PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A multi-centre, prospective observational study of the correlation between the Glasgow Admission Prediction Score and adverse outcomes
AUTHORS	Jones, Dominic; Cameron, Allan; Lowe, David; Mason, Suzanne; O'Keeffe, Colin; Logan, Eilidh

VERSION 1 - REVIEW

REVIEWER	Demetrios James KUTSOGIANNIS Department of Critical Care Medicine and Public Health Sciences, The University of Alberta, Edmonton, Alberta, Canada
REVIEW RETURNED	25-Oct-2018

GENERAL COMMENTS	The authors have presented a very relevant cohort study validating the predictive ability of the Glasgow Admission Prediction Score performed at the time of emergency room (ER) triage on 1) inpatient length of stay 2) 6-month hospital readmission rate and 3) 6-month all cause mortality. The motivation of the study, analysis plan and result were well outlined. The STROBE checklist was adhered to however the authors should include the nature of any hospital ethics approval within the methods section. Although the NEWS score and TRIAGE Category were used within the GAPS score the authors should explicitly outline how these scores are calculated within the manuscript or in an appendix. The results section is succinct and communicates the major findings well. The authors should include the median hospital lengths of stay (including confidence intervals) for those patients admitted per 3-group strata. The remaining analysis is well described. With respect to the discussion section, the authors should outline some more limitations and future planned research questions resultant from this research. Specifically, the study was performed in a narrow time period in the spring so there may (or may not) be some seasonal effects to the predictive value of this score. Moreover, although 2 sites were used in this study, further validation internationally may be in order to make this tool more widespread. Future studies may include health services evaluation on whether grouping admission strata into hospital cohorts would actually reduce resources and improve outcome as well as an intervention of discharge planning for those patients at high risk of re-admission.

REVIEWER	Dr Camille SCHWAB Hôpital Tenon, Assistance Publique - Hôpitaux de Paris Paris France
REVIEW RETURNED	06-Dec-2018

GENERAL COMMENTS	This paper presents a topic which attracts much attention in recent years: predicting readmission However, I have some remarks: 1) Title and Abstract: The study design (prospective observational study) is not indicated in the title or the abstract. Furthermore, it would have been interesting to indicate in the title which prognostic values are studied in this study, in order to inform the reader from the title. 2) Introduction section: Why were you interested in the 6 month readmission or mortality? Is it planned or unplanned readmission? The worldwide recognized quality indicator for hospital performance is the 30-day unplanned readmission. The GAPS should be better presented. I haven't heard of this score before and I had to read the external validation study of this score to understand that this score estimates the probability of admission at the time of triage ("to predict patient outcomes" is not clear enough). Furthermore, the Triage Category should be detailed, as well as the NEWS (National Early Warning Score). At last, "This paper demonstrates GAPS ability to predict inpatient …" is for a discussion, and not an objectives section. 3) Methods section: The paragraph "Data were collected at each site…between the 5th and 26th of May 2016" should be in the Data collection section. Furthermore, it is not clear how readmission and mortality were assessed. How the patients were followed up? 4) Statistical analysis: The aim of this study is to assess the ability of the GAPS score to predict hospital lengh of stay, sixmonth hospital readmission and mortality. It is therefore an external validation of the GAPS score, a ROC curve or a c-statistic value are missing. 5) Results section: A flow diagram would have been welcomed. This study assesses a score, yet no score results appear. What is the mean score of the population study? The demographics characteristics of the patients are presented. In both hospitals, the age group 2029 is largely represented, which is uncommon in a hospital, but you have not explained that, what are the clinical characteristics of the population? The missing data are not indicated. 6) Discussion section: This discussion is all about how and why the GAPS can be used. There are no interpretations considering results from similar studies or relevant evidence. Furthermore, the limitations of the study are not discussed; there are just two sentences in the abstract.

REVIEWER	Blanca Gallego Luxan UNSW, Sydney, Australia
REVIEW RETURNED	11-Feb-2019

GENERAL COMMENTS	This study looks at the association between the Glasgow admission prediction score (GAPS) and hospital LOS, time to death and time to readmission (in the following 6 months) for 1,420 patients presenting to ED. The manuscript is well written, and it is good to see an analysis based on time-to-event as opposed to the binary outcome models that are often presented in these type of studies. I have some questions about the survival analyses. By building a survival model the authors demonstrate an association between GAPS and time to event using log rank test and Hazard Ratios). Is this Cox PH model univariate (that is only a function of GAPS)? How does this compare to other simple scores? This analysis does not provide information on the accuracy of 'survival' predictions for new patients. For this to happen, the authors should provide an out-of-sample (e.g. using cross validation) measure of discriminative ability such as Chambless and Diao's or Harrell's extensions of c-statistics. The authors claim that knowing this score in real time can be utilised by hospital bed managers and ED managers to improve patient flow. As a reader, with no expertise in hospital management I would have liked to see more detail on who would this be achieved. Similarly when it comes to clinical decision support: can the authors specify what would be the clinical action in ED associated with an algorithm identifying a patient who has higher probability of longer LOS, higher risk of readmission and higher risk of death in the next few months? The authors also claim that "GAPS does not require the use of historical data or aggregation of electronic health records to identify a score". However, this may not be true for all settings. GAPS requires a NEWS score (based on physiological parameters and clinician feedback), which is not readily available in the EMR for all patients on admission to ED (at least not outside the UK). It also makes use of information on previous admission, which is generally not known if the patient was previously admitted to a different hospital.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Demetrios James Kutsogiannis

