emergency department. The PIIPED risk stratification tool had a high predictive ability, with an area under the receiver operating characteristic curve of 0.895 in the validation cohort. The PIIPED risk stratification tool may allow clinicians to recognize patients at high risk of severe outcomes.

2 | METHODS

2.1 | Design

This is a single-center retrospective cohort study. This study was approved by the institutional review board of the academic medical center, approval #201709155.

2.2 | Setting

The study was conducted at a large urban tertiary care academic ED that registers 83,500 individual patient encounters on average each year. The demographic breakdown of all patients evaluated in the studied ED between 2019 and 2022 is 55% female, 45% male, 55% black, 44% white, and <2% other self-identified race.

2.3 | Selection of subjects

In the derivation cohort, we included all patients with a positive clinical influenza test obtained during the course of their ED encounter between February 1, 2008 and March 31, 2018. Derivation cohort data were retrieved from the hospital's electronic medical record (EMR) on April 17, 2019. The validation cohort consisted of all patients with a positive influenza test obtained during the course of an ED visit between August 1, 2018 and April 30, 2020. Validation cohort data were pulled from the EMR on February 15, 2022. We collected validation cohort data after performing initial analysis and deriving the risk stratification tool. We excluded any subjects where the ED disposition listed in the EMR indicated that the subject was transferred to another hospital for any reason, left against the medical advice of the ED practitioner, or left without being seen in the ED despite the influenza test being performed while the patient was in triage. This ensured adequate

information about the index hospital stay was available in the EMR for all included subjects. Additional details about the data pull are found in the Supplementary Methods.

2.4 | Measurements

We assembled the following information obtained during each individual subject's ED encounter when available: age, sex, race, first recorded ED vital signs (including pulse oximetry value and the amount of oxygen administered), complete blood cell count results, basic metabolic panel results, blood lactate results, and chest radiography reports. Candidate predictor variables were chosen in a blinded fashion to outcome variables as a convenience of basic studies and findings commonly performed on influenza subjects in the ED. We included laboratory and chest radiography results for admitted subjects only if these tests were performed while the subject was physically located in the ED. We obtained comorbidity data by calculating Elixhauser comorbidity index values for each subject, which were used as a surrogate of past medical history. Complete details of the Elixhauser comorbidity index calculations are listed in the Supplementary Methods.

Radiologist reports for any ED-performed chest radiography exam during the index encounter were reviewed. The senior author evaluated all radiologist reports in the derivation cohort. They recorded any mention in the report of the presence or absence of a pleural effusion, the presence or absence of an infiltrate, and its character as multifocal (>1 infiltrate described by the reading radiologist) or unifocal (only 1 infiltrate described). The authors did not review chest radiograph images and were blinded to outcome information while abstracting radiologist reports. If the reading radiologist did not comment on infiltrates or the presence/absence of a pleural effusion in their written report, then this was coded as not reported. The first author independently evaluated and coded all chest radiography radiologist reports in the validation cohort. To cross-validate chest radiography coding, the first and senior author each reviewed 100 randomly selected chest radiography reports from the other cohort and agreement between the 2 reviewers was calculated using kappa.

2.5 | Outcomes

We collected the following outcomes for each subject: ED disposition (left against medical advice, left without being seen, discharged, transferred to another facility, admitted, admitted to ICU, died in ED), total hospital length of stay for admitted subjects, total ICU length of stay, ultimate hospital discharge status (in-hospital death, transfer to facility, discharge), use of mechanical ventilation, and total ventilator days. We evaluated the composite primary outcome of subjects who died during the index hospitalization or required intubation at any point during the index hospitalization. We defined intubation as any subject where the EMR indicated a positive "use of mechanical ventilation" field or any subject with any recorded length of ventilator days.

