PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Association of Socioeconomic Status with Medical Assistance in Dying: A Case Control Analysis
AUTHORS	Redelmeier, Donald; Ng, Kelvin; Thiruchelvam, Deva; Shafir, Eldar

VERSION 1 – REVIEW

REVIEWER	Natalie McCormick Massachusetts General Hospital, USA
REVIEW RETURNED	16-Sep-2020

GENERAL COMMENTS	Thank you for preparing and submitting this manuscript on uptake of medically assisted dying in Canada by SES group. Figure 2 was particularly effective. It was intriguing how the SES discrepancy was present in nearly all subgroups, including the early and late periods of the study, despite the relatively low uptake of medically assisted dying overall, and despite the medically assisted dying and control groups being similar on many other characteristics. Your use of large sets of routinely collected data from a universal healthcare setting was a key strength, and neighbourhood income quintile is an established measure of SES. Still, I feel some additional details should be provided, and you may want to consider using an additional SES measure, if available, in a sensitivity analysis. The clinician survey was less useful. There seem to be several possible explanations for the discrepancy you report, and these warrant further exploration. Please see some specific comments and queries below: Major Comments • Methods, Patient Selection, page 7: Why did you limit to individuals age ≥ 65 years? While appreciating that the frequency of death will be lower among younger individuals, do you expect (perhaps from prior literature) the findings would differ if younger individuals were included? • Methods: While neighbourhood SES is an established measure of SES, agreement between individual- and neighbourhood SES has been lower in some older populations as compared to younger [PMID: 21453534]. I appreciate that few individual-level measures of SES are available in administrative data. However, some researchers have used receipt of government subsidies for provincial medical plan premiums [PMID: 15818655] or prescription drug coverage [PMID: 27213543] as a proxy measure of individual-level SES. If available in the Ontario data, you may want to use one of these measures in a sensitivity analysis. • Discussion, page 20, paragraph 1, sentence 3: It is not clear to me that the imbalance could not be easily attributed to “thoughtless impulsivity, reciprocal compensation, or community

	norms". I suggest providing more explanation or removing these factors. • Please provide more details about how the survey was designed and administered. Was this component prespecified? Was it based on an established set of questions? How were potential participants selected and approached? Did the individuals who administered the survey know the participating clinicians? Did you specifically target or exclude clinicians who were involved in palliative care/provided medical assistance in dying? What were the clinicians' specialities? Would they be representative of primary or palliative care physicians caring for eligible patients in the community setting? Minor Comments • Methods, Patient Selection, top of page 8: Do those pharmacy codes specifically pertain to the drug regimen prescribed for medical assistance in dying? • Methods, Patient Selection: The province of BC has a Palliative Care Drug Plan which can be used to identify recipients of palliative care drug benefits outside of an acute care setting. Does such a plan/code exist in Ontario? • Discussion, top of page 21: I would make it explicit here, or in the Methods, that data on race/ethnicity and religion were not available in the administrative data, since race/ethnicity data are available in administrative data from some other settings. • It would help to interpret for readers the difference between the main and matched-pair analysis. • Do your findings on the number of Ontario seniors who received palliative care, and who received medically assisted dying, fit with those from other sources, such as the Ministry of Health?

REVIEWER	Anna Santos Salas University of Alberta
REVIEW RETURNED	27-Nov-2020

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. The authors report findings from a research study that sought to determine socioeconomic differences in access to medical assistance in dying (MAID) in a large Canadian province. This is a novel research study that sheds light into a potential health equity issue around a recently established health care practice in Canada. The authors examined a large population cohort of individuals who received palliative care comparing those who underwent MAID with those who did not. Study findings suggest that persons from low socioeconomic status tend to access MAID less frequently than those from high socioeconomic status. The study unveils a socioeconomic disparity in the administration of MAID. A few issues need further consideration. These are described below. The authors state that on average, more than 1000 Canadians receive MAID per year. A report by Health Canada (2020) indicates that in 2019, there were 5631 cases of MAID in Canada, with 1747 of these in Ontario.

