

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The association of comorbidity and health service utilisation among patients with dementia in the UK: a population-based study
<b>AUTHORS</b>	Browne, Jorge; Edwards, Duncan; Rhodes, Kirsty; Brimicombe, James; Payne, Rupert

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Donovan Maust University of Michigan, USA
<b>REVIEW RETURNED</b>	03-Jun-2016

<b>GENERAL COMMENTS</b>	<p>The authors present a generally clearly-written analysis of an interesting data source. However, the conclusions are completely underwhelming—they show that sicker patients (those with more medical conditions) have higher rates of utilization, which (as they acknowledge) is entirely expected.</p> <p>Two main points:</p> <ol style="list-style-type: none"><li>1. I think the far more interesting analysis would be to compare utilization between patients with and without dementia, stratified by medical comorbidity. Are there ways in which the care of patients with dementia differs from what you might expect? This would be more interesting to consider in terms of how the “usual” system of care does not work for certain groups of patients with dementia than the current analysis. Maybe at a given level of medical comorbidity, dementia doesn’t really make much of a difference. Perhaps it is among patients with fewer comorbid conditions that patients with dementia get either more care or perhaps they get less care.</li><li>2. I fundamentally think simply counting conditions is problematic. Do the authors truly think that “prostate disorders” = “COPD” = “psoriasis or eczema” = “chronic sinusitis” = “cancer” etc? That these conditions are all equivalent in their impact on healthcare utilization? I think the authors should reconsider how they measure accumulating medical comorbidity rather than a simple count of conditions.</li></ol> <p>Minor points:</p> <p>Introduction:</p> <ul style="list-style-type: none"><li>- p.3, line 10: “those diagnosed with dementia have significantly higher consultation rates”—please clarify what you mean by “consultation”? Is this referring to a specific type of outpatient visit (e.g., from specific providers?)</li><li>- p.3, line 20: one reason patients with dementia in Medicaid have high costs is b/c Medicaid covers the cost of long-term care in the US, which is different than more acute and outpatient care that I believe the authors are addressing</li></ul> <p>Methods:</p>
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	<p>- p.4, line 5: in addition to minimum follow-up period, would be better to censor observation some period of time before death. As currently described, you are still capturing utilization in individuals in the period immediately before death, provided they survey &gt;3months from incident dementia.</p> <p>- p.4, line 38: from what data source is death determined?</p> <p>- p.5, line 9: I would include the details re: observation period</p> <p>Results:</p> <p>- p.5, line 48: seems concerning that a full 1/3 of individuals were lost to follow-up. Is it possible that those patients that transferred practices were related to progression of their dementia and/or change in living situation—in other words, those remaining patients are less ill. You do discuss this in the Discussion (p.8); seems might you like compare distribution of clinical and demographic characteristics among those lost to follow-up, as you do for patients for whom hospitalization data is not available.</p>
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<b>REVIEWER</b>	Amaia Calderón-Larrañaga Aging Research Center - Karolinska Institutet, Sweden
<b>REVIEW RETURNED</b>	03-Jun-2016

<b>GENERAL COMMENTS</b>	<p>This is a well written paper showing the impact of comorbidity on health services utilisation among patients with dementia. The interest of the article would be enhanced if the authors provided answers to the following key questions: 1) to what extent is this increased used of services avoidable; 2) what is the impact of this increased use of services on patients well-being and quality of life?; 3) do patients with comorbidities and increased use of services still receive quality care.</p> <p>Still, I consider this a publishable work in this journal, once the following minor issues have been considered:</p> <ul style="list-style-type: none"> <li>- I guess the authors used the exposure option in STATA (did they use STATA?) when carrying out the negative binomial regressions, in order to account for the differing follow-up times among subjects. If this was the case, the authors should state it in the methods. If it was not the case, they should rerun the analyses adjusting for the time each individual was followed.</li> <li>- If all data available in CPRD was used (according to Figure 1), then why do the authors perform a sample size calculation?</li> <li>- What do the authors mean by “baseline death” in the Results section? Is this the overall 5-year follow-up death rate?</li> <li>- In the discussion, the authors talk about the need to change health services in order to respond to the needs of patients with dementia, who should be provided care that differs from that received by the rest of patients. There is evidence to believe that health systems with strong and resourceful primary care services are best suited to assist patients with multimorbidity, regardless of their specific comorbidities, assuring both horizontal (equal access to resources for people with the same needs) and vertical (greater resource provision for people with greater needs) equity in care provision.</li> </ul>
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<b>REVIEWER</b>	Leena Forma, PhD, postdoctoral researcher School of Health Sciences and Gerontology Research Center (GEREC), University of Tampere, Finland
<b>REVIEW RETURNED</b>	27-Jun-2016

