PEER REVIEW HISTORY

This paper was submitted to the BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Predicting risk of emergency admission to hospital using primary care data: derivation and validation of QAdmissions score
AUTHORS	Hippisley-Cox, Julia; Coupland, Carol

VERSION 1 - REVIEW

REVIEWER	Howe, Amanda University of East Anglia, School of Medicine Health Policy and Practice
REVIEW RETURNED	20-May-2013

GENERAL COMMENTS	Good paper, interesting and relevant should be published

REVIEWER	Purdy, Sarah University of Bristol
REVIEW RETURNED	20-May-2013

GENERAL COMMENTS	Is the article important? The importance of trying to identify those at high risk of future hospital admission is clear - especially for those working in the NHS. However, the relevance for readers from other countries is less apparent. The prediction model is similar to previously described models although the authors are to be lauded for the transparency of their approach and the offer to share the model for use in primary care. However, it is unclear how readily the model can be implemented by practices. The article reads well and make sense. It does have a clear message which is that the authors were able to derive and validate a model to predict emergency admissions using data from primary care. However, as with all such models, the sensitivity and PPV is low. Originality As above, the work adds to a field where previous similar models (PEONY, PARR, Combined model) have already been described. The validation model for this study was derived from primary care

	practice data only which is original. However, the generalisability to non QRisk practices where coding of admissions may be less robust is not assured. As previous admissions are such a big driver of future admissions this data is vital to a 'real time' model and my experience is that such data are not well recorded on GP systems. The research question is clearly defined and appropriate to the methods used. In principal the overall design of study is appropriate and adequate to answer the research question. However, there are some concerns about the methods used. The population is adequately described apart from the fact that the coding of admissions in this sample may not reflect coding in a general sample of practices (see above). My main concern relates to the explanatory variables used. The outcome is all emergency admissions yet the predictive variables are limited and do not include all possible relevant variables. For example only a small number of drug groups are included (statins, NSAIDS, anticoagulants, corticosteroids, antidepressants and antipsychotics). The logic for including this group of drugs is unclear. There is no inclusion of drugs likely to prevent/precipitate other sorts of admissions e.g. triple therapy for COPD (Philip Short et al Chest 2012, 141; 81-86) or therapies recommended by NICE etc to optimise treatment. This is a major shortcoming of the study. It is difficult to how generic emergency admissions can be predicted effectively using this sort of approach - perhaps a disease specific approach would be more appropriate? A similar comment applies to the reporting of investigations as explanatory variables - renal function is not included, nor is albumin. The inclusion of PCT rather than SHA would be a better reflection of local service delivery. The main outcome measure is clear. However, I am concerned about the reporting of 'methods of admission; e.g. bed bureau etc. These are notoriously unreliable in HES and reflect local practices and coding rather than clinical pathways e.g. a patient may be admitted via A&E even though the GP sent them to the hospital for admission. There is no attached reporting statement - the STROBE guidelines could have been used for reporting a cohort study? There are no ethical concerns. Results With the caveats above the results are well presented and answer the research question. Discussion The authors do not discuss regression to the mean and the implications for this study. Despite the 2 year duration of follow up this is still an issue.

	The abstract should acknowledge some of the issues described above.

REVIEWER	Freund, Yonathan Hôpital Pitié-Salpêtrière, Emergency Department
REVIEW RETURNED	30-May-2013

GENERAL COMMENTS	The authors present a study that develops and validates an algorithm to estimate tisk of emergency hospital admission in primary care. This study addresses a very important topic, and is well written. The results seem very promising and the study of very high methodological quality. Results are generalisable to all UK, although the international validity of this method is very unlikely. Major queries: 1) Difficulty for a non statistical specialist to follow your method and result. We don't know what results are relevant, and especially, what are the performances of your model that support its interest. Are we looking at D stat? sensitivity? PPV? Performances for top tenth? top 1%? comparison between predicted risk and observed? We understand that you provide statistical proofs that your model is robust. However we would like to see that it is accurate for a specific use. 2) The lack of the primary complaint as a variable in the model. The same results will apply for the same patient that consult his GP for routine follow up, than for typical chest pain or acute onset of neurological deficit for example. It feels like we are missing a major component. 3) How did you take into account the patients that were actually admitted with elective admission? Those one would not have emergency admission, then no primary endpoint. However, should be incorporated as very high risk of admission. 4) It is not clear how and when should this algorithm be used. At the time a patient consult his GP? Or is it a continuous measure for each patient of the primary care, that is to be updated continuously (eg when the GP receive a new lab results for his patient, ...)? I) ABSTRACT: - It is unclear what you mean with 2.8 millions patients studied with 4.6 millions person years (and same for validation cohort). What does the 4.6 millions person years correspond to? - Endpoint: would need a time frame. Awkward formulation, i would say "Emergency admission to hospital ... within the study period (or 2 years). It is unclear what time frame you are considering. 2 years starting from inclusion, or 2 years from the begining of the study? As your cohort is open, it seems very important - Risk factor: Haven't you recorded reason for consultation / primary complaint? - Results: It would be interesting to report the raw rate of your primary endpoint. II) INTRODUCTION

