

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	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
<b>AUTHORS</b>	Wang, Te-Hao; Jheng, Jing-Cheng; Tseng, Yen-Ting; Chen, Li-Fu; Chung, Jui-Yuan

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Huang, Chien-Cheng National Cheng Kung University
<b>REVIEW RETURNED</b>	30-Sep-2020

<b>GENERAL COMMENTS</b>	<ol style="list-style-type: none"><li>1. The management of missing data and information was not mentioned; please include an explanation in the method section.</li><li>2. You did mention that your population may be unusual in comparison to other hospitalized groups of older people, however, you did not comment on the local cause of the high prevalence of COPD in your population.</li><li>3. It would be useful to include a comparison of other available scoring systems, such as PSI, APACHE II Score and SOFA score, as the utility of these data would be much more significant if NEWS performs similarly to other more complicated scoring systems.</li><li>4. Whether the low flu vaccination rate would affect the research outcome is not discussed in this study, as flu vaccination is reported to be effective in preventing illness, hospitalization and death.</li><li>5. The number of included patients over 5 years is relatively low without explanation as of why; is it because local practice relies more on clinical diagnosis of flu rather than swabs?</li><li>6. The false positive and negative swab results are mentioned, however, the relevant numbers for their specific test were not specified.</li><li>7. Although this article is well written, some minor grammar mistakes were found: p. 7, line 169: "oseltamivir" and "zanamivir" should start with capital letters.</li><li>8. It would be better to adjust the sentence "NEWS had an equivalent or even superior value for quick sequential organ failure assessment and SIRS assessment in predicting mortality and ICU admission" in the p.9, line 202-204 to "NEWS had an equivalent or even superior value than quick sequential organ failure assessment score and SIRS criteria</li></ol>
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	in predicting mortality and ICU admission."
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<b>REVIEWER</b>	Nannan Panday, Rishi S Lee Kong Chian School of Medicine
<b>REVIEW RETURNED</b>	26-Nov-2020

<b>GENERAL COMMENTS</b>	<p><b>INTRODUCTION:</b></p> <ul style="list-style-type: none"> <li>- Please report some numbers on hospitalizations in other countries</li> <li>- Line 87-92: Please add a reference or add how this selection was made</li> </ul> <p><b>METHODS:</b></p> <ul style="list-style-type: none"> <li>- Lines 124-128: Why did you use data from 2010 to 2015? That seems like quite some time ago. Please elaborate further.</li> <li>- Please elaborate a bit more about the power calculation (i.e. 0.8, allows you to detect what difference?)</li> </ul> <p><b>RESULTS:</b></p> <ul style="list-style-type: none"> <li>- Line 174-178, you mention that the GCS is lower. Please use a more common used score for the ICU patients to compare this (e.g. APACHE score)</li> <li>- The variables that you report in lines 179-186 seem to be selected randomly. Please elaborate/justify why these were selected</li> <li>- Lines 187, the use of antiviral medication also is one of the inclusion criteria it seems. Please adjust accordingly in the methods section.</li> <li>- Line 202: Explain what the Youden index is in your results section</li> </ul> <p><b>DISCUSSION:</b></p> <p>Line 219-220: You have missed an important systematic review on this subject. I feel your manuscript is not complete without this paper. Please add it to improve the quality of your paper. The manuscript is entitled: "Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review", publish in the European Journal of Internal Medicine.</p> <ul style="list-style-type: none"> <li>- Why did you not consider using the NEWS2? Please elaborate in your discussion section</li> <li>- Line 267: How many patients in your sample had in hinsight false-positive or false-negative test results?</li> <li>- A section on the strengths of your study is missing</li> </ul> <p><b>CONCLUSION:</b></p> <p>You only conclude something, but I am missing a recommendation in this section</p>
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<b>REVIEWER</b>	Spångfors, Martin Centralsjukhuset Kristianstad Anestesi
<b>REVIEW RETURNED</b>	16-Jan-2021

<b>GENERAL COMMENTS</b>	I thank the authors for the opportunity to read and revise
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this manuscript. The research question is of great interest not only in these pandemic times but due to the fact that the old and frail often is at greater risk of catastrophic events.