	The article suggests that MAID is equivalent to physician-assisted suicide. Clarification is needed concerning the two types of MAID that are available to Canadians (administered by a practitioner or self-administered). A distinction needs to be made between MAID and palliative care. The authors state that, “medical assistance in dying became a benefit under universal health insurance in Ontario on June 6, 2016, listed as palliative care” (p. 8 lines 35-40). This statement is misleading as it conveys the sense that medical assistance in dying (MAID) became a palliative care practice. The authors should note that persons accessing MAID who did not opt for palliative care services were not included in the study. Is it also possible that some individuals who received palliative care were excluded? A 2020 Health Canada report shows that more than 80% of those who accessed MAID received palliative care. Were the number of MAID cases identified by the authors close to those expected based on MAID statistics reported in Ontario and Canada? The validity of the 4-question survey is difficult to assess given limited details provided. How were the surveys ‘randomly assigned’? What was the rationale for the survey? The authors seem to dichotomize the populations in poor and rich groups. Socioeconomic status is somewhat simplified as in reality it encompasses much more than having had a life of luxury or hardship. I would suggest to remove survey data from the article. There seems to be a tendency to interpret differences found in the study to either patient or physician-related behavioural factors such as ‘faulty doctor-patient communication’ or ‘faulty intuition’. Further discussion of the underlying roots of health inequities is needed given the focus of the study. Health inequities originate in complex interactions that are not well understood. Inequities deeply rooted in institutional and social practices go beyond practitioners’ approaches and assumptions or the abilities of patients to voice their needs and advocate for themselves. Discussion of how these inequities take root in the health care system to generate and perpetuate health inequities would be useful. Clarification of the following statement would be helpful “More broadly, the data might inform patient engagement in less extreme cases of inequities where poor patients may feel disempowered and physicians may be disinclined to push” (p. 23 lines 30-35) References Health Canada (2020) First Annual Report on Medical Assistance in Dying in Canada 2019. https://www.canada.ca/content/dam/hc-sc/documents/services/medical-assistance-dying-annualreport-2019/maid-annual-report-eng.pdf

	Government of Canada (2020). Medical assistance in dying. https://www.canada.ca/en/healthcanada/services/medical-assistance-dying.html Government of Ontario Ministry of Health Ministry of Long Term Care (2018). Medical Assistance in Dying. http://www.health.gov.on.ca/en/pro/programs/maid/

VERSION 1 – AUTHOR RESPONSE

REVIEWER #1 COMMENTS (n = 10)
1) Additional Sensitivity Analysis based on Different SES Measure
The review begins with a positive general review of the manuscript and then raises a first suggestion to test an additional socioeconomic status measure as another sensitivity analysis. We agree because no single indicator is ideal and further measures can test the robustness of results. In response, we have now obtained data on a direct social services indicator for “Low-income Seniors”, rerun the primary analysis, and again observed those with low socioeconomic status are less likely to receive medical assistance in dying. These new findings are now added to the methods and results sections to help strengthen the manuscript.

2) Restriction to Individuals ≥ 65 years
The review asks why our analysis was restricted to older patients since young adults can also be candidates. We agree because Canadian laws consider all adults potentially eligible; however, restrictions in Ontario confine our drug database primarily to adults age ≥ 65 years (exclusion of young patients retains most cases of medical assistance in dying). In response, we now state this limitation more clearly in the methods and discussion sections.

3) Individual-Level Indicator of SES
The review suggests that receipt of government subsidies might provide a proxy measure of individual-level socioeconomic status that avoids assessments based on home neighborhood characteristics. We agree this is an opportunity for a sensitivity analysis. In response, we now add the new sensitivity analysis based on low-income indicator, find similar results, and report the new findings in the methods and results sections.

4) Disclaimer about Impulsivity, Compensation, and Norms
The review seeks more discussion on why some factors are unlikely to explain the results. We agree that many explanations can arise for social gradients; however, our case is different by design since it focuses on medical assistance in dying. In particular, this treatment has a mandatory reflection interval, which implies decisions are unlikely to be thoughtless impulsivity. The treatment prohibits direct conflicts of interest or interpersonal pressure, which implies decisions are unlikely to be reciprocal compensation. The treatment is viewed positively in diverse communities, which implies decisions are unlikely to be community norms. In response, we have now revised the points gently in the introduction and discussion sections (space limitations preclude longer discussion).

5) More Details about Validation Survey
The review invites more details on the validation survey. We agree such details can help researchers elsewhere interested in replicating our findings. In response, we now explain the survey was pre-specified; questions were created based on experiments outside medicine; participants were a convenience sample of clinicians at a coffee shop inside a large hospital; most were unlikely to be directly participating in medical assistance in dying; the survey did not directly target those involved in

palliative care; and we elicited no information on specialty training. These additional technical details appear in the appendix.