- 'Although the NEWS score and TRIAGE Category were used within the GAPS score the authors should explicitly outline how these scores are calculated within the manuscript or in an appendix.'

Details on how NEWS and the Manchester triage system are calculated have been added in appendices and highlighted in the main body of the text.

-'The authors should include the median hospital lengths of stay (including confidence intervals) for those patients admitted per 3-group strata.'

This is now included in the main body of the results section

-'With respect to the discussion section, the authors should outline some more limitations and future planned research questions resultant from this research. Specifically, the study was performed in a narrow time period in the spring so there may (or may not) be some seasonal effects to the predictive value of this score. Moreover, although 2 sites were used in this study, further validation internationally may be in order to make this tool more widespread. Future studies may include health services evaluation on whether grouping admission strata into hospital cohorts would actually reduce resources and improve outcome as well as an intervention of discharge planning for those patients at high risk of re-admission.'

Thank you for these suggestions. These additions have all been considered and another section of the discussion has been included addressing limitations and further work.

Reviewer: 2

Reviewer Name: Dr Camille Schwab

-'The study design (prospective observational study) is not indicated in the title or the abstract. Furthermore, it would have been interesting to indicate in the title which prognostic values are studied in this study, in order to inform the reader from the title.'

Thank you for pointing this out the title has been updated to include both of these suggestions

-'Why were you interested in the 6 month readmission or mortality? Is it planned or unplanned readmission? The worldwide recognized quality indicator for hospital performance is the 30-day unplanned readmission.'

This is a good point and hopefully I can explain our reasoning below. The readmissions were all unplanned. I've made this explicit in the methods now. The reason for follow-up out to 6-months was threefold. Firstly, we planned our follow-up period to be that long to ensure that we had endpoint data for all hospital discharges. Secondly, we wanted to ensure our study was adequately powered to show a difference in mortality, and our preliminary data suggested that, given our sample size, 6 months of follow-up was required to adequately power the study to reveal a significant difference. Thirdly, we reasoned that 6-month follow-up would incorporate 30-day follow-up. The divergence in the Kaplan-Meier curves at 30 days is clear in the figures, but we take the point that we should specifically mention this in the text. Thank you for pointing out the quality indicator and a 30-day readmission analysis has been added in the results.

-'The GAPS should be better presented. I haven’t heard of this score before and I had to read the external validation study of this score to understand that this score estimates the probability of admission at the time of triage (“to predict patient outcomes” is not clear enough). Furthermore, the Triage Category should be detailed, as well as the NEWS (National Early Warning Score).'

The introduction has been updated to better explain what GAPS is. How the manchester triage system and national early warning scores are calculated have been explained in appendices and indicated in the text.

-'At last, “This paper demonstrates GAPS ability to predict inpatient …” is for a discussion, and not an objectives section.'

I've removed this statement from the introduction

-'The paragraph “Data were collected at each site…between the 5th and 26th of May 2016” should be in the Data collection section. Furthermore, it is not clear how readmission and mortality were assessed. How the patients were followed up?'

This has been moved to the data collection section. The method for following up the patients is now highlighted in the data collection section

-'The aim of this study is to assess the ability of the GAPS score to predict hospital lengh of stay, sixmonth hospital readmission and mortality. It is therefore an external validation of the GAPS score, a ROC curve or a c-statistic value are missing.'

This is a valid point, we have already published the data that describes an external validation of GAPS. I have made this clear in the introduction

-'A flow diagram would have been welcomed.'

Figure 1 displays this flow chart

-'This study assesses a score, yet no score results appear. What is the mean score of the population study?'

We felt a median score would be more meaningful. The median score and 95% confidence intervals are now in the results section.

-'The demographics characteristics of the patients are presented. In both hospitals, the age group 20-29 is largely represented, which is uncommon in a hospital, but you have not explained that, what are the clinical characteristics of the population?'

Our figures are very typical for UK EDs. According to our national statistics, there are approximately 300 ED attendances per 1000 adults per year in the 20-29 age range. This then falls away with increasing age until a nadir of 190 attendances per 1000 adults at age 60 before rising again. The rate of attendances per 1000 population for those in their mid-70s is approximately the same as that for those in their 20s. Although the rate is as high as 500 attendances per 1000 people in the over 85 group, the number of people in their 20s is far higher, so we simply see more people in their 20s attending. Of course, the rate of admission to hospital is far lower in the younger age group than in

the older age group, so the inpatient population would have a very different demographic from the ED demographic included in our study, since it is a selected subset of it.

