PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Is loneliness associated with increased health and social care utilisation in the oldest old? Findings from a population-based longitudinal study
AUTHORS	Wang, Hanyuying; Zhao, Emily; Fleming, Jane; Dening, Tom; Khaw, Kay-Tee; Brayne, Carol

VERSION 1 - REVIEW

REVIEWER	Joseph Puyat UBC, Canada
REVIEW RETURNED	10-Jul-2018

GENERAL COMMENTS	The authors examined the association between loneliness and use of health/social services among the elderly (>80 years). They used longitudinal self-reported data to estimate the association using GEE. They found that lonely elderly people, compared with those who were not lonely, have shorter time interval between their last visit to their GPs, and were more likely to visit their community nurses and were more likely to have accessed the meals on wheels services. They concluded that "loneliness was a significant risk factor for certain types of health and social care utilisations. Findings ... have several implications, including the need for awareness-raising and prevention of loneliness to be priorities for public health policy and practice." I have a number of concerns about the paper, most importantly about the conclusions the authors made. Assuming the authors' results are correct, I'm not sure why they would imply that increased use of health and social services is an undesirable finding. Would it not be more problematic to find that lonely people are less likely to be engaged with health and social services, especially given the robust link between loneliness and health outcomes? It was also not clear to me what the authors were really trying to achieve with their second objective when they said that they wanted to investigate whether 'time-varying loneliness' and health/social services were related. It looked like their model was estimating the association between loneliness, averaged across time points, and the outcome. It that was their intention (to average the loneliness level) then their analysis does not actually make good use of the fact that they have loneliness data that vary over time. On the other hand, if what they wish to imply is that

	changes in loneliness from one time point to another is associated with relative differences in health/social service use, then the models used should explicitly account for that. Last, I have some concerns about how the outcome variables were modeled. The authors truncated the number of community service contacts, hospital visits and possibly the time interval in their last GP visit. There were no information provided on how these data changes may have influenced their results. Mean values, which is basically what their GEE models are comparing, can be quite sensitive to suppression of extreme values. When changes to raw data such as what's been done in the study, supplementary sensitivity analyses usually help in demonstrating that the results are not an artifact of the data preparation process carried out. Below are other comments for consideration: 1) Time since last GP visit was modeled using a Gaussian distribution. I doubt that this variable follows the Gaussian distribution. Using a more appropriate analytic approach should be considered. 2) It would be more helpful to have row percent and not column percent on Table 1. Adding another column containing the raw counts for each demographic characteristics would also help. 3) Have the authors considered mixed-effects models that can accommodate missingness instead of GEE with IPW? 4) There were factors used in the adjustment that could be measuring largely the same construct, ie. depression and loneliness, physical impairments and physical functioning. Have the authors considered running their analyses with only variables that are distinct from each other and see if the point estimates and/or confidence interval changes?

REVIEWER	Dr Antonia Ypsilanti Senior Lecturer in Cognitive Psychology/Psychobiology Sheffield Hallam University UK
REVIEW RETURNED	07-Nov-2018

GENERAL COMMENTS	This is a well-written paper, with clear and concise sections that allows the reader to identify the key objectives and follow the clear rationale of the study. Below are some minor corrections that need to be addressed: 1. I think the introduction could be expanded slightly to include a brief discussion of the covariates that are examined in the study and the importance of selecting these covariates. More specifically, depression is highly linked to loneliness and there is a bulk of research discussing this association. Also, general cognition as measured with MMSE has also been linked to loneliness, so it would be helpful to add a couple of references to show why these covariates are important to consider. In the manuscript the authors actually mention that differences in findings between studies may be due to differences in covariates examined, so this makes it all the more important to include some information about the covariates of the present study and their importance.

