PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Efficacy of prehospital National Early Warning Score to predict outpatient disposition at an emergency department of a Japanese tertiary hospital: a retrospective study
AUTHORS	Endo, Takuro; Yoshida, Toru; Shinozaki, Tomohiro; Motohashi, Takako; Hsu, Hsiang-Chin; Fukuda, Shunsuke; Tsukuda, Jumpei; Naito, Takaki; Morisawa, Kenichiro; Shimozawa, Nobuhiko; Taira, Yasuhiko; Fujitani, Shigeki

VERSION 1 – REVIEW

REVIEWER	Win Sen Kuan National University Health System, Singapore
REVIEW RETURNED	26-Oct-2019

GENERAL COMMENTS	Thank you for the opportunity to review the manuscript entitled "Prehospital national early warning score predicts outpatient disposition at the Emergency Department in a Japanese tertiary hospital". The study addresses a unique patient population, i.e. a rapidly aging population in Asia, where the proportion of elderly are one of the highest in the world. Many other developed countries are approaching such a demographic and thus the results may still be relevant to those countries in years to come. The results of this study add to the literature on the utility of NEWS across various settings and populations. The manuscript is largely well-written with easy readability and minor grammatical, spelling, punctuation and typographical errors. For example, the figure for proportion aged 65 years and higher in Hong Kong is missing (line 58). What is the emergency department load of the study site? This would determine the proportion of patients conveyed by ambulance versus those who went to the emergency department on their own. Certain terminology e.g. "sick call" (line 33) should be described more clearly in the Methods or Results as the phrase carries different connotations in different countries. While the authors acknowledge limitations in the retrospective and single-centre nature of the study, they should also elaborate on the almost 20% incomplete vital data of pre-hospital observations and whether these patients are inherently significantly different from the included cases.

	Would the authors be able to study the outcomes (e.g. unscheduled return visits, subsequent admission, death) of the seemingly high proportion (217/1330) of patients with high-risk level NEWS discharged from the ED (Table 2)? Supplementary Tables 2-5 should be condensed and may be combined into one.

REVIEWER	Rungsun Bhurayanontachai Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, THAILAND
REVIEW RETURNED	24-Dec-2019

GENERAL COMMENTS	Thank you the editor for giving me an opportunity for reviewing this interesting article. The author aim to identified the application of NEWS during prehospital evaluation to predict the patient deposition in ED. This article is the retrospective study in fashion that reviewed the medical records from one large center in Japan. Overall: - The article is well narrated with few missed spelling and some grammatical error. Please review. STATISTICAL ANALYSIS - The author used ROC curves as a tool to identify the power of discrimination of NEWS for hospital disposition, which classified into 4 categories as noted. In addition, the author needed to find out the cut off values of NEWS in each outcome category, but the method to identify the cut off value has not been declared in the manuscript. Please clarify and state in this part. RESULTS: - No comments Discussion - The discussion part is easily to comprehend and well constructed. - The author hypothesized that the higher aging population in Japan may influence the result of NEWS in prehospital setting comparing to the other surrounding countries, but there is no discussing regarding this point. From the patient characteristic, the mean age of the current study did not significantly difference from the previous studies. Please clarify and discuss. - The author did not discuss regarding the application of these study results into current clinical practice in the place. Prehospital NEWS could be from the non-resuscitation periods and possible changed during transportation and at ED arrival. Furthermore, NEWS may be changed after appropriated resuscitation in ED. Does the author reckon that prehospital NEWS can be used as a triage tool for disposition? Please discuss. TABLE: - TABLE 1: Chief complaint row is a bit difficult to understand, please list the chief complaint in the left column and show only the number and percentage in each group. - TABLE 3: The row of age, gender and trauma could be omitted. FIGURES: - Supplement figure 1: The ROC curve of interested outcomes were plot against the discharge from ED. I am a bit skeptic regarding the ROC curve of discharged from ED, I am not quite sure what parameter of this ROC curve plot against, please clarify. However, this figure could be omitted from presentation.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Win Sen Kuan
Institution and Country: National University Health System, Singapore
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below Thank you for the opportunity to review the manuscript entitled "Prehospital national early warning score predicts outpatient disposition at the Emergency Department in a Japanese tertiary hospital". The study addresses a unique patient population, i.e. a rapidly aging population in Asia, where the proportion of elderly are one of the highest in the world. Many other developed countries are approaching such a demographic and thus the results may still be relevant to those countries in years to come. The results of this study add to the literature on the utility of NEWS across various settings and populations.