6) Checking that Codes Pertain to Medical Assistance in Dying
The review inquires whether the six Ontario Drug Benefit codes (93877101 to 93877106) are specific for medical assistance in dying. We agree that other regions use different codes that may have a different sensitivity or specificity. We now state in the methods these six codes are specifically defined for medical assistance in dying and have no other indications.

7) Alternative Drug Benefit Codes in British Columbia
The review mentions some regions have a palliative care drug benefit plan that covers care outside an acute care setting. We agree that each Canadian province has somewhat different systems. In response, we now mention the Ontario approach is similar to other regions. In both cases, the treatment is provided free-of-charge to patients as we now state in the introduction.

8) Declaration that Race/Ethnicity Data are Unavailable
The review suggest inserting an explicit comment in the limitations section that data on race/ethnicity were not available in the database. We agree that other regions have more extensive social information than our region. In response, we now state this limitation in the methods section and also mention this conceptual limitation in the discussion section as a potential opportunity for future research.

9) Distinguishing Main Analysis from Matched Pairs Analysis
The review suggests adding more interpretation of the difference between the findings of the main analysis and the matched pairs analysis. We agree this is an important test of robustness because the main analysis was based on the total patient sample (all individuals who died) whereas the matched analysis was based on a smaller subset sample (1-to-1 matching based on characteristics). In response, we now comment that the main analysis and matched paired analysis yielded similar results with overlapping 95% confidence intervals.

10) Correspondence of Counts from Other Sources
The review ends with a question on how well our study sample (patients who died while receiving palliative care) fit with other documented counts (total cases of medical assistance in dying reported to government sources). We agree these sources are not identical because our study had stringent selection criteria. In response, we now explain more carefully in the methods section that the study undercounts cases compared to total federal data sources.

REVIEWER #2 COMMENTS (n = 8)
1) Estimated Annual Frequency in Canadian Population
The review begins with an accurate review of the manuscript and then raises a report from Health Canada indicating more total cases of medical assistance in dying in Ontario. We agree that comprehensive population counts are higher than reported in our study because of our explicit selection criteria that differs from public health surveillance (eg, we excluded patients who were younger, not receiving palliative care, or hospital inpatients). In response, we now explain in the methods section that our selection criteria are designed to be specific (not fully sensitive) to allow links to detailed healthcare databases of diagnoses and treatments. We also note this approach is not likely to bias the observed estimates of socioeconomic gradients (internal validity of correlation coefficients).

2) Distinguishing MAID from Physician-Assisted Suicide
The review stresses the medical assistance in dying is not precisely the same as physician assisted suicide. We agree since the former is administered by a practitioner whereas the latter is self-

administered. In response, we now delete the term “physician assisted suicide” since it has different connotations in other regions and can lead to unnecessary confusion.

3) Debate over MAID as a Palliative Care Practice
The review raises a caution over the prevailing debate on whether MAID should be excluded or included under the category of palliative care. We agree this debate is not central to our analysis and the manuscript needs to avoid antagonizing readers. In response, we have now removed the statement that can be prone to misinterpretation.

4) Correspondence between Study Sample and Population Statistics
The review cautions our study is not a comprehensive sample due to the methods for identifying individuals. We agree because patients included in our study needed to be older (age ≥ 65 years), receiving palliative care (2 contacts in last month), identifiable in databases (valid healthcard number), and selected during the initial 3 years (2016-2019). Cases of medical assistance in dying included in our study, furthermore, additionally needed to be identifiable from outpatient pharmacy prescriptions (would not count cases of medical assistance in dying obtained by other channels). In response, we now state the criteria explicitly in the patient selection paragraph of the methods section because clinical research is not the same as population health surveillance. In addition, we now show in the results section that our patients amount to 1-in-5 total deaths (50,095 of 243,880).

5) Validity of Brief Survey
The review highlights that the validity of the survey is hard to assess without more technical details. We agree that further details would be helpful, in accord with the suggestions of the other reviewer. In response, we have now expanded the appendix to better explain the background purpose, the randomization procedure, and the limitation that socioeconomic status is more complicated than a binary classification of luxury or hardship. We continue to include the survey because it is another method for validating the results and supporting the interpretation of the primary analysis.

6) Alternative Interpretations of Observed Differences
The review emphasizes the potential complexity of the underlying roots of health inequities. We agree that disparities prevailing among vulnerable adults are multifactorial and extend beyond difficulties in communication between patients and providers. In response, we have now cited more relevant literature on the complex factors that perpetuate shortfalls of healthcare. Of course, more can be said that could be included as a topic for an accompanying editorial.

