PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Neighborhood Socioeconomic Position and Risks of Major Chronic Diseases and All-Cause Mortality: A Quasi-Experimental Study
AUTHORS	Kim, Daniel; Glazier, Richard; Zagorski, Brandon; Kawachi, Ichiro; Oreopoulos, Philip

VERSION 1 – REVIEW

REVIEWER	Christo Albor Queen Mary University of London, United Kingdom
REVIEW RETURNED	09-Aug-2017

GENERAL COMMENTS	Thank you for asking me to review this manuscript. It was an interesting read. Strengths include the longitudinal design and analysis, the number of health outcomes, and the relative homogeneity of the sample included (publicly-housed), amongst other things. The findings are intriguing, given an apparent threshold up to what point a more affluent neighbourhood may exert protective effects. This fits well with arguments on a balance between material and social benefits of a 'nice' area and psychosocial disadvantages of relative deprivation through status incongruity. Below are some points that I considered important to take into account whilst reading the manuscript. Introduction: Perhaps a mention/citation of Riva, Gauvin & Barnett's review of small area effects on health from 2007 (JECH 61:853-861), as this review synthesised 86 separate studies. Methods: Not entirely clear whether the MTCH application procedure had been the same points system from before the mid-1990s. Perhaps some of the differences between quartiles are because selection bias was introduced before the quasi-random allocation of housing. Clearly shown is the population size of the census enumeration areas, but what is the mean population size of the census tracts?

	Discussion: Although residual confounding was reduced by having all sample in public housing, and adjustment by proxy indicators of socio-economic status, it is possible that residual confounding could account for some of the findings, given that there does appear to have been some selection bias. Relating to findings on hypertension, Diez-Roux, Nieto, Muntaner et al. in 1997 published a paper in the American Journal of Epidemiology (Vol 146, No.1) that had similar findings in a subset analysis. For one group of African-American men living of low social class, cholesterol was increased in richer neighbourhoods. However, the same pattern was not found for their blood pressure. Nevertheless, an interesting parallel. One other alternative explanation to some of the census tract effects may be the structural differences in the public housing projects built in these different neighbourhoods of different levels of affluence. Especially in the case of asthma incidence. Many thanks.

REVIEWER	Lennert Veerman Cancer Council NSW, Australia
REVIEW RETURNED	04-Sep-2017

GENERAL COMMENTS	This is an interesting study with an innovative and strong design, relative to the standard in the field. The study exploits the fact that public housing was assigned 'primarily based on factors other than personal choice'. I think these findings should be published, but would like to see some additional analysis, and would also challenge the authors on the interpretation of the findings. Table 1 shows that unfortunately, the assignment turned out not to be quite as random as would have been ideal for this study. The residents in the highest SEP quartile neighbourhood were younger, more likely to be black and less likely to be immigrant, less likely to be living alone, and had a higher median household income. This not only means that this group cannot be compared to the rest, but also puts a question mark around the randomness in the allocation across the other quartiles. Do the authors think this influenced the results? Some comments on this matter could be included in the discussion section. These data are ordinal. Therefore, rather than analysing the data by comparing quartiles, should they not be analysed for trends across quartiles, rather than by comparing Q2-Q4 to Q1? The 'dropping out' of Q4 leaves three quartiles that seem broadly comparable in composition. Table 2 and 3 show some statistically significant differences of Q2 and Q3 with Q1 (lowest income/SEP), but to this reviewer, a clear pattern does not really emerge, except perhaps for asthma, and possibly a trend towards a higher risk of hypertension with rising neighbourhood income and SEP.

	Are data on ambient air quality available, to explore this as a possible explanation for the finding that higher neighbourhood income and SEP are associated with lower risk of asthma? In their interpretation of the data, the authors seem to emphasize the results that confirm their (not clearly stated) hypotheses, and ignore findings that challenge these assumptions. In Table 2 (though not in Table 3), all-cause mortality is higher in Q2 than that in Q1, but this is mentioned neither in the results, nor in the discussion. To avoid the impression of bias, if not to ensure a balanced interpretation, the authors should note and, if possible, explain this finding. To a lesser extent, the same may be true with respect to hypertension, if the trend in that condition makes it across the line of statistical significance in a trend analysis. In contrast, the results for acute MI in Q3 compared to Q1 are the first finding reported in the abstract, although this is not statistically significant by commonly used standards. One can have reservations with the quest for statistical significance, but an impression of selective application of such rules-of-thumb is to be avoided. The summary (page 18) concludes that “this quasi-experimental study provides new evidence to support protective influences of higher neighborhood SEP on selected chronic diseases and all-cause mortality”. That is too strong and broadly formulated for my liking. The ‘selected chronic conditions’ should be specified as ‘asthma’, and the mortality results don’t show a clear trend. Q3 has lower mortality than Q1, but given borderline statistical significance and the fact that allocation was not entirely random, I would hesitate to make too much of that finding.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Christo Albor
Institution and Country: Queen Mary University of London, United Kingdom