<b>GENERAL COMMENTS</b>	<p>This is a manuscript with a rich data but unfortunately missing the information on round-the-clock long-term-care (LTC). The paper presents important new information and is well written. However, some clarifications would make the paper easier to read and interpret.</p> <p>Major comments to the authors:</p> <ol style="list-style-type: none"> <li>1. In the abstract and other parts of the paper you assess the care needs on the basis of service use. However, other demand side and supply side factors have an effect on service use. Please, clarify the relation of need for and use of services.</li> <li>2. For a reader it is important to know from the beginning, that LTC was not included in the study. Please mention this already in the abstract or bullet points describing limitations.</li> <li>3. You refer to the resource allocation several times, what exactly is the message for resource allocation of this study? Please, clarify this.</li> <li>4. p. 3, r. 32 you write about dementia population, but you study only incident cases, please mention it here. In the Discussion, please consider how the results are affected by studying the incident cases, and those with a more advanced dementia are not included.</li> <li>5. p. 4, r. 32 hospital encounters: does this include only inpatient care, or also ambulatory services?</li> <li>6. All readers in other countries than the UK are not familiar with the Read codes, please describe them briefly. In addition, why did you not use e.g. ICD-10 codes?</li> <li>7. p. 5, r.19: Please clarify the description of multi-level negbin analyses. How many levels did you include, and which were the levels?</li> <li>8. How did the length of the follow-up period vary between the comorbidity-categories? How did you take this variation into account in the analyses?</li> <li>9. It would be interesting to test, whether multi-morbidity is similarly associated with service use in different age groups. Age and multi-morbidity may have an interaction effect.</li> <li>10. In Table 1 consider presenting also column "All" including all comorbidity-categories.</li> <li>11. To me the number of health service contacts is surprisingly high, please compare this also to other studies, if available.</li> <li>12. p. 8, r. 30: 50% of people in the highest comorbidity-group died during the study period. Therefore, palliative care decision-making is not easy to perform on the basis of number of comorbidities, please modify this.</li> <li>13. It is very important that you consider the possible selection bias in the page 8, r. 12-16. I think it would be important to perform some kind of loss analysis: can you evaluate the possibility to enter long-term care in different comorbidity groups?</li> </ol> <p>Minor comments:</p> <ol style="list-style-type: none"> <li>1. p. 3, r. 10: which consultations?</li> <li>2. Does use of these data presume some permission from the register official? Please give the details.</li> <li>3. p. 4, r. 6: please remind the reader that your minimum follow-up</li> </ol>
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	<p>period was 3 months</p> <p>4. p. 4, r. 7: please give some references to this “are known to be...”</p> <p>5. Consider replacing “dementia treatment” by “dementia medications” (as you do on p. 4, r. 42)</p>
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## VERSION 1 – AUTHOR RESPONSE

### REVIEWER 1

The authors present a generally clearly-written analysis of an interesting data source. However, the conclusions are completely underwhelming—they show that sicker patients (those with more medical conditions) have higher rates of utilization, which (as they acknowledge) is entirely expected.

Two main points:

1. I think the far more interesting analysis would be to compare utilization between patients with and without dementia, stratified by medical comorbidity. Are there ways in which the care of patients with dementia differs from what you might expect? This would be more interesting to consider in terms of how the “usual” system of care does not work for certain groups of patients with dementia than the current analysis. Maybe at a given level of medical comorbidity, dementia doesn’t really make much of a difference. Perhaps it is among patients with fewer comorbid conditions that patients with dementia get either more care or perhaps they get less care.