However, I found some major concerns in your manuscript.

There were 49 patients in the ICU-group but only 15 had a NEWS of 8 or more. This means that the majority of patients that were admitted to the ICU were missed by using a cut off at 8 points. This does not justify your conclusion in the article.

The authors state that a high specificity is a better trade off than a high sensitivity. This trade off will however result in in the apparent risk that patients at risk will be missed. In the EWS literature it is more common to reach for a high sensitivity since missing patients can lead to catastrophic events like cardiac arrests or unexpected death. Furthermore, you need to specify both the sensitivity and the specificity.

In the supplementary table 1 the V, P, U in the level of consciousness only generates two points instead of three points. If you have used this faulty scoring in your analyses, you need to recalculate them.

Minor revisions:

Line 37. Repeated use of "We" in this section. Consider revising to "Demographic data, vital signs, medical history, subtype of influenza, national early warning score (NEWS), and outcomes was analyzed."

Line 39. It is unclear what you mean by "outcomes". Consider specifying.

Line 39. Consider revising "accuracy" to ability.

Line 44. Revise to "predicted"

Line 48. Consider revising to "A NEWS  $\geq$  8 is associated with ICU-admission and may help to triage elderly patients with influenza infections during the flu epidemic season."

Line 58. Revise to "The high specificity of NEWS  $\geq$  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"

Line 76. Revise to "Of all the age groups, the elderly are at the highest risk of developing serious complications from influenza"

Line 83. When you write dispositioning do you mean triage? If so please revise to triage in the manuscript.

	<p>Line 87. Revise to "There are several scoring systems in use to predict poor prognosis among elderly patients with influenza infections, for....."</p> <p>Line 92. Revise to "Patients scoring <math>\geq 3</math> points on this scale should be considered for ICU admission"</p> <p>Line 95. Triage?</p> <p>Line 96. Revise to "which can lead to worsening the overcrowding."</p> <p>Line 101. Altered</p> <p>Line 106. Revise to "by a clinical team with critical care competence and may be transferred to a higher-dependency care area"</p> <p>Line 125. Revise to "fulfilling the following criteria, were included in the study....."</p> <p>Line 132. Revise to "(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."</p> <p>Line 140. Revise to "The study endpoint was admission to the ICU."</p> <p>Line 143. Revise to "A retrospective medical record review was performed on the patients who fulfilled the inclusion criteria."</p> <p>Line 150. Consider changing "setting" to "design"</p> <p>Line 154. Please state if the sample size calculation was performed a priori or not?</p> <p>Line 178. Please report the GCS in the non-ICU group.</p> <p>Line 181. Please report the WBC and CRP in the non-ICU group.</p> <p>Line 192. Revise to "The ICU group had a higher mortality percentage (21.7%) than the non-ICU group (3.4%)."</p> <p>Line 198-200 needs revision to clarify</p> <p>In table 3 you should specify both the unadjusted and adjusted results.</p>
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#### VERSION 1 – AUTHOR RESPONSE

# Reviewer 1:

1. The management of missing data and information was not mentioned; please include an explanation in the method section.

Response: In response to the reviewer's comment, any required variable that is not recorded in the patient's medical chart will be marked negative and eventually be excluded. We added "Required data that is not recorded in the patient's medical chart was considered negative, and the patient will be eventually excluded." in the Method section (line 137~139) of the revised manuscript to explain this issue.

2. You did mention that your population may be unusual in comparison to other hospitalized groups of older people, however, you did not comment on the local cause of the high prevalence of COPD in your population.

Response: In response to the reviewer's comment, we added "The high prevalence of chronic obstructive pulmonary disease (COPD) in this study, compared to 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." in the Discussion section (line 273~276) of the revised manuscript. Additional reference is also listed in the revised manuscript: "Wang YC, Lin JM, Li CY, et al. Prevalence and risks of chronic airway obstruction: a population cohort study in Taiwan. *Chest* 2007;131:705-10."

