

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Development of a risk predictive scoring system to identify patients at risk of re-presentation to emergency department: a retrospective population-based analysis in Australia
AUTHORS	Ahn, Euijoon; Kim, jinman; Rahman, Khairunnessa; Baldacchino, Tanya; Baird, Christine

VERSION 1 – REVIEW

REVIEWER	Aracely Díaz Oviedo Unidad de Posgrado e Investigación de la Facultad de Enfermería y Nutrición de la Universidad Autónoma de San Luis Potosí México.
REVIEW RETURNED	15-Jan-2018

GENERAL COMMENTS	Add ethics committee approval and informed consent approval procedure
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REVIEWER	Shen Yuzeng Department of Emergency Medicine, Singapore General Hospital, Singapore
REVIEW RETURNED	26-Jan-2018

GENERAL COMMENTS	<p>This is a well intentioned study with major limitations.</p> <ol style="list-style-type: none">1. RUSS-ED needs to cater to the general patient population, for it to meet the study objective. However, the RUSS-ED excludes patients with "certain chronic conditions" and elderly >70yo patients. It would be important then to justify why are these groups excluded. For example, are they excluded because they are already frequent attenders, and may further skew outcomes for the rest of the general patient population? An idea of the patient demographics and profile of the population which the study centre serves would be useful. Most of the emergency departments globally are facing an increased number of elderly attendees, and there are studies which show increase in proportion of frequent attenders for the elderly population, compared to the non elderly population. Hence, RUSS-ED, which is limited to an under 70 year old patient cohort, will not be practical or generalizable to most other EDs.2. What is the burden of frequent attenders within the study set? What is the study setting like (urban, rural etc) Would serve as an important comparator to other published studies regarding ED frequent attenders.3. More information needs to be given regarding the validation set. Why was validation sample limited to 77 patients? Why were these patients chosen? How did the physicians chose them?
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	<p>4. In contrast to most published studies on frequent attenders, there seems to be a skew of frequent attenders towards the younger (20-39) age group, compared to the more elderly (60-70) age group. This finding can be elaborated upon more.</p> <p>5. There should be more discussion regarding limitations:</p> <ul style="list-style-type: none"> - single centre study - doesn't account for individual patient complexity and reason for coming to the ED - has survival bias been accounted for or discussed? for example, more patients who are younger would have very frequent ED visits >10, because the patients in the elderly age group would have passed away within the same period. <p>6. There needs to be broader lit review, as there are multiple ED frequent attender studies demonstrating increased proportion of frequent attenders related to drug, alcohol and psychiatric issues.</p> <p>It would be good to include all comers to RUSS-ED to have a more generalizable study.</p>
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REVIEWER	Colineaux, H�el�ene Department of Epidemiology, Toulouse University Hospital, France, LEASP UMR 2017, Toulouse III University, France
REVIEW RETURNED	01-Mar-2018

