PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	FACTORS ASSOCIATED WITH 30-DAY READMISSION AFTER HOSPITALIZATION FOR COMMUNITY-ACQUIRED PNEUMONIA IN OLDER PATIENTS. A CROSS-SECTIONAL STUDY IN SEVEN SPANISH REGIONS
AUTHORS	Toledo, Diana; Soldevila, Núria; Torner, Nuria; Perez, Mª José; Espejo, Elena; Navarro, Gemma; Egurrola, Mikel; Dominguez, Angela; Working Group, Project FIS PI12/02079

VERSION 1 – REVIEW

REVIEWER	Gregory Ruhnke University of Chicago, USA
REVIEW RETURNED	27-Nov-2017

GENERAL COMMENTS	This paper by Toledo et al is an impressive and rigorously-constructed analysis of the reasons for which elderly patients admitted for community-acquired pneumonia (CAP) are readmitted. An important strength of this study is a robust sample of nearly 2000 patients derived from 20 hospitals in Spain. The results are interesting, important, and confirm in a non-US population that discharge disposition (home with home health care) is a clinically and statistically significant predictor of readmission risk. Suggestions: (1) The first paragraph under methods: outcomes (page 6, beginning with line 15) describes that readmission was ascertained by "re-review of medical records." It is not clear whether this is the facility of the index hospitalization or across all hospitals. (2) The method by which comorbid (underlying) diseases was ascertained and codified is not clear. For example, page 6, line 51 does not indicate with any specificity the methods of ascertainment and codification. (3) Page 7, line 30: analyses are not made, but rather conducted. (4) Your finding regarding the importance of discharge disposition (Reference #16, Int J Clin Pract.Int J Clin Pract. 2017 Mar;71(3-4). doi: 10.1111/ijcp.12935. Discharge disposition as an independent predictor of readmission among patients hospitalised for community-acquired pneumonia. Dong T1, Cursio JF2, Qadir S2, Lindenauer PK3,4, Ruhnke GW1 is consistent with our findings and worthy of an addition to the discussion. We had hypotheses regarding our findings, but, given the consistency of your results with ours, some additional comments

	may be useful for the readership. (5) The discussion section should include some additional information regarding the most important predictors of readmission (cohabitants, chronic respiratory failure, discharge disposition), particularly regarding policy implications. (6) The paragraph on page 12, beginning with line 42 is important, but should reference the pneumonia PORT study regarding this issue. (7) In the discussion, page 14, beginning on line 22, you reference our study on the relationship of discharge disposition and readmission risk. Although we were not able to explain this association with confidence, it is also the most significant predictor of readmission in a sample of patients in another country. This is an extremely important finding. Even if simply assertions, some suggestion about why this finding exists in US and Spanish populations would be important for the readership. Minor suggestions: (1) Abstract Objective, page 2, line 6: Patients are not discharged due to CAP. They are admitted for CAP. (2) Abstract setting: "stydy" is incorrect spelling and the sentence requires a period at the end. (3) Introduction, page 4, line 22: by "notifiable disease," I believe you mean "reportable." (4) Page 4, line 32, "discharge due to CAP" is not a correct description, as is mentioned in comment #1. Same issue on page 4, line 42. (5) Page 4, line 37, I suppose the 9 is a reference and that the next sentence beginning with "30-day" is a new sentence. This should be rectified. (6) Page 7, line 46 refers to an adjusted odds ratio as OR, but the abstract refers to an aOR (presumably an adjusted odds ratio) without defining the acronym. I suggest consistency. (7) Page 12, line 21, "al" is not correct. (8) Page 12, line 23, "reference centres" is not the usual term, which would be referral centers. (9) First paragraph of the discussion "variations in the number of people assigned" is an unusual method of referring to the mechanism by which patients are admitted to a given facility. In most countries, patients are not assigned hospitals, but rather admitted to a given hospital based on de facto geographic considerations.

REVIEWER	Francesco Cacciatore, MD, PhD Department of Internal Medicine and Geriatrics - University of Naples "Federico II", Italy
REVIEW RETURNED	08-Dec-2017

GENERAL COMMENTS	The study is designed to determine factors associated with 30-day readmission in elderly patients with CAP. The analysis was carried out on 1756 patients discharged alive from 20 hospitals in seven Spanish regions during two influenza seasons. Factors associated with 30-day readmission were male sex, living with a person aged < 15 years, moderate-to-high degree of dependency, chronic respiratory failure, heart failure, chronic liver disease and discharge to home with home health care. No associations were found with pneumoccocal or seasonal influenza vaccination in any of the three previous seasons. The manuscript is of interest. Several point should be addressed.Flowchart is not clear. Readmission 200 pts.