3. It would be useful to include a comparison of other available scoring systems, such as PSI, APACHE II Score and SOFA score, as the utility of these data would be much more significant if NEWS performs similarly to other more complicated scoring systems.

Response: Thank you for the reviewer's comment, the aim of our study is to identify the accuracy of qSOFA score for mortality prediction in geriatric patients with influenza infection; perhaps in the future, if you agree, we could conduct a research in comparison of qSOFA score performance with other available scoring systems.

4. Whether the low flu vaccination rate would affect the research outcome is not discussed in this study, as flu vaccination is reported to be effective in preventing illness, hospitalization and death.

Response: In response to the reviewer's comment, the mortality benefits of influenza vaccination in elderly people is still controversial. We added "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. Further researches are needed to clarify this issue." in the Discussion section (line 277~280) of the revised manuscript. Additional reference is also listed in the revised manuscript: "Simonsen L, Taylor RJ, Viboud C, et al. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *Lancet Infect Dis* 2007; 7:658-66."

5. The number of included patients over 5 years is relatively low without explanation as of why; is it because local practice relies more on clinical diagnosis of flu rather than swabs?

Response: In response to the Reviewer's comment, the low number of included patients over 5 years is because of local practice relies more on flu swabs rather than clinical diagnosis. Furthermore, our study defines influenza infection as positive influenza pharyngeal or throat swab test.

6. The false positive and negative swab results are mentioned, however, the relevant numbers for their specific test were not specified.

Response: In response to the Reviewer's comment, we added the following in the revised manuscript: "we used BD Directigen Flu A+B Kit for influenza test, and according to literature review, BD Directigen Flu 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 B." in the Method section (line 114~119) of the revised manuscript. Additional reference is also listed in the revised manuscript: "Gröndahl B, Puppe W, Weigl J, et al. Comparison of the BD Directigen Flu A+B Kit and the Abbott TestPack RSV with a multiplex RT-PCR ELISA for rapid detection of influenza viruses and respiratory syncytial virus. Clin Microbiol Infect. 2005 Oct;11(10):848-50"

7. Although this article is well written, some minor grammar mistakes were found: p. 7, line 169: "oseltamivir" and "zanamivir" should start with capital letters.

Response: In response to the Reviewer's comment, we agree with the reviewer, and adjusted "oseltamivir" and "zanamivir" to "Oseltamivir" and "Zanamivir" in the revised manuscript (line 185).

8. It would be better to adjust the sentence "NEWS had an equivalent or even superior value for quick sequential organ failure assessment and SIRS assessment in predicting mortality and ICU admission" in the p.9, line 202-204 to "NEWS had an equivalent or even superior value than quick sequential organ failure assessment score and SIRS criteria in predicting mortality and ICU admission"

Response: In response to the Reviewer's comment, we agree with the reviewer, and adjusted the sentence to "NEWS had an equivalent or even superior value than quick sequential organ failure assessment score and SIRS criteria in predicting mortality and ICU admission" in the revised manuscript (line 232~234).

#### #Reviewer 2:

1. Please report some numbers on hospitalizations in other countries

Response: In response to the Reviewer's comment, we added "Meanwhile, up to over 30,000 excess hospitalizations per year was noted in France, Germany, Italy, United Kingdom and Ukraine during the seasonal influenza pandemics." in the Introduction section (line 62~64) of the revised manuscript to strengthen this issue. We also added "Gasparini R, Amicizia D, Lai PL, Panatto D. Clinical and socioeconomic impact of seasonal and pandemic influenza in adults and the elderly. Hum Vaccin Immunother. 2012 Jan;8(1):21-8." in the Reference section of the revised manuscript.