This is an important point. This study included participants diagnosed with dementia with the aim of exploring differences within this population. As mentioned by the reviewer, it would be of great interest also knowing if the impact of multimorbidity over health use is different in dementia population compared with those with comorbidities, which unfortunately was not explored in this study. However, we believe that understanding differences within the dementia population, and quantifying the extent of service utilisation, is nevertheless very important for strengthening the arguments for the provision of health services which move away from single-condition care towards holistic management of multimorbidity. There is only limited published data at present, and we therefore believe the findings of this paper, although as the reviewer states “entirely expected”, are nonetheless a valuable contribution to the literature. We hope in future research to be able to explore the differences in the impact of multimorbidity between those with and without dementia, but unfortunately do not have this data available at present.

2. I fundamentally think simply counting conditions is problematic. Do the authors truly think that “prostate disorders” = “COPD” = “psoriasis or eczema” = “chronic sinusitis” = “cancer” etc? That these conditions are all equivalent in their impact on healthcare utilization? I think the authors should reconsider how they measure accumulating medical comorbidity rather than a simple count of conditions.

We agree that treating all conditions as equivalent is potentially problematic. Alternative strategies include (i) use of categorical data to consider specific comorbid conditions, (ii) use of continuous data extracted from comorbidity scores that weight comorbidities differently (eg. Charlson score), (iii) Use of categorical data obtained through patterns of comorbidity, which groups comorbidities that occurs frequently together. Our decision to use a simple count was based in part on pragmatism and transparency. However, there are also challenges with the use of the alternative methods. For example, weighted scores perform best if applied to specific outcomes, so weighting according to risk of death will not necessarily perform well in predicting quality of life or certain aspects of health service use. Furthermore, we have found more sophisticated measures of quantifying morbidity to perform no better than simple counts in terms of predicting service utilisation (Payne, CMAJ 2013;185:E221-8). The simple count approach has been used effectively by others too (e.g. Barnett,

Lancet 2012;380:37-43). Nevertheless, to address concerns that a simple count would not be able to capture the impact of specific comorbidities, we ran a model that considered the 10 most frequent comorbidities adjusting for the number of other comorbidities (Table 4), and found no clear clinically relevant differences, supporting the argument that a more sophisticated comorbidity score is unlikely to have significant benefit over the parsimonious approach.

Minor points:

Introduction:

- p.3, line 10: “those diagnosed with dementia have significantly higher consultation rates”—please clarify what you mean by “consultation”? Is this referring to a specific type of outpatient visit (e.g., from specific providers?)

We have clarified that this refers to contact with a GP and defined this accordingly.

- p.3, line 20: one reason patients with dementia in Medicaid have high costs is b/c Medicaid covers the cost of long-term care in the US, which is different than more acute and outpatient care that I believe the authors are addressing

Indeed, long-term care derives much of the Medicaid dementia care costs. However, when excluding long term care, Boyd et al (2010) found that care costs of comorbid dementia was 61% higher than dementia alone suggesting that costs differences are not only due to long-term care. Unfortunately for this study long term care data was not available, nevertheless as suggested it would be helpful to include this variable in future research. We have now clarified that long-term costs were excluded from these results.

Methods:

- p.4, line 5: in addition to minimum follow-up period, would be better to censor observation some period of time before death. As currently described, you are still capturing utilization in individuals in the period immediately before death, provided they survey >3months from incident dementia.

The reviewer raises the important issue of variability in care use leading up to death. For this paper we sought to capture an overall picture including leading up to death, and therefore did not censor the observation period. We have now clarified the length of the minimum follow-up period, and also now acknowledge the issue of variation in care use in the limitations section of the discussion.

- p.4, line 38: from what data source is death determined?

This information was captured within the CPRD data collected by primary care services; this has been clarified in the manuscript. As GPs in the UK provide the coordination of health care to virtually all UK residents, the recording of death in primary care records is generally very reliable.

