

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Utility of models to predict 28-day or 30-day unplanned hospital readmissions: An updated systematic review
<b>AUTHORS</b>	Zhou, Huaqing; Della, Phillip; Roberts, Pam; Goh, Louise; Dhaliwal, Satvinder

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Kukuh Noertjojo, MD MHSc MSc The Evidence-Based Practice Group, Clinical Services, WorkSafeBC, British Columbia. CANADA
<b>REVIEW RETURNED</b>	22-Jan-2016

<b>GENERAL COMMENTS</b>	<ul style="list-style-type: none"> <li>- Please check spelling (at least I found one spelling mistake)</li> <li>- If the authors have registered the protocol of this systematic review please provide the registration information</li> <li>- perhaps the objective of this systematic review would be clearer if it say something like ".. to update previous systematic review..." as opposed to "..to synthesize evidence..."</li> <li>- in methods - search strategy perhaps the fact that manual search was done should also be stated in here</li> <li>- in methods - inclusion/exclusion perhaps the fact that abstract only articles were excluded should be stated in here replacing ...in English with full text access...</li> <li>- in methods - inclusion/exclusion criteria stated that eligible studies were peer reviewed with clear evidence of research methodology. I think this statement needs to be defined</li> <li>- in methods - study selection and data extraction, perhaps the roles of reviewers need to be clarified (name abbreviation for e.g.) on each of these issues</li> <li>- on page 9 last sentence just above the Study Characteristics" there is a statement ...that overall risk of bias was low so there was no further exclusion of studies. If this was the intention of the authors, I think they need to mention this in their methods - inclusion/exclusion criteria and defined what is high and low risk of bias.</li> </ul> <p>Thank you for the opportunity of reviewing this rather complex systematic review.</p>
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<b>REVIEWER</b>	Rhema Vaithianathan Auckland University of Technology
<b>REVIEW RETURNED</b>	01-Feb-2016

<b>GENERAL COMMENTS</b>	I would suggest that they provide more detail on the methods used by each author. Eg, type of data mining method - regression/
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	machine learning etc; and also whether the test statistics (AUR) where calculated for a validation sample. Some discussion of how well the methodologies are undertaken would be helpful. There are also some grammatical errors that need cleaning up.
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<b>REVIEWER</b>	Paolo Eusebi University of Perugia, Italy
<b>REVIEW RETURNED</b>	26-Feb-2016

<b>GENERAL COMMENTS</b>	The paper is interesting and reads well. The addressed issue is a relevant one in the public health field. The adopted methodology seems appropriate. I would prefer to see clearly stated in the title that this is an updated systematic review. I suggest including, in the presentation of results, a more in depth illustration of the ability of predictive models of classifying patients in terms of clinical risk categories (if appropriate).
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

- Please check spelling (at least I found one spelling mistake)

Response:

Ginger software has been used to check any spelling errors, which were corrected and highlighted as coloured text.

- If the authors have registered the protocol of this systematic review please provide the registration information

Response:

Not applicable. There is no registered protocol of this systematic Review.

- perhaps the objective of this systematic review would be clearer if it say something like ".. to update previous systematic review..." as opposed to "..to synthesize evidence..."

Response:

The objective has been revised as:

"...to update previous systematic review..." (Also refer to Review 3 – revised title as ‘...an update SR...’)

- in methods - search strategy perhaps the fact that manual search was done should also be stated in here

Response:

Under search strategy and the PRISMA flow chat, we have already stated that

“A hand search reference list of the remaining 60 articles was also conducted and no additional studies were identified” (highlighted as colored text)

- in methods - inclusion/exclusion perhaps the fact that abstract only articles were excluded should be stated in here replacing ...in English with full text access...

Response:

Under exclusion criteria, we have added that

“...abstract only articles were excluded...”

- in methods - inclusion/exclusion criteria stated that eligible studies were peer reviewed with clear

evidence of research methodology. I think this statement needs to be defined

Response:

It has been revised as:

..Peer reviewed journals with details of study design clearly stated...

- in methods - study selection and data extraction, perhaps the roles of reviewers need to be clarified (name abbreviation for e.g.) on each of these issues

Response:

The roles of reviewers have been added under study selection and data extraction as:

Initial literature searches were conducted by HZ and PD. Two authors (HZ and LG) independently screened titles, ... and only a handful of studies warranted discussion between the authors (HZ, LG, SD, PD and PR), and to reach consensus as to whether they met the inclusion criteria.

Data were extracted from the final included studies by three authors (HZ, LG and SD).

The assessment of risk for bias was completed by two independent reviewers (HZ and SD).

