Author's response to reviews

Title: The association of cold weather and all-cause and cause-specific mortality in the island of Ireland between 1984 and 2007

Authors:

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Author's response to reviews: see over
To the Environmental Health Editorial Team:

Dear Dr Kristie Ebi,

We appreciate the helpful comments you have provided to aid in strengthening our manuscript. Thank you for allowing us the opportunity to submit our revised manuscript (MS:2101583410137976), “The association of cold weather and all-cause and cause-specific mortality in the island of Ireland between 1984 and 2007” by Ariana Zeka, Stephen D Browne, Helen McAvoy, and Patrick Goodman as a Research Article for your journal. We have addressed all the formatting issues required by the journal, as well as have updated the author contribution section to reflect journal format and contributions to this manuscript. We have included the exact reviewer comments provided, and have addressed these in a point-by-point manner in this response letter. Our manuscript now consists of 3360 words (excluding Abstract of 274 words). We are grateful to you for considering our manuscript for publication in Environmental Health.

Respectfully,

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**Comments from Reviewer #1:**

1. This was a classic time-series study of cold that was well written and well executed. The pattern of results was as expected, with stronger associations at short lags that tails away, and stronger associations in the elderly. The results are not new internationally, but could well have important local implications.

*Authors’ Response (AR): We appreciate the Reviewer comments, and have attempted to highlight more the differences between the results from the two jurisdictions on the small island of Ireland.*

Major Compulsory Revisions:
2. I encourage the authors to include time as an effect modifier to answer the important question of is things getting better or worse? Given the long time series this would be worth testing. I would recommend winter season as a linear effect modifier, i.e., 2004=1, 2004/05=2, 2005/06=3, etc. This would test if things are gradually getting worse or better.

Authors’ Response: We understand the Reviewer’s point; however, the way in which the Reviewer advises to explore this issue is not possible in the case-crossover approach. We used a time-stratified case-crossover design for this study, in which each event (day of death) is compared to controls (all other days, of the same day of the week, in the same month) for varying risk factors (referent window/strata). In the case of the winter/year definition as the Reviewer specifies, this is a non-varying factor within each referent window (determined by the event month, and day of the week), therefore it is not possible to compare within each risk set.

We have, however, explored the changes over time, by stratifying the models for different definitions of time (period), and we have detected small decreases in response over time in both jurisdictions. We have included wording in the text to reflect this point.

In agreement with the Reviewer, we do consider the long-term changes in the cold weather-mortality relationship very important to explore. However, the issue of long term effects on the cold weather-mortality relationship is much more complex, considering temporal and jurisdiction-specific policy, socioeconomic, health care and demographic differences. We are investigating these issues further, through extensive analyses which will be presented in another substantive paper in preparation. We also wish to refer the Reviewer to our response to Point 3 below on a similar issue.

3. One of the ways that things might be getting better is because of the fuel payments (noted in the discussion). It may be worth looking at individual years around the time of the fuel payments.

Authors’ Response: We agree with the Reviewer on this very important issue. We are indeed looking at the contribution of fuel policy, poverty, and socioeconomics on the cold weather and mortality association in both jurisdictions of Ireland. Further analyses will include test for temporality effects of the policy, such as for example testing whether cold weather-mortality associations pre- and post-policy differ amongst the two jurisdictions. In preliminary analyses, we tested the cold weather-mortality relationship for different time periods defined by the presence of fuel policy for each jurisdiction (1989-1990; 1991/1992). We observed some differences over time, with effects diminishing in more recent years were observed in both jurisdictions (Tables A and B in this response letter). However, the temporal separation in these preliminary analyses is quite crude, and does not take into account other immediate and gradual changes in public policies and health care in the two jurisdictions. Further extensive analyses, which are part of the second stage of the study, will explore in depth influences of fuel poverty, socioeconomic, demography, health care and other important factors on the cold-weather mortality association, and will be presented as a separate publication. We do consider these issues very important; however, due to the comparative nature of this research, we feel that the present paper is sufficiently
complex to stand as it is. We have, however, revised the manuscript to include findings of these temporal analyses; these extensions of the discussion section are also in agreement with comments by the other two Reviewers.