- p.5, line 9: I would include the details re: observation period

As suggested this was addressed in this version

Results:

- p.5, line 48: seems concerning that a full 1/3 of individuals were lost to follow-up. Is it possible that those patients that transferred practices were related to progression of their dementia and/or change in living situation—in other words, those remaining patients are less ill. You do discuss this in the Discussion (p.8); seems might you like compare distribution of clinical and demographic characteristics among those lost to follow-up, as you do for patients for whom hospitalization data is not available.

We now compare the age and comorbidity characteristics of the two groups in the first paragraph of the results, as well as commenting on how this might impact upon the effect estimates in the discussion section.

## REVIEWER 2

This is a well written paper showing the impact of comorbidity on health services utilisation among patients with dementia. The interest of the article would be enhanced if the authors provided answers to the following key questions:

- 1) to what extent is this increased use of services avoidable;
- 2) what is the impact of this increased use of services on patients well-being and quality of life? do patients with comorbidities and increased use of services still receive quality care.

The three issues of whether or not the health service use is avoidable, the impact upon well-being and quality of life, and an assessment of the quality of service provision, are all very important points. Unfortunately, the nature of the data we had available is such that we cannot conduct these analyses. We have, nevertheless, acknowledged these points in the discussion, and already refer to the need for further study into some of these issues in the conclusions.

- I guess the authors used the exposure option in STATA (did they use STATA?) when carrying out the negative binomial regressions, in order to account for the differing follow-up times among subjects. If this was the case, the authors should state it in the methods. If it was not the case, they should rerun the analyses adjusting for the time each individual was followed.

The reviewer is correct in their assumption – we have clarified this in the methods.

- If all data available in CPRD was used (according to Figure 1), then why do the authors perform a sample size calculation?

We consider this good practice. A sample size calculation was conducted to ensure the proposed study time period would allow identification of an adequate number of incident cases, whilst reducing the potential for variations in service utilisation over time.

- What do the authors mean by “baseline death” in the Results section? Is this the overall 5-year follow-up death rate?

Baseline death refers to overall 5-year follow-up death rate. We have rephrased this accordingly and changed to “overall” death.

- In the discussion, the authors talk about the need to change health services in order to respond to the needs of patients with dementia, who should be provided care that differs from that received by the rest of patients. There is evidence to believe that health systems with strong and resourceful primary care services are best suited to assist patients with multimorbidity, regardless of their specific comorbidities, assuring both horizontal (equal access to resources for people with the same needs) and vertical (greater resource provision for people with greater needs) equity in care provision. This is a fair point, although the argument we make is not that the needs of those with dementia are different, but that the needs of those with multimorbidity are different. We accept the argument that primary care systems are already well suited to care of multimorbidity. We have therefore rephrased the final paragraph of this section to better address these concerns.

## REVIEWER 3

This is a manuscript with a rich data but unfortunately missing the information on round-the-clock long-term-care (LTC). The paper presents important new information and is well written. However, some clarifications would make the paper easier to read and interpret.

We agree with the relevance of long-term care over overall dementia care costs and the need to

understand the factors associated to this. Unfortunately, social care data is not available in CPRD data.

Major comments to the authors:

1. In the abstract and other parts of the paper you assess the care needs on the basis of service use. However, other demand side and supply side factors have an effect on service use. Please, clarify the relation of need for and use of services.

We agree that there are factors beyond simply health care need that determine levels of service use. We have attempted to rephrase the third paragraph of the discussion to acknowledge this issue.

2. For a reader it is important to know from the beginning, that LTC was not included in the study. Please mention this already in the abstract or bullet points describing limitations.

We now acknowledge this issue in the limitations section.

3. You refer to the resource allocation several times, what exactly is the message for resource allocation of this study? Please, clarify this.

We have clarified that we are particularly referring to health care resource allocation, and now provide some examples in the conclusions section of the manuscript.

4. p. 3, r. 32 you write about dementia population, but you study only incident cases, please mention it here. In the Discussion, please consider how the results are affected by studying the incident cases, and those with a more advanced dementia are not included

As requested, we now explicitly state on page 3 we are examining only incident cases. We also now discuss the implications of using incident (cf prevalent) cases in the limitations section.