2. Line 87-92: Please add a reference or add how this selection was made

Response: In response to the Reviewer's comment, we added "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  $\geq$  7) should be assessed immediately by a clinical team capable of critical care and may be transferred to a higher-dependency care area" in the Introduction section (line 88~93) of the revised manuscript to clarify this issue. We also revised reference 8 to "Hawkes N. Royal College recommends national system to recognize deteriorating patients. BMJ. 2012;345" in the Reference section of the revised manuscript.

3. Lines 124-128: Why did you use data from 2010 to 2015? That seems like quite some time ago. Please elaborate further.

Response: In response to the Reviewer's comment, we have published several articles about the geriatric influenza infection issue since 2018, such as "Geriatric influenza death (GID) score: a new tool for predicting mortality in older people with influenza in the emergency department", "Shock index predicted mortality in geriatric patients with influenza in the emergency department" and "Quick-SOFA score to predict mortality among geriatric patients with influenza in the emergency department" by using the data collected from 2010 to 2015 in the emergency department of Cathay General Hospital. However, we have never conduct a study about the use of early warning system in dispositioning elderly patients with influenza infection via the database. Furthermore, under the covid-19 pandemic, we think it is crucial to utilize medical resources wisely by using an accurate and precise tool, such as National Early Warning Score; therefore, we conducted this study to delineate this issue.

4. Please elaborate a bit more about the power calculation (i.e. 0.8, allows you to detect what difference?)

Response: In response to the Reviewer's comment, we calculated the power of this study to confirm whether the study sample size (n=409) was sufficient to analyze the current issue. We therefore adjusted "The statistical power of this study was 0.80 calculated via G-power 3.0, which indicate sufficient sample size to analyze this issue" in the Method section (line 147) in the revised manuscript to clarify this issue.

5. Line 174-178, you mention that the GCS is lower. Please use a more common used score for the ICU patients to compare this (e.g. APACHE score)

Response: In response to the Reviewer's comment, we actually meant Glasgow Coma Scale, we therefore adjusted the sentence to "Furthermore, consciousness level, GCS, was lower in the ICU group at  $12.6 \pm 3.8$ , with a p value  $< 0.01$ ." in the Result section (line 172~174) of the revised manuscript to clarify this issue.

6. The variables that you report in lines 179-186 seem to be selected randomly. Please elaborate/justify why these were selected

Response: In response to the Reviewer's comment, we addressed the variables according to the order of table 1. We added "Vital signs showed..." and "While the laboratory data showed higher white blood cell count and CRP level in the ICU group, at  $12.8 \pm 6.4$   $10^3$  /mm<sup>3</sup> and  $12.5 \pm 10.8$  mg/dl, respectively." in the Result section (line 169~177) of the revised manuscript to justify this issue.

7. Lines 187, the use of antiviral medication also is one of the inclusion criteria it seems. Please adjust accordingly in the methods section.

Response: In response to the Reviewer's comment, we added "(3) antiviral therapy with either Oseltamivir or Zanamivir within 24-hours of the diagnosis of influenza infections." in the Method section (line 114~115) of the revised manuscript to clarify this issue.

8. Line 202: Explain what the Youden index is in your results section

Response: In response to the Reviewer's comment, the Youden's indices for NEWS was 0.32. We added "the Youden's index of NEWS was 0.32" in the Result section (line 196)

of the revised manuscript to explain this issue.

9. Line 219-220: You have missed an important systematic review on this subject. I feel your manuscript is not complete without this paper. Please add it to improve the quality of your paper. The manuscript is entitled: "Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review", publish in the European Journal of Internal Medicine.

Response: In response to the Reviewer's comment, we agree with the reviewer that "Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review" should be added to improve the quality of our study, we therefore added "a literature review conducted by Nannan Panday RS and colleagues showed that ICU admission among ED patients was best predicted by NEWS" in the Discussion section (line 237~238) of the revised manuscript to clarify this issue. We also added "Nannan Panday RS, Minderhoud TC, Alam N, Nanayakkara PWB. Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): A narrative review. Eur J Intern Med. 2017 Nov;45:20-31." in the Reference section of the revised manuscript.