	2. I think the following needs clarification: "However, with only two measures, researchers were not able to capture the fluctuating nature of loneliness[9-11], therefore, the complicated association between time-varying loneliness and health and social care utilisation could not be examined". why does the fluctuating nature of loneliness pose difficulty when measured twice? Please clarify. 3. The following sentence suggests that these issues were improved in the current study but you don't clarify how they were improved. "The heterogeneity in existing evidence is likely to be due to the differences in study sample, selection of covariates, length of follow-up time, and the measures of loneliness". You state that in this study the sample is older old adults that are underrepresented, which is true and that the length and number of waves are much better in your study. However, as I mentioned earlier, you must explain why you selected the specific covariates but also why you used a single item to measure loneliness. The vast majority of research on loneliness use questionnaires (such as the UCLA) rather than a single item to capture different aspects of loneliness. Since loneliness is defined the perceived discrepancy between one's desired and actual social contacts it is useful to justify why you selected a single item for loneliness. I appreciate that you have it as a limitation in the discussion but I think that since loneliness is the key variable of the paper it's measurement should be justified. 4. Perhaps it would be useful to state whether you measured "medication use/ prescribed medication" because this would be another reason to visit the GP. If you haven't measured this please add a note on the discussion in the limitations and/or future studies.

REVIEWER	asma tarjoman Iran
REVIEW RETURNED	13-Nov-2018

GENERAL COMMENTS	The topic is not new Good luck

VERSION 1 – AUTHOR RESPONSE

Comments from Reviewer #1:

Comment #1 I have a number of concerns about the paper, most importantly about the conclusions the authors made. Assuming the authors' results are correct, I'm not sure why they would imply that increased use of health and social services is an undesirable finding. Would it not be more problematic to find that lonely people are less likely to be engaged with health and social services, especially given the robust link between loneliness and health outcomes?

Reply:

According to Andersen’s behavioural model, there are three factors influencing individuals’ engagement in medical care use: predisposing characteristics, enabling resources, and need.

Within enabling resources, social relationships serve as a means to provide and transfer health information including the availability of health services within social networks (1995). Social isolation, which is defined as lack of social connections and social engagement, is associated with lack of access to services (Jopling, 2015).

Using Andersen's behavioural model, 'need' is considered as the major contributor to medical care use. 'Need' is represented by health conditions, such as physical health. In the current study, we were interested in exploring whether loneliness, after controlling for physical health (and mental health), is associated with health and social services consumption.

Loneliness may have impacts on the use of health services in two ways: higher or lower service use. (1) Lonely individuals could visit GPs or communicate with community nurses more often than non-lonely individuals because the element of social interaction in such contacts may alleviate loneliness. Conversely, loneliness could be associated with worse health, increasing health service and social care consumption. To rule out the confounding effect of health conditions and to investigate whether loneliness has direct impact on service use, participants' health conditions were adjusted for in the current study. (2) In the case of lower use of health and social services, it may be that those who are lonely do not know about existing services or how to access them. Given the strong link between loneliness and health, it is likely that lonely individuals are at higher risk of health decline, which would result in consuming more health services when little is enough.

In either situation (here: higher or lower service use), it is crucial to raise public awareness of loneliness, identifying at-risk group, and making relevant services readily available.

As suggested, we added the following sentences to the last second paragraph in the discussion session.

Despite strong associations between loneliness and increased use of GP and community-based services, it is possible that lonely individuals have less knowledge about appropriate access to health and social care services or do not have the means to access them than non-lonely individuals. Given the robust link between loneliness and health outcomes reported in previous studies, individuals who are lonely may be at higher risk of health decline, and consequently are likely to have greater need of health services. However, in the current analysis, health conditions were adjusted for, implying that there might be other mechanisms underlying the association between loneliness and health and social care services usage. This again emphasises the importance of developing services that are sensitive to loneliness.

Comment #2 It was also not clear to me what the authors were really trying to achieve with their second objective when they said that they wanted to investigate whether 'time-varying loneliness' and health/social services were related. It looked like their model was estimating the association between loneliness, averaged across time points, and the outcome. It that was their intention (to average the loneliness level) then their analysis does not actually make good use of the fact that they have loneliness data that vary over time. On the other hand, if what they wish to imply is that changes in loneliness from one time point to another is associated with relative differences in health/social service use, then the models used should explicitly account for that.

Reply:

Loneliness is likely fluctuate with circumstances and context across time. The aim of our analysis is to investigate the association between time-varying loneliness and health service and social care usage. In GEE with this time-varying covariate, each participant's data is divided into different time spaces, and the analysis creates a specific value of the time-varying covariate for that specific time space. Then a final weighted average of short-term effects is calculated.