	- It is not obvious what you define as emergency admission, although you define it later on. We understand that it opposes to elective or planned admission, likely through A&E. The reader (including myself) might not understand what other kind of emergency admissions exist in your country. Maybe it is worth to explain succintly this major concept for your study. - What is the rate of emergency admission / elective admissions / others? This is of great interest for the reader to understand the situation, more than the cost of it. Whether it is extra cost vs elective admission or raw cost is unclear too. - One of the major poblem of emergency admissions is emergency admissions through A&E, recently reported by NHS medical director and health minister, as A&E are facing serious problems with no clue of solution in the future. - p1l43: Might want to cite the recent study by Donze et al., JAMA Intern Med. 2013;173(8):632-638. III) METHODS There is one point that needs clarification. You enrolled patients in an open cohort settings for 2 years inclusions. Primary endpoint was sought then for different time frame. If i understand correctly, say a patient is recruited in november 2011 then he will have only a short time follow up, and the analysis won't predict his 2 years risk of re admission, but rather his 2 months readmission risk! How do you cope with that bias? Why then having chosen an open cohort, or a fixed 2 years follow up? - Were all hospitals in the country linked to the HES database? this needs further clarification for reader not familiar with NHS. - Primary complaint / Diagnosis of the visit could not hve been taken into account? note that p2L24 you mention your using "clinical diagnosis" in your algorithm - p4L49 no coma after "final model". - The methods section is no very easy to understand for a non statistician specialist. It is unclear what you are relying on to validate your model. Are you aiming for PPV? sensitivity? AUC ROC? It is unclear what D stat is, is it somehow similar to C stat of AUC ROC? I let the statistical reviewer report on this. IV) RESULTS On the whole, this section is not very easy to read. We don't know exactly what is it you are looking for. For what i understand, you are firstly looking for factors associated to readmission using cox model and other adjustments.Then evaluate an algorithm with the variables that have been selectioned. Are you using all of these or some of them have no impact? Then assess the statistical performances of your model, being sensitivity/PPV/AUC ROC? Are you looking for threshold? Then you are evaluating the correlation of observed and predicted rate? Then discrimination and calibration of the model? Apology if i misunderstand, but i think you should rearrange results so that we can follow your method, and explain better what is it you are relying on. I understand all of these values are important but for the study to be readable by non-statistician you should probably help the reader with hierachization and organization of your results.

	p6L21 " error ref source not found" please correct. Do you mean "table 1"? I think that table 1 would be more suitable as an appendix Table 2: it is not clear why you present only some variables, being age, location and ethnicity. what about the others? p6 L32: I am confused. You mention in the text 9.3% of emergency admission, and 5.78% in the table 2. Apologies if i am missing something. Same applies for the validation cohort p8 L8: mention of figure 2 although probably refers to figure 1. V) DISCUSSION - p10 l30 It is not obvious what are the differences between the datas of GP alone and linked GP-HES datas. What information could be missing in the GP datas alone? It appears in your description of factors included in the model that they all can be extracted from the GP / Primary care practice software. - p11l5 You chose a cut off a 1%. In the results section you chose 10%. Although you state that these are only examples, it can gives the impression that you are "choosing" threshold with good performances, rather than define a priori cut-off (maybe derived from the ROC Curve?), or make a sensitivity analysis. To be fair, the next paragraph expresses this question, and we agree that determining a threshold for intervention is beyond scope of this study, however, one (or more, with "gray zone" approach) threshold for statistical analysis could be interesting. - One limitation that needs to be expressed is the classification bias for patients with elective admission. If I understand correctly, a patient with high risk of emergency admission could have been referred by his primary care practicioner to the hospital for elective admission. Then, he will not have the primary endpoint of your study, although being at very high risk of admission. - Other limitation includes the different length of follow up for different patients. -The authors address the limitation in the international generalization of their results.

