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

TITLE (PROVISIONAL)	Here one year, gone the next? Investigating persistence of frequent emergency department attendance, a retrospective study in Australia.
AUTHORS	Lago, Luise; Westley-Wise, Victoria; Mullan, Judy; Lambert, Kelly; Zingel, Rebekah; Carrigan, Thomas; Triner, Wayne; Eagar, Kathy

VERSION 1 – REVIEW

REVIEWER	Susana Garcia-Gutierrez Reserach Unit. Hospital Galdakao-Usansolo. Osakidetza-Servicio Vasco de Salud
REVIEW RETURNED	19-Nov-2018

GENERAL COMMENTS	This is a very important question and this works is an opportunity to quantify and explain factors realted to revisits to emergeny departments. Nevertheless, I think there are methological concerns to be solved: 1.- Deniition of outcome: I read the reference used by the authors to defined frequent users(Doupe MB, Palatnick W, Day S, et al. Frequent Users of Emergency Departments: Developing Standard Defintions and Defining Prominent Risk Factors. Ann Emerg31 Med 2012;60:24–32). Doupe et al defined less frequent users and highly frequent users,asumming all of them were frequent users. You used this definition to explain non-FA and FA, and I think the cutoff point must be revised. - In a large study like this, with all the centrs of a helath system included in the analysis is requiered to perfom a multilevel analysis or at least, adjust by the center. -In adittion to that, other measures orf control for counding must be developed, propensity score matching for example. -This is an oportunity to create predicition models in order to create profiles of FA. You should do an effort in this way. -As a minor question, you should be careful with the contents incuded in each of the sections of the manuscript, that is, the inclusion of explanation of bibliography in outcomes section, for example, makes the text confusing.

REVIEWER	Leonardo Palombi Department of Biomedicine and Prevention, University of Rome Tor Vergata, Italy
REVIEW RETURNED	10-Dec-2018

GENERAL COMMENTS	The study is an important contribution to the knowledge of FA predictors in ED and I agree with the conclusions of the authors on: "This study has provided a unique, longitudinal perspective on ED, contrasting the demographic and diagnostic profile of

	temporary, repeat and persistent FA. However, I must stress that a large amount of analysis and processing produced by the authors, almost 1.2 million visits for more than 300.000 patients over 10 years has not generated or confirmed hypothesis, despite having the full epidemiological potential to do so. I am convinced that a study so important in terms of size, observation time and the number of variables analyzed can and should produce far-reaching conclusions. I would like to suggest to the authors to express more clearly some of these conclusions: for example, we understand that ED represents a social "mirror" of discomfort, poverty and some failures of the welfare system in the continuum of care, with particular regard to psychiatric diseases or addictions. It is also understood that population subgroups present different profiles of FA, for example, those of young and older people. The study could even provide important cost-benefit information for patients who evidently resort to ED for lack of alternatives. I, therefore, propose to the authors of such an important study to widen and enrich their conclusions. It would then be useful to dedicate part of the analyzes to the outcome data of the ED admissions. It could be interesting to analyze the differences among FA/ non FA groups and in terms of hospitalization, death, discharge at home. Finally, the list of bibliographic references could be more complete In conclusion, the paper can be accepted with the proposed revision.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer 1 Susana Garcia-Gutierrez

1. **Definition of outcome: I read the reference used by the authors to defined frequent users (Doupe MB, Palatnick W, Day S, et al. Frequent Users of Emergency Departments: Developing Standard Definitions and Defining Prominent Risk Factors. Ann Emerg31 Med 2012;60:24–32). Doupe et al defined less frequent users and highly frequent users, assuming all of them were frequent users. You used this definition to explain non-FA and FA, and I think the cutoff point must be revised.**

   We agree with the reviewer that the highly frequent threshold identifies an interesting sub-group. There are significant issues with comparability of international research findings due to inconsistent definitions (Moe et al, 2017, Doupe et al 2012). The lower threshold, 7 or more visits (Doupe et al 2012), was used because the authors wanted to use an objective and internationally recognised standard. The higher threshold, 18 or more visits, was also investigated. Summary counts are tabulated below:

   Table 1 Frequent attenders by duration and high vs less frequent attendance, 05-06 to 14-15

	Temporary FA	Repeat FA	Persistent FA	All FA
Less frequent[1]	6,744	1,000	418	8,162
Highly frequent[2]	122	104	189	415
All FA	6,866	1,104	607	8,577