2.6 | Data analysis

Patient characteristics were assessed using frequencies (n [%]) for all categorical variables and median ± interquartile ranges (IQR) for continuous variables. The proportion of patients with the composite primary outcome (death and/or intubation) was calculated and predictors of death/intubation were identified using univariate and multivariate analysis. For univariate analysis, Fisher exact test, chi-square test, or univariate logistic regression analysis were performed for categorical variables and Mann–Whitney U or Wilcoxon tests were performed for continuous variables. Multivariable logistic regression analysis included age, sex, and race, as well as all variables with a P value < 0.05 in the univariate analysis.

To develop a risk stratification tool, we included all variables significantly associated with intubation or death in the univariate analysis that also exhibited clear and clinically relevant differences between median values or frequency between individuals who required intubation or died and those that did not. This included common laboratory studies that also had some established basis in the literature for predicting influenza severity.[11–15] We weighed the values in the resultant risk prediction tool based upon the multivariate analysis, providing 2 points for each factor associated with severe outcome in the multivariate analysis and 1 point for all factors associated with severe outcome in the univariate analysis. Cutoffs for oxygen saturation, respiratory rate, glucose, blood urea nitrogren, lactate, and red cell distribution width were set based upon comparisons of the median and IQR of values between the 2 severity groups as well as clinical practicality.

Area under the receiver operating curve (AUC) analysis, receiver operating characteristic curve graphs, 95% confidence intervals (CIs), and sensitivity/specificity values for the validation cohort were calculated and visualized using Prism software (Version 9.4.1). Sensitivity and specificity with 95% CIs were calculated for the derivation cohort with internal validation by bootstrapping using *proc survey select*. Descriptive, univariate, multivariate, and bootstrapping statistical analyses were performed using SAS 9.4 (SAS Inc., Cary, NC). Absolute risk and 95% CIs for the combined cohorts were calculated and visualized using Prism software (Version 9.4.1). Calibration plots were assembled by calculating predicted risk of outcome for each cohort using binomial logistic regression analysis in SPSS version 28.0.0.0 (IBM Corporation). Actual risk and 95% CIs of the primary outcome were then plotted against the predicted risk using Prism software (Version 9.4.1). All significance tests were performed using 2-tailed hypotheses and α of 0.05.

3 | RESULTS

The derivation cohort data pull from the EMR retrieved 2259 subjects (Figure 1). We excluded 62 subjects because they were transferred to another hospital, left against medical advice, or left the ED without being seen. One medical record represented a duplicate encounter, which was excluded from further analysis. Ultimately, we included 2196 subjects in the derivation cohort analysis. Seventy subjects in the
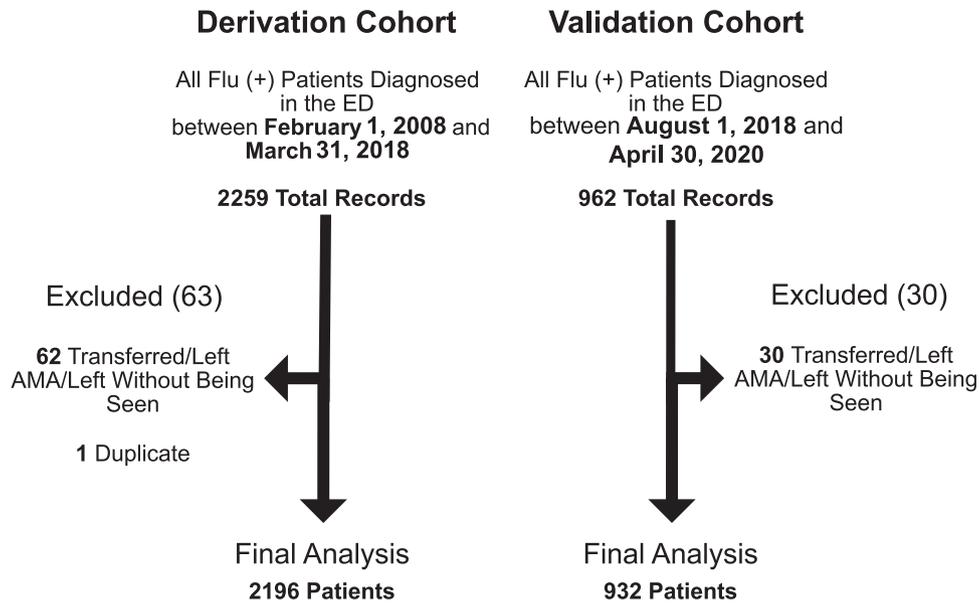
Derivation Cohort