GENERAL COMMENTS	<p>Thank you for giving me the opportunity to review this paper since it deals with the ED use and with the phenomenon of frequent visits to this health care.</p> <p>My major concern is the generalizability of the results:</p> <ul style="list-style-type: none"> - This is a monocentric study. - The authors do not give much information on the context (ED organization, alternative care services, population socio-demographic characteristics, etc.) => representativeness of the NSW situation is difficult to evaluate - I do not understand the choice of the sample used for external validation. These patients seem very particular and not representative of the patients for which the authors wish to use the score. <p>Minor revisions:</p> <ul style="list-style-type: none"> - Are FV characteristics stable over the 7 analysed years? - To evaluate the performance of the score in a more practical way, it would have been useful to indicate the positive and negative predictive values for the chosen thresholds. - The description of patterns of FV based on the time of arrival should be in Results and not in Discussion - The authors do not give much information on how they think they will improve the management of the FV once the algorithm has identified them. The usefulness of such a score is therefore questionable if we do not propose specific management for patients at risk of re-presentation. But since "many FV did not wait to complete their treatment or leave the EDs at their own risk", how to implement these specific management ?
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REVIEWER	Jackie Cooper Queen Mary University of London, United Kingdom
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REVIEW RETURNED	28-Mar-2018
GENERAL COMMENTS	<p>1) Main comment: The objective of the study is to predict patients likely to re-present to emergency departments. The authors have used ED presentation as the unit of analysis, but do not appear to have taken account of the within patient correlations in their models. This approach will give too much weight to patients with a large number of visits. They could use a mixed effects model to take account of this and develop a score based on the fixed effects. Alternatively a per-patient analysis would be valid using data from the first presentation to predict whether the patient will become a FV. I certainly think the developed score should be applied at the patient level not the ED presentation level and the external validation dataset should be at the patient level as they are predicting which patients will re-present, not which visits will be re-presentations.</p> <p>2) Minor comments:</p> <p>a) The validation method needs to be clarified. Ten-fold cross validation involves dividing the data into ten parts, fitting the model on 90% and using that model to predict for the remaining 10%. This process is repeated using each of the 10 sets as the validation data. As the authors have used a 50% split it is unclear what they have done.</p> <p>b) Confidence intervals should be presented for the AUROC and other evaluation metrics.</p> <p>c) P 11 The authors should clarify that a AUROC of 0.5 indicates no discrimination and so the higher the curve above the diagonal the better the predictive accuracy.</p> <p>d) I think the sensitivity presented in the abstract is misleading as it comes from a very high risk selected population (patients with an average of 40 presentations) and is much higher than the value from the internal validation.</p>

VERSION 1 – AUTHOR RESPONSE

We would like to thank the Editor and the Reviewers for their valuable and constructive feedbacks. We have revised and improved our manuscript based on the Reviewers' comments and provide a point-by-point response to them below.

Reviewer 1 (R1)

1. Add ethics committee approval and informed consent approval procedure

Ethics approval was obtained from the Human Research Ethics Committees (HRECs) at the Nepean Blue Mountains Local Health District (NBMLHD), NSW, Australia. This is now added in page 5.

Reviewer 2 (R2)

1. RUSS-ED needs to cater to the general patient population, for it to meet the study objective. However, the RUSS-ED excludes patients with "certain chronic conditions" and elderly >70yo patients. It would be important then to justify why are these groups

excluded. For example, are they excluded because they are already frequent attenders, and may further skew outcomes for the rest of the general patient population? An idea of the patient demographics and profile of the population which the study centre serves would be useful. Most of the emergency departments globally are facing an increased number of elderly attendees, and there are studies which show increase in proportion of frequent attenders for the elderly population, compared to the non elderly population. Hence, RUSS-ED, which is limited to an under 70 year old patient cohort, will not be practical or generalizable to most other EDs.

Our primary aim was to identify frequent visitors (FVs) to ED among younger and general population (age \leq 70) as their characteristics were more complex and heterogenous compared to older age group (age $>$ 70). Recent studies suggest that the FVs to ED are not only highly associated with elderly age groups, but also with younger age groups^{1 2} and suggests the importance of understanding the younger age groups³. In addition, identification of FVs from older age group was relatively trivial as many of them were already FVs of the hospital, often suffering from certain chronic diseases. Such patients also tend to have distinct characteristics with a skewed distribution, introducing confounding (e.g., survival) bias in the analysis. We therefore targeted younger and general patients with age \leq 70 in our analysis. We included all of patients' information (including any chronic conditions) if they visited the ED during 1 January 2009 to 30 June 2016.

Many of predictive models were specifically designed to predict patients with high risk of a future re-admission rather than a future re-presentation to EDs, often targeting only older patients with certain chronic diseases⁴⁻⁷. We hence respectfully suggest that our derivation of RPSS-ED is an important addition to the literature and research in this area.

These are now clarified in page 5.

2. What is the burden of frequent attenders within the study set? What is the study setting like (urban, rural etc) Would serve as an important comparator to other published studies regarding ED frequent attenders.