   1. At least 7 and at most 17 visits in any 12-month period during the study
   2. 18+ visits in at least one 12-month period during the study

The authors avoided reference to the higher threshold in the submitted version as there were concerns with incorporating of this threshold in the analysis. Firstly, there was a low sample size of highly frequent attenders (n=415 total, 104 to 189 in each FA cohort), which prevented separate models for less/highly frequent attenders within temporary and ongoing FA groups. Whilst separate risk factor models could be fitted for low and high volume attenders (combining temporary and ongoing FAs), the authors felt this was already addressed in the Doupe paper (Table 2&3 pp.28-29). Secondly, as this was a longitudinal study, people were frequent attenders in some 12-month periods and not in others, and highly frequent in some frequent attendance periods and less frequent in others. This additional complexity was considered a distraction from the main message. The authors felt it was more a more novel finding, and potentially more important (Krieg et al 2016), that future intervention studies consider the likelihood and characteristics of *temporary vs persistent* frequent use, than *low vs high* use.

Based on the reviewer's recommendation we have made the following changes:

- *Methods:* Added the highly frequent threshold (p.8).
- *Results*: Added a result showing highly frequent use is more prevalent among ongoing frequent attenders (p.14).
- *Discussion*: Added a discussion point concerning the overlap between persistent and highly frequent attendance and potential implications for health policy (p16).

2. In a large study like this, with all the centers of a health system included in the analysis is required to perform a multilevel analysis or at least, adjust by the center.

Multilevel analysis is appropriate when modelling visits, which are clustered within patients, within facilities, and within regions. This would involve a crossover structure as frequently attending patients may, and often do, visit more than one facility. However, this paper includes results modelled at patient level and within only a single region. Visits are only used to describe whether each patient me the FA threshold, and to describe other patient characteristics (most common diagnosis, socio-demographics).

The dependent variable was whether a person met a FA threshold at any time during the study, which is not clustered within centres. In addition, FA are known to attend multiple EDs, therefore we have not focused on measuring facility-level effects.

3. In addition to that, other measures or control for confounding must be developed, propensity score matching for example.

The paper includes a descriptive analysis, which by definition does not require control or matching. The paper also includes predictive analysis, which identifies risk factors for ongoing and temporary FA. These models assess each risk factor controlling for the other confounders.

Risk factors such as those identified in this paper should be used to control for differences between groups when evaluating an intervention. However, there is no treatment / intervention in this study.

4. This is an opportunity to create prediction models in order to create profiles of FA. You should do an effort in this way.

We agree that prediction models for ongoing FA need to be developed and validated. This paper identifies factors that should be tested in a predictive model, however we felt this could not be comprehensively covered within this paper. Existing models are scarce; Billings et al (2006) predicts emergency re-admissions within 12 months of a trigger admission, and Smits et al (2009) predict persistent GP attendance. Developing and validating these models is an area of active research by the authors, which will use future years of data for development and testing.

We have made the following changes:

- *Title:* The title of the paper has been amended to reflect the focus on persistence of frequent attendance, rather than prediction of frequent attendance (p1).
- *Discussion*: An additional paragraph notes the recommendation for the development of predictive models in future research. We also note this paper provides a starting point by characteristics associated with temporary and ongoing FA (p17).

- *Tables & Figures*: The labels of Table 3, Table 4 and Figure 2 have been updated to make clear we are modelling characteristics associated with ongoing frequent attendance, rather than predicting ongoing frequent attendance (pp.27-29).

5. **As a minor question, you should be careful with the contents included in each of the sections of the manuscript, that is, the inclusion of explanation of bibliography in outcomes section, for example, makes the text confusing.**

We thank the reviewer for this suggestion. We have made the following changes:
- *Outcomes:* The existing text has been moved to the *Measurements* section, and with an additional clarification added after the second paragraph (p8). The primary and secondary outcomes have now been more clearly stated (p7).

Reviewer 2 Leonardo Palombi

1. **I must stress that a large amount of analysis and processing produced by the authors, almost 1.2 million visits for more than 300.000 patients over 10 years has not generated or confirmed hypothesis, despite having the full epidemiological potential to do so.**

We agree there is a large potential in this longitudinal dataset. The analysis in this paper is both descriptive and analytic. The study aimed to quantify short and long-term frequent attendance, describe each group, and identify associated common and contrasting risk factors. This has now been made clearer by a re-write of the outcomes section. This analysis has been used inform the design of future intervention studies which will be designed to test hypotheses.