REVIEWER	Wong, Hannah York University, School of Health Policy and Management
REVIEW RETURNED	05-Jun-2013

GENERAL COMMENTS	This paper develops and validates a risk prediction algorithm for emergency admissions to hospital. The authors analyze 2 years worth of primary care practice data and randomly allocated two thirds of practices to a derivation cohort and one-third to the validation. The final algorithm incorporates 30 variables and explains ~42% of variation in the validation cohort. This is a very well written paper and well conducted observation study. The rationale for the study was clear and well written and the authors have described their methods and results clearly and succinctly. A few suggestions for the authors to consider:

	1. Would type of services (nursing services in domiciliary or nursing home, receiving home health care services) be a patient-level predictor? In addition to prior hospital admission, would longer length of stay also be a significant predictor? 2. Studies have demonstrated that hospitalizations/readmissions vary by hospital. Future versions of the model may want to consider hospital-level characteristics. 3. Future versions of the model may also want to look at an additional outcome measure: emergency department episodes that did not result in inpatient hospitalization. Would this be difficult to incorporate? 4. Please comment on how the risk prediction algorithm might be a valuable tool with respect to proposed changes to English NHS policy that connects readmissions to hospital income. 5. Please comment on what elements primary care should be collecting to better predict emergency admissions to hospital. 6. The authors may wish to consider including or commenting on the following articles: Kansagara D, Englander H, Salanitro A, et al. Risk prediction models for hospital readmission: a systematic review. Jama 2011; 306:1688-1698. van Walraven C, Wong J, Forster AJ. LACE+ index: extension of a validated index to predict early death or urgent readmission after hospital discharge using administrative data. Open Med 2012; 6:e80-90. Lemke KW, Weiner JP, Clark JM. Development and validation of a model for predicting inpatient hospitalization. Med Care 2012; 50:131-139. Mathison DJ, Chamberlain JM, Cowan NM, et al. Primary care spatial density and nonurgent emergency department utilization: a new methodology for evaluating access to care. Acad Pediatr 2013; 13:278-285. Wallace E, Hinchey T, Dimitrov BD, Bennett K, Fahey T, Smith SM. A systematic review of the probability of repeated admission score in community-dwelling adults. J Am Geriatr Soc 2013; 61:357-364.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 – had no specific comments to address.

Reviewer: 2

The prediction model is similar to previously described models although the authors are to be lauded for the transparency of their approach and the offer to share the model for use in primary care. However, it is unclear how readily the model can be implemented by practices.
Response: The Qadmissions model can be used either by the public facing web calculator (www.qadmissions.org) or can be integrated into the GP clinical computer system in the same way that QRISK2, QDiabetes and QFracture have been implemented. We have added this to section 4.1 of the discussion. Since the model can run on GP data alone, the practicalities of implementation are much simpler than models which can only run on primary care data linked to secondary care data as described in the introduction.

The validation model for this study was derived from primary care practice data only which is original. However, the generalisability to non QResearch practices where coding of admissions may be less robust is not assured. As previous admissions are such a big driver of future admissions this data is vital to a 'real time' model and my experience is that such data are not well recorded on GP systems. The population is adequately described apart from the fact that the coding of admissions in this sample may not reflect coding in a general sample of practices (see above).
Response: We agree with the reviewer that coding, generalizability and the performance of the model in an external sample is very important. In light of the comment regarding coding of admissions on GP data used for the validation (which is also highlighted by another reviewer), we have refined our definition of emergency admission recorded on the GP data and provided more detail on how this was done in the methods (section 2.6). We have now included a supplementary table A which includes the clinical codes used to search the GP data.
Also, since our original submission of the paper of the BMJ, we obtained approval from the CPRD ISAC committee to test the performance of QAdmissions on a separate group of practices and patients contributing to the Clinical Research Data Link (ISAC reference 13_079). Practices contributing to this database use a different clinical computer system (In Practice Systems) from QResearch (which uses EMIS). We have included the results of this external validation as an extra column alongside the results for QResearch in tables 1, 2, 4 and 5. The results demonstrate very similar characteristics both for coding for the outcome and predictor variables in the CPRD as in the original QResearch derivation and validation samples. Also, the validation statistics show comparable performance in each validation cohort. This provides stronger evidence regarding the likely generalizability of the findings to practices using the two most commonly used GP computer systems (EMIS, which is used by 55% of GPs and INPS which is used by 20% of GPs).