Nepean Blue Mountains Local Health District (NBMLHD) covers both urban and semi-rural areas, covering approximately 9,179 kilometers. The estimated resident population of NBMLHD in 2011 is 345,564 which includes an indigenous community (2.6%). The number of younger aged profiles and indigenous people have been steadily increasing in recent years⁸. The number of ED presentations is projected to increase by 33% in 2022 along with increases in mental health care, rehabilitation and recovery, cancer care, and renal dialysis⁸. The increasing populations of both younger and elderly people introduce new and unique challenges in health care demands, planning, and service delivery.

Different from other published studies^{1 2}, we observed that FVs are highly associated with socially disadvantaged groups such as people who have been divorced, widowed, or separated (See Table 2). These are now clarified in the revised manuscript.

3. More information needs to be given regarding the validation set. Why was validation sample limited to 77 patients? Why were these patients chosen? How did the physicians chose them?

The tailored integrated intervention providers at the Nepean hospital manually targeted patients 1) with multiple health and social care needs or 2) who have presented to ED 10 times in the past year. The enrolled 77 patients were the total number of patients who were receiving the targeted interventions at the Nepean hospital. We have therefore initially tested our RPSS-ED using the enrolled 77 patients to measure the efficacy of the predictive model. These are clarified in the revised manuscript in page 6.

4. In contrast to most published studies on frequent attenders, the there seems to be a skew of frequent attenders towards the younger (20-39) age group, compared to the more elderly (60-70) age group. This finding can be elaborated upon more.

Recent studies suggest that the FVs to ED are not only highly associated with elderly age groups but also with younger age groups^{1 2}. Unlike FVs in older age group who often have chronic illnesses such as diabetes and heart disease, our findings indicate that FVs in younger aged patients are highly associated with mental health related diseases along with alcohol, and drug related diagnosis. This is now stated in page 14.

5. There should be more discussion regarding limitations:

- single centre study
- doesn't account for individual patient complexity and reason for coming to the ED
- has survival bias been accounted for or discussed? for example, more patients who are younger would have very frequent ED visits >10, because the patients in the elderly age group would have passed away within the same period.

We have now taken individual patient complexities (i.e., patient correlations) using a mixed-effects model and develop a scoring system based on the fixed effects. We also articulated the limitations of the paper as suggested in the revised manuscript.

6. There needs to be broader lit review, as there are multiple ED frequent attender studies demonstrating increased proportion of frequent attenders related to drug, alcohol and psychiatric issues.

As suggested we have added and discussed other similar studies in the revised manuscript. Please refer to page 14.

Reviewer 3 (R3)

1. This is a monocentric study. The authors do not give much information on the context (ED organization, alternative care services, population socio-demographic characteristics, etc.) => representativeness of the NSW situation is difficult to evaluate

Nepean Blue Mountains Local Health District (NBMLHD) covers both urban and semi-rural areas, covering approximately 9,179 kilometers. The estimated resident population of NBMLHD in 2011 is 345,564 which includes an indigenous community (2.6%). The number of younger aged profiles and indigenous people have been steadily increasing in recent years. The number of ED presentations is projected to increase by 33% in 2022 along with increases in mental health care, rehabilitation and recovery, cancer care, and renal dialysis. The increasing populations of both younger and elderly people introduce new and unique challenges in health care demands, planning, and service delivery. These statements are now included in page 5.

2. I do not understand the choice of the sample used for external validation. These patients seem very particular and not representative of the patients for which the authors wish to use the score.

The tailored integrated intervention providers at the Nepean hospital manually targeted patients 1) with multiple health and social care needs or 2) who have presented to ED 10 times in the past year. The enrolled 77 patients were the total number of patients who were receiving the tailored targeted interventions at the Nepean hospital. We have therefore initially tested our RPSS-ED using the enrolled 77 patients to measure the efficacy of the predictive model. These are clarified in the revised manuscript in page 6.