Minor Essential Revisions

4. Page 12, in terms of confounding by air pollution see the excellent recently commentary: Commentary: Does Air Pollution Confound Studies of Temperature? Buckley, Jessie et al, Epidemiology, Volume 25(2), March 2014, p 242–245

Authors’ Response: We appreciate the Reviewer’s useful comment and for drawing our attention to the recent paper by Buckley et al. (2014) [1]. We agree with the conclusions of this commentary article which strengthen the findings of our study further. In response, we have revised the section where we discuss the issue of air pollution adjustment in the analyses and also findings of other studies that have controlled for air pollution as potential confounding in the cold temperature-mortality relationship. We are now citing the article by Buckley et al. (2014) as a key reference in this section to emphasize the robustness of our study findings. We are also including findings from other studies that did in fact adjust for air pollution and did not observe confounding effect as a confirmation of the underlying hypothesis for the cold temperature and mortality relationship that Buckley et al. discuss.

5. Table 6, the stars for statistical differences are for what test? cold versus winter?

Authors’ Response: The symbols (double stars) relate to the effect differences for the respective age-specific groups (highlighted with the symbol), and these are only presented for statistically different associations at the 95% confidential interval. However, due to updates of our study results, no statistically important differences in the associations (by age and gender) were observed, therefore this symbol is no longer used.

6. The tables were quite large with a lot of numbers to take in. It might be worth considering a couple of plots to show the key results in a condensed form.

Authors’ Response: We have adjusted a number of the tables and reduced the content where possible in the attempt to provide a more concise and clearer guidance to the reader. We are now presenting only the results for winter months, and only briefly discuss (in text) findings for other seasonal definitions. The inclusion of some plots to show the key results in a condensed form may detract from the complete picture, considering that (for example) for the effects by age and gender for each country would mean plotting 40 estimates and their confidence limit values. We found it difficult in previous attempts to show these clearly and without clustering the figures. Hence, we feel that keeping the tables instead would make it easier for the reader.
Discretionary Revisions

7. Page 5, It took a while to understand definition of winter/cold. I think it would be easier to understand if the days were removed and just the months given.

Authors’ Response: We have now edited the text in our revised manuscript to reflect this comment of the Reviewer.

8. Page 6, ”averaged over 3 days,” use a colon rather than a comma

Authors’ Response: We have now replaced the comma with a colon.

9. Page 11, the greater size of your estimates could also be due to a longer lag compared with other studies. One argument against using a longer lag is that very long lags can start to pick up seasonal effects. Also longer lags are more prone to measurement error compared with shorter lags, as we need to assume that people remained in the same place for longer.

Authors’ Response: There is not a great amount of variation in the temperature dispersion in both jurisdictions, and we think that mobility would not be an issue in these circumstances. Our study results suggested no cold weather-mortality associations remaining in week 6, and only in a few cases these effects were prolonged up to 5 weeks prior to death; these were mainly observed in the Republic of Ireland. Considering that most of the effects observed were amongst older people in both jurisdictions (≥65 years old), we assumed little mobility within a period of 4 to 5 weeks. We are however not excluding the possibility of this factor, but we think its influence may be quite small in our study. The lack of statistical importance of these longer lags also reassured us that we are not picking up seasonal effects. In addition, the use of the time-stratified case-crossover approach controls by seasonality. We also tested our models for different lag structures and durations, including shorter lags and non-mean weekly (daily and 2-day) lags. However, these other lag definitions either did not capture the full effects or were less efficient, and overall findings were similar to the weekly-mean temperature lags. Therefore, we feel confident that we are capturing real effects in our data. We have updated the methods section of our paper to make this clearer for the reader, and also to reflect our response to this comment.

Comments from Reviewer #2:
1. This paper examined the cold effects on mortality in Republic of Ireland and Northern Ireland. It addresses a very important extreme weather-related topic, which is relevant to this journal. This manuscript is recommended to be published after addressing several major issues.

Authors’ Response: We wish to thank the reviewer for their comments and advice that we believe has substantially improved the paper.

Major compulsory revisions:

2. The statistical analysis need be refined to adjust time trends (not mentioned in the methods section), to explore whether cold has a linear effects, and to add separate effects of cold spells in addition to cold. For example, Anderson and Bell (2009) used a spline term to account for non-linear associations between cold and mortality [2].

Authors’ Response: In response to this comment we would like to point out that the time-stratified case-crossover approach used in this study does in fact adjust for a function of time (St). This function appropriately controls for time-varying confounders and time trends if there is no over-dispersion present in the data [3, 4]. In response to a similar comment (1) by Reviewer 3, we tested our data prior to choosing the modelling approach and found no important over-dispersion in data in both jurisdictions. We therefore considered the case-crossover approach as the most appropriate for estimating the cold weather-mortality relationship in our study.

