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)	Likelihood of death amongst hospital inpatients in New Zealand: prevalent cohort study
AUTHORS	Gott, Merryn; Broad, Joanna; Zhang, Xian; Jarlbaek, Lene; Clark, David

VERSION 1 – REVIEW

REVIEWER	Kate Grundy Canterbury Integrated Palliative Care Service Christchurch Hospital New Zealand
REVIEW RETURNED	09-Apr-2017

GENERAL COMMENTS	I note with interest that the Scottish study chose a Sunday in spring (31/3/10) and this study chose a Wednesday in Autumn (10/4/13). Why was this done and could it have in anyway influenced the findings?? In the discussion it is quoted that 8% died during the index admission. This was the case in the 2016 publication (ref 16) but NOT in the 2014 publication (ref 12) which was the definitive study and had this figure at 9.3%. There was a contradictory figure quoted - on page 8 it states 43% >60yrs and on page 2 states 42% >65yrs. I believe the latter is correct. Finally, ref 16 and ref 17 are a duplication.

REVIEWER	Ji Won Yoo University of Nevada School of Medicine, Department of Internal Medicine, Nevada, USA No Competing Interest
REVIEW RETURNED	03-Jul-2017

GENERAL COMMENTS	Authors achieved their aims to identify the proportion of hospitalized patients dying within 12 months and factors associated with death. Approximately 47% of study patients were aged 60 or older, authors should consider geriatric syndrome such as functional impairment, delirium, cognitive impairment in logistic regression models. Geriatric syndrome is well known risk factor of determining long-term mortality in other countries. In materials and methods, mixed multi-level model was preferred because this model might adjust hospital characteristics in regression models. Authors cited Scottish studies that were similar to study design.

	Other European or Asian studies need to be more cited to ensure replication of current study's findings. Finally, advance directives could be key variable of understanding long-term morality or palliative necessity of hospitalized patients. I recommend authors to add advance directives variable in regression models.

REVIEWER	Evangelos I. Kritsotakis School of Health and Related Research, University of Sheffield, United Kingdom
REVIEW RETURNED	19-Jul-2017

GENERAL COMMENTS	Minor revision comments: 1) Page 3, Strengths and limitations: the statement that the study provides "novel insight into international trends at end of life" is vague and unclear. The authors should explicitly state the insights provided by their findings. Also, 'trends' may be taken to imply comparisons over time, which was not done in this study. 2) Pages 6-7, materials and methods: the authors should specify clearly how outcome data were collected. What exactly is meant by "mortality information" in the first paragraph of the methods? Does this refer to total mortality (i.e. no censoring) or is it in-hospital mortality that was recorded? The former seems to be true from a mentioning of the use of "death registration records" in the results (page 8). This would justify the use of observed mortality proportions and logistic regression in data analysis. If so, it should be stated clearly and the methods used for data linkage with national death registration databases should be described. If, in contrast, in-hospital mortality was assessed then survival analysis methods would be more appropriate to account for censoring, incomplete follow up and the possibility of discharge-alive acting as a competing risk to in-hospital death. 3) Pages 6-7, materials and methods: The authors categorise patient specialty as medical, surgical or procedure. The term "procedure" seems too broad to make sense. Also, how was patient specialty assessed? Does this refer to the specialty of the attending physician or does it simply reflect the ward in which the patient was located on the census day? 4) Page 7, materials and methods: How was clustering at the hospital level accounted for in the analysis? Isn't this relevant to this study? (e.g. by inflating standard errors) 5) Page 7, materials and methods: The authors state that they used the AIC to assess the logistic regression models. I could not locate AIC values in results or tables. 6) Results, page 10: The authors interpret the c-index as indicating the degree of the variability explained by the model. This is a misinterpretation of the c-index in logistic regression. The c-index is a probability value indicating the ability of model predictions to discriminate between those who died and those who survived. See for example BMC Medical Research Methodology, 2012;12:82 (DOI: 10.1186/1471-2288-12-82).