Comment 1-1
The manuscript is largely well-written with easy readability and minor grammatical, spelling, punctuation and typographical errors. For example, the figure for proportion aged 65 years and higher in Hong Kong is missing (line 58).
Reply : Thank you very much for your comments.

・The figure for proportion aged 65 years and higher in Hong Kong is 15.1% in page 6.

・There was no comment from the reviewer, but when I reviewed it again with the co-author, the ROC curve (s) was changed to ROC (s), so I revised it throughout the paper in Discriminative performance of NEWS in the prehospital setting, page 10.

・We added citation number this sentence; "In 2017, a study7 showed that high-risk patients (those with NEWS ≥7) demonstrated a relatively higher risk for a one-day mortality rate of …" in page12.

Comment 1-2
What is the emergency department load of the study site? This would determine the proportion of patients conveyed by ambulance versus those who went to the emergency department on their own.
Reply : The emergency department of our hospital is the largest lifesaving center in the study site. Between April 2016 and March 2017, the number of patients conveyed by ambulance was 5,640 and the number of walk-in patients was 16,922.

Change to text : "Between April 2016 and March 2017, the number of patients conveyed by ambulance was 5,640 and the number of walk-in patients was 16,922." in page7.

Comment 1-3
Certain terminology e.g. "sick call" (line 33) should be described more clearly in the Methods or Results as the phrase carries different connotations in different countries.
Reply : I am very sorry, but the description of the chief complaint was partially incorrect. Specifically, "Sick Call" was a mistake of "Sick Person".
We adopted the MPDS category for the chief complaint. The definition follows the MPDS classification. The prior study (Silcock DJ, et al. Validation of the National Early Warning Score in the prehospital setting. Resuscitation 2015) also adopted the MPDS category. In Japan, MPDS wasn't used, therefore the main complaint of the transport paper described by paramedics was changed to the MPDS number.

Change to text : "Sick Call" to "Sick Person" was changed in all applicable places.

Change to text : "However, in Japan, this code was not used in practice. The appropriate code

number was added using the chief complaint item of the paper written by the paramedics after transport." in page 8

Comment 1-4
While the authors acknowledge limitations in the retrospective and single-centre nature of the study, they should also elaborate on the almost 20% incomplete vital data of pre-hospital observations and whether these patients are inherently significantly different from the included cases.
Reply : We could get vital data from Kawasaki area but could not get from other areas. Vital signs of patients transported from Kawasaki City were written on the report after transported by paramedics. On the other hand, vital signs of patients transported from other areas (Tokyo, Yokohama next to Kawasaki) were not written on the report after transportation. These data could not be allowed to access for the personal privacy. Definitely we excluded 20% of the data for which no vital signs were obtained but the only difference is the area that has been transported and it is presumed to be essentially the same as the other 80% of patients.

Change to text : Discussion in page 11.
In this case, there is 20% incomplete data for which no vital signs were obtained. Vital signs of patients transported from Kawasaki City were written on paper by paramedics and we got it.
On the other hand, vital signs of patients transported from other areas (Tokyo, Yokohama next to Kawasaki) were not written on the report after transportation. These data could not be allowed to access for the personal privacy. Definitely we excluded 20% of the data for which no vital signs were obtained but the only difference is the area that has been transported and it is presumed to be essentially the same as the other 80% of patients.