All Flu (+) Patients Diagnosed
in the ED
between **February 1, 2008** and
March 31, 2018

2259 Total Records

Excluded (63)

62 Transferred/Left
AMA/Left Without Being
Seen

1 Duplicate

Final Analysis
2196 Patients

Validation Cohort

All Flu (+) Patients Diagnosed
in the ED
between **August 1, 2018** and
April 30, 2020

962 Total Records

Excluded (30)

30 Transferred/Left
AMA/Left Without Being
Seen

Final Analysis
932 Patients

FIGURE 1 Flow chart of subjects included and excluded in the derivation and validation cohorts. Abbreviations: AMA, against medical advice; ED, emergency department.

derivation cohort experienced the primary outcome of death or intubation. For the validation cohort, the EMR data pull retrieved 962 records (Figure 1). We excluded 30 subjects who were transferred to another hospital, left against medical advice, or left the ED without being seen. We ultimately analyzed 932 subjects in the validation cohort, including 21 who experienced the primary outcome of death or intubation. Chest radiography reviewers displayed excellent agreement as evidenced by kappa statistic (Table S1).

The median age of the derivation cohort was significantly higher than that of the validation cohort, but the demographic characteristics of the 2 cohorts were otherwise similar with respect to race and sex (Table 1). Both cohorts exhibited a preponderance of female subjects and subjects who reported their race as black, reflecting the overall demographic composition of the studied ED. There was a modest difference in the ICU admission frequency between the 2 cohorts; however, there was no difference in the primary outcome of death or intubation. To assess for potentially missed severe outcomes in study subjects discharged during the index hospital visit, we quantified return admissions within 3 days, 7 days, and 30 days to the same hospital or to any hospital in the 15-hospital health care system for all discharged subjects in the validation cohort (Table S2). There was no significantly increased frequency of return admissions in influenza positive subjects discharged from the studied ED (Table S2). Individual chart review of 18 validation cohort study subjects who returned to the studied ED and required hospital admission within 30 days of the index ED visit revealed that only 7 return admissions were related to the recent influenza infection. None of the 7 individuals were admitted to the ICU, intubated, or died on the second visit to the hospital. Only 1 of the 7 required supplemental oxygen administration. This individual was diagnosed with a secondary bacterial pneumonia 2 days after their index ED visit. They required 2 days of inpatient hospital care before discharge on oral antibiotics.

We performed a univariate analysis of how each measured variable affected the primary composite outcome of death or intubation in the derivation cohort (Table 2). Subjects who died or required intubation were significantly older than those with a less severe outcome. They were also more likely to have multifocal infiltrates and a pleural effusion on chest chest radiograph. They tended to have more respiratory distress at triage as indicated by higher respiratory rates and lower pulse oximetry readings. Indeed, several common laboratory studies performed in the ED were significantly different between those subjects who died or required intubation and those who did not. We also found that medical comorbidities associated with severe influenza infection as defined by the CDC[16] predicted death or intubation (Table 2).

We then performed multivariable logistic regression analysis including all significantly different variables from the univariate analysis along with age, sex, and race. We excluded neutrophil and monocyte counts from the multivariable logistic regression model due to the collinearity of these variables with total white blood cell count. The multivariable analysis revealed 4 variables significantly associated with death or intubation: the number of CDC-defined medical comorbidities, respiratory rate, the presence of a pleural effusion on chest radiograph, and the blood lactate level (Table 2).