3. Are FV characteristics stable over the 7 analysed years?

We have further conducted yearly break-down age analysis below. Our results show that FVs were highly likely to be between middle (20-39) to late-middle (40-59) aged patients, consistent with the characteristics derived using whole consolidated data.

Frequent Visitors (4+ per annum)							
Age Group	2009 Percent (Freq)	2010 Percent (Freq)	2011 Percent (Freq)	2012 Percent (Freq)	2013 Percent (Freq)	2014 Percent (Freq)	2015 Percent (Freq)
0-9	6.14% (26)	8.04% (51)	9.87% (75)	9.61% (87)	11.06% (129)	12.65% (169)	12.49% (173)
10-19	10.71% (45)	12.46% (79)	9.87% (75)	12.71% (115)	13.55% (158)	10.63% (142)	10.90% (151)
20-39	32.86% (138)	33.44% (212)	30.13% (229)	34.25% (310)	32.33% (377)	34.96% (467)	32.35% (448)
40-59	32.38% (136)	30.60% (194)	30.00% (228)	26.63% (241)	27.87% (325)	26.27% (351)	26.93% (373)
60-70	17.86% (75)	15.46% (98)	20.13% (153)	16.80% (152)	15.18% (177)	15.49% (207)	17.33% (240)

4. **To evaluate the performance of the score in a more practical way, it would have been useful to indicate the positive and negative predictive values for the chosen thresholds.**

As suggested we have now included positive and negative predictive values for the chosen thresholds in page 13. For instance, using a risk score threshold of 15.38, our model had a positive predictive value and negative predictive value of 23.53% and 89.85% respectively.

5. **The description of patterns of FV based on the time of arrival should be in Results and not in Discussion**

As suggested we have now moved the description of patterns of FVs based on the time of arrival to Results section in revised manuscript.

6. **The authors do not give much information on how they think they will improve the management of the FV once the algorithm has identified them. The usefulness of such a score is therefore questionable if we do not propose specific management for patients at risk of re-presentation. But since "many FV did not wait to complete their treatment or leave the EDs at their own risk", how to implement these specific management ?**

The tailored integrated care providers at the Nepean hospital is currently manually searching for potential at-risk patients and offer tailored interventions to them. Using the RPSS-ED, an initial search can be performed which can then ease the current manual search requirements, and therefore allows clinicians to focus more on patient cares and service delivery. These statements are added in page 14.

Reviewer 4 (R4)

1. **The objective of the study is to predict patients likely to re-present to emergency departments. The authors have used ED presentation as the unit of analysis, but do not appear to have taken account of the within patient correlations in their models.**

This approach will give too much weight to patients with a large number of visits. They could use a mixed effects model to take account of this and develop a score based on the fixed effects. Alternatively a per-patient analysis would be valid using data from the first presentation to predict whether the patient will become a FV. I certainly think the developed score should be applied at the patient level not the ED presentation level and the external validation dataset should be at the patient level as they are predicting which patients will re-present, not which visits will be re-presentations.

We thank the Reviewer for the constructive comments. As suggested we have now taken individual patient complexities (i.e., patient correlations) using a mixed-effects model and develop a scoring system based on the fixed effects in the revised manuscript. We have also computed the risk scores at the patient level for the external validation dataset in the revised manuscript.

- 2. The validation method needs to be clarified. Ten-fold cross validation involves dividing the data into ten parts, fitting the model on 90% and using that model to predict for the remaining 10%. This process is repeated using each of the 10 sets as the validation data. As the authors have used a 50% split it is unclear what they have done**

We thank the Reviewer for the constructive comments. As suggested we have now divided the data into ten groups from the training data, fitting the model on 90% (i.e., derivation group) and using the model to predict remaining 10% of the data (i.e., internal validation group). This process was repeated 10 times using each set (i.e., 10-fold cross validation).

- 3. Confidence intervals should be presented for the AUROC and other evaluation metrics.**

We have included the Confidence Intervals (CIs) in all our evaluation metrics in the revised manuscript.