Comment 1-5
Would the authors be able to study the outcomes (e.g. unscheduled return visits, subsequent admission, death) of the seemingly high proportion (217/1330) of patients with high-risk level NEWS discharged from the ED (Table 2)?
Reply : Thank you very much for your comments. It's a very interesting and important research question. I'm sorry to say that now we don't have outcome data (unscheduled return visits, subsequent admission, death) of patients. We would like to work it as a research next issue.
Aiming for using prehospital NEWS as a triage tool, it is necessary to clarify what kind of cases are "Go home despite high score" and "ICU hospitalization despite low score". We recognize that the result of the statistical analysis that combines the chief complaint and prehospital NEWS will provide a practical transport triage.

In this study, "Go home despite high score" includes reversible diseases such as asthma attacks and influenza infections. And "ICU hospitalization despite a low score" includes patients who were transported for headache alone and required surgery for subarachnoid hemorrhage and those who were transported for chest pain and required catheterization for myocardial infarction.

Change to text : Discussion in page 14.
We are also currently analyzing the relationship between prehospital NEWS and mortality rate with more extensive data and exploring the possibility of predicting death more accurately by integrating other factors (chief complaints etc.). This study is the first step towards implementation of prehospital NEWS as a prehospital triage tool. In Japan there is no triage tool in the prehospital setting. The Japan Triage and Acuity Scale (JTAS) is currently used in the outpatient setting but it does not assume an emergency site. Aiming for using prehospital NEWS as a triage tool, additional analysis of "false positive" and "false negative" would be required. It is necessary to clarify what kind of cases are "Go home despite high score" and "ICU hospitalization despite low score". Next step we will analyze these data.

Comment 1- 6
Supplementary Tables 2-5 should be condensed and may be combined into one.
Reply : Thank you very much for your comments. Supplementary Tables 2-5 were condensed and combined into one as new Supplementary Tables 2.
Change to text : Supplementary Table 2, Breakdown of number of presentations by AMPDS category is changed as below.

Reviewer: 2
Reviewer Name: Rungsun Bhurayanontachai
Institution and Country: Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, THAILAND
Please state any competing interests or state 'None declared': Non declared

Please leave your comments for the authors below
Thank you the editor for giving me an opportunity for reviewing this interesting article. The author aim to identified the application of NEWS during prehospital evaluation to predict the patient deposition in ED. This article is the retrospective study in fashion that reviewed the medical records from one large center in Japan.

Overall:
Comment 2-1
- The article is well narrated with few missed spellings and some grammatical error. Please review.
Reply : Thank you very much for your comments. I reviewed my article again and fixed some. I am very sorry, but the description of the chief complaint was partially incorrect. Specifically, "Sick Call" was a mistake of "Sick Person".

Change to text :
・AMPDS code chief complaints "Sick Call" was changed to "Sick Person" in all applicable places.
・The figure for proportion aged 65 years and higher in Hong Kong is 15.1% in page 6.
・There was no comment from the reviewer, but when I reviewed it again with the co-author, the ROC curve (s) was changed to ROC (s), so I revised it throughout the paper in page 10.

STATISTICAL ANALYSIS

Comment 2-2
- The author used ROC curves as a tool to identify the power of discrimination of NEWS for hospital disposition, which classified into 4 categories as noted. In addition, the author needed to find out the cut off values of NEWS in each outcome category, but the method to identify the cut off value has not been declared in the manuscript. Please clarify and state in this part.
Reply : Thank you very much for your comments. Because there is no principled statistical criterion for selecting an optimal cutoff point without information on "cost", we carefully chose the cut points (4.5 and 6.5) from the combinations of three sets of sensitivity and 1 - specificity presented in Supplement Table 4 from a clinical practice viewpoint. As a starting point, we calculated Youden's index, which is defined as a difference between sensitivity and 1 - specificity, or "sensitivity + specificity - 1"; we found the following values to be considered as candidate cut points for NEWS:
Youden's index
Cut point Ward/ICU/Death ICU/Death Death
3.5 0.303 0.354 0.377
4.5 0.329 0.412 0.47
5.5 0.339 0.447 0.577