	What is the meaning of Nreadmission? In the result section you stated that you collected information on readmission in 188 cases - 99 cases (comorbidities in 80 and other causes in 19) and pneumonia-related in 80 cases. The sum is 179. I do not understand if the analysis was conducted on 200 patients or on the 188/179 cases in which you collected information. Why did you decided to treat Barthel index as dichotomous variable? Did you try to analyze age as continuous variable? It could be of interest to measure the effect of comorbidity, i.e. the sum of disease, or Charlson Comorbidity Index or Cumulative illness rating scale Parmalee PA, Thuras PD, Katz IR, Lawton MP: Validation of the Cumulative Illness Rating Scale in a geriatric residential population. J Am Geriatr Soc 1995;43:130-137 Introduction row 36 – ref 9 brackets. Congestive heart disease. Consider to use heart failure.

VERSION 1 – AUTHOR RESPONSE

Editors comments:

- Please revise the title of your manuscript to include study design (cross-sectional). Research question, study design and setting is the preferred title format of the journal.

We have modified the title.
"FACTORS ASSOCIATED WITH 30-DAY READMISSION AFTER HOSPITALIZATION FOR COMMUNITY-ACQUIRED PNEUMONIA IN OLDER PATIENTS. A CROSS-SECTIONAL STUDY IN SEVEN SPANISH REGIONS"

- Along with your revised manuscript, please include an updated copy of the STROBE checklist indicating the page/line numbers of your manuscript where the relevant information can be found (https://strobe-statement.org/index.php?id=strobe-home). Please include all items indicating any items that are Not applicable to your study.

We have modified the STROBE checklist.

- We recommend that you thoroughly proofread your revised article before submission to improve the quality of the English. For example, we noted several typos in your abstract and some remaining Spanish words within Table 1.

We have sent the manuscript to be reviewed by a native English speaker.

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: Gregory Ruhnke

Institution and Country: University of Chicago, USA

Suggestions:
(1) The first paragraph under methods: outcomes (page 6, beginning with line 15) describes that readmission was ascertained by "re-review of medical records." It is not clear whether this is the facility of the index hospitalization or across all hospitals.

The Spanish health system assigns to each citizen a primary care centre and a referral hospital to be treated. Consequently, if there is a readmission it would be at the same hospital.
Patients who did not have their principal residence in any of the 7 participating regions were excluded from the study because we did not have access to their clinical records.
We have modified this sentence in the Outcomes section:
"Information on readmission was collected by re-review of index hospital medical records up to 30 days after initial discharge."
And we have added this sentence to the Study population section:
"…patients whose main residence was not in any of the seven participating regions …"

(2) The method by which comorbid (underlying) diseases was ascertained and codified is not clear. For example, page 6, line 51 does not indicate with any specificity the methods of ascertainment and codification.

Comorbidities were recorded according to the diagnoses documented in the patient's medical record. We have changed the expression "underlying disease" by "comorbidities" and rewritten the sentence for clarity.

(3) Page 7, line 30: analyses are not made, but rather conducted.

We have modified the sentence.

(4) Your finding regarding the importance of discharge disposition (Reference #16, Int J Clin Pract.Int J Clin Pract. 2017 Mar;71(3-4). doi: 10.1111/ijcp.12935.
Discharge disposition as an independent predictor of readmission among patients hospitalised for community-acquired pneumonia.
Dong T1, Cursio JF2, Qadir S2, Lindenauer PK3,4, Ruhnke GW1 is consistent with our findings and worthy of an addition to the discussion. We had hypotheses regarding our findings, but, given the consistency of your results with ours, some additional comments may be useful for the readership.

We have rewritten the Discussion section.

(5) The discussion section should include some additional information regarding the most important predictors of readmission (cohabitants, chronic respiratory failure, discharge disposition), particularly regarding policy implications.

We have rewritten the Discussion section.