-'The missing data are not indicated.'

We have described who was excluded from the study and why. The patients who were lost to followup are also indicated in the results section.

-'This discussion is all about how and why the GAPS can be used. There are no interpretations considering results from similar studies or relevant evidence. Furthermore, the limitations of the study are not discussed; there are just two sentences in the abstract.'

Thank you for bringing this to our attention. There is a section in the discussion comparing GAPS to relevant other prediction tools available. I've also included a discussion on limitations and future work relating to GAPS.

Reviewer: 3

Reviewer Name: Blanca Gallego Luxan

-'By building a survival model the authors demonstrate an association between GAPS and time to event using log rank test and Hazard Ratios). Is this Cox PH model univariate (that is only a function of GAPS)? How does this compare to other simple scores?'

Yes this is a univariate analysis of GAPS. I have made this explicit in the text. There is limited data on other simple scores to compare GAPS to. Two studies comparing GAPS to the ambulatory care score and nurses abilities are referenced in the text.

-'This analysis does not provide information on the accuracy of ‘survival’ predictions for new patients. For this to happen, the authors should provide an out-of-sample (e.g. using cross validation) measure of discriminative ability such as Chambless and Diao’s or Harrell’s extensions of c-statistics. '

Thank you for pointing this out. We feel that this would fall under further work which is now included at the end of the discussion

-'The authors claim that knowing this score in real time can be utilised by hospital bed managers and ED managers to improve patient flow. As a reader, with no expertise in hospital management I would have liked to see more detail on who would this be achieved. Similarly when it comes to clinical decision support: can the authors specify what would be the clinical action in ED associated with an algorithm identifying a patient who has higher probability of longer LOS, higher risk of readmission and higher risk of death in the next few months?'

I've tried to make this more explicit in the discussion. We didn't think that an algorithm would be a useful way of displaying this as clinical judgement plays a role in decision making for clinicians.

-'The authors also claim that “GAPS does not require the use of historical data or aggregation of electronic health records to identify a score”. However, this may not be true for all settings. GAPS requires a NEWS score (based on physiological parameters and clinician feedback), which is not readily available in the EMR for all patients on admission to ED (at least not outside the UK). It also makes use of information on previous admission, which is generally not known if the patient was previously admitted to a different hospital.'

The point about NEWS is a very important consideration and I have included this as a limitation in the discussion. With regards to the information of previous admissions, the triaging member of staff can ask the patient this question at triage.

VERSION 2 – REVIEW

REVIEWER	Camille SCHWAB Assistance Publique - Hôpitaux de Paris Hôpital Tenon Paris, France
REVIEW RETURNED	05-Apr-2019

GENERAL COMMENTS	I would like to thank the authors to have taken some of my remarks into account. However, I still have some comments regarding the manuscript. The manuscript has been renamed "a multi-centre, prospective observational study assessing the prognostic value of the GAPS...", but if the objective, linked to the title, is clearly define in the abstract:” To assess whether the Glasgow admission prediction score (GAPS) is predictive of hospital length of stay, six-month hospital readmission and six-month all-cause mortality.”, it is different of the one mentioned in the main document:” This study represents a six-month follow-up of patients who were included in an external validation of the GAPS score’s ability to predict admission at the point of triage. The results of this validation are described in an earlier paper (30)”. A predictive value implies to conduct an external validation study, which means to calculate the c-statistics. However, no c-statistics have been calculated. If the objective of this study is to represent a six-month follow-up of patients, then the statistical analyses conducted are appropriate, but the title needs to be changed. Lastly, in the previous version, the fact that this study used the patient data from a first study was not mentioned. This point is important for the method and should be described in the method and not presented in the objective.

VERSION 2 – AUTHOR RESPONSE

Dear reviewer(s)

Thank you for your further comments and suggestions on our manuscript. We have taken all of your suggestions into account and I will detail all changes below:

Thank you for your point on our use of the word 'predict' throughout the manuscript. We have renamed the manuscript 'A multi-centre, prospective observational study of the correlation between the Glasgow Admission Prediction Score and adverse outcomes'. We hope this better describes the study conducted and matches the statistical analyses conducted.

In addition, we have made multiple changes throughout the manuscript to remove use of the word 'predict'. These are detailed in the marked copy. We have used words such as 'correlation' and 'association' to better match the statistical analyses used in the study.

Finally, we have moved the sentence 'this study represents a six-month follow-up of patients who were included in an external validation of the GAPS score’s ability to predict admission at the point of triage. The results of this validation are described in an earlier paper (30)' to the methods section of the manuscript. We have also included this statement in the abstract.