6.5 0.339 0.461 0.661
7.5 0.306 0.451 0.732
8.5 0.262 0.431 0.709
For a "high/middle-risk" cut point, sensitivity for death and ICU admission is crucial. Among the values lower than 7.5 (sensitivity of 1 for death), we chose a value 6.5 because relatively higher sensitivity of ICU admission or death (about 3/4, or 75%).
Next, we considered that a "middle/low-risk" cut point should have had high sensitivity for a ward admission and minimal degree of specificity, e.g., over 50%-60%. Such points may be 3.5 or 4.5; we chose 4.5 because it has a better balance of sensitivity and specificity for ICU admission, too.
We added the above explanation below Supplement Table 4. We also added the following sentences in "Statistical Analysis" (Methods) and "Cut-off NEWSs for clinical risk categories" (Results)
Change to text :
・"We started with Youden's index (sensitivity + specificity - 1) to obtain candidate cutoff values for hospital disposition. Among the range, we carefully chose high/middle-risk and middle/low-risk cut points that appropriately reflect clinical requirement." (Statistical Analysis, Methods in page 8-9)
・"How to choose these values is described in Supplementary Table 4 as below." (Cut-off NEWSs for clinical risk categories, Results in page 10)

RESULTS:
- No comments

Discussion
- The discussion part is easily to comprehend and well-constructed.

Comment 2-3
- The author hypothesized that the higher aging population in Japan may influence the result of NEWS in prehospital setting comparing to the other surrounding countries, but there is no discussing regarding this point.
Reply : It has been confirmed that prehospital NEWS fully predicts outpatient disposition even in Japan -an aging society. Following the results of previous studies predicting outpatient disposition in the UK and other countries, where the aging rate is lower than in Japan, this result suggests that prehospital NEWS may be available globally. It suggests that NEWS can be used when countries become an aging society like Japan in the future.

Change to text : Discussion in page12
It has been confirmed that prehospital NEWS fully predicts outpatient disposition even in an aging society, such as in Japan. Addition to our result and following the results of previous studies predicting outpatient disposition in the UK and other countries, these results suggest that prehospital NEWS might be available globally. It suggests that NEWS could be used when countries become an aging society like Japan in the future.

- From the patient characteristic, the mean age of the current study did not significantly difference from the previous studies. Please clarify and discuss.

Reply : In the prior study; Shaw J, et al. Emergency Med J 2017, the mean age of the sample was 63 years (ranging from 16 to 97 years) and in this study the mean age of the sample was 66.5 years (ranging from 16 to 101 years). As you mentioned, the difference between the averages is not big. In this study, median age is 73 years (lower to upper quartile: 53-82), with a bimodal (modes around 44 and 82) instead of unimodal, symmetric distribution. The median and IQR in previous studies are unknown with published information. The average does not have a big difference but recognizes that the difference by IQR may be different.
Since the effects of age cannot be shown from the data unless it is tracked before transportation, it

must be a qualitative discussion in this study. It is true that Japan is an aging society, and we believe that analyzing cases only transported to one hospital in such a society will contribute to the generalization of prehospital NEWS availability.

Change to text : Results in page 9
"The mean (±standard deviation) age of the participants was 66.5 ±19.6 years, median age is 73 years (lower to upper quartile: 53-82), with a bimodal (modes around 44 and 82) and asymmetric instead of unimodal, and the proportion of male participants was 53.5%."

Comment 2-4
- The author did not discuss regarding the application of these study results into current clinical practice in the place.
Reply: Thank you very much for your comments. I will add a discussion on this point. This study is the first step towards implementation of prehospital NEWS as a prehospital triage tool. In Japan there is no triage tool in the prehospital setting. Japanese famous triage tool, The Japan Triage and Acuity Scale (JTAS) is currently used in the outpatient setting and it does not assume an emergency site. Prehospital NEWS aims the practical application as a prehospital triage tool.

