ORIGINAL ARTICLE

Manon Fleury · Dominique F. Charron · John D. Holt · O. Brian Allen · Abdel R. Maarouf

A time series analysis of the relationship of ambient temperature and common bacterial enteric infections in two Canadian provinces

Received: 29 July 2005 / Revised: 24 January 2006 / Accepted: 7 February 2006 / Published online: 31 March 2006 © ISB 2006

Abstract The incidence of enteric infections in the Canadian population varies seasonally, and may be expected to be change in response to global climate changes. To better understand any potential impact of warmer temperature on enteric infections in Canada, we investigated the relationship between ambient temperature and weekly reports of confirmed cases of three pathogens in Canada: Salmonella, pathogenic Escherichia coli and Campylobacter, between 1992 and 2000 in two Canadian provinces. We used generalized linear models (GLMs) and generalized additive models (GAMs) to estimate the effect of seasonal adjustments on the estimated models. We found a strong non-linear association between ambient temperature and the occurrence of all three enteric pathogens in Alberta, Canada, and of Campylobacter in Newfoundland-Labrador. Threshold models were used to quantify the relationship of disease and temperature with thresholds chosen from 0 to -10°C depending on the pathogen modeled. For Alberta, the log relative risk of Salmonella weekly case counts increased by 1.2%, Campylobacter weekly case counts increased by 2.2%, and E. coli weekly case counts increased by 6.0% for every degree increase in weekly mean temperature. For Newfoundland-Labrador the log relative risk increased by 4.5% for Campylobacter for every degree increase in weekly mean temperature.

M. Fleury () · D. F. Charron
Foodborne, Waterborne and Zoonotic Infections Division,
Public Health Agency of Canada,
160 Research Lane, Unit 206,
Guelph, Ontario, N1G 5B2, Canada
e-mail: Manon D Fleury@phac-aspc.gc.ca

Tel.: +1-519-8262185 Fax: +1-519-8262244

J. D. Holt · O. B. Allen Department of Mathematics and Statistics, University of Guelph, Guelph, Ontario, Canada

A. R. Maarouf Meterological Service of Canada, Environment Canada, Toronto, Ontario, Canada **Keywords** Foodborne disease · Ambient temperature · Time series analysis · Climate change · Canada

Introduction

Foodborne illnesses are defined as diseases, usually either infectious or toxic in nature, that are acquired through the ingestion of food. Every person is at risk of foodborne diseases. In Canada, the most commonly reported bacterial enteric pathogens are Campylobacter, Salmonella and Escherichia coli. These pathogens are generally foodborne in Canada (Canadian Integrated Surveillance Report 2003). Advances in food protection have not resolved all public health concerns about foodborne infections, even in developed countries. While most foodborne diseases occur sporadically and are often not reported, foodborne disease outbreaks can take on massive magnitudes. For example, in 1998, an outbreak of Salmonella due to contaminated cheese occurred in Canada, affecting approximately 800 people (Canadian Medical Association Journal 2003).

A number of studies have shown an effect of ambient temperature on the occurrence of certain enteric diseases. A study exploring growth rates of salmonellosis under varying temperatures found that the growth rate increased as the temperature increased (Mackey and Kerridge 1988). It has been noted that enteric diseases in temperate latitudes have a seasonal pattern, with the highest incidence of illness during the summer months (Isaacs et al. 1998). A study of foodborne illness in the United Kingdom found a relationship between the incidence of disease and the temperature in the month preceding the illness (Bentham and Langford 2001). It is believed that the survival and growth of certain enteric pathogens are, within limits, positively correlated with ambient temperature (Hall et al. 2002). In a study of five cities in Australia, D'Souza et al. (2004) found a significant positive association between mean temperature in the previous month and the number of notifications of cases of Salmonella in the current month. A multinational European study presented results of a time

series of weekly notifications of *Campylobacter* and average ambient temperature (Kovats et al. 2004). These studies imply that factors related only to behaviour and dietary choices are unlikely to explain all of the seasonal summer increase in certain bacterial gastroenteritis noted in temperate latitudes. Warmer ambient temperature in combination with differences in eating behaviour may therefore contribute to the foodborne portion of the increased incidence of enteric diseases.