We have also amended the text to incorporate a comment on the changes in response of the population over time.

3. The authors pointed out that lack of air pollution adjustment may not affect their results. The previous studies cited by the authors are not sufficient to support this statement because those studies have not examined PM2.5. The authors are encouraged to conduct an additional analysis to evaluate whether air pollution affect their estimates because it makes this study more convincing and comprehensive.

Authors’ Response: In response to this comment, we would like to point out that air pollution data are very inconsistent across Ireland. More importantly, Reviewer 1 also raised a very similar point, addressing us at a recent paper by Buckley et al. [1] which shows that there is no known mechanism by which air pollution confounds the cold temperature and mortality (health) relationship. The authors of this recent article suggest that, if such adjustment is warranted, then a very clear rationale on why this takes place needs to be provided, and we support their conclusions [1]. This issue is also corroborated by findings of several epidemiological studies assessing the cold weather-mortality relationship which find little or no effect of air pollution on temperature-mortality relationship (references included in the manuscript in corresponding section). Hence, these findings strengthen the confidence in the robustness
of our study results. In reflection, we have now appropriately revised the discussion section where we address this issue.

3. Some discussions need to be expanded, e.g., discussion on differences of estimates between Republic of Ireland and Northern Ireland. The authors need to further explore or discuss which factors may likely result in larger cold effects in Republic of Ireland compared to Northern Ireland. Also, Table 5 shows cold affected more on people above 75 years of age than those between 65 and 74 in Republic of Ireland, however, this pattern is reversed in Table 6. This should be discussed.

Authors’ Response: We have amended the text in an attempt to highlight the differences, between the two jurisdictions. We think that the underlying mechanisms for the observed difference in the cold weather-mortality associations in the two jurisdictions are quite complex, as there are different societal factors at play. In response to this Reviewer’s comment, we have extended our discussion section to explore key differences in context of several issues such as fuel poverty, demographic and socioeconomic differences between the two jurisdictions, using our best knowledge and evidence. These extensions are also in response to similar comments by the other two Reviewers. However, we are currently investigating these discussed differences in depth as the next stage of this study, findings of which will be presented in another publication.

4. The authors stated that “The ability of the case-crossover …. may also support the greater size of our estimates than those observed in most of the previous”. This statement is suggested to be deleted. Theoretically, for analyses like this study without including personal risk factors, case-crossover design is equivalent to Poisson regression models (Lu and Zeger, 2007) [5].

Authors’ Response: We appreciate and support your comments and we have deleted that statement.

Comments from Reviewer #3:
1. MAJOR - primarily all points in the concluding section, which could be strengthened.

Authors’ Response: We agree with the reviewer; however, we think the conclusion section needs to remain short and concise. We have revised and amended the text to strengthened key relevant points in the discussion section.

2. p 13 conclusions: has the impacts of temp on mortality changed over these 24 years? I would guess so.

Authors’ Response: This point has been raised by the other Reviewers. Please see our response to comment 2 of Reviewer 1.
3. Conclusions:
There was no mention of the role of sudden drops in temperatures, and increasing volatility; focussing solely on means misses a lot.

Authors’ Response: We thank you for your insightful comments. We tested different temperature lag structures (including daily, 2-day lags); the application of weekly mean temperature lag structures in the models revealed more efficient and stable results, and the overall results were not different, whether using finer or average lag structures. To assess temperature variability (such as sudden drops in temperature), we also tested the temperature difference between maximum and minimum temperature, between maximum and mean temperature, and between weekly mean maximum temperature lags and weekly mean minimum temperature lags as independent variables in the models. However, we found that there were no important associations in regard to these definitions of temperature; hence these findings were not presented in the manuscript. We have clarified this further in our methodology section.

4. Conclusions:
There was no comment on whether climate warming might help or exacerbate the problem - it might be nice to say something about the future to help policy makers.