Aiming for using prehospital NEWS as a triage tool, additional analysis of false positive and negative items is required. It is necessary to clarify what kind of cases are "Go home despite high score" and "ICU hospitalization despite low score".

In this study, "Go home despite high score" includes reversible diseases such as asthma attacks and influenza infections. And “ICU hospitalization despite a low score” includes patients who were transported for headache alone and required surgery for subarachnoid hemorrhage and those who were transported for chest pain and required catheterization for myocardial infarction.
Next step we will analyze and combine information obtained at the scene and hope to bring it closer to practical use.

Change to text : Discussion in page14
We are also currently analyzing the relationship between prehospital NEWS and mortality rate with more extensive data and exploring the possibility of predicting death more accurately by integrating other factors (chief complaints etc.). This study is the first step towards implementation of prehospital NEWS as a prehospital triage tool. In Japan there is no triage tool in the prehospital setting. The Japan Triage and Acuity Scale (JTAS) is currently used in the outpatient setting but it does not assume an emergency site. Aiming for using prehospital NEWS as a triage tool, additional analysis of “false positive” and “false negative” would be required. It is necessary to clarify what kind of cases are "Go home despite high score" and "ICU hospitalization despite low score". Next step we will analyze these data.

- Prehospital NEWS could be from the non-resuscitation periods and possible changed during transportation and at ED arrival. Furthermore, NEWS may be changed after appropriated resuscitation in ED. Does the author reckon that prehospital NEWS can be used as a triage tool for disposition? Please discuss.
Reply : Hypothetically that post-intervention vitals are the most predictive of outpatient disposition, but we have little interest in verifying at which stage vital can be predicted for outpatient disposition.
We assume this score for the triage in prehospital setting on the purpose of selecting hospital. In Japan, when there is an emergency request, emergency ambulance is performed in all cases. The patient will be contacted at the scene, and then a disease and severity are judged. Calculating risk categories from vital score may help paramedics make decision. The scene where we use this score is limited to the destination selection, therefore in this study we examined the vitals only of that situation, not vitals during transportation and at ED arrival.

Change to text : Discussion in page11

The aim of this study was not to clarify when to use NEWS to predict outcomes more accurately, but to verify whether the paramedics could determine the severity from vital sign scores at the time of patient contact.

TABLE:

Comment 2-5

- TABLE 1: Chief complaint row is a bit difficult to understand, please list the chief complaint in the left column and show only the number and percentage in each group.

Reply : I changed Table 1 as an above comment.

Comment 2-6

- TABLE 3: The row of age, gender and trauma could be omitted.

Reply : Given the rapidly aging society, an increasing number of ambulance deliveries for patients with multiple comorbidities is expected to become more common than before. The present study aimed to examine the use of prehospital NEWS in the aging society of Japan and its application to emergency transportation. Then, this study also examined how age contributes to improved outcome prediction when used with the NEWS risk score.

We thought that a high contribution of age would indicate that the NEWS risk score with age was better than the NEWS risk score alone. But the results of the analysis shown in Table 3 suggest that the use of the NEWS risk score without considering age, gender and trauma was justified. This table is listed to explain this. The following comment was added to the discussion section.

Change to text : Discussion in page 12.

This study also examined how age gender and trauma contributes to improved outcome prediction when used with the NEWS risk score. The results of the analysis shown in Table 3 suggest that the use of the NEWS risk score without considering age, gender and trauma was justified.

FIGURES:

Comment 2-7

- Supplement figure 1: The ROC curve of interested outcomes were plot against the discharge from ED. I am a bit skeptic regarding the ROC curve of discharged from ED, I am not quite sure what parameter of this ROC curve plot against, please clarify. However, this figure could be omitted from presentation.