The objective of this study was to investigate the relationship between weekly occurrence of enteric bacterial disease notifications and short-term variations in ambient temperature between 1992 and 2000 in two Canadian provinces, Alberta and Newfoundland-Labrador, while adjusting for possible confounding influence of seasonal effects and long-term trends. An understanding of such short-term relationships could be useful in further studies of the potential impacts of climate change.

Materials and methods

All Canadian provinces were approached to participate. Due to time and resource constraints, as well as data availability, only data from Alberta (population in 1996 ~2,696,826) and Newfoundland-Labrador (population in 1996 ~551,792, Statistics Canada 2002) were included. These provinces have very different climates. Alberta, in continental western Canada, is characterized by mainly dry and warm summer weather and cold winters while Newfoundland-Labrador, in coastal eastern Canada, experiences moderate to cool wet weather in summer and

Fig. 1 Map of Canada highlighting the two study provinces, Alberta and Newfoundland-Labrador

cold winter temperatures that are moderated by a coastal effect (Environment Canada 2002).

Weekly laboratory confirmed cases of Salmonella, Campylobacter and entero-pathogenic E. coli were collected from the Notifiable Disease Registries (NDR) for Alberta and Newfoundland-Labrador. Maximum, minimum and average weekly temperatures, recorded at 92 geographically representative weather stations in Alberta and 59 stations in Newfoundland-Labrador, were obtained from the Meteorological Service of Canada, Environment Canada. The study period was from January 1992 to December 2000, and included the most up-to-date data on bacterial enteric disease infections in the two provinces. The number of NDR observations from Alberta consisted of 6,282 cases of Salmonella, 1,743 cases of Campylobacter and 9,664 cases of E. coli, and from Newfoundland-Labrador, 986 cases of Salmonella and 1,188 cases of Campylobacter.

Cases of disease and meteorological data were geographically identified by health region (17 regions in Alberta and 6 regions in Newfoundland-Labrador). The scarcity of data in some health regions was addressed by grouping health regions according to climate zones: seven groups for Alberta (two were from two large urban centres: Edmonton and Calgary) and two for Newfoundland-Labrador (Fig. 1).

Generalized linear models (GLM) and generalized additive models (GAM), assuming a log link and Poisson errors, were used to accommodate the non-normality, heteroscedasticity, and non-linearity typical of count data. Because of controversy in the air pollution literature, which has raised issues with GAM (Dominici et al. 2002), we have included both GAM and GLM in this analysis. The B-



spline and loess smoothers were included in the model to control for any confounding effect of season, and to ward against any masking short-term effects of temperature on enteric disease, choosing degrees of freedom (*df*) and spans that minimize Akaike's information criterion (AIC) and the sum of the absolute partial autocorrelations (Hastie and Tibshirani 1990). Generalized cross-validation and Dominici's (Dominici et al. 2002) sensitivity parameter were used as additional criteria for selection of the loess span. We chose a span of 0.025 (12 weeks) for the loess smoother and an average *df* of 73 (corresponding to 6.5 weeks per *df*) for the B-spline. In addition to the B-spline, a categorical variable (season) provided additional control of seasonal confounding in the GLM model.

To explore the shape of the relationship between temperature and disease case counts, after accounting for the potential confounding effects of seasonal and holiday variation, temperature was modelled using a loess smoother with a smoothing window of 15°C for the GAM model and a B-spline with a smoothing window of 15°C for the GLM model. Average weekly temperature lagged by 0–6 weeks prior to the incidence of weekly disease case counts was modeled separately in the model.

Enteric disease counts are typically highly correlated from week to week. This may result from the existence of local contagion, seasonal effects, or other unmeasured effects. Therefore, transitional regression models, with lagged outcome variables and residuals from prior days included as covariates, were included in the models to see if serial-correlation appeared in the partial autocorrelation plots (Brumback et al. 2000). All analyses were conducted using S-Plus 2000 (Mathsoft 1999).

