Appendix 1 (as supplied by the authors): Expanded methods and supplementary data

Assessment of the impact of cold and hot temperatures on mortality in Ontario, Canada: population-based study

Hong Chen PhD, 1,2,3 Jun Wang MSc, 1 Qiongsi Li MMath, 1 Abderrahmane Yagouti MSc, 4 Eric Lavigne PhD, 5,6 Richard Foty MSc, 2,7 Richard T Burnett PhD, 8 Paul J Villeneuve PhD, 2,9 Sabit Cakmak PhD, 8 Ray Copes MD^{1,2}

¹ Public Health Ontario, Toronto, ON, Canada

- ² Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada
- ³ Institute for Clinical Evaluative Sciences, Toronto, ON, Canada
- 4 Climate Change and Health Office, Health Canada, Ottawa, ON, Canada
- 5 Air Health Science Division, Health Canada, Ottawa, ON, Canada
- 6 Population Studies Division, Health Canada, Ottawa, ON, Canada
- 7 Sick Kids Hospital, Toronto, ON, Canada
- 8 Department of Health Sciences, Carleton University, Ottawa, ON, Canada
- ⁹ Climate Change and Health Office, Health Canada, Ottawa, ON, Canada

Correspondence:

Hong Chen, PhD Public Health Ontario 480 University Avenue, Suite 300 Toronto, Ontario M5G 1V2 Tel: 647-260-7109 Email: hong.chen@oahpp.ca

Table of Contents

EXPANDED METHODS

Mortality Outcomes

Deceased residents were identified using data linkage to the Ontario Registrar General's Death database using the residents' unique, encrypted health card number. We selected *a priori* a total of eight outcomes including non-accidental deaths and deaths from five cardiovascular causes (any cardiovascular, coronary heart, acute myocardial infarction [AMI], stroke, and heart failure, cardiac arrest and related), diabetes, and any respiratory illness. The *International Classification of Diseases, Ninth Revision*, ICD-9 code and *Tenth Revision*, ICD-10 code for our study outcomes are listed in Table S3.

Hospital, laboratory, and physician services in Ontario are funded by the provincial government through a single-payer universal Medicare system that covers virtually all residents.¹

Humidex and Windchill

From Environment Canada, we collected hourly weather data including air temperature, relative humidity, dew point temperature and wind speed. We then calculated the daily mean, minimum and maximum of air temperature and relative humidity. We also derived daily average and maximum values of windchill for cold season and humidex for warm season.

Humidex is a popular temperature metric in warm season across Canada, which takes into account temperature and humidity. According to Environment Canada, humidex is equal to air temperature when air temperature is equal to or less than 25° C. When air temperature exceeds 25° C, humidex can be derived using the following formula:²

Humidex = air *temperature* $) + (0.5555) * (vapour pressure in hPa(mbar) - 10.0);$ Where $e = 6.11 * \exp^{[(5417.7530*(1/273.16)-(1/dew point))]}$ and $\exp = 2.7182$.

Similarly, wind chill is a temperature metric commonly used for cold season across Canada, which takes into account temperature and wind velocity values. Wind chill can be derived using the following formula: 2

$$
\begin{cases} W = 13.12 + 0.6215 \cdot T_{air} - 11.37 \cdot V_{10m}^{0.16} + 0.3965 \cdot T_{air} \cdot V_{10m}^{0.16}, when T_{air} \le 0 and 0 < wind speed < \frac{5km}{h} \\ W = T_{air} + \frac{-1.59 + 0.1345 \cdot T_{air}}{5} \cdot V_{10m}, when T_{air} \le 0 and 0 < wind speed < \frac{5km}{h} \end{cases}
$$

Where W is wind chill, T_{atr} is air temperature in ^oC, and V_{1cm} is wind speed at 10 metres above ground, in kilometres per hour.

Five Regions in Ontario

We classified 49 census divisions of Ontario into five regions (north, west, east, central east and central west), according to the Ontario health region classification. Table S4 shows census divisions in each region.

Ascertainment of Influenza Activity

To control for potential confounding by influenza, we obtained daily number of physician-office visits for influenza (diagnostic code 487) for each CD using data from the Ontario Health Insurance Plan Database (OHIP). As the diagnostic code 487 may contain patient visits for influenza vaccination, we excluded the visits with an OHIP fee code that is typically associated with vaccination (G538, G539, G590, G591, Q003, and Q130).

Further Details of Statistical Analysis

Our analysis was carried out in two stages. In the first stage, we modeled the relationship between daily mortality (non-accidental and cause-specific) and daily mean temperature in each census division using a conditional logistic regression model, adjusting for daily mean relative humidity, NO_2 , O_3 , influenza visits, and holidays. Due to considerable missing data for $PM_{2.5}$, we did not include it in the main model, but considered it in a sensitivity analysis. We fitted air pollutants using lag 0-2 (average of the concurrent day and two previous days) based on evidence from published Canadian studies, but we also conducted sensitivity analyses by fitting air pollution using lag structures from 0 to 6 days (Table S5). We chose daily mean air temperature as our primary exposure because it represents the exposure throughout the entire day and night, and it has been positively linked to mortality at diverse locations including several Canadian cities.³ Cold and heat were separately analyzed.

