Reviewer’s report

Title: Treatment patterns and burden of behavioral disturbances in patients with dementia in the United States: a claims database analysis

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Reviewer: Stuart MacDonald

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Dr. Qi-Hao Guo
Associate Editor - Dementias
BMC Neurology

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Title: Treatment patterns and burden of behavioral disturbances in patients with dementia in the United States: a claims database analysis

This is a timely manuscript, emphasizing an important research focus - the differential impact of behavioral disturbances (BD) on clinical characteristics, treatment patterns, healthcare resource utilization, and costs among patients with dementia. The authors employ a retrospective analysis of claims data from the well-regarded Truven Health MarketScan® database (2012-2015), with the originality and importance of this manuscript representing definitive strengths. The primary research foci were clear, and the findings clearly support the exacerbating impact of BD on select outcomes including clinical characteristics of dementia, medication use, and healthcare resource utilization. Based on their findings, the authors demonstrated that dementia coupled with BD resulted in significantly more medical and psychiatric disease comorbidities, increased pharmacotherapy (e.g., antidementia drugs, antidepressants, antipsychotics), and substantially greater healthcare resource utilization (e.g., hospitalizations, number of skilled nursing visits) and a corresponding increase in healthcare costs. Conclusions focused on the increased economic burden of BD in dementia, with implications for easing such burdens by liaising with caregivers, for example. On balance, I believe this paper will be of particular interest to the readership of BMC Neurology.

Having perused the manuscript several times, I have but a few comments or queries (beyond those raised during initial review) for the authors’ consideration.

(1) At several points in the manuscript, the authors clearly cite evidence demonstrating that patients with dementia and neuropsychiatric symptoms often require more medication, and typically transition earlier to subsequent levels of long-term care. Complementing Dr. Guo's earlier query re: dementia severity, to what extent might the well-documented issues of polypharmacy or multimorbidity influence the more complex clinical manifestations of dementia with BD?
(2) On page 14 of the discussion, and related to the issue of polypharmacy, the authors note that "The higher use of antipsychotics and antidepressants among the dementia patients with BD compared with patients without BD, in the current study, highlights potential off-label use of these medications for BD, underscoring the unmet need for a therapy with demonstrated effectiveness to treat BD in dementia". Given the risks of polypharmacy for older adults (particularly those with dementia), I wonder if the authors have (or can) reflect further on what these alternative therapies (or strategies) might be? For example, as implied in the discussion, might one of these approaches entail the stable presence of a caregiver who is actively involved in treatment? Going forward, it would be of great interest to evaluate whether patients with dementia and BD had more limited access to a caregiver. Recent intervention evidence from various literatures (e.g., physical activity, social connectedness, music) suggests that key neuropsychiatric symptoms may be mitigated for those with dementia. Might such active engagement of caregivers, in concert with care providers, mitigate transition risk to subsequent levels of care (e.g., institutionalization)?

Accordingly, I wonder whether the authors can further augment their conclusion section (on page 16). For example, what are the authors' suggestions regarding next steps for caregivers to contemplate when BD are manifest in addition to dementia? For example, relevant research and commentary over the past several decades (e.g., Silverstir et al., 2004) indicates widespread agreement that behavioral disturbances for those with dementia are effectively controlled with non-pharmacological support.

(3) The authors have focused their analysis on all-cause dementia with BD. Do the authors anticipate distinct patterns if the focus was restricted to those with Alzheimer Disease with BD?

(4) I have no qualms per se with the statistical analyses performed. The techniques employed for the comparisons made were appropriate, with patterns of significance always in the expected direction. However, I do have a minor comment regarding the presentation of the results. Given the population, the authors have ample statistical power to detect group differences; I wonder whether it might also be useful to quantify the magnitude of such differences? Have the authors also considered including a suitable estimate of effect size to formally quantify the magnitude of group differences between BD vs non-BD? Alternatively, the authors could include further comment in the discussion that addresses the practical implications of observed differences between those with vs. without BD.

I sincerely appreciated the opportunity to review your scholarship - with very best wishes,

Stuart W.S. MacDonald, PhD

Professor and Member of the Royal Society of Canada College of New Scholars, Artists and Scientists

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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