A delayed effect of temperature on foodborne illness (Bentham and Langford 1995) was addressed by lagging the mean weekly temperature by between 0 and 6 weeks. Two variables were incorporated variously into the regression model in order to model temporal trends of enteric illness: an index variable labelled "Week," identified weeks beginning 1 January 1992 to 31 December 2000; a second categorical variable, "Season," classified data by winter (December, January and February), spring (March, April and May), summer (June, July and August) and fall (September, October and November). Prior research has found that major holidays affect the reporting of enteric diseases in Canada (Aramini et al. 2000). Hence a categorical variable was included to allow for differing effects of Canadian statutory holidays. Climate zone health region groups were incorporated as a categorical variable to control for variation in population size, and other characteristics associated with each health region and regional climate.

Although it would have been preferable to control for records of cases of disease linked to known outbreaks, such information on outbreaks was available only from 1998 to 2000. Exclusion of these records would artificially inflate case counts of illness prior to 1998. In the analysis of the Salmonella case counts in Alberta, a test for residual outliers identified three influential points. These were

down-weighted in the model since these inflated weekly counts were clearly attributable to outbreaks.

Since the smoothed models suggested a piecewise linear effect of temperature on log mean case counts and because the biology of enteric disease suggests a meaningful change in the behaviour of pathogens at certain temperatures, threshold models were also considered. These allowed for no effect of temperature up to a certain temperature and a linear effect above this point (Ulm and Salanti 2003). Exploratory modeling and deviance tests of temperature effects for each pathogen suggested one or two cut-off points. Likelihood (deviance)-based confidence intervals were then constructed for these apparent thresholds. With these in hand, cut-off points were incorporated into the models for each of the pathogens in each of the provinces.

For all models, the selection methods included comparing nested models using the likelihood ratio test (deviance test) as well as the AIC. The final log-linear GAM and log-linear GLM were:

GAM

log(Counts)

- = loess(Temperature(lag 0 6 weeks), span
- = 15 degrees Celsius) + factor(Holiday)
 - + Lagged Count + factor(Health Region Group)
 - + loess(Week, span = 12 weeks)

GLM

```
log(Counts) = bs(Temperature(lag 0 - 6 weeks), df
= 15 degrees Celsius) + factor(Holiday)
+ Lagged Count + factor(Health Region Group)
+ bs(Week, df = 6.5 weeks) + factor(Season)
```

Results

Figures 2 and 3 show plots of weekly incidence of infection, from 1992 to 2000, for pathogens *Salmonella*, *Campylobacter* and *E. coli* in Alberta, and *Salmonella*, and *Campylobacter* in Newfoundland-Labrador, respectively. Peaks were evident in early summer and the large spikes that appear outside the regular seasonal trend may correspond to unidentified outbreaks of disease. Some of the large spikes were down-weighted by averaging the days before and after this value, because they masked the seasonal pattern. Figures 4 and 5 show seasonal patterns averaged across the 9 years of data. Similar seasonal patterns were seen for the three pathogens and for temperature.

Average weekly temperatures from 0 to 6 weeks prior to the incidence of weekly disease were found to be significant for all pathogens in each location. The temperature 1 week prior to illness was selected as the best fitting lag, according to the AIC. The estimates, relative risks and confidence

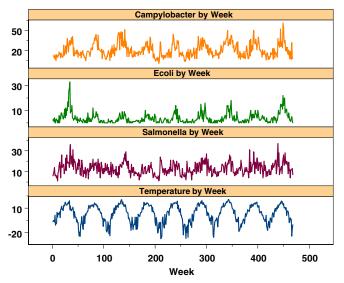


Fig. 2 Weekly temperatures (°C), and case counts of *Campylobacter*, *Escherichia coli* and *Salmonella* from 1992 to 2000, in Alberta. Note that the extreme case counts were down-weighted by taking the average of the day(s) before and after

limits for each of the lags for threshold models for *Salmonella*, *Campylobacter* and *E. coli* in Alberta and *Campylobacter* in Newfoundland-Labrador are presented in Table 1. All temperature estimates suggest a relative risk increase for lags zero to six in each of the models.