10. Why did you not consider using the NEWS2? Please elaborate in your discussion section

Response: In response to the Reviewer's comment, NEWS2 was designed to improve safety for patients with hypercapnic respiratory failure, with SpO2 adjustments. However, a multi-center retrospective observational study, conducted in the United Kingdom, which identified 48,898 patients, showed that NEWS2 do not improve discrimination of adverse outcomes in patients with type 2 respiratory failure, while compared to the original NEWS. Furthermore, a Danish study also showed similar result with decreased sensitivity for 48-hour mortality and intensive care unit (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. We therefore choose NEWS rather than NEWS2. We added "We consider NEWS instead of NEWS2 to identify intensive care unit admission among elderly patients with influenza infections in the emergency department because several studies showed NEWS2 non-superior to NEWS in discriminating patients with adverse outcomes. NEWS2 was originally designed to improve safety for patients with hypercapnic respiratory failure, with SpO2 adjustments. However, a multi-center retrospective observational study, conducted in the United Kingdom, which identified 48,898 patients, showed that NEWS2 do not improve discrimination of adverse outcomes in patients with type 2 respiratory failure, while compared to the original NEWS. Furthermore, a Danish study also showed similar result with decreased sensitivity for 48-hour mortality and intensive care unit (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." in the Discussion section (line 209~221) of the revised manuscript to elaborate this issue. We also added "Pimentel MAF, Redfern OC, Gerry S, Collins GS, Malycha J, Prytherch D, Schmidt PE, Smith GB, Watkinson PJ. A comparison of the ability of the National Early Warning Score and the National Early Warning Score 2 to identify patients at risk of in-hospital mortality: A multi-centre database study. Resuscitation. 2019 Jan;134:147-156" and "Pedersen NE, Rasmussen LS, Petersen JA, Gerds TA, Østergaard D, Lippert A. Modifications of the National Early Warning Score for patients with chronic respiratory disease. Acta Anaesthesiol Scand. 2018 Feb;62(2):242-252. in the Reference section of the revised manuscript.

"



11. Line 267: How many patients in your sample had in hindsight false-positive or false-negative test results?

Response: In response to the Reviewer's comment, as Reviewer #1 had brought out a similar question, we added the following in the revised manuscript: "we used BD Directigen Flu A+B Kit for influenza test, and according to literature review, BD Directigen Flu 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 B." in the Method section (line 115~119) of the revised manuscript. Additional reference is also listed in the revised manuscript: "Gröndahl B, Puppe W, Weigl J, et al. Comparison of the BD Directigen Flu A+B Kit and the Abbott TestPack RSV with a multiplex RT-PCR ELISA for rapid detection of influenza viruses and respiratory syncytial virus. Clin Microbiol Infect. 2005 Oct;11(10):848-50"

12. A section on the strengths of your study is missing

Response: In response to the Reviewer's comment, we added "the strength of this study is that this is 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." in the Discussion section (line 284~286) of the revise manuscript to clarify this issue.

13. You only conclude something, but I am missing a recommendation in this section

Response: In response to the Reviewer's comment, we added "In conclusion, NEWS  $\geq$  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 flu pandemic season, and the limited medical resources may be reserved to the actual critical patients." in the Conclusion section (line 302~305) of the revised manuscript to clarify this issue.

#Reviewer 3:

1. There were 49 patients in the ICU-group but only 15 had a NEWS of 8 or more. This means that the majority of patients that were admitted to the ICU were missed by using a cut off at 8 points. This does not justify your conclusion in the article.

Response: In response to the Reviewer's comment, we agree with the reviewer, however, this (the majority of patients that were admitted to the ICU were missed by using a cut off at 8 points) is due to the high specificity setting of NEWS, which may benefit in lower false-positive rate, and could further avoid unnecessary ICU admission during the flu epidemic season. We therefore adjusted "In conclusion, NEWS  $\geq$  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 flu pandemic season, and consequence in reserving medical resources for the actual critical patients." in the Conclusion section (line 302~305) of the

revised manuscript to clarify this issue.