The final model for the Predicting Intubation in seasonal Influenza Patients diagnosed in the ED (PIIPED) risk stratification tool (Figure 2) included a total of 9 factors and tests that are easily obtained and measured in the ED: (1) age, (2) past medical history, (3) pulse oximetry, (4) respiratory rate, (5) chest radiograph, (6) blood glucose concentration, (7) blood urea nitrogen concentration, (8) blood lactate concentration,

TABLE 1 Demographics.

Demographics	Derivation		Validation		Odds ratio (95% CI)
	N	%	N	%	
Age (years, mean, 95% CI)	(47.3)	(46.4–48.1)	(43.5)	(42.3–44.6)	
Sex					
Female	1253	57.1	522	56.0	1.04 (0.89–1.22)
Male	943	42.9	410	44.0	0.96 (0.82–1.12)
Race					
White	496	22.6	190	20.4	1.14 (0.94–1.37)
Black	1582	72.0	697	74.8	0.87 (0.73–1.03)
Other	118	5.4	45	4.8	1.12 (0.79–1.59)
ED disposition					
Admitted to hospital	858	39.1	301	32.3	1.34 (1.14–1.58)
Discharged from ED	1338	60.9	631	67.7	0.74 (0.63–0.87)
Outcome					
In-hospital death	17	0.8	4	0.4	1.81 (0.63–4.98)
Intubation during hospital stay	53	2.4	17	1.8	1.33 (0.76–2.34)
Composite of intubation or death	70	3.2	21	2.3	1.43 (0.88–2.30)
Required admission to ICU during hospital stay	66	3.0	51	5.5	0.54 (0.37–0.78)
Hospitalized with a total hospital length of stay of ≥4 days	151	6.9	80	8.6	0.79 (0.59–1.04)
Hospitalized with a total hospital length of stay ≥2 days but <4 days	238	10.8	94	10.1	1.08 (0.84–1.40)
Discharged from the emergency department after diagnosis, or admitted to the hospital for <2 days.	1671	76.1	686	73.6	1.14 (0.96–1.36)

Abbreviations: CI, confidence interval; ED, emergency department.

and (9) red cell distribution width. We also evaluated a simplified tool, the PIIPED triage model, which excluded components requiring blood laboratory testing and chest radiography imaging. The PIIPED triage model consisted of (1) age, (2) past medical history, (3) pulse oximetry, and (4) respiratory rate (Figure 2).

The receiving operator characteristic curve generated from the derivation cohort using the PIIPED tool had an AUC of 0.8988 (95% CI: 0.8695–0.9281, Figure 3). A PIIPED cutoff score of 3 or more exhibited high sensitivity for the prediction of intubation or death in a bootstrapped analysis of the derivation cohort, and a score of 9 or more was highly specific (Table 3). The PIIPED triage model revealed an AUC of 0.8518 (95% CI: 0.8180–0.8857) in the derivation cohort (Figure 3). A PIIPED triage cutoff score of 1 manifested very high sensitivity for prediction of intubation or death in a bootstrapped analysis of the derivation cohort, and a score of 5 or more was very specific for severe disease (Table 3). We validated the PIIPED and PIIPED triage models in the independently collected validation cohort. The AUC for the full PIIPED model in the validation cohort was 0.8948 (95% CI: 0.8534–0.9361) and PIIPED triage exhibited an AUC of 0.8233 (95% CI: 0.7632–0.8834, Figure 3). Score cutoffs in the unadjusted validation cohort analysis revealed high sensitivity and specificity for severe disease (Table 3). Subjects with a PIIPED score from 0 to 3 exhibited a very low actual risk of intubation or death in the combined derivation and validation cohorts (0.15%, 95% CI: 0.04%–0.44%,

Figure 4). Subjects with PIIPED triage scores of 0 or 1 also had very low risk of intubation or death in the combined cohort (0.13%, 95% CI: 0.02%–0.48%, Figure 4). Both the PIIPED and PIIPED triage models were well calibrated in both cohorts (Figure S1).