7) Methods pages 7-8 (or results, pages 9-10): The authors should consider providing the reasoning behind fitting three logistic regression models. I can understand fitting models 1 and 3 (model 1 using same set of variables as in the Scottish study and model 3 including the additional data available to the authors). But what is the added value of fitting model 2?

8) Strengths and limitations, pages 13-14. The authors are right to point out the potential for length-time bias in a prevalent cohort design. However, simply stating that patients experiencing longer hospital stays are over-represented does not tell much on potential impacts on the interpretation of their findings. The authors should try to provide some more insight, if possible, of both the direction and magnitude of the impact of length-time bias on their findings (e.g. on accurately estimating cumulative mortality proportions or the effects of the covariates). This is also a requirement in STROBE guidelines (no. 19), which the authors have not fully met.

REVIEWER	Mark Joy School Of Health Sciences, Surrey University, UK No Competing Interest
REVIEW RETURNED	31-Jul-2017

GENERAL COMMENTS	This paper employs suitable techniques to address the research objectives and they have been satisfactorily employed but I would have much preferred to see one logistic regression. Harrel's index could be used to compare predictive information of variables. Whilst not faulted, this paper adds little to the knowledge of the risk factors for in-hospital death. In addition, none of the model predictors are what I would call "hospital service variables" (e.g. what type of clinician is present on admission etc) In table 1, column 2 "died within 7 days", I understand the %ages but why two rows under column "n"?

VERSION 1 – AUTHOR RESPONSE

Many thanks to all reviewers for taking the time to provide us with valuable feedback to improve the paper. We have addressed their comments as follows:

Reviewer: 1
Reviewer Name: Kate Grundy
Institution and Country: Canterbury Integrated Palliative Care Service, Christchurch Hospital, New Zealand
Competing Interests: None declared

Comment: I note with interest that the Scottish study chose a Sunday in spring (31/3/10) and this study chose a Wednesday in Autumn (10/4/13). Why was this done and could it have in anyway influenced the findings??

Response: There were 2 Scottish studies using the same methods for different time periods (ref11 and ref12). This NZ paper used the same census date as ref12. There are inherent seasonal differences in cross-hemisphere research. We chose the same census date for pragmatic reasons, making sure that it was not during the winter months in either country.

Comment: In the discussion it is quoted that 8% died during the index admission. This was the case in the 2016 publication (ref 16) but NOT in the 2014 publication (ref 12) which was the definitive study and had this figure at 9.3%.

Response: As above, we were comparing with ref12

Comment: There was a contradictory figure quoted - on page 8 it states 43% >60yrs and on page 2 states 42% >65yrs. I believe the latter is correct.

Rsponse: Thank you for spotting this typo. Now corrected on page 8.

Comment: Finally, ref 16 and ref 17 are a duplication.

Response: Thank you. Amended.

Reviewer: 2
Reviewer Name: Ji Won Yoo
Institution and Country: University of Nevada School of Medicine, Department of Internal Medicine, Nevada, USA
Competing Interests: None

Comment: Authors achieved their aims to identify the proportion of hospitalized patients dying within 12 months and factors associated with death. Approximately 47% of study patients were aged 60 or older, authors should consider geriatric syndrome such as functional impairment, delirium, cognitive impairment in logistic regression models. Geriatric syndrome is well known risk factor of determining long-term mortality in other countries.

Response: Interesting hypothesis. For this national level study we could only use data gathered by MoH and they do not collect this information.

Comment: In materials and methods, mixed multi-level model was preferred because this model might adjust hospital characteristics in regression models. Authors cited Scottish studies that were similar to study design. Other European or Asian studies need to be more cited to ensure replication of current study's findings.

Response: Currently no other studies using this method, but we agree additional national comparative studies would be valuable.

Comment: Finally, advance directives could be key variable of understanding long-term morality or palliative necessity of hospitalized patients. I recommend authors to add advance directives variable in regression models.