My main concern relates to the explanatory variables used. The outcome is all emergency admissions yet the predictive variables are limited and do not include all possible relevant variables. For example only a small number of drug groups are included (statins, NSAIDS, anticoagulants, corticosteroids, antidepressants and antipsychotics). The logic for including this group of drugs is unclear. There is no inclusion of drugs likely to prevent/precipitate other sorts of admissions e.g. triple therapy for COPD (Philip Short et al Chest 2012, 141; 81-86) or therapies recommended by NICE etc to optimise treatment. This is a major shortcoming of the study. It is difficult to how generic emergency admissions can be predicted effectively using this sort of approach - perhaps a disease specific approach would be more appropriate?
Response: We did not test every possible diagnosis or every possible drug as there are a huge number which could generate spurious associations. Instead we focused on regular medication already thought to be predictive of emergency admission[1] or events likely to result in an emergency admission. For example, NSAIDS, anticoagulation, antidepressants, antipsychotics were all significant in the PEONY study[1]. A number of these drugs have also been included in related risk prediction algorithms associated with acute events likely to lead to hospital admission such as corticosteroids and antidepressants (predictive of osteoporotic fracture[2]), antipsychotics (predicted of venous

thrombosis[3]), and NSAIDs (predictive of moderate to severe renal failure[4]). We tested anti-hypertensives[5] as part of a composite variable 'treated hypertension' but this was not significant on multivariate analysis so was not included in the final model. We think the current text in the paper is sufficient in what is already a detailed paper. Should this paper be published in BMJ Open then the review and this response will be available for the interested reader.

We decided to focus this initial paper on the global outcome of emergency hospital admissions since that is what NHS England have mandated all practices to do and existing tools all have problems which make them difficult or inappropriate to implement. We did consider a more disease specific approach (to complement the risk prediction tools which already exist for conditions which might result in an emergency admission such as QRISK, QFracture and QThrombosis) and have flagged this in the discussion as an area for future research.

A similar comment applies to the reporting of investigations as explanatory variables - renal function is not included, nor is albumin.
Response; whilst renal blood tests are not included, the model does include chronic renal disease as a predictor variable which we think is a more robust variable than glomerular filtration rate or creatinine. Whilst we have not included albumin, we have included abnormal liver function tests which includes significantly raised ALT, bilirubin and GGT levels (ie > 3 times the upper limit of normal). There is a difficult balance to be struck between inclusion of every possible variable and ensuring the model is robust and can be implemented.

The inclusion of PCT rather than SHA would be a better reflection of local service delivery.
Response; we included SHAs in the model as we had sufficient number of patients in each of the 10 SHAs to undertake the modeling. We did not include PCTs as these have now been abolished as part of the latest NHS re-organisation and have been replaced by 212 CCGs. At present we do not have enough data to model each CCG separately and also the configuration of CCGs is likely to change as the health service reforms become established. SHA's are more durable units for inclusion in a prediction model.

The main outcome measure is clear. However, I am concerned about the reporting of 'methods of admission; e.g. bed bureau etc. These are notoriously unreliable in HES and reflect local practices and coding rather than clinical pathways e.g. a patient may be admitted via A&E even though the GP sent them to the hospital for admission.

Response; we have removed the text in section 3.2 which reports on the methods of admission.

There is no attached reporting statement - the STROBE guidelines could have been used for reporting a cohort study?
Response: STROBE was included in the submission and is provided for the submission to BMJ open

The authors do not discuss regression to the mean and the implications for this study.
Despite the 2 year duration of follow up this is still an issue.
Response: This is a survival analysis and we don't think that regression to the mean is relevant here.

Reviewer: 3

Major queries:
Difficulty for a non statistical specialist to follow your method and result. We don't know what results are relevant, and especially, what are the performances of your model that support its interest. Are we looking at D stat? sensitivity? PPV? Performances for top tenth? top 1%? comparison between predicted risk and observed? We understand that you provide statistical proofs that your model is robust. However we would like to see that it is accurate for a specific use.
Response: We realize this type of paper can be difficult for the generalist reader although it does follow a format used in a number of related papers. We have included some additional explanatory text in the foot of table 4 which we hope will go some way to addressing this point. We had already included some discussion of the performance measures in section 4.1 of the discussion. The ROC value and positive predictive value of the score at a given threshold are likely to be the most important

statistical measures for comparisons between scores as these have been reported in other studies whereas the R^2 and D statistics generally have not.