Additional studies are also underway, including the development and validation of predictive models (as noted in response to reviewer 1), and analysis of patient sub-groups such as older patients and those with mental health and drug and alcohol problems.

We have made the following changes to the paper:
- *Outcomes*: The primary and secondary outcomes have now been more clearly stated.
- *Discussion*: An additional paragraph notes the recommendation for the development of predictive models in future research. We also note this paper provides a starting point by characteristics associated with temporary and ongoing FA (p16).

2. **I am convinced that a study so important in terms of size, observation time and the number of variables analyzed can and should produce far-reaching conclusions. I would like to suggest to the authors to express more clearly some of these conclusions: for example, we understand that ED represents a social "mirror" of discomfort, poverty and some failures of the welfare system in the continuum of care, with particular regard to psychiatric diseases or addictions. It is also understood that population subgroups present different profiles of FA, for example, those of young and older people.**

We thank the reviewer for pointing out the need to highlight important conclusions in with regards to social determinants of health, service gaps, and the heterogeneity of the FA cohort.

We have made the following changes to the paper:
- *Keywords:* Added MeSH term ‘social determinants of health’ (p1)
  Discussion: Added a paragraph describing the heterogeneity of the FA cohort, the differing needs of patient sub-groups, and potential policy implications. (p16)

3. **The study could even provide important cost-benefit information for patients who evidently resort to ED for lack of alternatives. I, therefore, propose to the authors of such an important study to widen and enrich their conclusions.**

We agree with the reviewer that the use of ED is unlikely to be a cost-effective solution for patients who could be treated elsewhere. While a cost-effectiveness analysis is beyond the scope of this paper, a statement has been added to the discussion (p16) to expand on this point.

4. **It would then be useful to dedicate part of the analyzes to the outcome data of the ED admissions. It could be interesting to analyze the differences among FA/ non FA groups and in terms of hospitalization, death, discharge at home.**

We agree that outcomes data are useful to inform the description of the cohort, and in particular when evaluating interventions. We are investigating linkage with mortality data to investigate deaths and how often this is the cause of frequent attenders no longer using the ED. Our available data was restricted to deaths in hospital, which were not considered sufficiently complete (<80% of deaths) to draw conclusions. Admission to hospital was considered as a descriptor in the analysis, and a further paper could expand on this and include discharge home and mortality as additional outcomes.

5. **Finally, the list of bibliographic references could be more complete.**

Changes to manuscript:

- *References*: We have included additional references describing:
    - evidence on predictive models for frequent ED attendance (Rask et al 1998, Okuyemi et al 2001);
    - social determinants related to frequent ED use (Hunt et al 2006);
    - increasing rates of ED attendance among older patients (Lowthian et al 2010, Lowthian et al 2012, Xu et al 2009, Aboagye-Sarfo et al 2015, Arendts and Lowthian 2013); and
    - potential implications for older ED attenders (Arendts and Lowthian 2013, Legramante et al 2016, Lowthian et al 2012, McCusker et al 2008, McCusker et al 2006).

VERSION 2 – REVIEW

REVIEWER	Susana Garcia-Gutierrez Hospital Galdakao-Usansolo, Basque Country, Spain
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	The main limitation I know in this work is the confounding definition of outcome variable and statistical analysis performed. You have a great amount of data and, if I understood well, from a lot of EDs. You must perform multilevel analysiss and apply multiple comparisons adjustment. It is for that reason I think you must consult with an expert in statistics. In adittion to taht, you must clearly define dependent variables in each of the models performed and give information about their discrimination and calibration properties

REVIEWER	Leonardo Palombi University of Rome Tor Vergata, Department of Biomedicine and Prevention
REVIEW RETURNED	27-Jan-2019

GENERAL COMMENTS	The authors responded very positively to my comments and I hope they can produce further work on the basis of this promising analysis

VERSION 2 – AUTHOR RESPONSE

Reviewer 1 changes:

1. **The main limitation I know in this work is the confounding definition of outcome variable and statistical analysis performed. You have a great amount of data and, if I understood well, from a lot of EDs. You must perform multilevel analysis and apply multiple comparisons adjustment. It is for that reason I think you must consult with an expert in statistics.**

See comments above responding to statistical adviser recommended changes. We have carried out the revised modelling controlling for centers and attendance at more than one centre and updated the methods and results.