(6) The paragraph on page 12, beginning with line 42 is important, but should reference the pneumonia PORT study regarding this issue.

We agree. We have modified the sentence and added the reference.

(7) In the discussion, page 14, beginning on line 22, you reference our study on the relationship of discharge disposition and readmission risk. Although we were not able to explain this association with confidence, it is also the most significant predictor of readmission in a sample of patients in another country. This is an extremely important finding. Even if simply assertions, some suggestion about why this finding exists in US and Spanish populations would be important for the readership.

We have rewritten the Discussion section.

Minor suggestions:
(1) Abstract Objective, page 2, line 6: Patients are not discharged due to CAP. They are admitted for CAP.

The reviewer is right. We have modified the sentence.

(2) Abstract setting: “stydy” is incorrect spelling and the sentence requires a period at the end.

The reviewer is right. We have modified the word.

(3) Introduction, page 4, line 22: by “notifiable disease,” I believe you mean “reportable.”

The reviewer is right. We have modified the sentence.

(4) Page 4, line 32, “discharge due to CAP” is not a correct description, as is mentioned in comment #1. Same issue on page 4, line 42.

We agree and we have modified the sentences.

(5) Page 4, line 37, I suppose the 9 is a reference and that the next sentence beginning with “30-day” is a new sentence. This should be rectified.

The reviewer is right. We have rectified the reference.

(6) Page 7, line 46 refers to an adjusted odds ratio as OR, but the abstract refers to an aOR (presumably an adjusted odds ratio) without defining the acronym. I suggest consistency.

We agree and we have modified the sentence.

(7) Page 12, line 21, “al” is not correct.

The reviewer is right. We have corrected the word.

(8) Page 12, line 23, “reference centres” is not the usual term, which would be referral centers.

We have modified the sentence.

(9) First paragraph of the discussion “variations in the number of people assigned” is an unusual method of referring to the mechanism by which patients are admitted to a given facility. In most countries, patients are not assigned hospitals, but rather admitted to a given hospital based on de facto geographic considerations.

The Spanish health system assigns each citizen a primary healthcare centre and a referral hospital to be treated. The assignation of the population to each hospital is made according to geography. Consequently, if there is a readmission it would be in the same hospital. However, in an emergency, the patient may be treated in any hospital.
We have rewritten the paragraph for clarity.

Reviewer: 2
Reviewer Name: Francesco Cacciatore, MD, PhD

Institution and Country: Department of Internal Medicine and Geriatrics - University of Naples "Federico II", Italy

(1) Flowchart is not clear. Readmission 200 pts. What is the meaning of Nreadmission? In the result section you stated that you collected information on readmission in 188 cases - 99 cases (comorbidities in 80 and other causes in 19) and pneumonia-related in 80 cases. The sum is 179. I do not understand if the analysis was conducted on 200 patients or on the 188/179 cases in which you collected information.

The reviewer is right. We have rewritten the flowchart and the paragraph for clarity.
"Reasons for 30-day readmission were unrelated to pneumonia in 49.5% (99 cases), pneumonia-related in 44.5% (89 cases) and unknown diagnosis in 6% (12 cases)."

(2) Why did you decided to treat Barthel index as dichotomous variable?

We treated the Barthel Index as have our group and other authors in the following publications:

Sanz F, Morales-Suárez-Varela M, Fernández E, Force L, Pérez-Lozano MJ, Martín V, Egurrola M, Castilla J, Astray J, Toledo D, Domínguez Á; Project PI12/02079 Working Group. A Composite of Functional Status and Pneumonia Severity Index Improves the Prediction of Pneumonia Mortality in Older Patients.J Gen Intern Med. 2018 Jan 4. doi: 10.1007/s11606-017-4267-8.

Domínguez À, Soldevila N, Toledo D, Torner N, Force L, Pérez MJ, Martín V, Rodríguez-Rojas L, Astray J, Egurrola M, Sanz F, Castilla J; Working Group of the Project PI12/02079. Effectiveness of 23-valent pneumococcal polysaccharide vaccination in preventing community-acquired pneumonia hospitalization and severe outcomes in the elderly in Spain. PLoS One. 2017 Feb 10;12(2):e0171943. doi: 10.1371/journal.pone.0171943

Torner N, Izquierdo C, Soldevila N, Toledo D, Chamorro J, Espejo E, Fernández-Sierra A, Domínguez A; Project PI12/02079 Working Group. Factors associated with 30-day mortality in elderly inpatients with community acquired pneumonia during 2 influenza seasons. Hum Vaccin Immunother. 2017 Feb;13(2):450-455.