4 | LIMITATIONS

Though the results of our study are promising, there are several limitations. This study was retrospective, observational, and confined to a single center with a predominant population of subjects who are female and black. Prospective, multicenter validation must be performed to verify the wider applicability of our results and the PIIPED tools to other ED populations. Not all included subjects obtained chest chest radiography imaging and full laboratory workups in the ED due to the retrospective design. We used Elixhauser comorbidity index as a surrogate of past medical history, which may have limited the completeness of past medical history in some subjects. We did not have access to information about antiviral medications provided to subjects; therefore, we cannot assess the impact of these medications on outcomes in the present study. Finally, this single-center study was performed at an ED that triages non-critically ill pregnant patients who are more than 20 weeks gestation to a separate obstetric triage location for evaluation. Therefore, the present results may not necessarily

TABLE 2 Predictors of intubation and/or death—Derivation cohort (univariate and multivariate analyses).

	All other outcomes, N = 2126		Death or intubation, N = 70		Univariate odds ratio (95% CI)	Multivariate odds ratio (95% CI)
	N	%	N	%		
Demographics						
Age (median, IQR)	46	30–61	58	49–71	1.03 (1.02–1.04)	1.00 (0.98–1.03)
Sex						
Female	1214	57.1	39	55.7	Reference	Reference
Male	912	42.9	31	44.3	1.06 (0.66–1.71)	1.88 (0.70–5.08)
Race						
White	469	22.1	27	38.6	Reference	Reference
Black	1541	72.5	41	58.6	0.46 (0.28–0.76)	0.52 (0.20–1.34)
Other	116	5.4	2	2.8	0.30 (0.07–1.28)	–
Chest radiography findings (not performed/reported in 434)						
Clear	1357	80.0	33	50.0	Reference	Reference
Unifocal	187	11.0	12	18.2	2.64 (1.34–5.20)	1.36 (0.40–4.60)
Multifocal	152	9.0	21	31.8	5.68 (3.21–10.07)	1.38 (0.39–4.92)
Pleural effusion on chest radiography (not performed/reported in 459)						
No	1560	93.1	42	67.7	Reference	Reference
Yes	115	6.9	20	32.3	6.46 (3.67–11.37)	6.81 (2.34–19.83)
	Median	IQR	Median	IQR	Univariate odds ratio (95% CI)	Multivariate odds ratio (95% CI)
Vitals						
First temperature (°F)	99.7	98.4–101.1	99.2	98.1–100.8	0.83 (0.72–0.95)	0.77 (0.59–1.02)
First systolic blood pressure	132	119–148	134.5	118–155	1.00 (0.99–1.01)	
First diastolic blood pressure	80	72–89	79	67–90	1.00 (0.97–1.02)	
First pulse oximetry (%)	97	95–98	95	91–97	0.88 (0.85–0.92)	0.98 (0.89–1.07)
First respiratory rate	18	18–20	22	18–27	1.13 (1.09–1.18)	1.08 (1.00–1.16)
First heart rate	101	89–114	109.5	98–123	1.02 (1.01–1.04)	1.01 (0.98–1.03)
Labs						
White blood cells (WBC; thousand/mm^3)	6.8	5.2–9.0	9	6.1–12.7	1.08 (1.04–1.19)	1.04 (0.96–1.12)
Neutrophils (thousand/mm^3)	4.9	3.4–7.1	7.5	4.9–10.0	1.09 (1.04–1.14)	
Lymphocytes (thousand/mm^3)	0.9	0.6–1.4	0.8	0.4–1.4	1.18 (0.96–1.45)	
Monocytes (thousand/mm^3)	0.7	0.5–0.9	0.7	0.4–1.0	1.68 (1.17–2.41)	
Sodium (mmol/L)	137	135–140	138	135–141	1.03 (0.97–1.10)	
Bicarbonate (mmol/L)	25	22–27	25	22–28	0.99 (0.93–1.06)	
Creatinine (mg/dL)	1	0.8–1.2	1	0.8–1.5	1.05 (0.94–1.18)	
Blood urea nitrogen (BUN; mg/dL)	13	9–18	18	12–36	1.03 (1.02–1.04)	0.99 (0.96–1.01)
Glucose (mg/dL)	108	94–131	145.5	107–193	1.01 (1.00–1.01)	1.00 (0.99–1.01)
Lactate (mmol/L)	1.2	0.9–1.7	1.8	1.5–3.1	1.49 (1.24–1.80)	1.52 (1.01–2.28)
Red cell distribution width (RDW; %)	14.0	13.2–15.2	15.9	13.9–17.8	1.23 (1.14–1.33)	1.03 (0.83–1.28)
Number of CDC-defined influenza-relevant comorbidities	1	0–3	5	3–7	1.64 (1.51–1.79)	1.72 (1.37–2.16)