Thank you for asking me to review this manuscript. It was an interesting read. Strengths include the longitudinal design and analysis, the number of health outcomes, and the relative homogeneity of the sample included (publicly-housed), amongst other things.

The findings are intriguing, given an apparent threshold up to what point a more affluent neighbourhood may exert protective effects. This fits well with arguments on a balance between material and social benefits of a "nice" area and psychosocial disadvantages of relative deprivation through status incongruity.

We greatly appreciate Reviewer 1’s detailed and helpful comments.

Below are some points that I considered important to take into account whilst reading the manuscript.

Introduction:
Perhaps a mention/citation of Riva, Gauvin & Barnett"s review of small area effects on health from 2007 (JECH 61:853-861), as this review synthesised 86 separate studies.

Response: This paper is now cited as Reference 1 in the Introduction section.

Methods:
Not entirely clear whether the MTCH application procedure had been the same points system from before the mid-1990s. Perhaps some of the differences between quartiles are because selection bias was introduced before the quasi-random allocation of housing.

Response: As described in the original paper, up until the mid-1990s, applicants on the Metropolitan Toronto Housing Corporation (MTHC) waiting list were assigned to public housing projects according to factors primarily other than personal choice i.e., using a points system, with households being given points primarily based on financial need. Families who reached the top of the waiting list were offered accommodation according to the first available unit with the requested number of bedrooms. Families in subsidized housing could request a transfer based upon a change in employment location or family size, but moving between projects on the basis of poor neighborhood environments was not permitted. Oreopoulos previously showed that there were limited baseline differences in public housing residents across projects based on observable background differences in 1978, and thus there was no evidence of significant selection at that time.

Starting in the mid-1990s, the new application for MTCH housing included space for the choice of neighborhood, and eventually one could specify the specific projects of interest (although each project had long waiting times, roughly 4-6 years). Hence, beginning in the mid-1990s, there was some opportunity for selection as compared to previously. This may account for some of the baseline differences in our study.

Comment: Clearly shown is the population size of the census enumeration areas, but what is the mean population size of the census tracts?

Each Census tract contains between 2500 and 8000 individuals, and an average of 4000 individuals. This is now stated in the text on page 7.

Discussion:
Although residual confounding was reduced by having all sample in public housing, and adjustment by proxy indicators of socio-economic status, it is possible that residual confounding could account for some of the findings, given that there does appear to have been some selection bias.

Response: We fully agree with this statement. The possibility of residual confounding is acknowledged in the study limitations on page 15: "…while we controlled for baseline patterns of health care, to the extent that individual/household income (for which EA-level income was an imperfect proxy) and co-morbid conditions and their treatments could influence staying versus moving out of the neighborhood and the outcomes, residual confounding is still possible."

Comment: Relating to findings on hypertension, Diez-Roux, Nieto, Muntaner et al. in 1997 published a paper in the American Journal of Epidemiology (Vol 146, No.1) that had similar findings in a subset analysis. For one group of African-American men living of low social class, cholesterol was increased in richer neighbourhoods. However, the same pattern was not found for their blood pressure. Nevertheless, an interesting parallel.

Response: We thank the reviewer for noting this interesting parallel. We now cite this finding in the paper on page 17: “Likewise, although we did not examine cholesterol as an outcome, another study observed that in African-American men, low SEP was associated with higher serum cholesterol in the least socioeconomically disadvantaged neighborhoods, and with lower serum cholesterol in the most disadvantaged neighborhoods.”
One other alternative explanation to some of the census tract effects may be the structural differences in the public housing projects built in these different neighbourhoods of different levels of affluence. Especially in the case of asthma incidence.

We agree that physical and structural features of Census tracts, such as the built environment and environmental factors, may also contribute to the observed associations such as for asthma. This is now noted on page 15: “Physical and structural features of neighborhoods, such as the built environment and air quality, were not specifically controlled for in the models, and could further contribute to residual confounding including for the observed asthma associations.”