For each census division, we verified the assumption of linearity for the relationship between temperature and mortality by using restricted cubic spline functions with two, three, and four degrees of freedom (df), using SAS macro '%LGTPHCURV9'.⁴ We examined plots of temperature-response curves, and conducted likelihood ratio test to determine whether the nonlinear model offered a significant improvement over the linear model. Cold and hot effects were separately analyzed.

As a second test of sensitivity of results to the use of a non-linear model versus linear model, we implemented a distributed lag non-linear model.^{5, 6} Details of the distributed lag non-linear model have been described elsewhere.^{5, 6} Briefly, a distributed lag non-linear model allows for

representing the non-linear relationship of temperature with mortality and the delayed effects of temperature simultaneously. To do this, a bi-dimensional space of functions is used to describe the shape of the relationship along both the space of the predictor and the lag dimension of its occurrence. The relative risk of the outcome (Y_i) of daily death counts is estimated using a generalized linear model, with a quasi-Poisson link function to account for over-dispersion. The model formula is described as follows:

$$
\log[E(Y_i)] = \alpha + \sum_{j=1}^p g_j(x_{ij}) + m(t_i)
$$

Where T_i represents temperature exposure, X_i represents covariates, and $g(\cdot)$ and $m(\cdot)$ represent functions.

For each census division, we compared the estimated percentage increase in daily mortality for each 5^oC increase in temperature in warm season as estimated by the linear model to the measurement from the distributed lag non-linear model for a 5° C change in temperature centered at the census division's $75th$ percentile of temperature in warm season during study period.

Appendix to: Chen H, Wang J, Li Q, et al. Assessment of the effect of cold and hot temperatures on mortality in Ontario, Canada: a population-based study. *CMAJ Open* 2016. Similar to previous studies,⁷ we selected cubic b-splines to model temperature effect and natural cubic splines for lag effect. To be consistent with our main analysis, we considered a maximum lag period of 7 days. We evaluated a range of df for temperature and lag, and we found that the use of 7 df for temperature and 2 df for lag resulted in the best model fit according to Akaike information criterion (AIC) and also yielded plausible shape of temperature-response curves based on the literature.^{6, 7} As a result, we chose 7 df for temperature and 2 df for lag. To control for time trend, we used natural cubic functions for day of week and day of the year. In addition, we adjusted for humidity, O_3 , NO_2 , influenza activity, and statutory holidays.

DOI:10.9778/cmajo.20150111. Copyright © 2016 8872147 Canada Inc. or its licensors.

Because of the relatively small number of deaths in most census divisions, we applied the sensitivity analysis with a distributed lag non-linear model to the 10 largest census divisions in Ontario. These include Ottawa, York, Toronto, Peel, Hamilton, Niagara, Waterloo, Essex, Middlesex, and Simcoe.

In the first analysis, we found little evidence that modeling temperature using restricted cubic splines would improve model fit for cold and hot temperatures. In 26 of the 27 census divisions in Ontario, using restricted cubic splines did not provide significantly better fit relative to the models that assumed linearity for cold and hot temperatures (*p*-value of likelihood ratio test ranged from 0.06 to 0.93, depending on census division and season), with the exception of a nonlinear model of heat effect in Toronto (*p*-value = 0.03).

Because of no evidence of departure from linearity for the cold effects in any census division, we focused the second analysis on heat effects only. Table S6 shows the effect estimates of hot temperature from the linear model and estimates from the distributed non-linear model for a 5° C change in daily mean temperature centered at the census division's 75th percentile of temperatures in warm season. Across the 10 largest census divisions, the effect estimates from linear models were similar to those derived from non-linear models (Table S6).

Overall, there is little evidence of non-linearity for the relationship of temperatures and mortality in the warm and cold season, respectively. In addition, effect estimates did not alter materially when using a non-linear model. As a result, we used the linear models to examine the relationship between cold and hot temperatures and mortality in remaining analyses. We report adjusted odds ratio and associated 95% confidence interval (95% CI) for every 5° C change in

temperature, which were scaled to represent a mean percent increase in daily mortality per 5°C change (referred to as MPC₅), using the following formula: (odds ratio – 1) \times 100%.

To identify potentially vulnerable subpopulations, we conducted stratified analyses for each census division by age, sex, place of death, history of AMI, heart failure, COPD, hypertension, and diabetes, as well as recent hospitalization for AMI, heart failure, stroke, diabetes, COPD, and respiratory illness. The effect estimates were then pooled across Ontario.⁸ To avoid losing substantial power, we restricted the analyses to cardiovascular- and respiratory-related deaths, respectively. We also investigated potential effect modification by different time periods (1996- 2000, 2001-2005, and 2006-2010) and regions (north, west, east, central east, and central west).