Abbreviations: CDC, Centers for Disease Control and Prevention; CI, confidence interval; IQR, interquartile range.

(A)

PIIPED Model	
Score Component	**Points**
Age ≥ 50	1
2 or more flu-relevant comorbid conditions	2
Oxygen saturation < 96%	1
Respiratory rate > 21	2
Multifocal opacities on chest x-ray	1
Pleural effusion on chest x-ray	2
Glucose >129	1
BUN > 17	1
Lactate ≥ 1.7	2
Red blood cell distribution width ≥ 15	1

PIIPED Triage Model	
Score Component	**Points**
Age ≥ 50	1
2 or more flu-relevant comorbid conditions	2
Oxygen saturation < 96%	1
Respiratory rate > 21	2

(B)

CDC flu-relevant comorbid conditions
Obesity - body mass index ≥ 40
Asthma or other chronic pulmonary disease
Heart disease (congestive heart failure, coronary disease, chronic arrhythmia)
Chronic neurologic and neurodevelopmental conditions (including previous stroke)
Blood disorders (sickle cell disease, chronic coagulopathy)
Chronic endocrine disorders (diabetes mellitus, thyroid disorders)
Chronic kidney disease of any stage
Chronic liver disease
Chronic immunosuppression (HIV infection, due to medications, autoimmunity)
Solid and hematologic malignancies
Metabolic disorders (inheritied metabolic disease and mitochondrial disorders)

FIGURE 2 Components of the model. (A) Individual components and weight for each component in the PIIPED model and the PIIPED triage model. (B) CDC-defined comorbid medical conditions that put individuals at risk for severe disease that are included in the PIIPED model. Abbreviations: BUN, blood urea nitrogen; CDC, Centers for Disease Control and Prevention; PIIPED, Predicting Intubation in seasonal Influenza Patients diagnosed in the ED.

TABLE 3 Sensitivity and specificity of full PIIPED model and the PIIPED triage model for predicting intubation or death.

	% (95% CI)		% (95% CI)	
	Derivation cohort[a]		Validation cohort[b]	
PIIPED	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Score = 3	97.3 (93.2–100)	53.3 (51.2–55.3)	100 (84.5–100)	60.8 (57.6–63.9)
Score = 6	78.7 (68.9–88.2)	83.4 (81.7–85.0)	71.4 (50.0–86.2)	84.7 (82.3–86.9)
Score = 9	34.3 (22.8–45.1)	96.9 (96.1–97.6)	23.8 (10.6–45.1)	97.0 (95.7–98.0)
	Derivation cohort[a]		Validation cohort[b]	
PIIPED triage	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Score = 1	100 (100–100)	31.5 (29.7–33.3)	100 (84.5–100)	38.5 (35.4–41.7)
Score = 3	92.8 (85.5–98.4)	62.6 (60.4–64.8)	85.7 (65.4–95.0)	69.5 (66.4–72.4)
Score = 5	51.2 (38.8–63.6)	90.9 (89.8–92.1)	33.3 (17.2–54.6)	92.5 (90.6–94.1)