The investigation of changing pattern of loneliness over time was intended to provide evidence that loneliness varies over time. However, we now see that this was confusing and suggested the objective of the current study was to examine the effect of loneliness changes on the changes of health and social service use. This section has been removed. Please see changes in the main text.

Investigating the impact of loneliness on health and social service use by using change model would be useful for understanding how changes of loneliness from one time point to another affect the changes of service use, but this is beyond the scope of the current study.

Comment #3 Last, I have some concerns about how the outcome variables were modeled. The authors truncated the number of community service contacts, hospital visits and possibly the time interval in their last GP visit. There were no information provided on how these data changes may have influenced their results. Mean values, which is basically what their GEE models are comparing, can be quite sensitive to suppression of extreme values. When changes to raw data such as what's been done in the study, supplementary sensitivity analyses usually help in demonstrating that the results are not an artifact of the data preparation process carried out.

Reply:

When asking participants how often they used community services in the past week answers were coded as 6 for 6 or >6 contacts. When asking how many times they have been admitted into hospitals in the last year responses were coded as 2 for 2 or >2 hospital admissions. Participants were asked how long it was since they last visited a GP, coded in the months since last visit, but there was no data collected on the number of GP visits in the last year. It is possible that there were extreme values (outliers) for each health service use measure. We understand that GEE model is sensitive to suppression of outliers, but we do not have the data to conduct sensitivity analyses. To clarify this issue, we added the following sentences as one of weaknesses in the discussion session.

Responses about health and social care service use were coded with maximum values, without recording the true maximum. It is possible that some participants are heavy users of services, resulting in higher service use than measured. It is possible that this led to a loss of ability to identify relationships for heavy use of services, and no sensitivity analyses are possible to test this. However, for each type of health and social service, the largest proportion of participants who were in the maximum category was less than 6%. Therefore, results from the current study are unlikely to be influenced by the extreme values of service use.

Comment #4 Time since last GP visit was modeled using a Gaussian distribution. I doubt that this variable follows the Gaussian distribution. Using a more appropriate analytic approach should be considered.

Reply:

As suggested by the reviewer, we have now chosen a more appropriate approach to model the non-normally distributed continuous variable. As the distribution of variable “time since last visiting a GP” fits into one of the Gamma distribution shapes, we assumed a Gamma distribution for this variable, and used gamma family and the natural logarithm as the link function in the GEE model. Briefly, results from this model did not differ from the results in the previous model (using Gaussian family) substantively, except that depression was found to be significantly associated with shorter time since last visiting a GP in associations between either baseline loneliness or time-varying loneliness and health and social care usage. Please see the changes:

In terms of associations between baseline loneliness and health and social care utilisation, the only significant association was that feeling slightly lonely was positively associated with GP visits after adjusting for demographic characteristics and health problems (Table 3). Neither feeling lonely nor feeling slightly lonely were found to be related to home help use, community nurse contacts, meals on

wheels service use, day centre or hospital visits. Results also indicated that moderate and high levels of physical impairment were significantly associated with home help use and with hospital visits. Having three or more chronic diseases was associated with community nurse contacts. Having disabilities in both IADL & ADL was related to increased frequency of day centre visits. On the other hand, depression was significantly and negatively associated with day centre visits. However, being depressed was associated with shorter time since last seeing a GP. Moreover, being female and having at least three chronic diseases was also associated with GP visits.

Comment #5 It would be more helpful to have row percent and not column percent on Table 1. Adding another column containing the raw counts for each demographic characteristics would also help.

Reply:

As suggested, we have added an additional table to describe the characteristics of participants at wave 3 using the raw data. This table (Table 1 in the revised version) presents the raw counts for each demographic characteristic as well as the corresponding percentages.

Because our baseline data were drawn from wave 3, we adjusted for the dropout from wave 1 to wave 3 by computing inverse probability weights. In addition, as there were a few participants who did not have data on loneliness at wave 3, a weight was calculated to adjust for loneliness non-response. In order to make the study sample as representative of the original study population as possible, we thought it would be reasonable to describe the study sample by applying the weight (a product of the weight adjusting for dropout between wave 1 and wave 3 and the weight adjusting for loneliness non-response). Therefore, we kept the table 'The distribution of characteristics according to loneliness level measured at wave 3, weight applied' (Table 2 in the revised version). Following this reviewer's comment, we present the row percent instead of column percent. The description of participants' characteristics in the results session was revised accordingly. Please see the changes in the main text.