2. The authors state that a high specificity is a better trade off than a high sensitivity. This trade off will however result in the apparent risk that patients at risk will be missed. In the EWS literature it is more common to reach for a high sensitivity since missing patients can lead to catastrophic events like cardiac arrests or unexpected death. Furthermore, you need to specify both the sensitivity and the specificity.

Response: In response to the Reviewer's comment, we agree with the reviewer that high specificity may miss out patients at risk and result in catastrophic events like cardiac arrests or unexpected death. However, in the setting of high sensitivity, the false positive rate may increase during the pandemic season, resulting in excessive unnecessary ICU admission, and eventually crowd out the actual critical patients. In addition, the purpose of this study is to avoid unnecessary ICU admission during the pandemic season. Perhaps the most ideal method to solve this issue is to develop a screening tool with both high sensitivity and specificity. We added "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" and "As medical resources are usually deficient during the flu epidemic season, it is crucial to avoid unnecessary ICU admissions and ensure proper medical resource utilization" in the Discussion section (line 243~246) of the revised manuscript to clarify this issue.

3. In the supplementary table 1 the V, P, U in the level of consciousness only generates two points instead of three points. If you have used this faulty scoring in your analyses, you need to recalculate them.

Response: In response to the Reviewer's comment, we calculated the level of consciousness by alert = 0; confusion, voice, pain, and unresponsive = 3. However, we make an error while creating supplementary table 1. We therefore adjusted "alert = 0; confusion, voice, pain, and unresponsive = 3." in the revised supplementary table 1.

4. Line 37. Repeated use of "We" in this section. Consider revising to "Demographic data, vital signs, medical history, subtype of influenza, national early warning score (NEWS), and outcomes was analyzed."

Response: In response to the Reviewer's comment, we revised the sentence "Demographic data, vital signs, medical history, subtype of influenza, national early warning score (NEWS), and outcomes were analyzed." in line 37-38. of the revised manuscript.

5. Line 39. It is unclear what you mean by "outcomes". Consider specifying.

Response: In response to the Reviewer's comment, we added "(mortality)" in line 39. of the revised manuscript to clarify this issue.

6. Line 39. Consider revising "accuracy" to ability.

Response: In response to the Reviewer's comment, we revised the word "ability" in line 39. of the revised manuscript.

7. Line 44. Revise to "predicted"

Response: In response to the Reviewer's comment, we revised the word "predicted" in line 44. of the revised manuscript.

8. Line 48. Consider revising to "A NEWS  $\geq$  8 is associated with ICU-admission and may help to triage elderly patients with influenza infections during the flu epidemic season."  
Response: In response to the Reviewer's comment, we revised the sentence "A NEWS  $\geq$  8 is associated with ICU-admission and may help to triage elderly patients with influenza infections during the flu epidemic season." in line 46-48. of the revised manuscript.

9. Line 58. Revise to "The high specificity of NEWS  $\geq$  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"  
Response: In response to the Reviewer's comment, we revised the sentence "The high specificity of NEWS  $\geq$  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" in line 50-51. of the revised manuscript.

10. Line 76. Revise to "Of all the age groups, the elderly are at the highest risk of developing serious complications from influenza"  
Response: In response to the Reviewer's comment, we revised the sentence "Of all the age groups, the elderly are at the highest risk of developing serious complications from influenza" in line 57-58. of the revised manuscript.

11. Line 83. When you write dispositioning do you mean triage? If so please revise to triage in the manuscript.  
Response: In response to the Reviewer's comment, we added the sentence "(discharge, admission to ward or ICU)" in line 66. of the revised manuscript to clarify this issue.