Abbreviations: CI, confidence interval; PIIPED, Predicting Intubation in seasonal Influenza Patients diagnosed in the ED.
[a]Derivation cohort values calculated from a bootstrapping analysis of 1000 random samples of the derivation cohort.
[b]Validation cohort values calculated on the total 932-subject cohort, without bootstrapping.
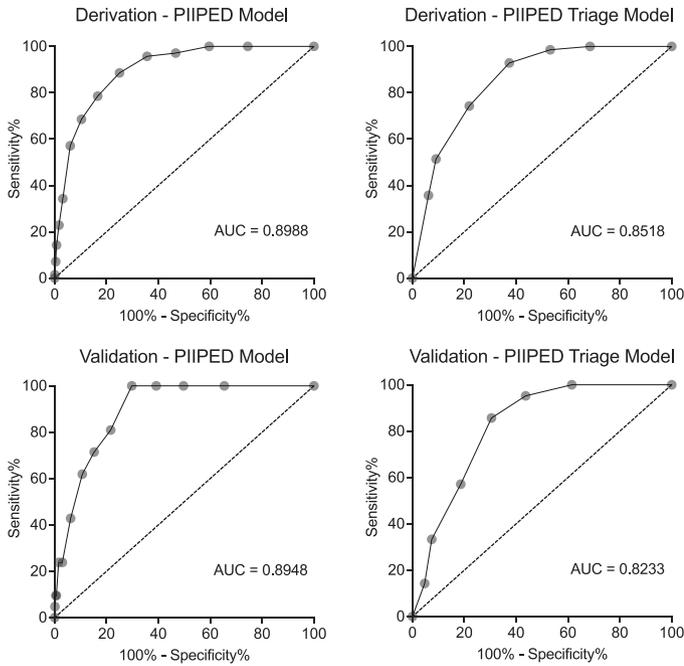
FIGURE 3 Receiver operating characteristic curves for the PIIPED and PIIPED triage models in both the derivation (upper panels) and validation (lower panels) cohorts. All reported AUC values are statistically significant (P < 0.0001). Abbreviations: AUC, area under the receiver operating characteristic curve; PIIPED, Predicting Intubation in seasonal Influenza Patients diagnosed in the ED.
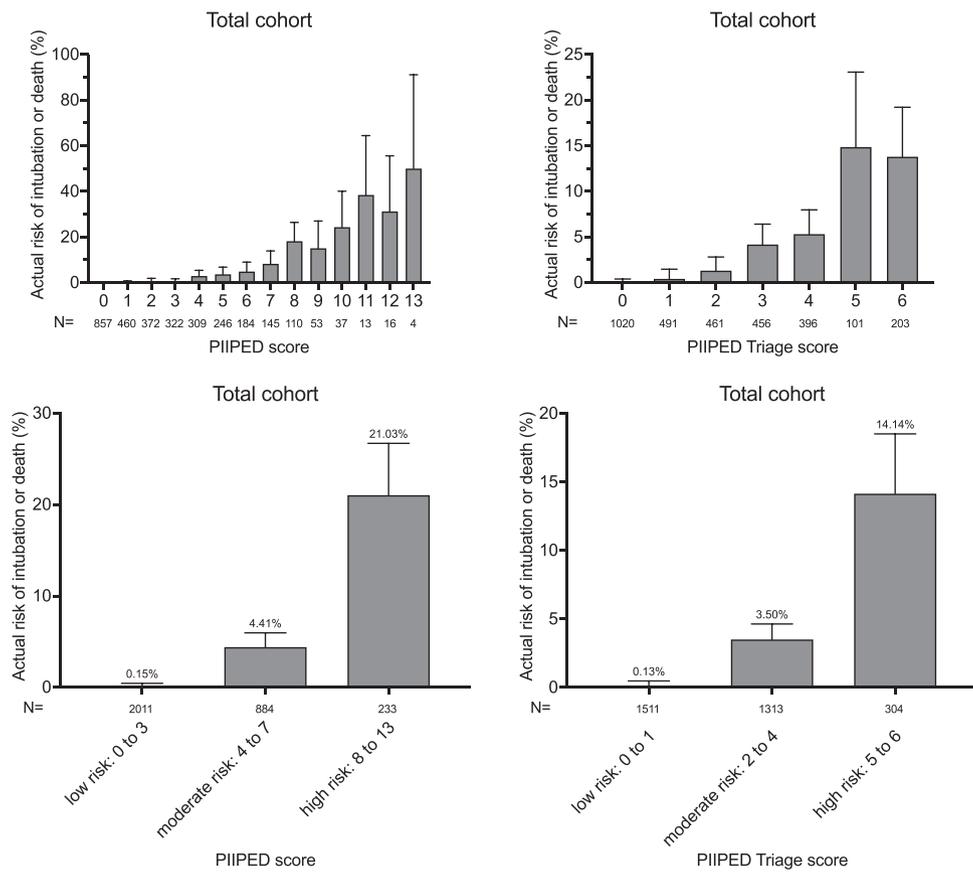