Reviewer: 2
Reviewer Name: Lennert Veerman
Institution and Country: Cancer Council NSW, Australia

Comment: This is an interesting study with an innovative and strong design, relative to the standard in the field. The study exploits the fact that public housing was assigned ‘primarily based on factors other than personal choice’. I think these findings should be published, but would like to see some additional analysis, and would also challenge the authors on the interpretation of the findings.

Response: We greatly appreciate Reviewer 2’s detailed and helpful comments.

Comment: Table 1 shows that unfortunately, the assignment turned out not to be quite as random as would have been ideal for this study. The residents in the highest SEP quartile neighbourhood were younger, more likely to be black and less likely to be immigrant, less likely to be living alone, and had a higher median household income. This not only means that this group cannot be compared to the rest, but also puts a question mark around the randomness in the allocation across the other quartiles. Do the authors think this influenced the results? Some comments on this matter could be included in the discussion section.

Response: We agree that the differences between Q4 and other quartiles suggests the presence of some selection. At the same time, however, as evidenced by the similarity of baseline characteristics of public housing residents across Q1-Q3 quartiles, we believe that there is more limited evidence of selection in the lower three quartiles. We have added this caveat to the Discussion section on page 15: “While we cannot fully eliminate confounding in the lower quartiles (Q1-Q3) of neighborhood SES, the relative baseline comparability among their public housing residents suggests that any confounding bias is likely to be less than in the absence of assignment to public housing projects primarily according to factors other than personal choice.”

Comment: These data are ordinal. Therefore, rather than analysing the data by comparing quartiles, should they not be analysed for trends across quartiles, rather than by comparing Q2-Q4 to Q1?

Response: To clarify, in Table 1 we had compared Q1-Q3 to Q4 because Q4 showed evidence of sizeable differences from characteristics of public housing residents in the other three quartiles (Q1-Q3). Under the assumption of quasi-random variation of assignment to neighborhoods, we would expect to see comparability of these characteristics of residents across all four quartiles, and not any specific trend, linear or otherwise.

Hence, we do not believe that a trend analysis is warranted here.

Comment: The 'dropping out' of Q4 leaves three quartiles that seem broadly comparable in composition. Table 2 and 3 show some statistically significant differences of Q2 and Q3 with Q1 (lowest income/SEP), but to this reviewer, a clear pattern does not really emerge, except perhaps for asthma, and possibly a trend towards a higher risk of hypertension with rising neighbourhood income and SEP.

Are data on ambient air quality available, to explore this as a possible explanation for the finding that higher neighbourhood income and SEP are associated with lower risk of asthma?

Response: We agree that examining air quality/air pollutants would be interesting to look at as a possible explanation for the asthma association. We mention this in the Discussion section on page 15: "Physical and structural features of neighborhoods, such as the built environment and air quality, were not specifically controlled for in the models, and could further contribute to residual confounding including for the observed asthma associations." Unfortunately, however, such data on air quality/air pollutants are not available to us.

Comment: In their interpretation of the data, the authors seem to emphasize the results that confirm their (not clearly stated) hypotheses, and ignore findings that challenge these assumptions. In Table 2 (though not in Table 3), all-cause mortality is higher in Q2 than that in Q1, but this is mentioned neither in the results, nor in the discussion. To avoid the impression of bias, if not to ensure a balanced interpretation, the authors should note and, if possible, explain this finding. To a lesser extent, the same may be true with respect to hypertension, if the trend in that condition makes it across the line of statistical significance in a trend analysis. In contrast, the results for acute MI in Q3 compared to Q1 are the first finding reported in the abstract, although this is not statistically significant by commonly used standards. One can have reservations with the quest for statistical significance, but an impression of selective application of such rules-of-thumb is to be avoided.

Response: In order to be clear about the interpretation of findings, we have now added our general study hypothesis as follows on page 7: "Based on the past literature, we hypothesized that neighborhood SEP would have protective influences on the risks of developing these diseases/conditions and all-cause mortality."

We now note the findings that are consistent and inconsistent with our study hypotheses, including that the hazard ratio estimate for Q2 is greater than 1 for the associations with all-cause mortality and acute MI on pages 12 and 13 of the Results, and further offer selection bias as a possible explanation at the bottom of page 15 of the Discussion.

In addition, we mention the unexpected association for hypertension (while also noting on page 13 it exhibited no statistically significant trend across Q1-Q4), and offer a possible explanation for it in relation to status incongruity on page 17: "Our findings of a positive relation between higher neighborhood SEP and hypertension is also compatible with past evidence of associations between neighborhood SEP and worse CHD risk factor profiles for low-income individuals in high-income neighborhoods, although the specific association observed in a prior study was with cholesterol and not hypertension. As has been previously posited, such findings may reflect the adverse health effects of status incongruity, whereby feelings of relative deprivation and social exclusion for low-income individuals living in high-income neighborhoods may generate psychosocial stress."