- on page 9 last sentence just above the Study Characteristics" there is a statement ...that overall risk of bias was low so there was no further exclusion of studies. If this was the intention of the authors, I think they need to mention this in their methods - inclusion/exclusion criteria and defined what is high and low risk of bias.

Response:

The statement has been revised as:

The overall risk of bias of the 60 studies were low when evaluated against the six domains of potential bias. All studies described the population of interest adequately for key characteristics, the response rate information was clearly stated, adequate proportion of the study population had complete data on all independent variables, the outcome variable readmission was measured with sufficient accuracy, and the method of statistical analysis was appropriate for the design of the study.

Reviewer: 2

-I would suggest that they provide more detail on the methods used by each author. Eg, type of data mining method - regression/ machine learning etc; and also whether the test statistics (AUR) were calculated for a validation sample. Some discussion of how well the methodologies are undertaken would be helpful.

Response:

We have added that

Multivariable logistic regression model was used in all included studies. In logistic regression the outcome variable is the log of the odds of the event (probability of readmission / (1 – probability of readmission)). Once the final model is determined, the multivariable logistic regression allows for the calculation of probability of readmission for cohort studies. The predicted probabilities of the final multivariable logistic model are also used for computing the ROC curve and the calculation of the ROC, a measure of model discrimination.

The AUC for validation studies ranged from 0.5362 – 0.8385, being slightly lower than those for the derivation study 0.2174 – 0.8885.

-There are also some grammatical errors that need cleaning up.

Response:

Ginger software has been used to check any grammatical errors, which were corrected and highlighted in blue.

Reviewer: 3

- I would prefer to see clearly stated in the title that this is an updated systematic review.

Response:

The title has been revised as:

“Utility of models to predict 28-day or 30-day unplanned hospital readmissions: An updated systematic review”

-I suggest including, in the presentation of results, a more in depth illustration of the ability of predictive models of classifying patients in terms of clinical risk categories (if appropriate).

Response:

We have added that:

Predictive risk of readmission was assessed in all included studies, but only 14 of the included 60 studies specified thresholds for risk categories. Thresholds were ranged from 4% to 80%.

Risk of Bias Assessment: The assessment of risk for bias was completed by two independent reviewers. The ratings of “Yes”, “Partly”, “No” or “Unsure” was given to each domain and then an overall risk of “low” or “high” was assigned to each study

Six Domains (Study participation Study attrition Prognostic factor measurement Outcome measurement Confounding measurement and account Analysis) and Overall level of risk of bias