Comment #6 Have the authors considered mixed-effects models that can accommodate missingness instead of GEE with IPW?

Reply:

Mixed-effects models are likelihood based, requiring much less strong assumptions for missing data mechanisms. Only Missing At Random is required for a valid inference. This approach is useful when modelling individual trajectories as it is conditional on random effects that describe the behaviours of a response that vary for a specific individual. However, the objective of the analysis is to examine population-averaged (marginal) effects of risk factors on outcomes, therefore, the generalised estimating equations (GEE) was chosen as the most appropriate statistical model. In addition, our cohort is unusual in that all participants have now died so outcome is known on all, so we calculated the inverse probability weight based on probability of staying in the current study on the condition of responding to the previous wave and being alive at the current wave. After taking all these factors into consideration, the GEE with the inverse probability weighting adjusting for dropout during follow-up is used to test the paper's hypotheses.

Comment #7 There were factors used in the adjustment that could be measuring largely the same construct, ie. depression and loneliness, physical impairments and physical functioning. Have the authors considered running their analyses with only variables that are distinct from each other and see if the point estimates and/or confidence interval changes?

Reply:

Depression and loneliness are related but are distinct concepts. They were conceptually distinguished by Weiss (1973) who defined loneliness as how individuals feel about their social relationships in

particular, whereas depression is a far broader concept in which loneliness may be expressed. In practice, some of the cluster of depression's symptoms are similar to those of loneliness. For example, in several earlier studies examining the association between loneliness and depression, depression was measured by using the Centre for Epidemiologic Studies Depression Scale (CES-D), which includes the item "I am feeling lonely". To avoid circularity, the authors removed this item when measuring depression. In the current study, depression was measured using series of 10 items whose validity was tested in CC75C (Girling et al, 1995). None of these items was intended to measure loneliness.

Although the variables physical impairment, physical functioning and number of chronic diseases are health-related, they were operationalised in different ways. Physical impairment was intended to capture general health conditions including poor vision, poor hearing, back pain, chest pain and so on. Physical functioning, in contrast, focused on measuring a broad spectrum of activities of daily living including bathing, dressing, getting to the toilet on time, grooming, cooking and housework. Finally, the number of chronic diseases measures the specific self-reported doctor-diagnosed diseases, such as angina, stroke, diabetes, etc. This is all described in the methods section to clarify the differences in these measures to the reader.

Although these variables related to health were collected in distinctive ways we have, as suggested by the reviewer, performed an additional analysis to test the impact of loneliness on health and social service use using only physical functioning.

In statistical analysis section, we added:

Because several covariates included in the analyses were health-related, such as physical impairment, physical functioning and number of chronic diseases; despite that they were collected in distinctive ways, a sensitivity analysis was performed to test the impact of loneliness on health and social service use adjusting only for physical functioning. The results of the sensitivity analysis are available upon request.

The results from sensitivity analysis did not differ from the presented results substantively, generally supporting the conclusions made based on the current analysis. We have therefore retained all three variables as covariates to control for as much confounding as possible.

Comments from Reviewer #2:

Comments #1 I think the introduction could be expanded slightly to include a brief discussion of the covariates that are examined in the study and the importance of selecting these covariates. More specifically, depression is highly linked to loneliness and there is a bulk of research discussing this association. Also, general cognition as measured with MMSE has also been linked to loneliness, so it would be helpful to add a couple of references to show why these covariates are important to consider. In the manuscript the authors actually mention that differences in findings between studies may be due to differences in covariates examined, so this makes it all the more important to include some information about the covariates of the present study and their importance.

Reply:

As suggested, we have added a few references on the association between loneliness and covariates, and the importance of how these are selected for analysis. The inserted text is provided below.

There have been consistent reports both from longitudinal and cross-sectional studies on the association of loneliness with mental health (Nolen-Hoeksema and Ahrens, 2002), cognitive decline

(O'Luanaigh et al., 2012; Wilson et al., 2007), poor physical health (Hawkley et al., 2010; Keysor et al., 2003; Kurina et al., 2011) and mortality (Luo et al., 2012; Holt-Lunstad et al., 2015). Those on mental health have been consistent across age groups studied.