2) The lack of the primary complaint as a variable in the model. The same results will apply for the same patient that consult his GP for routine follow up, than for typical chest pain or acute onset of neurological deficit for example. It feels like we are missing a major component.
Response: We think this is a good point – we did consider at the design stage having the outcome subdivided by the diagnosis/reason for admission. On exploring the data, we realized there were many hundreds of different ICD10 codes used as the primary diagnosis field and that there isn't a standard approach to grouping these. It would also have made the model much more complicated. It's possible that for future iterations of this model, we will look at multiple outcomes.

3) How did you take into account the patients that were actually admitted with elective admission? Those one would not have emergency admission, then no primary endpoint. However, should be incorporated as very high risk of admission.
Response: In section 2.3 we describe our definition of emergency admission which is the UK standard definition used across the NHS and used in other studies. We have amended the text to make this clearer.

4) It is not clear how and when should this algorithm be used. At the time a patient consult his GP? Or is it a continuous measure for each patient of the primary care, that is to be updated continuously (eg when the GP receive a new lab results for his patient, ...)?
Response: The intention for this algorithm is to be used in batch processing mode, applied to patients registered with a general practice, to generate a rank ordered list of patients at high risk for further management. It can be run on a regular basis (e.g. every day) or ad hoc, depending on the requirements of the practice. We have added this to section 4.1 of the discussion.

I) ABSTRACT:
- It is unclear what you mean with 2.8 million patients studied with 4.6 million person years (and same for validation cohort). What does the 4.6 million person years correspond to?
Response: we have clarified in the abstract that this is 4.6 million person years of follow-up.

- Endpoint: would need a time frame. Awkward formulation, i would say "Emergency admission to hospital ... within the study period (or 2 years). It is unclear what time frame you are considering. 2 years starting from inclusion, or 2 years from the beginning of the study? As your cohort is open, it seems very important
Response; we have clarified in the abstract that the endpoint is first emergency admission to hospital in the next two years.

- Risk factor: Haven't you recorded reason for consultation / primary complaint?
Response: see above

- Results: It would be interesting to report the raw rate of your primary endpoint.
Response: the numbers of admissions and their characteristics are reported in the text in section 3.2 and this refers to the rates which are included in Table 2.

II) INTRODUCTION

- It is not obvious what you define as emergency admission, although you define it later on. We understand that it opposes to elective or planned admission, likely through A&E. The reader (including myself) might not understand what other kind of emergency admissions exist in your country. Maybe it is worth to explain succinctly this major concept for your study.
Response: we have clarified this in section 2.3 (also see response above).

- What is the rate of emergency admission / elective admissions / others? This is of great interest for the reader to understand the situation, more than the cost of it. Whether it is extra cost vs elective admission or raw cost is unclear too.
Response: We have included the emergency admission rate in section 3.2 and table 2. We haven't added the admission rates for other types of admission as this was outside the scope of the study and might confuse readers.

- One of the major problems of emergency admissions is emergency admissions through A&E, recently reported by NHS medical director and health minister, as A&E are facing serious problems with no clue of solution in the future.
Response: We had included this information in section 3.2 but have since removed it in response to reviewer 2 (see above).

- p1l43: Might want to cite the recent study by Donze et al., JAMA Intern Med. 2013;173(8):632-638.
Response: thank you for this suggestion. Whilst this score by Donze is about 30 hospital re-admission, we think it is useful to include it in the discussion so have referenced in section 4.1. In particular, the C statistic in our study was 0.77 which is significantly higher than 0.71 in the Donze study.

III) METHODS
There is one point that needs clarification.
You enrolled patients in an open cohort settings for 2 years inclusions.
Primary endpoint was sought then for different time frame.
If i understand correctly, say a patient is recruited in November 2011 then he will have only a short time follow up, and the analysis won't predict his 2 years risk of re admission, but rather his 2 months readmission risk! How do you cope with that bias? Why then having chosen an open cohort, or a fixed 2 years follow up?
Response: just to clarify, our outcome was first emergency admission to hospital in the study period not re-admission. We chose to use an open cohort which allows patients to enter the cohort during the calendar study period as this best reflects the realities of primary care which has a dynamic population. By using survival analysis we accounted for censoring before two years follow-up and were able to predict risk of admission within 2 year by using the estimated baseline survivor function evaluated at 2 years.