(3) Did you try to analyze age as continuous variable?

Following your suggestions we have repeated the analyses and have treated age as a continuous variable in this revised version.
Analysis of age as a categorical variable showed no significance in the crude analysis and thus it was not included in the final model. Treating age as a continuous variable also showed no significance in the crude analysis, but even so age was included in the final model.

(4) It could be of interest to measure the effect of comorbidity, i.e. the sum of disease, or Charlson Comorbidity Index or Cumulative illness rating scale Parmalee PA, Thuras PD, Katz IR, Lawton MP: Validation of the Cumulative Illness Rating Scale in a geriatric residential population. J Am Geriatr Soc 1995;43:130-137

We have introduced the Charlson Comorbidity index in the unadjusted and multilevel analysis. In the unadjusted analyses we found a significant association but this disappeared in the multilevel analysis. Due to the importance of the association between comorbidities and readmission after CAP we did not use this variable in the final analysis. We analysed the importance of identifying comorbidities independently.
Below we show the multilevel model considering the variable "Charlson index".

(5) Introduction row 36 – ref 9 brackets.

The reviewer is right. We have corrected the reference.

(6) Congestive heart disease. Consider to use heart failure.

We agree and have modified this.

VERSION 2 – REVIEW

REVIEWER	Gregory Ruhnke University of Chicago, USA
REVIEW RETURNED	23-Jan-2018

GENERAL COMMENTS	Regarding my prior suggestion #2, it might be helpful to state that comorbidities were obtained from the patient's medical record through chart review (if that is what was done). The authors make very clear in their response to my suggestions regarding how the structure of the Spanish health care system "assigns" patients to hospitals. The paper might benefit from a clear statement about this, perhaps under study population. Readers not familiar with the system in Spain may have questions similar to those that I raised. Very optional, but the authors mention the association between discharge home with home health care demonstrated in admissions for diseases other than CAP. A statement regarding the findings in these other diseases might be helpful, especially since this is the strongest risk factor for readmission in the adjusted analysis.

REVIEWER	Francesco Cacciatore, MD, PhD Salvatore Maugeri Foundation, IRCCS, Institute of Telese (Bn), Italy Heart Transplant Section, Monaldi Hospital, Naples, Italy
REVIEW RETURNED	02-Feb-2018

GENERAL COMMENTS	All comments were addressed. The manuscript is globally improved.

VERSION 2 – AUTHOR RESPONSE

a. Editors comments:

- Please update the 'Participants' section of your abstract to include the sample size.

We have added a sentence explaining the final sample size.

“Finally, 1756 CAP cases were included and of these, 200 (11.39%) were readmitted.”

b. Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Gregory Ruhnke

Institution and Country: University of Chicago, USA

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

a. Regarding my prior suggestion #2, it might be helpful to state that comorbidities were obtained from the patient's medical record through chart review (if that is what was done).

We have rewritten the second paragraph in the outcomes section for clarity.

"All participating hospitals had a specifically-trained team of health professionals who used a structured questionnaire to obtain sociodemographic information and lifestyle factors by patient interview and the review of patient's medical record to collect immunization history, risk medical conditions and the CAP hospital care process."

And, we have rewritten the next sentence

"…were collected from the patient's medical record through chart review."

b. The authors make very clear in their response to my suggestions regarding how the structure of the Spanish health care system "assigns" patients to hospitals. The paper might benefit from a clear statement about this, perhaps under study population. Readers not familiar with the system in Spain may have questions similar to those that I raised.

We have added the next paragraph in the study population section.

"The Spanish health system assigns each citizen a primary healthcare centre and a referral hospital to be attended. The assignation of the population to each hospital is made according to geography. Consequently, if there is a readmission, it would be in the same hospital. However, in an emergency, the patient may be treated in any hospital.·

c. Very optional, but the authors mention the association between discharge home with home health care demonstrated in admissions for diseases other than CAP. A statement regarding the findings in these other diseases might be helpful, especially since this is the strongest risk factor for readmission in the adjusted analysis.

We have added a sentence and 3 new references.