Reply : Thank you for constructive comments on the supplementary Figure 1. It contains ROC curves for 4 different binary outcomes: (1) Discharged from ED (1) or others (0) , (2) Admitted to a ward (1) or others (0), (3) Admitted to the ICU (1) or others (0), (4) Died in ED (1) or others (0). Note that ROC curves 1 and 4 are the same as those presented in Figure 3 ("Admitted to a ward or the ICU or died in ED" and "Died in ED", respectively). On the contrary, it may be hard to interpret ROC curves 2 and 3 in a clinically relevant way because they contain both "good" and "bad" prognosis in "others". We agreed that this figure can be omitted from presentation because of the lack of interpretability.

Change to text : This figure is omitted from the presentation.

VERSION 2 – REVIEW

REVIEWER	Win Sen Kuan National University Health System, Singapore
REVIEW RETURNED	05-Feb-2020

GENERAL COMMENTS	Thank you for comprehensively addressing our comments. The manuscript has been greatly improved. Some grammatical issues and colloquial terms will need to be addressed during the copy editing process to enhance readability.

REVIEWER	Rungsun Bhurayanontachai Critical Care Medicine Unit, Division of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla , Thailand.
REVIEW RETURNED	19-Feb-2020

GENERAL COMMENTS	COMMENTS: Thank you the editor for giving the opportunity for me to review the manuscript regarding NEWS application in prehospital setting for patient disposition in Japan. OVERVIEW: - The author has changed and rewritten several points according to my comments, but there are still some grammatical error, missed spelling and missed punctuation. Please recheck it again INTRODUCTION: - METHOD: - RESULTS: 1. The author identified the new cut-off values of NEWS by using ROC analysis and Youden index, which the author selected the NEWS > 0.65 as a cut-off value for ICU admission/Death in ED and NEWS > 4.5 as a cut-off value for ward/ICU admission/death in ED. However in the following analysis for risk category by patient disposition group, the author still used the NEWS classification according to RCPL classifications. For my opinion, the new finding for cut-off NEWS should be used instead of RCPL classification because this is a new finding from your research and will match to the current situation in your area. As you may know, NEWS was initially recommended in IPD setting to detect the risk of patient deterioration as an EWS. Therefore, the application of ED particularly in prehospital setting is limited. The new cut off value of NEWS should be differed from the current IPD classification. 2. In binary logistic regression model, author used the current RCPL classification instead of the new classification. I would suggest to use the new finding (cut-off values) into the model. 3. As a result, table 2 and 3 may need to be changed. DISCUSSION: 1. The revised paragraph " In this case, there is 20% incomplete data for which no vital signs were obtained. Vital……." should be move in to RESULTS. This paragragh is the explanation of patient characteristic, not a discussion of the finding. Therefore, this could be moved to RESULTS. TABLE,FIGURE:-

VERSION 2 – AUTHOR RESPONSE

Reviewer 1: Win Sen Kuan / National University Health System, Singapore
Comment:
Thank you for comprehensively addressing our comments. The manuscript has been greatly improved. Some grammatical issues and colloquial terms will need to be addressed during the copy editing process to enhance readability.
Reply : Thank you very much for your comments. The manuscript has been reviewed by a native English speaker and changes have been made to the manuscript.

Reviewer 2 Rungsun Bhurayanontachai / Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, THAILAND
OVERVIEW Comment
- The author has changed and rewritten several points according to my comments, but there are still some grammatical error, missed spelling and missed punctuation. Please recheck it again
Reply : Thank you very much for your comments. The manuscript has been reviewed by a native English speaker and changes have been made to the manuscript.