5. p. 4, r. 32 hospital encounters: does this include only inpatient care, or also ambulatory services? Only inpatient encounters – this has been clarified in the text.

6. All readers in other countries than the UK are not familiar with the Read codes, please describe them briefly. In addition, why did you not use e.g. ICD-10 codes?

Read Codes are the standard clinical terminology used in CPRD to classify conditions, and cover administrative, treatment and other areas not covered by ICD-10. We have added a brief explanation to the text as requested.

7. p. 5, r.19: Please clarify the description of multi-level negbin analyses. How many levels did you include, and which were the levels?

Two levels models were used to analyse the differences at individual level (1st level) and also to take into account that individuals could be clustered by primary care facilities (2nd level). The methods section was modified to further clarify this point.

8. How did the length of the follow-up period vary between the comorbidity-categories? How did you take this variation into account in the analyses?

Those with higher number of comorbidities had lower follow-up period compared with those with low number of comorbidities. This was addressed by using rates, which allow comparing risks of individuals with different follow up times.

9. It would be interesting to test, whether multi-morbidity is similarly associated with service use in different age groups. Age and multi-morbidity may have an interaction effect.

This was considered and explored; yet no significant interaction effect was found between age and multimorbidity. For simplicity purposes we did not include this analysis in this paper.

10. In Table 1 consider presenting also column “All” including all comorbidity-categories.

In the interests of brevity, we have decided not to complicate this table further by adding a further column. We already report overall gender distribution and age in the main text.

11. To me the number of health service contacts is surprisingly high, please compare this also to other studies, if available.

This was compared with the Chen et al. (BMC Geriatrics 2014, 14:76) mentioned in the paper which reports comparable primary care consultations rates for patients with dementia in the UK. Chen et al described a consultation rate of 16.1 per person per year for patients with dementia. Differences in the consultation rate could be explained by differences in the types of consultations included and by the mean severity of dementia. Compared with Chen et al mortality was higher in this study. Hence, probably more people with an advanced stage of disease were included, producing higher consultation rates. We have now added this to the discussion (“comparison with other studies”)

12. p. 8, r. 30: 50% of people in the highest comorbidity-group died during the study period.

Therefore, palliative care decision-making is not easy to perform on the basis of number of comorbidities, please modify this.

We disagree; although numbers may be small, and case fatality high, this does not necessarily mean that decisions taken about palliative care should not account for co-morbidity.

13. It is very important that you consider the possible selection bias in the page 8, r. 12-16. I think it would be important to perform some kind of loss analysis: can you evaluate the possibility to enter long-term care in different comorbidity groups?

Thank you for you comment. Risk of selection bias and its possible effect is described in the discussion section. Unfortunately data on long-term care was not available for this study.

Minor comments:

1. p. 3, r. 10: which consultations?

Consultations types are described in the Participants, Exposure and Outcomes section and further detailed in Appendix 3.

2. Does use of these data presume some permission from the register official? Please give the details.

CPRD is regulated by the UK Government Department of Health. Ethical permission to use the data was granted through the required means by the CPRD Independent Scientific Advisory Committee following the protocol 15\_106R, as noted in the manuscript.

3. p. 4, r. 6: please remind the reader that your minimum follow-up period was 3 months  
p4 r6 was modified as requested.

4. p. 4, r. 7: please give some references to this “are known to be...”

We have now referenced this statement accordingly.

5. Consider replacing “dementia treatment” by “dementia medications” (as you do on p. 4, r. 42)

This has been done throughout as suggested.



## VERSION 2 – REVIEW

<b>REVIEWER</b>	Amaia Calderón-Larrañaga Aging Research Center, Karolinska Institutet, Sweden
<b>REVIEW RETURNED</b>	13-Nov-2016

<b>GENERAL COMMENTS</b>	The authors appropriately addressed all my comments
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<b>REVIEWER</b>	Leena Forma School of Health Sciences and Gerontology Research Center (GEREC), University of Tampere, Finland
<b>REVIEW RETURNED</b>	08-Nov-2016

<b>GENERAL COMMENTS</b>	The comments of reviewers are sufficiently covered.
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