Authors’ Response: Although there is a trend of increasing mean temperatures, the variability in temperature will also increase, thus potentially contributing to increased frequency of weather extremes [6]. On this basis only, it may be possible that winter mortality may change; however, whether this change will be an increase or decrease is much more complex, and it is largely dependent on societal adaptation capacity. Other researchers suggest that climate change (increasing mean temperatures) will do little to reduce morbidity and mortality in winter [7-9]. In agreement with previous comments of this Reviewer and similar comments from the other two Reviewers, we have now extended the discussion section to explore some of these issues, including temperature forecasting, potential effects on mortality and influential societal factors. For example, there is already scrutiny of the impact and effectiveness of the winter fuel payment (based on the current climate) in Northern Ireland [10], although it is difficult to assess at this stage if it will consider the warming trend in winter temperatures, or the increased variability in the temperatures (and their extremes) [6]. Further exploration of the influence of these societal actors on the cold weather-mortality relationship will be carried out as part of the next stage of this research.

5. There are a few very recent papers and comment pieces which the authors may find interesting and worthwhile to include:

Authors’ Response: Thank you for highlighting some recent papers and comment pieces which we have found both interesting and informative, and have cited these where appropriate.

MINOR

6. On p12, I think the link between cold deaths and age is quite clear - the majority of people affected by the excess winter deaths effect for example are over 65 yrs.

Authors’ Response: We appreciate the Reviewer’s comment. We recognise that there is an age trend in the cold weather mortality association, and have addressed this point by extending the relevant section in the discussion, also in response to a similar comment (3) from Reviewer 2.

7. p12 yes, there must be many other differences between Northern Ireland and the Republic which could account for this. The point about housing stock and healthcare etc, is presented in a recent paper that you quote: reference 6.

Authors’ Response: We do agree with this comment, and wish to refer the Reviewer to our response to comment 4 above and to similar comments from the other two Reviewers. In response to these, we have extended our discussion section to explore the influence of some of these key issues on the observed differences in the cold weather mortality effects in the two jurisdictions.

8. p13 what level of air pollution are we talking about in Ireland - I would guess very low compared to say London or Beijing...

Authors’ Response: We appreciate your observation. The levels of air pollution in Ireland have been lower than London or Beijing, and this may be due to population size, density and distribution, the prevailing weather patterns, economic activity and output and nature and extent of industrialisation [11-13]. However, we wish to draw the Reviewer attention to a recent paper by Buckley et al., identified by Reviewer 1. In this paper, Buckley et al. suggest that there is no known mechanism which indicates that air pollution affects temperature and health relationship [1], and we support their conclusions. On reflection to this, we have amended our discussions section of the paper to make this clearer for the reader. Please also refer to similar comments (and our responses) from Reviewer 1 (comment 4) and 2 (comment 3).
9. p13 'showed different trends' - so not significant?

Authors’ Response: The authors referred to different cold weather effect trends by age and gender in the two jurisdictions. In response to this comment, we have now edited the section where this appears to make it clearer.

10. p13 not sure that the statement that cold weather mortality is a topical health issue is particularly revealing - this has been known for a long time.

Authors’ Response: We appreciate the Reviewer’s observation. However, we believe that cold weather mortality is a topical health issue in Ireland, especially in light of the recent debate on the provision and future of the winter fuel payment [10]. In the context of the island of Ireland, there is a focus on reducing fuel poverty/excess winter mortality, a potential contributor to the cold weather mortality association [14, 15]. As such, from a policy and societal point of view, this topic is quite coherent. We have now edited the section to reflect this comment, and discuss the issue within the context of policy and other contributing factors on this relationship (cold weather-mortality).

11. Regarding the analysis (all tables):
It is a shame that no test of change over time was carried out - how valid is it to perform averages over years if the relationship is changing? I think more explanation of the rational for taking this approach in the analysis should be provided.

Authors’ Response: We appreciate the Reviewer comment. We would like to refer to our response to comment 2 of Reviewer 1 and comment 2 of Reviewer 2 on a similar issue. The time-stratified case-crossover approach was chosen as most appropriate after exploring our data in depth. This is also in agreement with previous research showing that if all assumptions are correctly met, the time-series and case-crossover approaches can perform quite similar [3]. Potential changes in the relationship in the two jurisdictions are quite complex, and is greatly influenced by many societal factors (comment 2 of Reviewer 1 and comment 2 of Reviewer 2). Further tests on how the relationship has changed over time will be carried out in the next stage of this research, where in depth exploration of these contributing factors will take place.