FIGURE 4 Actual risk of intubation or death in the total combined derivation and validation cohorts (N = 3128). Top panels report mean risk and 95% confidence intervals for each individual PIIPED (left) or PIIPED triage (right) score. Number of subjects in the cohort with each reported score is listed below the appropriate column (N). Bottom panels show mean risk and 95% confidence intervals for the PIIPED score (left) and PIIPED triage score (right) grouped into low-risk, moderate-risk, and high-risk groups. Mean risk value is reported above each column. Abbreviation: PIIPED, Predicting Intubation in seasonal Influenza Patients diagnosed in the ED.

apply to pregnant influenza patients who are known to be at increased risk for severe disease.

5 | DISCUSSION

Seasonal influenza is frequently encountered and diagnosed in the ED. In the absence of a reliable and validated risk stratification tool for these patients, emergency clinicians lack robust or standardized objective methods to assist in translating clinical findings into safe dispositions. This may lead to unnecessary testing and hospital admissions in some individuals at very low risk for severe disease.

The performance of the PIIPED risk stratification tool shows promise in filling this current void. PIIPED uses information routinely obtained over the course of an ED visit and detects patients at risk for death or intubation with high sensitivity. One of the most promising aspects of this study is the preservation of tool performance characteristics with the PIIPED triage tool that excludes any lab or imaging components. Laboratory and imaging evaluation add substantial length of stay to a standard ED visit. Quick identification of low-risk patients with non-concerning vital signs and no more than one influenza-relevant comorbid condition (PIIPED triage score of ≤1) could limit laboratory or imaging evaluation in this group, improve ED throughput, and reduce costs during influenza season. Patients with 2 or more influenza-relevant comorbid conditions and those who otherwise require additional workup due to their clinical picture could be further risk-stratified with the full PIIPED. The possibility exists that some of these individuals may still be deemed low risk (full PIIPED score ≤3) and might be able to avoid admission to hospital, if appropriate.

The PIIPED and PIIPED triage risk stratification tools perform substantially better than existing tools that demonstrate limited applicability to this patient population.[4–9] If appropriately validated, PIIPED and PIIPED triage will assist emergency clinicians determine which patients with a positive influenza test during ED evaluation are most at risk for progression to severe disease. Prospective validation is needed to determine whether these 2 novel tools can reliably identify those most at risk for severe disease and expedite care for low-risk patients during influenza season.

AUTHOR CONTRIBUTIONS

CONFLICT OF INTEREST STATEMENT

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Pajor MJ, Munigala S, Reynolds D, et al. Predicting severe disease in patients diagnosed with seasonal influenza in the emergency department. *JACEP Open*. 2023;4:e13045. https://doi.org/10.1002/emp2.13045

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