We have also revised the Abstract to note these inconsistent findings, as follows: “By contrast, the associations corresponding to living in the highest vs. lowest quartile of median household income (Q4 vs. Q1) were neither consistent in direction nor statistically significant. The inconsistent associations may be attributed in part to selection and status incongruity.”

Comment: The summary (page 18) concludes that “this quasi-experimental study provides new evidence to support protective influences of higher neighborhood SEP on selected chronic diseases and all-cause mortality”. That is too strong and broadly formulated for my liking. The ‘selected chronic conditions’ should be specified as ‘asthma’, and the mortality results don’t show a clear trend. Q3 has lower mortality than Q1, but given borderline statistical significance and the fact that allocation was not entirely random, I would hesitate to make too much of that finding.

Response: This statement has been revised accordingly as follows, to tone down the strength of the statement: “This quasi-experimental study provides new evidence that is compatible with protective influences of higher neighborhood SEP on asthma and to a lesser degree all-cause mortality.” (page 19)

VERSION 2 – REVIEW

REVIEWER	Christo Albor Queen Mary, University of London UK
REVIEW RETURNED	23-Nov-2017

GENERAL COMMENTS	Thank you for the amendments based on my previous review of this manuscript. I am happy with the changes.

REVIEWER	Lennert Veerman Cancer Council NSW, Australia
REVIEW RETURNED	10-Nov-2017

GENERAL COMMENTS	The paper has improved, but I still have some reservations with the interpretation. The trend analysis shows that there is no statistically significant trend in health outcomes, going from high to low neighbourhood SEP. Given that there are reasons to think that the allocation of the exposure was not random, and the possibility of selective migration out of the areas, my conclusion is that there is no evidence for an independent effect of neighbourhood SEP on these health outcomes, with the possible exception of asthma. The result of an increased mortality in Q2 compared to Q1, and a p for trend of 0.26 (Table 2) do not warrant the statement that these results are ‘compatible with protective influences of higher neighborhood SEP on […] all-cause mortality’. Such a statement can be made on the basis of any underpowered study. Specific comments: Selective out-migration is a potential threat to this analysis. Can you provide information on the percentage in each quartile that moved out?

	I agree that a p for trend is not warranted for Table 1, but thank you for adding those for Tables 2 and 3. "Physical and structural features of neighborhoods, such as the built environment and air quality, were not specifically controlled for in the models, and could further contribute to residual confounding including for the observed asthma associations." – Such features could be regarded as mediators (explanatory variables) rather than confounders, depending on how 'neighbourhood SEP' is defined. It is not included in the definition at the start of the paper, but the authors could consider amending the paper on this point. Hypothesis: good, but please add 'higher' to 'neighbourhood SEP'. In addition to 'status incongruity' as an explanation for the (trend towards) a higher risk of hypertension in 'better' neighbourhoods, could it be that residents in higher SEP neighbourhood had better access to better quality primary health care, leading to a higher chance of being diagnosed? This would be less of an issue for the more easily diagnosed conditions (like death), but could be for asymptomatic conditions like hypertension.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2 Reviewer Name: Lennert Veerman Institution and Country: Cancer Council NSW, Australia Please state any competing interests or state 'None declared': None declared. Please leave your comments for the authors below The paper has improved, but I still have some reservations with the interpretation. The trend analysis shows that there is no statistically significant trend in health outcomes, going from high to low neighbourhood SEP. Given that there are reasons to think that the allocation of the exposure was not random, and the possibility of selective migration out of the areas, my conclusion is that there is no evidence for an independent effect of neighbourhood SEP on these health outcomes, with the possible exception of asthma. The result of an increased mortality in Q2 compared to Q1, and a p for trend of 0.26 (Table 2) do not warrant the statement that these results are 'compatible with protective influences of higher neighborhood SEP on […] all-cause mortality'. Such a statement can be made on the basis of any underpowered study.

R: We have now removed the statements of a protective influence on all-cause mortality in the Abstract and throughout the main text of the manuscript. As described below, there was statistical evidence of a linear trend across the Q1-Q3 quartiles for asthma.

C: Specific comments: Selective out-migration is a potential threat to this analysis. Can you provide information on the percentage in each quartile that moved out?