Figure 6 shows the log-relative risk plots for the association between weekly disease notifications versus weekly temperature, lagged 1 week, for both provinces controlling for holidays, weekday, season, health region and autocorrelation of weekly case counts. All explanatory variables were significant in the model. The plots suggest a hockey-stick shape with little or no effect of temperature for all pathogens below -10°C to 0°C depending on the pathogen. There is no statistically significant association

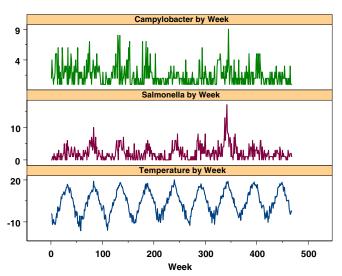


Fig. 3 Weekly temperatures (°C), and case counts of *Campylobacter* and *Salmonella* from 1992 to 2000, in Newfoundland-Labrador. Note that the extreme case counts were down-weighted by taking the average of the day(s) before and after

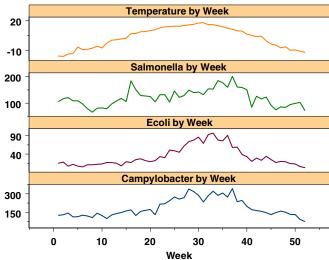


Fig. 4 Average weekly temperature (°C) and case counts for *Campylobacter*, *E. coli* and *Salmonella* from 1992 to 2000, for Alberta

between temperature and the risk of weekly case counts of *Salmonella* in Newfoundland-Labrador for any temperature lags.

In order to estimate the slope of the roughly linear portions of the temperature-disease relationships in each of the models (Fig. 6), threshold models with fixed cut-off points were applied to the data. The cut-off points were selected and modeled for a range of temperatures between -10° C and 0° C. These assumed no temperature effect up to the threshold temperature and a linear temperature effect beyond this threshold. An advantage of these models is that the slopes of the linear portions are easily interpreted as the log relative risk of disease per degree temperature change. Not surprisingly, AIC values (Table 2) indicate a poorer fit

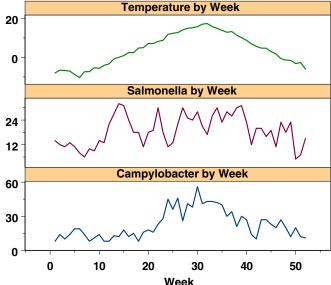


Fig. 5 Average weekly temperature (°C) and case counts for *Campylobacter*, and *Salmonella* from 1992 to 2000, for Newfoundland-Labrador

Table 1 Estimates and relative risks of temperature 0–6 weeks prior to illness for *Salmonella*, *Campylobacter* and *Escherichia coli* in Alberta and *Campylobacter* in Newfoundland-Labrador

		Lag	Relative risk	95% Confidence intervals
Alberta	Salmonella	0	1.010	(1.007,1.013)
		1	1.012	(1.009, 1.015)
		2	1.016	(1.013, 1.020)
		3	1.013	(1.010, 1.016)
		4	1.011	(1.008, 1.014)
		5	1.011	(1.008, 1.014)
		6	1.009	(1.006, 1.012)
	Campylobacter	0	1.016	(1.014, 1.019)
		1	1.022	(1.019, 1.024)
		2	1.018	(1.016, 1.021)
		3	1.025	(1.022, 1.027)
		4	1.017	(1.014, 1.020)
		5	1.017	(1.014, 1.020)
		6	1.014	(1.012, 1.017)
	E. coli	0	1.006	(0.997, 1.016)
		1	1.060	(1.050, 1.069)
		2	1.039	(1.029, 1.048)
		3	1.026	(1.017, 1.036)
		4	1.026	(1.017, 1.036)
		5	1.041	(1.032, 1.051)
		6	1.039	(1.029, 1.049)
Newfoundland-	Campylobacter	0	1.060	(1.047, 1.073)
Labrador		1	1.045	(1.033, 1.058)
		2	1.054	(1.041, 1.067)
		3	1.029	(1.016, 1.042)
		4	1.070	(1.057, 1.084)
		5	1.028	(1.015, 1.041)
		6	1.037	(1.024, 1.050)

for threshold models when compared to loess or B-spline models. However, imbedding the threshold model in a B-spline hierarchy suggests that, for *E. coli* in Alberta, the B-spline is not significantly better (*P*=0.06) than the threshold model

Threshold models suggest that for every degree increase in weekly temperature above the threshold, the log relative risk of *Salmonella* (threshold –10°C) in Alberta increased by 1.2%, *Campylobacter* by 2.2% (threshold –10°C), and *E. coli* by 6.0% (threshold 0°C). A threshold for *Campylobacter* in Newfoundland-Labrador was set to 0°C and the log relative risk increased by 4.5% per degree increase in weekly temperature.