#### All-Cause UHRs (14)

Escobar et al. (2015) Yes Yes Yes Yes Yes Yes Low

Yu et al. (2015) Yes Yes Yes Yes Yes Yes Low

Baillie et al. (2013) Yes Yes Yes Yes Yes Yes Low

Choudhry et al. (2013) Yes Yes Yes Yes Yes Yes Low

Gildersleeve et al. (2013) Yes Yes Yes Yes Yes Yes Low

Kruse et al. (2013) Yes Yes Yes Yes Yes Yes Low

Richmond (2013) Yes Yes Yes Yes Yes Yes Low

Shulan et al. (2013) Yes Yes Yes Yes Yes Yes Low

van Walraven et al. (2013) Yes Yes Yes Yes Yes Yes Low

Cotter et al. (2012) Yes Yes Yes Yes Yes Yes Low

Khan et al. (2012) Yes Yes Yes Yes Yes Yes Low

Lee (2012) Yes Yes Yes Yes Yes Yes Low

van Walraven et al. (2012a) Yes Yes Yes Yes Yes Yes Low

van Walraven et al. (2012b) Yes Yes Yes Yes Yes Yes Low

#### Cardiovascular Disease Related UHRs including Pneumonia (11)

Hebert et al. (2014) Yes Yes Yes Yes Yes Yes Low

Iannuzzi et al. (2014a) Yes Yes Yes Yes Yes Yes Low

Keyhani et al. (2014) Yes Yes Yes Yes Yes Yes Low

Rana et al. (2014) Yes Yes Yes Yes Yes Yes Low

Shahian et al. (2014) Yes Yes Yes Yes Yes Yes Low

Shams et al. (2014) Yes Yes Yes Yes Yes Yes Low

Sharif et al. (2014) Yes Yes Yes Yes Yes Yes Low

Lucas et al. (2013) Yes Yes Yes Yes Yes Yes Low

Wallmann et al. (2013) Yes Yes Yes Yes Yes Yes Low

Wasfy et al. (2013) Yes Yes Yes Yes Yes Yes Low

Krumholz et al. (2011) Yes Yes Yes Yes Yes Yes Low

#### Cardiovascular Disease Related UHRs including Pneumonia – Heart Failure only (11)

Betihavas et al. (2015) Yes Yes Yes Yes Yes Yes Low

Di Tano et al. (2015) Yes Yes Yes Yes Yes Yes Low

Huynh et al. (2015) Yes Yes Yes Yes Yes Yes Low

Raposeiras-Roubin et al. (2015) Yes Yes Yes Yes Yes Yes Low

Sudhakar et al. (2015) Yes Yes Yes Yes Yes Yes Low

Fleming et al. (2015) Yes Yes Yes Yes Yes Yes Low  
 Wang et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Eapen et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Zai et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Au et al. (2012) Yes Yes Yes Yes Yes Yes Low  
 Watson et al. (2011) Yes Yes Yes Yes Yes Yes Low  
 Cardiovascular Disease Related UHRs including Pneumonia – Pneumonia only (2)  
 Mather et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Lindenauer et al. (2011) Yes Yes Yes Yes Yes Yes Low  
 General Medical Condition Related UHRs (10)  
 Shadmi et al. (2015) Yes Yes Yes Yes Yes Yes Low  
 Tsui et al. (2015) Yes Yes Yes Yes Yes Yes Low  
 Donzé et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 He et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Taha et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Donzé et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Tan et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Billings et al. (2012) Yes Yes Yes Yes Yes Yes Low  
 Zapatero et al. (2012) Yes Yes Yes Yes Yes Yes Low  
 Gruneir et al. (2011) Yes Yes Yes Yes Yes Yes Low  
 Medical Condition UHRs – Cirrhosis only (2)  
 Singal et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Volk et al. (2012) Yes Yes Yes Yes Yes Yes Low  
 Medical Condition UHRs – Chronic Kidney Disease only (1)  
 Perkins et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Medical Condition UHRs – HIV only (1)  
 Nijhawan et al. (2012) Yes Yes Yes Yes Yes Yes Low  
 Medical Condition UHRs – Acute Pancreatitis (1)  
 Whitlock et al. (2011) Yes Yes Yes Yes Yes Yes Low  
 Surgical Conditions Related UHRs (6)  
 Taber et al. (2015) Yes Yes Yes Yes Yes Yes Low  
 Lawson et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Iannuzzi et al. (2014b) Yes Yes Yes Yes Yes Yes Low  
 Mesko et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Moore et al. (2014) Yes Yes Yes Yes Yes Yes Low  
 Graboyes et al. (2013) Yes Yes Yes Yes Yes Yes Low  
 Mental Health Conditions Related UHRs (1)  
 Vigod et al. (2015) Yes Yes Yes Yes Yes Yes Low

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Kukuh Noertjojo, MD MHSc MSc Evidence-Based Practice Group, Clinical Services, WorkSafeBC
<b>REVIEW RETURNED</b>	14-Apr-2016

<b>GENERAL COMMENTS</b>	The authors have fully revised this paper as suggested by Editor and reviewers and I think it is ready for publication. Thank you for letting me review this good research paper.
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<b>REVIEWER</b>	Rhema Vaithianathan
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	Auckland University of Technology , New Zealand and Singapore Management University, Singapore
<b>REVIEW RETURNED</b>	27-Apr-2016

<b>GENERAL COMMENTS</b>	Please could they check their cited work (74) as it seems strange that it has a C-Statistic of 0.21 (how can you get a c-stat less than 0.5??!!).  Maybe a typo - please clean that up. Then all good to go.
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<b>REVIEWER</b>	Paolo Eusebi University of Perugia, Italy
<b>REVIEW RETURNED</b>	20-Apr-2016

<b>GENERAL COMMENTS</b>	The authors have amended the text according to what suggested by the reviewers.
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### VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

The authors have fully revised this paper as suggested by Editor and reviewers and I think it is ready for publication.

Thank you for letting me review this good research paper.

Reviewer: 3

The authors have amended the text according to what suggested by the reviewers.

Reviewer: 2

Please could they check their cited work (74) as it seems strange that it has a C-Statistic of 0.21 (how can you get a c-stat less than 0.5??!!).

Maybe a typo - please clean that up. Then all good to go.

Response:

We thank the reviewer for the comment. A C-statistic value of less than 0.5 is possible, as stated by Hand D 2009 (Page 106), as it indicates that the likelihood of readmission is lower. The referenced manuscript confirms the 0.21 value. To clarify the interpretation of this value we have included the following statement in the manuscript:

The C-statistic of 0.21(Zai et al 2013) was obtained for heart failure patients in the Telemonitoring program were less likely to be admitted. This indicates that the Telemonitoring program was effective in identifying and intervening in patients who were reporting symptoms and thus reduce the likelihood of readmission.

Reference

Hand. D. Measuring classified performance: a coherent alternative to the area under the ROC curve. Mach Learn (2009); 77:103-23.