Response: As noted above we could only use the data available via MoH and they don't collect AD completion.

Reviewer: 3
Reviewer Name: Evangelos I. Kritsotakis
Institution and Country: School of Health and Related Research, University of Sheffield, United Kingdom
Competing Interests: None declared

Minor revision comments:

1) Page 3, Strengths and limitations: the statement that the study provides "novel insight into international trends at end of life" is vague and unclear. The authors should explicitly state the insights provided by their findings. Also, 'trends' may be taken to imply comparisons over time, which was not done in this study.

Response: Thank you revised (Page 3).

2) Pages 6-7, materials and methods: the authors should specify clearly how outcome data were collected. What exactly is meant by "mortality information" in the first paragraph of the methods? Does this refer to total mortality (i.e. no censoring) or is it in-hospital mortality that was recorded? The former seems to be true from a mentioning of the use of "death registration records" in the results (page 8). This would justify the use of observed mortality proportions and logistic regression in data analysis. If so, it should be stated clearly and the methods used for data linkage with national death registration databases should be described. If, in contrast, in-hospital mortality was assessed then survival analysis methods would be more appropriate to account for censoring, incomplete follow up and the possibility of discharge-alive acting as a competing risk to in-hospital death.

Response: Data from national death registration records were used to establish fact and date of death. Hospital discharge data were used to identify deaths that occurred during the hospital stay of interest. No cause of death data were obtained or analysed. Data linkage was conducted by the Ministry of Health using each person's national health identifier that was then removed from the dataset before delivery to the investigators. (See page 5-6)

3) Pages 6-7, materials and methods: The authors categorise patient specialty as medical, surgical or procedure. The term "procedure" seems too broad to make sense. Also, how was patient specialty assessed? Does this refer to the specialty of the attending physician or does it simply reflect the ward in which the patient was located on the census day?

Response: Routinely collected data were used: the codes were provided by hospital coders and processed in a routine manner by national data centre clearing offices. Specialty was defined as the specialty for the patient at the time of discharge. "Procedure" was used where a person came in for a particular procedure (investigation or treatment), usually as an arranged or booked admission. Because the procedure may have been for either medical or surgical investigations, such as a CT scan, we grouped them together (page 6).

4) Page 7, materials and methods: How was clustering at the hospital level accounted for in the analysis? Isn't this relevant to this study? (e.g. by inflating standard errors)

Response: Hospitalisations could indeed have been regarded as clustered by ward, by hospital, by District Health Board, or by region. The data are regarded as being complete, i.e. all those in hospital on the survey date will have been included. There was therefore no need to adjust for sampling design or non-response, and no weighting was required in order to obtain estimates for the population in hospital on any one night. Further, large sample sizes mean that standard errors are not a concern. Thus, no adjustment for clustering was required.

5) Page 7, materials and methods: The authors state that they used the AIC to assess the logistic regression models. I could not locate AIC values in results or tables.

Response: Thank you for drawing this to our attention. Given the meaningful results that the models provide, we decided not to present the AIC. We have removed that from the Methods (page 7).

6) Results, page 10: The authors interpret the c-index as indicating the degree of the variability explained by the model. This is a misinterpretation of the c-index in logistic regression. The c-index is a probability value indicating the ability of model predictions to discriminate between those who died and those who survived. See for example BMC Medical Research Methodology, 2012;12:82 (DOI: 10.1186/1471-2288-12-82).

Response: Thank you for drawing this to our attention. We agree and have amended the text. (page 10).

7) Methods pages 7-8 (or results, pages 9-10): The authors should consider providing the reasoning behind fitting three logistic regression models. I can understand fitting models 1 and 3 (model 1 using same set of variables as in the Scottish study and model 3 including the additional data available to the authors). But what is the added value of fitting model 2?