R: Thank you for this helpful comment. We have now estimated the percentage who moved out over the 13-year follow-up period from each neighborhood SEP quartile at baseline, and observed this to range from 20-25% in each baseline quartile. We now mention this in the text on page 16 as follows: "Second, moves out of the baseline neighborhood SEP quartile (with approximately 20-25% of residents moving to a different quartile over the 13-year follow-up period) as well as differential attrition due to deaths prior to baseline could yield different observed associations than in the absence of such moves/attrition, thereby contributing to selection bias."

C: I agree that a p for trend is not warranted for Table 1, but thank you for adding those for Tables 2 and 3.

R: Thank you kindly for letting us know. Given that we believe there is evidence of selection primarily in the highest quartile Q4, we now additionally provide results in Tables 2 and 3 for the trend analysis for the Q1-Q3 quartiles. These results show a trend for hypertension and asthma (significant at the 10% and 5% levels, respectively), and no significant trend for the other outcomes examined. We detail this now in the text on page 13 as follows: “However, across the Q1 through Q3 quartiles, significant trends were observed at the 10% and 5% levels for hypertension and asthma, respectively (Table 3).”

C: “Physical and structural features of neighborhoods, such as the built environment and air quality, were not specifically controlled for in the models, and could further contribute to residual confounding including for the observed asthma associations.” – Such features could be regarded as mediators (explanatory variables) rather than confounders, depending on how ‘neighbourhood SEP’ is defined. It is not included in the definition at the start of the paper, but the authors could consider amending the paper on this point.

R: We have now amended the paper to reflect the above as follows:
“Neighborhood SEP is plausibly a determinant of amenities and resources including the local food environment (e.g., density of supermarkets), built environment (e.g., street connectivity), presence of tobacco and alcohol vendors (i.e., tobacco outlets), and air quality. In turn, such neighborhood attributes may mediate the health impacts of neighborhood SEP by influencing individual health behaviors and physical health, and ultimately shaping the risks of chronic health conditions.” (page 5)
“Physical and structural features of neighborhoods, such as the built environment and air quality, were not specifically controlled for in the models, and could further contribute to residual confounding and/or be potential mediators including for the observed asthma associations.” (bottom of page 15, top of page 16)

C: Hypothesis: good, but please add ‘higher’ to ‘neighbourhood SEP’.

R: We have now added ‘higher’ to ‘neighbourhood SEP’ on page 7.
In addition to ‘status incongruity’ as an explanation for the (trend towards) a higher risk of hypertension in ‘better’ neighbourhoods, could it be that residents in higher SEP neighbourhood had better access to better quality primary health care, leading to a higher chance of being diagnosed?

C: This would be less of an issue for the more easily diagnosed conditions (like death), but could be for asymptomatic conditions like hypertension.

R: This is a very interesting and plausible hypothesis. We agree that better access to better quality primary health care could possibly lead to a higher chance of being diagnosed. We have now added this to the revised manuscript as follows: “Finally, it is possible that with higher-quality health care services including primary health care being available in higher-SEP neighborhoods, such neighborhoods could be linked to a higher probability of being medically diagnosed with hypertension.” (page 18)

Reviewer: 1 Reviewer Name: Christo Albor Institution and Country: Queen Mary, University of London, UK Please state any competing interests or state ‘None declared’: None declared Please leave your comments for the authors below
C: Thank you for the amendments based on my previous review of this manuscript. I am happy with the changes.
R: Thank you kindly for letting us know.

VERSION 3 – REVIEW

REVIEWER	Lennert Veerman Cancer Council NSW, Australia
REVIEW RETURNED	26-Dec-2017

GENERAL COMMENTS	I am happy with the response of the authors and have no further comments, save to congratulate them on this very interesting paper.

Correction: *Neighbourhood socioeconomic position and risks of major chronic diseases and all-cause mortality: a quasi-experimental study*

Kim D, Glazier RH, Zagorski B, *et al*. Neighbourhood socioeconomic position and risks of major chronic diseases and all-cause mortality: a quasi-experimental study. *BMJ Open* 2018;8:e018793. doi: 10.1136/bmjopen-2017-018793.

The previous version of this manuscript contains an error in table 1 column headings.

The column headings should read respectively as:

Q1 (lowest income CTs)
Q2
Q3
Q4 (highest income CTs)

Instead of:

Acute MI
Hypertension
Diabetes
Asthma

BMJ Open 2019;**9**:e018793corr1. doi:10.1136/bmjopen-2017-018793corr1