The limitation of confounding between outcome and analysis has been noted in the limitation section, including noting the focus of the study on factors associated with patients with short and long term attendance patterns, rather than prediction models.

2. **In addition to that, you must clearly define dependent variables in each of the models performed and give information about their discrimination and calibration properties.**

Additional details describing dependent variables in each model have added to methods and results section for clarity.

Discrimination statistics (AUC) have been added to the footnotes of the tables to provide information on classification accuracy for each model. Calibration measures (Hosmer-Lemeshow) showed statistically significant lack-of-fit which is symptomatic of large-scale population-based data. Model fit statistics (Generalized Chi-Square/DF) indicated no over-dispersion. Each of these criteria have been added to the footnotes of Tables 3 and 4.

Reviewer 2 changes: Leonardo Palombi

1. **The authors responded very positively to my comments and I hope they can produce further work on the basis of this promising analysis**

We thank the reviewer for taking the time to read through the updated paper and for this encouragement.

VERSION 3 – REVIEW

REVIEWER	Susana Garcia-Gutierrez Hospital Gldakao-Usansolo. Osakidetza, Servicio vasco de salud
REVIEW RETURNED	27-Mar-2019

GENERAL COMMENTS	Just few comments: Conclusion in the abstract is not based on the results of the study, that is, first sentence must be deleted in my opinion It is confused the definition of outcome in the abstract, it´s seem that the only criteria is the year and not the threshold on occasions. Be clearer. When you explain measurements, you should explain the definition you choose and if you want to discuss other definitions because is important for the understanding of the paper, you should do in the discussion section.

	Tables should be informative enough, that is, it is not clear that table 1 and 2 are representing percentages?? You should explain in the footnote. You also have to give the confidence level in CI of multivariate regreesion models (95%??)

VERSION 3 – AUTHOR RESPONSE

Reviewer 1 (Editorial Board member)

3. **It may be helpful if they provide results from a statistical test comparing the crossed random effects model with the model without random effects. This can be done using Bayesian Information Criteria also known as Schwarz information Criteria. This is not necessary and can be added as a footnote to table 3.**

Model fit for generalised mixed models (with random effects) using pseudo likelihood methods is reported as a pseudo-Bayesian Information Criteria (pseudo-BIC). This cannot be compared with the BIC calculated using the generalised linear model. From the SAS output: "Fit statistics based on pseudo-likelihoods are not useful for comparing models that differ in their pseudo-data".[1]

References

1. Stroup WW, Milliken GA, Claassen EA, and Wolfinger RD (2018) SAS for Mixed Models: Introduction and Basic Applications. SAS Institute.

Reviewer 2: Susana Garcia-Gutierrez

2. **Conclusion in the abstract is not based on the results of the study, that is, first sentence must be deleted in my opinion**

Thank you for this observation. The first sentence of the conclusion in the abstract has been deleted.

3. **It is confused the definition of outcome in the abstract, it´s seem that the only criteria is the year and not the threshold on occasions. Be clearer.**

The participants and main outcome measures described in the abstract have been clarified to include the threshold.

4. **When you explain measurements, you should explain the definition you choose and if you want to discuss other definitions because is important for the understanding of the paper, you should do in the discussion section.**

Thank you for this suggestion, a sentence has been added to the discussion to draw attention to the generalisability of the findings, when the definition is varied to include planned return visits, or reduce the threshold number of visits.

5. **Tables should be informative enough, that is, it is not clear that table 1 and 2 are representing percentages?? You should explain in the footnote.**

The first column of Table 1 has been amended, and now specifies whether each estimate represents a '% of patients', '% of visits', or 'mean visits'.

The title of Table 2 has been amended, adding a clarification '(% of patients)'. This also appears in the top left cell of the table.

6. **You also have to give the confidence level in CI of multivariate regreesion models (95%??).**

Table 3 describes the significance level below the coefficients, but this was missing from Table 4 and has now been added:

"CI, 99.8% Confidence Interval (α adjusted for multiple comparisons, 1-α/m = 1-0.05/26 = 0.998)"

As per a previous reviewer suggestion, CIs were adjusted for multiple comparison, and are no longer 95% CIs. This is explained in the note above, which is now included in both tables 3 and 4.