All analyses were conducted using SAS version 9.3 and R statistical software version 3.0.3.

Further Details of Estimated Burden of Mortality Attributable to Temperature Changes

To quantify the burden of death attributed to short-term exposure to cold and hot temperatures, we derived attributable fraction which was applied to the observed mean daily non-accidental deaths for each census division during the period 1996 to 2010 using the formula as follows:^{9, 10}

$$
AF_i = (OR_i - 1)/OR_i \tag{1}
$$

Estimated excess deaths = $\sum (AF_i * \text{mean daily death counts } i)$ (2)

Where AF_i is the attributable fraction (*i.e.*, burden attributable to risk factor such as 5° C decrease in daily mean temperature in cold season) for census division i , OR_i is the adjusted odds ratio corresponding to each 5^oC change in daily mean temperature for census division *i*.

Supplemental Table S1. Distribution of selected air temperature variables in Ontario, by census division, 1996-2010

A. Cold Season

* Standard deviation

B. Warm Season

* Standard deviation

Supplemental Table S2. Correlation between different metrics of temperature and air pollutants

A. Cold season

B. Warm season

Supplemental Table S3. ICD-9 and ICD-10 codes for study outcomes

Supplemental Table S4. Census divisions in five regions in Ontario

Supplemental Table S5. Sensitivity analyses for the association of non-accidental mortality with every 5°C change in cold and hot temperatures across 27 selected census divisions in Ontario, 1996-2010

*** Cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0

Supplemental Table S6. Estimated percentage increase in daily non-accidental mortality for each 5^oC increase in hot temperatures using the linear model and the corresponding estimates from the non-linear model for a 5° C change in temperature centered at the census division's 75^{th} percentile of temperature in warm season, by the 10 largest census divisions in Ontario

Figure Legends

Supplemental Figure S1. Map of 27 selected census divisions, by regions in Ontario

Supplemental Figure S2. Pooled mean percent changes in daily mortality, by cause of death, by lag, and season, across 27 selected census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0).

Supplemental Figure S3 (A). Mean percent changes in daily cardiovascular-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (B). Mean percent changes in daily respiratory-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (C). Mean percent changes in daily coronary heart disease-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (D). Mean percent changes in daily acute myocardial infarctionrelated deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (E). Mean percent changes in daily heart failure-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (F). Mean percent changes in daily stroke-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Supplemental Figure S3 (G). Mean percent changes in daily diabetes-related deaths, by season and census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S1. Map of 27 selected census divisions, by regions in Ontario

Figure S2. Pooled mean percent changes in daily mortality, by cause of death, by lag, and season, across 27 selected census divisions in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0).

Figure S3 (A). Mean percent changes in daily cardiovascular-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S3 (B). Mean percent changes in daily respiratory-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S3 (C). Mean percent changes in daily coronary heart disease-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S3 (D). Mean percent changes in daily acute myocardial infarction-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0- 6; warm season: daily mean temperature at lag 0)

Figure S3 (E). Mean percent changes in daily heart failure-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S3 (F). Mean percent changes in daily stroke-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Figure S3 (G). Mean percent changes in daily diabetes-related deaths, by season and census division in Ontario, 1996-2010 (cold season: daily mean temperature at lag 0-6; warm season: daily mean temperature at lag 0)

Reference

- 1. Chen H, Burnett RT, Kwong JC et al. Risk of Incident Diabetes in Relation to Long-term Exposure to Fine Particulate Matter in Ontario, Canada. *Environ Health Perspect* 2013;121:804-10.
- 2. Climate Services. Environment Canada. http://climate.weather.gc.ca/data_index_e.html. [Accessed February 23, 2015].
- 3. Gasparrini A, Guo Y, Hashizume M et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 2015 DOI: http://dx.doi.org/10.1016/S0140-6736(14)62114-0
- 4. SAS LGTPHCURV9 Macro. Boston, MA: Harvard School of Public Health. http://www.hsph.harvard.edu/donna-spiegelman/software/lgtphcurv9/ [Accessed June 30, 2015]
- 5. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med* 2010;29:2224-34.
- 6. Guo Y, Gasparrini A, Armstrong B et al. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. *Epidemiology* 2014;25:781-9.
- 7. Goldberg MS, Gasparrini A, Armstrong B, Valois MF. The short-term influence of temperature on daily mortality in the temperate climate of Montreal, Canada. *Environ Res* 2011;111:853-60.
- 8. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177- 88.
- 9. Anderson GB, Dominici F, Wang Y, et al. Heat-related emergency hospitalizations for respiratory diseases in the Medicare population. *Am J Respir Crit Care Med* 2013;187:1098-103.
- 10. Ostro B. Outdoor air pollution: Assessing the environmental burden of disease at national and local levels. Geneva, World Health Organization, 2004 (*WHO Environmental Burden of Disease Series, No. 5*).