Discussion

We found that weekly counts of enteric bacterial disease cases generally increased with weekly temperature in Alberta and Newfoundland-Labrador after controlling for season and long-term trends. Other variables controlled in the model were holidays and health region group. An autoregressive term was included to control for residual autocorrelation in the model, which is typical of time series data. Our results are consistent with research carried out by Bentham and Langford (1995, 2001), D'Souza et al. (2004) and Kovats et al. (2004).

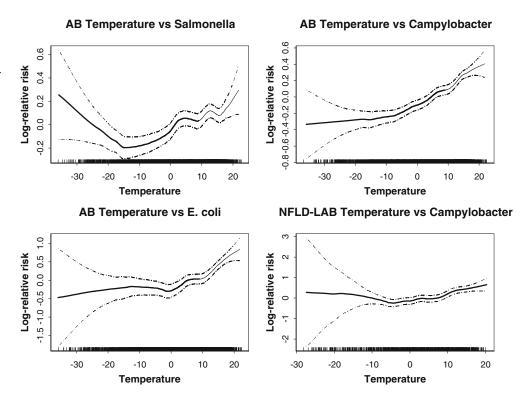
Bentham and Langford (2001) modeled lagged temperature and enteric bacterial notifications and found a strong association of foodborne illness with temperatures 2-5 weeks earlier, which could be due to factors occurring earlier in the food production system. We found an association between temperature and disease when looking at lags from 0-6 weeks prior to disease. All these lags had strong predictive effects on the incidence of illness for Alberta and Newfoundland-Labrador. This suggests that temperature may affect contamination at any point along the food chain, including the farm, the processing plant, or the home (Hall et al. 2002), and thus have an impact on the risk of disease, and may also indicate a need for more precise modelling of any lag effects of temperature on disease risk. To verify the models for any spurious significance of lag effects, temperature data lagged after disease events were modelled, and found not to be significantly associated with outcome, unlike temperature prior to disease events.

Threshold models were helpful in estimating the risk of enteric illness associated with temperature above a temperature threshold. These thresholds were generally compatible with nonparametric models, which suggested a linear relationship after a certain threshold. The thresholds were estimated for each of the pathogens and suggested a relative risk increase with temperature above the threshold for all modeled pathogens in both provinces.

The association between temperature and risk of salmonellosis in Newfoundland-Labrador differed from the results of the other pathogens in our study. There are several possible explanations for this difference in results. It may be that the risk of salmonellosis may truly not be associated with increased temperature in Newfoundland-Labrador. However, international evidence for an effect of temperature on Salmonella, and the results from Campylobacter in Newfoundland-Labrador suggest otherwise. We feel that there may be some unmeasured causes of Salmonella in Newfoundland-Labrador that are confounding the effect of temperature. Such unmeasured factors may include cases linked to point-source outbreaks, cases linked to travel outside of Newfoundland-Labrador, and cases linked to food behaviours in rural and northern parts of the province, where fish is consumed more than other meats therefore reducing the risk of exposure to Salmonella. Finally, the analysis has been hampered by a lack of power, given the smaller number of cases of this disease in the province (n=986).

Despite the fact that outbreak data could not consistently be differentiated from other sporadic cases, residual confounding and bias did not appear to be an issue. We successfully identified only three influential points in Alberta for *Salmonella* points using a residual test for

Fig. 6 Smoothed plots for the log-relative risk of *Salmonella*, *Campylobacter* and *E.coli* for Alberta (*AB*) and *Campylobacter* for Newfoundland-Labrador (*NFLD-LAB*) versus temperature lagged 1 week



outliers and down-weighted these to a value of one weekly case.

Our approach proved that the loess smoother in GAM was sufficient to control for seasonal variation in the model whereas GLM needed an extra seasonal parameter, "Season." This could be due to parametric splines used in the model not allowing for adequate control of seasonal confounding.