- 4. P 11 The authors should clarify that a AUROC of 0.5 indicates no discrimination and so the higher the curve above the diagonal the better the predictive accuracy.**

As suggested we have clarified that a AUROC of 0.5 indicates no discrimination and so the higher the curve above the diagonal the better the predictive accuracy.

- 5. I think the sensitivity presented in the abstract is misleading as it comes from a very high risk selected population (patients with an average of 40 presentations) and is much higher than the value from the internal validation.**

As suggested we have removed the sensitivity results using the external validation in the abstract.

Reference

1. Dinh MM, Berendsen Russell S, Bein KJ, et al. Trends and characteristics of short-term and frequent representations to emergency departments: A population-based study from New South Wales, Australia. *Emergency Medicine Australasia* 2016;28(3):307-12.
2. Jelinek GA, Jiwa M, Gibson NP, et al. Frequent attenders at emergency departments: a linked-data population study of adult patients. *Medical Journal of Australia* 2008;189(10):552.
3. Berry JG, Gay JC, Joynt Maddox K, et al. Age trends in 30 day hospital readmissions: US national retrospective analysis. *BMJ* 2018;360 doi: 10.1136/bmj.k497
4. Hamner JB, Ellison KJ. Predictors of hospital readmission after discharge in patients with congestive heart failure. *Heart & Lung: The Journal of Acute and Critical Care* 2005;34(4):231-39.
5. Risk factors for 30-day hospital readmission in patients? 65 years of age. Baylor University Medical Center Proceedings; 2008. Baylor University Medical Center.

6. Gupta S, Tran T, Luo W, et al. Machine-learning prediction of cancer survival: a retrospective study using electronic administrative records and a cancer registry. *BMJ open* 2014;4(3):e004007.
7. Shen Y, Tay YC, Teo EWK, et al. Association between the elderly frequent attender to the emergency department and 30-day mortality: A retrospective study over 10 years. *World Journal of Emergency Medicine* 2018;9(1):20-25. doi: 10.5847/wjem.j.1920-8642.2018.01.003
8. Nepean Blue Mountains Local Health District. Nepean Blue Mountains Local Health District Healthcare Services Plan 2012 to 2022. Kingswood: Nepean Blue Mountains Local Health District., 2013.

VERSION 2 – REVIEW

REVIEWER	Shen Yuzeng Singapore General Hospital, Singapore
REVIEW RETURNED	27-May-2018

GENERAL COMMENTS	<p>For abstract, instead of stating the study is looking at FVs to EDs under the Objective section, it would be more accurate to state that the study is attempting to work on ED FVs within the younger and general patient age groups. This has implications regarding the generalizability of the study.</p> <p>Also similarly, under the limitations section, it should be reflected that the study's predictive model does not apply to patients who are more than 70 years of age, for which another model needs to be applied.</p>
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REVIEWER	Jackie Cooper Queen Mary University of London
REVIEW RETURNED	09-May-2018

GENERAL COMMENTS	I am happy with the authors' response to my comments.
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VERSION 2 – AUTHOR RESPONSE

Reviewer 2 (R2)

1. For abstract, instead of stating the study is looking at FVs to EDs under the Objective section, it would be more accurate to state that the study is attempting to work on ED FVs within the younger and general patient age groups. This has implications regarding the generalizability of the study.

We thank the Reviewer for the constructive comments. As suggested we have now clarified the statement in the abstract (see page 2) as follows:

Objective: To examine the characteristics of frequent visitors (FVs) to emergency departments (EDs) and develop a predictive model to identify those with high risk of a future re-presentations

to ED among younger and general population (age \leq 70).

2. Also similarly, under the limitations section, it should be reflected that the study's predictive model does not apply to patients who are more than 70 years of age, for which another model needs to be applied.

We thank the Reviewer for the constructive comments. As suggested we have now included the following statement in page 14:

The model cannot be applied to predict FVs in older age group (age $>$ 70) since it was designed to predict FVs among younger and general population (age \leq 70).