Comments #2 I think the following needs clarification: "However, with only two measures, researchers were not able to capture the fluctuating nature of loneliness[9-11], therefore, the complicated

association between time-varying loneliness and health and social care utilisation could not be examined". why does the fluctuating nature of loneliness pose difficulty when measured twice? Please clarify.

Reply:

Consistent with previous studies, fluctuating loneliness is defined as the feeling of loneliness varying at different time points with changes not following a linear pattern. For example, if loneliness was measured at three time points, changing patterns can be lonely, not lonely, lonely; lonely, lonely, not lonely; not lonely, lonely, lonely; not lonely, lonely, not lonely; not lonely, lonely, not lonely. When loneliness is only measured at two time points only increase, stability or decline can be measured.

Comments #3 The following sentence suggests that these issues were improved in the current study but you don't clarify how they were improved. "The heterogeneity in existing evidence is likely to be due to the differences in study sample, selection of covariates, length of follow-up time, and the measures of loneliness". You state that in this study the sample is older old adults that are underrepresented, which is true and that the length and number of waves are much better in your study. However, as I mentioned earlier, you must explain why you selected the specific covariates but also why you used a single item to measure loneliness. The vast majority of research on loneliness use questionnaires (such as the UCLA) rather than a single item to capture different aspects of loneliness. Since loneliness is defined the perceived discrepancy between one's desired and actual social contacts it is useful to justify why you selected a single item for loneliness. I appreciate that you have it as a limitation in the discussion but I think that since loneliness is the key variable of the paper it's measurement should be justified.

Reply:

We have added the reasons why we selected the specific covariates in the introduction session (in the first paragraph). Please see the changes in the main text.

We recognised the limitations of using a single-item scale to measure loneliness, and the value of well-known multi-item scales such as UCLA or de Jong Gierveld Loneliness Scale. However, these measures were not included in CC75C, which started in 1984. The strength of a single-item scale is that it can measure loneliness directly by asking whether participants feel lonely or not. Single-items have been reported to have the advantage of ease of administration within large surveys where time for questions is at a premium, and that these are well accepted. The potential limitations of single-item loneliness scale are covered in the discussion section.

Comments #4 Perhaps it would be useful to state whether you measured "medication use/ prescribed medication" because this would be another reason to visit the GP. If you haven't measured this please add a note on the discussion in the limitations and/or future studies.

Reply:

In the CC75C study, participants were asked what medicines they are taking and how long they have been taking those medicines at each wave. This included all prescribed and taken medications, supplements and over the counter items. These are not distinguished in the study.

As suggested, we added the following sentences as one of the limitations in the discussion session:

Medication use may also serve as a confounder in this analysis, as individuals who are taking prescribed medications may need to visit their GPs more regularly. However, because of the unavailability of relevant data, we were unable to adjust for this variable. Although this might dilute the association between loneliness and health care utilisation, it is unlikely to change the direction of the association.

Comments from Reviewer #3:

Comments #1 The topic is not new. Good luck.

Reply:

The association between loneliness and health services use has indeed been investigated in numerous earlier studies. However, according to our systematic review (not yet published), there is little published on the association of loneliness with social services use. With a wide range of measurements of community and social care services in CC75C, we were able to explore the association between loneliness and both health and social care service use. We believe the current study adds to the evidence base in this area. Moreover, as stated in the text, the inclusion of repeated measurements of loneliness and service use (more than two measurements) provides the opportunity to test the hypothesis more thoroughly. Furthermore, to the best of our knowledge, this is the first study that focuses on older old people. In conclusion, despite the fact that the topic has been studied previously, the uniqueness and richness of our data allow us to extend previous analyses and contribute new findings to the literature, as well as provide new insights for future studies.

References:

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VERSION 2 – REVIEW

REVIEWER	Dr Antonia Ypsilanti Sheffield Hallam University, UK
REVIEW RETURNED	10-Feb-2019

GENERAL COMMENTS	The authors have addressed the points I raised when reviewing the paper and have provided sufficient feedback and have reasonably addressed all my concerns. I am happy to accept the manuscript without further revision.