12. Line 87. Revise to "There are several scoring systems in use to predict poor prognosis among elderly patients with influenza infections, for....."  
Response: In response to the Reviewer's comment, we revised the sentence "There are several scoring systems in use to predict poor prognosis among elderly patients with influenza infections" in line 70-71. of the revised manuscript.

13. Line 92. Revise to "Patients scoring  $\geq$  3 points on this scale should be considered for ICU admission"  
Response: In response to the Reviewer's comment, we revised the sentence "Patients scoring  $\geq$  3 points on this scale should be considered for ICU admission" in line 76. of the revised manuscript.

14. Line 95. Triage?  
Response: In response to the Reviewer's comment, we added the sentence "(discharge, admission to ward or ICU)" in line 78. of the revised manuscript to clarify this issue.

15. Line 96. Revise to "which can lead to worsening the overcrowding."  
Response: In response to the Reviewer's comment, we revised the sentence "which can lead to worsening the overcrowding" in line 84. of the revised manuscript.

16. Line 101. Altered  
Response: In response to the Reviewer's comment, we revised the word "altered" in line 84. of the revised manuscript.

17. Line 106. Revise to "by a clinical team with critical care competence and may be transferred to a higher-dependency care area"  
Response: In response to the Reviewer's comment, we revised the sentence "by a clinical team with critical care competence and may be transferred to a higher-

dependency care area" in line 90-91. of the revised manuscript.

18. Line 125. Revise to "fulfilling the following criteria, were included in the study....."  
Response: In response to the Reviewer's comment, we revised the sentence "fulfilling the following criteria, were included in the study" in line 108-109. of the revised manuscript.

19. Line 132. Revise to "(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."  
Response: In response to the Reviewer's comment, we revised the sentence "(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." in line 121-123. of the revised manuscript.

20. Line 140. Revise to "The study endpoint was admission to the ICU."  
Response: In response to the Reviewer's comment, we revised the sentence "The study endpoint was admission to the ICU" in line 130. of the revised manuscript.

21. Line 143. Revise to "A retrospective medical record review was performed on the patients who fulfilled the inclusion criteria."  
Response: In response to the Reviewer's comment, we revised the sentence "A retrospective medical record review was performed on the patients who fulfilled the inclusion criteria" in line 134-135. of the revised manuscript.

22. Line 150. Consider changing "setting" to "design"  
Response: In response to the Reviewer's comment, we revised the word "design" in line 143. of the revised manuscript.

23. Line 154. Please state if the sample size calculation was performed a priori or not?  
Response: In response to the Reviewer's comment, we revised the word "priori" in line 147. of the revised manuscript.

24. Line 178. Please report the GCS in the non-ICU group.  
Response: In response to the Reviewer's comment, we added "than the non-ICU group at  $14.2 \pm 2.0$ " in line 173. of the revised manuscript.

25. Line 181. Please report the WBC and CRP in the non-ICU group.  
Response: In response to the Reviewer's comment, we added "than the non-ICU group, at  $10.3 \pm 5.7$   $10^3$  /mm<sup>3</sup> and  $7.7 \pm 10.0$  mg/d" in line 179. of the revised manuscript.

26. Line 192. Revise to "The ICU group had a higher mortality percentage (21.7%) than the non-ICU group (3.4%)."  
Response: In response to the Reviewer's comment, we revised the sentence "The ICU group had a higher mortality percentage (21.7%) than the non-ICU group (3.4%)." in line 188-189. of the revised manuscript.

27. Line 198-200 needs revision to clarify

Response: In response to the Reviewer's comment, we revised the sentence "NEWS has also been used to identify early cardiac arrest..." in line 198. of the revised manuscript to clarify this issue.

28. In table 3 you should specify both the unadjusted and adjusted results.

Response: In response to the Reviewer's comment, we added the unadjusted result in the table 3 of the revised manuscript.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Spångfors, Martin Centralsjukhuset Kristianstad Anestesi
<b>REVIEW RETURNED</b>	12-Mar-2021
<b>GENERAL COMMENTS</b>	Thank you for the review of your paper. It has improved substantially.