7) Advocating for More Patient Engagement
The review calls for clarification of the point on how best to improve patient engagement and increase provider initiative to lessen healthcare inequities. We agree human fallibility may be one modifiable contributor to socioeconomic inequities around medical assistance in dying. In response, we have now edited the statement gently for better clarity. Again, much more can be said on this point that could be included as a topic for an accompanying editorial but would go beyond the available data in our statistical analyses.

8) Additional Relevant Citations
The review ends with offering 3 citations to governmental summary reports on medical assistance in dying. We agree these websites provide helpful background data. In response, we have now added each in the appropriate locations.

VERSION 2 – REVIEW

REVIEWER	McCormick, Natalie

	Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology
REVIEW RETURNED	17-Feb-2021

GENERAL COMMENTS

Thank you for your efforts in revising this manuscript on differences in the uptake of medical assistance in dying (MAID) by SES, including your additional sensitivity analysis defining SES based on low-income status in the ODB database. The overlap in results make your findings more robust, as does your stating that the ODB codes were specific to MAID. The additional explanation in the Introduction about aspects of the MAID protocols intended to minimise impulsivity and interpersonal pressure will help readers. Most other of my queries were addressed well in the response and revised manuscript. As mentioned in my initial review, it was intriguing how the SES discrepancy (according to the primary SES measure) was present in all subgroups, despite the MAID and non-MAID groups appearing similar on other characteristics, and you now mention that (understandably, in the interests of specificity), your analyses underestimated the number of MAID cases.

<p>However, I remain less enthused about the validation survey, despite the information that was provided. The main analysis has a number of strengths, including the population-based analysis of a few years' data (beginning from implementation of MAID in Ontario) covering nearly all seniors in a publicly-funded, 'universal' healthcare system, and use of drug codes specific to MAID. The primary case-control analysis employed a well-used measure of area-level SES, and the findings were supplemented by the matched-pairs analysis and individual-level SES measure. It's difficult to make inferences from the survey, but the main analysis could stand on its own and spur further, more granular investigation into the overall uptake of MAID and observed discrepancies by SES.

First, I appreciate your patience: I was involved in submitting two grant applications when the request for review arrived, including for my own career development/new investigator award, and could not complete a careful review until those were submitted. Thank you for the opportunity to review the revised version of this manuscript assessing socioeconomic disparities in the uptake of medical assistance in dying (MAID) within a universal healthcare setting (Canada's largest province, Ontario). When I reviewed the first version of this manuscript, I thought the main analysis was generally well conducted and the findings were intriguing; there was a significant SES discrepancy in uptake of MAID, with adjustment for several covariates, despite the low rates of uptake overall, and the discrepancy was present in nearly all available subgroups (data were not available on individuals' race, religion, educational attainment, or language). I posed some questions to the authors about the main analysis, and these were answered well in the response and revision; they even conducted an additional sensitivity analysis, using an individual-level measure of SES, and obtained similar findings as when using the area-level measure. MAID is an emerging topic and, as I mention in my comments to the authors, the main analysis has several strengths: it was a population-based analysis of a few years' data covering nearly all seniors in a publicly-funded, 'universal' healthcare system, which identified MAID cases using unique dispensing codes. Findings were similar across the primary case-control

	analysis, matched pairs analysis, and alternative definition of low SES. With that, I think the main analysis could be accepted for publication; it highlights a potential disparity in the uptake of MAID, in a setting where the direct medical costs should not be a barrier, and could incentivise more granular research into the many possible explanations and how any disparities might be addressed (by logistical means or otherwise). However, despite the additional information that was provided, I am still not convinced about the value of the survey. Whilst appreciating that any SES-related disparities in uptake of MAID would likely culminate from patients' encounters with multiple providers and settings over the course of illness (not just the 'final' provider/specialist), I think it would be more effective if the surveyed providers were involved in palliative care. Perhaps this component should be removed from the current manuscript, expanded, and reported separately. Or at least described as an exploratory analysis?

VERSION 2 – AUTHOR RESPONSE

REVIEWER #1 COMMENTS (n = 1)

1) Including the Validation Survey

The review begins with a gracious positive review and then expresses one main point about the survey. We agree that most database analyses can stand alone and do not require an additional controlled survey, yet the observed confirmatory findings add a further test to robustness because they reflect a randomized experimental approach. In response, we have followed the suggestions from the editor to move information about the survey into the main body of the manuscript, soften the language from "validation" to "confirmatory", and add a new additional paragraph about survey limitations in the discussion.