Response: Model 1, as the reviewer notes, replicates the model presented in the Scottish study. Model 2 incorporates additional variables that were hypothesised to improve the model (and indeed the c-index moves from 0.79 to 0.84), and in particular to examine the association of ethnicity and cancer with death, ethnicity being an important predictor of many measures of health in New Zealand, and cancer being the main reason people access specialist palliative care. Model 2 is important because deprivation no longer becomes an important predictor, suggesting that the association of deprivation with death within 12 months is related more to ethnicity (and related factors not measured) than to deprivation itself. This point has been added to the Discussion (page 13). Model 3 incorporates also other main diagnostic groupings, again attenuating the association with deprivation, and is the best simple model (ie no interactions or strata) we developed with these data.

8) Strengths and limitations, pages 13-14. The authors are right to point out the potential for length-time bias in a prevalent cohort design. However, simply stating that patients experiencing longer hospital stays are over-represented does not tell much on potential impacts on the interpretation of their findings. The authors should try to provide some more insight, if possible, of both the direction and magnitude of the impact of length-time bias on their findings (e.g. on accurately estimating cumulative mortality proportions or the effects of the covariates). This is also a requirement in STROBE guidelines (no. 19), which the authors have not fully met.

Response: Modelling data from a cross-sectional study, ie one based on a single night, limits the interpretation to all those on a particular night. The findings are not generalisable to all hospital admissions or discharges. To do that the simplest methods would be to analyse records from all discharges over a defined period, but that was not the purpose of this study nor the Scottish study that this replicates. However we acknowledge the risk that the results will be interpreted as such by readers.

If we were to use these data to generalise to all hospitalisations, then variables associated with longer stay, eg palliative care, frailty or complex conditions, would overly influence the findings, and those associated with shorter stays, e.g. day-stay procedures, lengthy (>3 hour) ED visits would be less influential. However the extent of these influences would be hypothetical at best, and we prefer not to go that route. Nor was this the purpose of the study.

On reflection, we believe the STROBE guidelines are not the most suited to this paper and we have therefore completed the RECORD checklist instead (attached).

Reviewer: 4
Reviewer Name: Mark Joy
Institution and Country: School Of Health Sciences, Surrey University, UK
Competing Interests: None

Comment: This paper employs suitable techniques to address the research objectives and they have been satisfactorily employed but I would have much preferred to see one logistic regression. Harrel's index could be used to compare predictive information of variables.

Response: Inclusion of the reasons for each of the models is now included, in response to the previous reviewer's comments. Fit of the models is not an issue as the purpose is achieved, and the changes in the c-index show how Model 1 is improved by the additional of other variables in Models 2 & 3.

Comment: Whilst not faulted, this paper adds little to the knowledge of the risk factors for in-hospital death. In addition, none of the model predictors are what I would call "hospital service variables" (e.g. what type of clinician is present on admission etc)

Response: The aim of the study was not just to explore risk factors for in-hospital death, but to identify the proportion of NZ patients in hospital on a given date that died within 12 months of that census date, to compare findings with a Scottish study and to explore the implications for the identification of these patients clinically. Few "hospital service variables" were available to model because they are not collected at a national level.

Comment: In table 1, column 2 "died within 7 days", I understand the %ages but why two rows under column "n"?
Response: Our apologies – the column boundaries within the tables were narrowed during final submission, and cell contents wrapped. Now corrected. (Table 1)

VERSION 2 – REVIEW

REVIEWER	Katherine (Kate) Grundy Canterbury District Health Board New Zealand
REVIEW RETURNED	13-Sep-2017

GENERAL COMMENTS	I have said no about statistical review as this is a revision and I don't believe another review is required on top of what has already been performed.

REVIEWER	Ji Won Yoo University of Nevada Las Vegas School of Medicine Las Vegas, Nevada, USA No Competing Interest
REVIEW RETURNED	20-Sep-2017

GENERAL COMMENTS	I reviewed the original draft and authors appropriately revised the 2nd version manuscript. Revisions are satisfactory. I recommend editorial office to accept the revised manuscript.