RESULTS Comment 1.
1. The author identified the new cut-off values of NEWS by using ROC analysis and Youden index, which the author selected the NEWS > 0.65 as a cut-off value for ICU admission/Death in ED and NEWS > 4.5 as a cut-off value for ward/ICU admission/death in ED.
However in the following analysis for risk category by patient disposition group, the author still used the NEWS classification according to RCPL classifications.
For my opinion, the new finding for cut-off NEWS should be used instead of RCPL classification because this is a new finding from your research and will match to the current situation in your area. As you may know, NEWS was initially recommended in IPD setting to detect the risk of patient deterioration as an EWS. Therefore, the application of ED particularly in prehospital setting is limited. The new cut off value of NEWS should be differed from the current IPD classification.
Reply : Thank you for your kind comments. We are sorry that our explanation has caused your misunderstanding. Our team's opinion is that we have NEWS 6.5 and 4.5 as cut-off values. When we round up this numbers, the cutoff values were the same as RCPL classification. So, we add in the discussion that the category classification did not follow the conventional method, but adopted it based on the results of the analysis.
Change to text: We added the following sentence to the Discussion section
"Furthermore, it is worth noting that the cut-off NEWS in the prehospital setting did not differ from that in the hospital setting.3 A few studies have reported the validity of the cut-off values for the NEWS in outpatient settings. In the previous four studies7-10, patients were categorized into low-, medium-, and high-risk groups, according to the guidelines of the Royal College of Physicians.3 After examining the cut-off value in our data, we divided the risk categories into three categories. This classification based on our results is the same as the conventional in-hospital NEWS category." in page 13.

RESULTS Comment 2.
2. In binary logistic regression model, author used the current RCPL classification instead of the new classification. I would suggest to use the new finding (cut-off values) into the model.
3. As a result, table 2 and 3 may need to be changed.
Reply : Thank you for your kind comments. Sorry for our lack of explanation on this matter. We did not use the in-hospital NEWS category by the RCPL but instead adopted a category obtained by our own analysis. Therefore, the current method and result in a binary logistic regression model are

considered appropriate.
Change to text: No change.

DISCUSSION Comment .
1. The revised paragraph " In this case, there is 20% incomplete data for which no vital signs were obtained. Vital……." should be move into RESULTS. This paragraph is the explanation of patient characteristic, not a discussion of the finding. Therefore, this could be moved to RESULTS.
Reply : Thank you for your kind comments.. The following sentence has been moved to the results:
Change to text :
"In the current study, there were 20% incomplete data for which no vital signs were obtained. The vital signs of patients transported from Kawasaki City were written on paper by paramedics and given to hospital staff. On the other hand, the vital signs of patients transported from other areas (Tokyo, Yokohama next to Kawasaki) were not written on the report after transportation. These data could not be accessed due to privacy regulations. We excluded 20% of the data for which no vital signs were obtained, but the only difference was the area that the patients were transported from; thus, we assume that there would be no significant differences in the baseline characteristics between these patients and the other 80%." in page 9.

VERSION 3 – REVIEW

REVIEWER	Rungsun Bhurayanontachai Faculty of Medicine, Prince of Songkla university, Hat Yai, Songkhla, Thailand
REVIEW RETURNED	22-Mar-2020

GENERAL COMMENTS	Thank you editor for giving me an opportunity to review a revision. After I have gone through the current revision of manuscript, I found that the current manuscript is in the perfect shape and suitable for published. However, there is few spelling error in the INTRODUCTION which could be easily corrected. Congratulation for the author and co-author for their success.

VERSION 3 – AUTHOR RESPONSE

Reviewer 2 Rungsun Bhurayanontachai / Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, THAILAND
OVERVIEW Comment
- Thank you, editor, for giving me an opportunity to review a revision. After I have gone through the current revision of manuscript, I found that the current manuscript is in the perfect shape and suitable for published. However, there is few spelling errors in the INTRODUCTION which could be easily corrected. Congratulation for the author and co-author for their success.
Reply : Thank you very much for your comments. The manuscript has been reviewed. I also corrected INTRODUCTION. The main changes are marked with a blue line.

Other change.
- 'gender' is generally taken to refer to psychological identity, while 'sex' refers to biological status. As I believe you intended the latter meaning, I have changed the term accordingly.
- I have formatted the software reference according to the instructions from the developers
- I have moved the tables within the text.