- Were all hospitals in the country linked to the HES database? This needs further clarification for reader not familiar with NHS.
Response; Yes all English NHS hospital trusts are included on the Hospital Episodes database. We have clarified this in section 2.3

- Primary complaint / Diagnosis of the visit could not have been taken into account?
Response: please see response above to the previous reviewer.

note that p2L24 you mention your using "clinical diagnosis" in your algorithm
- p4L49 no coma after "final model".
Response: thank you for spotting this - we have corrected both of these
- The methods section is not very easy to understand for a non-statistician specialist. It is unclear what you are relying on to validate your model. Are you aiming for PPV? sensitivity? AUC ROC? It is unclear what D stat is, is it somehow similar to C stat of AUC ROC?
I let the statistical reviewer report on this.
Response: please see response above which addresses the same point. We have updated the information in the results, table 4 and the discussion.

IV) RESULTS
On the whole, this section is not very easy to read. We don't know exactly what is it you are looking for. For what i understand, you are firstly looking for factors associated to readmission using cox model and other adjustments. Then evaluate an algorithm with the variables that have been selected. Are you using all of these or some of them have no impact?
Then assess the statistical performances of your model, being sensitivity/PPV/AUC ROC? Are you looking for threshold?
Then you are evaluating the correlation of observed and predicted rate?
Then discrimination and calibration of the model?
Apology if i misunderstand, but i think you should rearrange results so that we can follow your method, and explain better what is it you are relying on. I understand all of these values are important but for the study to be readable by non-statistician you should probably help the reader with hierachization and organization of your results.

Response: we haven't changed the order of this as two of the reviewers commented on how well the paper is presented and we think this follows a logical sequence and is similar to the reporting used for a number of related papers which have been published in the BMJ. If the editor would prefer this to change, we don't have a strong objection.

p6L21 " error ref source not found" please correct.
Do you mean "table 1"? I think that table 1 would be more suitable as an appendix
Response: yes its table 1. We have updated this. We realize table 1 is long but prefer to keep it in the main body of the paper to ensure the reader has a readily accessible understanding of the study population.

Table 2: it is not clear why you present only some variables, being age, location and ethnicity. what about the others?
Response: We have already presented a lot of data in the paper and decided to focus on these breakdowns to show how the absolute rates of emergency admission vary by these key demographic factors.

p6 L32: I am confused. You mention in the text 9.3% of emergency admission, and 5.78% in the table 2. Apologies if i am missing something. Same applies for the validation cohort
p8 L8: mention of figure 2 although probably refers to figure 1.
The 9.3% refers to 9.3% of the total study population (n=2,857,476) which had at least one incident emergency admission. The figures in the table 2 are rates. We have amended the text in section 3.2 to make it clear what the 9.3% refers to.

V) DISCUSSION
- p10 l30 It is not obvious what are the differences between the data of GP alone and linked GP-HES data. What information could be missing in the GP data alone? It appears in your description of factors included in the model that they all can be extracted from the GP / Primary care practice software
Response: the HES-GP linked data includes prior admissions as recorded on HES data whereas the GP data model includes prior hospital admissions recorded on the GP clinical record. This variable is now described more clearly in section 2.6 of the methods and also the codes used to identify the prior admissions on the GP data alone are now listed in supplementary table A of the results.

- p11l5 You chose a cut off a 1%. In the results section you chose 10%.
Response: In Table 5, we presented a range of thresholds including1%, 5%, 10% 20%. : on page 11 (section 3.4) of the results, we gave the example of 10% cut off rather than duplicating the information in the table. We think this is OK.

Although you state that these are only examples, it can gives the impression that you are "choosing" threshold with good performances, rather than define a priori cut-off (maybe derived from the ROC Curve?), or make a sensitivity analysis. To be fair, the next paragraph expresses this question, and we agree that determining a threshold for intervention is beyond scope of this study, however, one (or more, with "gray zone" approach) threshold for statistical analysis could be interesting.

Response: we didn't have an a priori cut off when designing the study and there is no nationally recommended threshold. Therefore, as the reviewers suspected, we presented performance at a range of thresholds so that others can then select a threshold which best meets their requirements or which could form the basis of further economic analyses which were outside the scope of our project.