References:


Table A. Estimated mortality percentage change per 1°C decrease in maximum temperature during the cold season in the Republic of Ireland, 1984-1991, 1992-2007.*

<table>
<thead>
<tr>
<th>Study Period</th>
<th>Lag of Week 1 % Change (95% CI)</th>
<th>Lag of Week 2 % Change (95% CI)</th>
<th>Lag of Week 3 % Change (95% CI)</th>
<th>Lag of Week 4 % Change (95% CI)</th>
<th>Lag of Week 5 % Change (95% CI)</th>
<th>Cumulative Effects % Change (95% CI)</th>
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<tr>
<td>All-cause Mortality</td>
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<td>1984-1991</td>
<td>1.1 (0.7, 1.5)</td>
<td>0.9 (0.6, 1.3)</td>
<td>0.8 (0.5, 1.1)</td>
<td>1.1 (0.8, 1.4)</td>
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<td>4.7 (3.7, 5.8)</td>
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<td>1992-2007</td>
<td>1.4 (1.1, 1.7)</td>
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<td>1984-1991</td>
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Abbreviations: CI = confidence intervals, COPD = chronic obstructive pulmonary disease, CVD = cardiovascular disease, IHD = ischemic heart disease, MI = myocardial infarction. % Change = estimated mortality percentage change. *Models were adjusted for Lag 0 of maximum temperature, relative humidity and air pressure average over 3 day lag, and day of week. Week 1 corresponds to the average of the temperature lag 1 – lag 7, week 2 to lag 8 – lag 14, week 3 to lag 15 – lag 21, week 4 to lag 22 – lag 28, and week 5 to lag 29 – lag 35. Models included mortality data for ages 18 years and above.
Table B. Estimated mortality percentage change per 1°C decrease in maximum temperature during the cold season in Northern Ireland, 1984-1991, 1992-2007.*

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<td>0.8 (0.0, 1.7)</td>
<td>0.6 (-0.2, 1.5)</td>
<td>0.6 (-0.3, 1.4)</td>
<td>2.4 (-0.2, 4.9)</td>
</tr>
<tr>
<td>IHD</td>
<td>1984-1991 1.6 (0.6, 2.7)</td>
<td>0.2 (-0.8, 1.3)</td>
<td>1.1 (0.2, 2.1)</td>
<td>1.0 (0.0, 2.0)</td>
<td>0.1 (-0.9, 1.1)</td>
<td>1.5 (-1.5, 4.5)</td>
</tr>
<tr>
<td>MI</td>
<td>1984-1991 1.8 (0.7, 3.0)</td>
<td>0.6 (-0.5, 1.7)</td>
<td>1.3 (0.3, 2.3)</td>
<td>0.8 (-0.2, 1.9)</td>
<td>0.2 (-0.9, 1.2)</td>
<td>1.6 (-1.5, 4.7)</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>1984-1991 2.7 (1.4, 4.1)</td>
<td>2.4 (1.1, 3.7)</td>
<td>2.6 (1.4, 3.8)</td>
<td>0.8 (-0.4, 2.0)</td>
<td>0.7 (-0.5, 1.9)</td>
<td>9.2 (5.5, 12.8)</td>
</tr>
<tr>
<td>COPD</td>
<td>1984-1991 5.4 (2.4, 8.4)</td>
<td>3.2 (0.3, 6.2)</td>
<td>1.0 (-1.7, 3.7)</td>
<td>1.3 (-1.4, 4.1)</td>
<td>0.7 (-2.1, 3.4)</td>
<td>11.6 (3.3, 19.8)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1984-1991 1.5 (-0.1, 3.2)</td>
<td>2.2 (0.6, 3.8)</td>
<td>2.8 (1.3, 4.2)</td>
<td>1.0 (-0.5, 2.5)</td>
<td>0.1 (-1.4, 1.6)</td>
<td>7.4 (2.9, 11.8)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1984-1991 1.2 (-0.4, 2.8)</td>
<td>1.5 (0.0, 3.0)</td>
<td>2.2 (0.8, 3.6)</td>
<td>0.8 (-0.6, 2.3)</td>
<td>0.1 (-1.4, 1.6)</td>
<td>5.7 (1.4, 10.1)</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence intervals, COPD = chronic obstructive pulmonary disease, CVD = cardiovascular disease, IHD = ischemic heart disease, MI = myocardial infarction. % Change = Estimated mortality percentage change. *Models were adjusted for Lag 0 of maximum temperature, and relative humidity average over 3 day lag, and day of week. Week 1 corresponds to the average of the temperature lag 1 – lag 7, week 2 to lag 8 – lag 14, week 3 to lag 15 – lag 21, week 4 to lag 22 – lag 28, and week 5 to lag 29 – lag 35. Models included mortality data for ages 18 years and above.