- One limitation that needs to be expressed is the classification bias for patients with elective admission. If I understand correctly, a patient with high risk of emergency admission could have been referred by his primary care practitioner to the hospital for elective admission. Then, he will not have the primary endpoint of your study, although being at very high risk of admission.
Response: We have clarified how the endpoint was defined in section 2.3 which should address this point (also see response to this mentioned above).

- Other limitation includes the different length of follow up for different patients.

Response: We designed the study and analysed the data using techniques which take account of the survival nature of the data. We think this is the preferred approach for developing such risk prediction tools.

Reviewer 4

Comments:
This paper develops and validates a risk prediction algorithm for emergency admissions to hospital. The authors analyze 2 years' worth of primary care practice data and randomly allocated two thirds of practices to a derivation cohort and one-third to the validation. The final algorithm incorporates 30 variables and explains ~42% of variation in the validation cohort.
This is a very well written paper and well conducted observation study. The rationale for the study was clear and well written and the authors have described their methods and results clearly and succinctly.
Response: thank you for these comments

A few suggestions for the authors to consider:

1. Would type of services (nursing services in domiciliary or nursing home, receiving home health care services) be a patient-level predictor? In addition to prior hospital admission, would longer length of stay also be a significant predictor?
   Response: We think this is a good suggestion and one which could be addressed in future versions of the score should type of nursing or home care service be recorded on the patients primary care electronic record. Also, whilst hospital admission is recorded on the GP record, the length of hospital admission is currently not recorded so had we included this as a predictor, then then it would make the score less applicable using GP data only (which was one of the key objectives of this work given the logistical problems in real time linkage between primary and secondary care data).

2. Studies have demonstrated that hospitalizations/readmissions vary by hospital. Future versions of the model may want to consider hospital-level characteristics.
   Response: We have included Strategic Health Authority as a proxy to take account of geographical variations in service provision. We considered a hospital level variable as has been used in other models but decided against this since hospitals change and merge, making the algorithm less applicable in future (indeed one of the problems of existing models is they include hospitals as parameters even though those hospitals no longer exist.)

3. Future versions of the model may also want to look at an additional outcome measure: emergency department episodes that did not result in inpatient hospitalization. Would this be difficult to incorporate?
   Response: This is another good suggestion. For emergency hospital admissions, then > 99% have a valid NHS number which enables reliable linkage of primary and secondary care records. For accident and emergency attendances, only 94% have a valid NHS number although this is increasing over time. We would hope to include A&E attendances in future versions of the tool once the recording of the NHS number is more complete.

4. Please comment on how the risk prediction algorithm might be a valuable tool with respect to proposed changes to English NHS policy that connects readmissions to hospital income.
   Response: We haven't commented on this in the paper since Qadmissions has been designed to be applied to patients in primary care who might not have had a recent hospital admission rather than apply to patients currently in hospital who might be at risk of a re-admission. It would be possible to develop a related tool for hospital re-admission but we think that should be the focus of a separate paper.

5. Please comment on what elements primary care should be collecting to better predict emergency admissions to hospital.

Response: All the variables needed to implement QAdmissions are already recorded on the primary care record although the clinical coding of prior admissions on the GP record does not always distinguish emergency from routine admission. An information recording standard could help this. We have commented on this in section 4.2 of the text.

6. The authors may wish to consider including or commenting on the following articles:
Response: thank you for these references – we have added one reference to readmission (see above) but didn't want to add further ones to avoid confusing the reader as this is a study about emergency admissions not re-admission. Of the references below, one (Lemke et al) is comparable to ours. However the full text of the article is not accessible.

References

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2. Hippisley-Cox J, Coupland C. Derivation and validation of updated QFracture algorithm to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study. Bmj 2012;**344**(may22 1):e3427-e27 doi: 10.1136/bmj.e3427[published Online First: Epub Date]|.
3. Hippisley-Cox J, Coupland C. Development and validation of risk prediction algorithm (QThrombosis) to estimate future risk of venous thromboembolism: prospective cohort study. BMJ 2011;**343**:d4656 doi: 10.1136/bmj.d4656[published Online First: Epub Date]|.
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5. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ 2008:bmj.39609.449676.25 doi: 10.1136/bmj.39609.449676.25[published Online First: Epub Date]|.