Some caution is required when applying GAM and GLM to enteric disease data. Specifically, Ramsay et al. (2003) note that the convergence criteria of the GAM procedure must be carefully monitored when using models with at least two loess smoothers. In this study, the default convergence parameters were adequate. Another issue is that the asymptotic standard errors are approximate; Dominici et al. (2002) provide methodology and software for determining exact asymptotic standard errors. Since B-splines are standard regression variables, the corresponding prediction errors are well understood. One difficulty is the determination of the spacing and number of knots. Current research (Woods 2004) suggests that the use of penalized regression splines may obviate these difficulties, but this research into the selection of corresponding smoothing

parameters is still at an early stage. B-splines in GLM also have disadvantages, including less flexibility when estimating smooth curves for temperature and week, and non-straightforward procedures for the selection of the smoothing parameters and their knots.

In summary, consistent with previous work from the United Kingdom and Australia, warmer ambient temperature in Canada is associated with an increase in the risk of bacterial enteric disease after controlling for seasonal and long-term trends. It is known that many pathogens in the environment are sensitive to ambient temperature. Given global climate change and projections for warmer summers, an increase in cases of foodborne illness may be expected. Problems may arise from production to consumption of food during warmer periods. Although some trends in enteric disease infections are decreasing, public health authorities may want to take action and focus public education programs and other polices to particularly vulnerable groups and to relevant occupational groups in the short term, and may consider new policies in anticipation of additional cases of foodborne disease due to climate change.

Table 2 Akaike's information criterion (AIC) values for the non-nested models with a B-spline or loess versus the model with a threshold parameter. *GLM* Generalized linear model, *GAM* Generalized additive model

		GLM		GAM	
Province	Pathogen	B-spline	Threshold	Loess	Threshold
Alberta	Salmonella	4,137.8	4,143.7	4,119.9	4,363.6
Alberta	Campylobacter	4,440.5	4,445.2	4,428.0	4,679.4
Alberta	E. coli	2,878.7	2,882.8	2,856.3	3,062.3
Newfoundland-Labrador	Salmonella	789.8	789.1	802.7	911.7

Acknowledgements We thank Alberta Public Health and Newfoundland and Labrador Centre for Health Information for the use of their notifiable disease data for this study. We also thank the cCASHh study for their support and collaboration and James R. Ferguson, a geographical consultant, for preparing the map for this article.

References

- Aramini J, McLean M, Wilson J et al (2000) Drinking water quality and health care utilization for gastrointestinal illness in greater Vancouver. Health Canada: Population and Public Health Branch. October
- Bentham G, Langford IH (1995) Climate change and the incidence of food poisoning in England and Wales. Int J Biometeorol 39:81–86
- Bentham G, Langford IH (2001) Environmental temperatures and the incidence of food poisoning in England and Wales. Int J Biometeorol 45:22–26
- Brumback BA, Ryan LM, Schwartz, J, Neas L, Stark P, Burge H (2000) Transitional regression models, with application to environmental time series. J Am Stat Assoc 95:16–27
- Canadian Integrated Surveillance Report (2003) Salmonella, Campylobacter, pathogenic E. coli and Shigella, from 1996–1999. Canadian Communicable Disease Report 2951
- Canadian Medical Association Journal (2003) Food irradiation: Let's do it (editorial). Can Med Assoc J 162:5
- Dominici F, McDermott A, Zeger SL, Samet JM (2002) On the use of generalized additive models in time-series studies of air pollution and health. Am J Epidemiol 156:193–203
- D'Souza RM, Becker NG, Hall G, Moodie KBA (2004) Does ambient temperature affect foodborne disease? Epidemiology 15:86–92

- Environment Canada (2002) "The Climate of Newfoundland." The Green Lane (Dartmouth, Nova Scotia) http://www.atl.ec.gc.ca/climate/nfld.html)
- Hall GV, D'Souza RM, Kirk MD (2002) Foodborne disease in the new millennium: out of the frying pan and into the fire? Med J Aust 177:614–618
- Hastie TJ, Tibshirani R (1990) Generalized additive models. Chapman and Hall, London
- Isaacs S, Leber C, Michel P (1998) The distribution of foodborne disease by risk setting—Ontario. Can Commun Dis Rep 24:61-64
- Kovats S, Edwards S, Hajat S, Armstrong BG, Ebi KL, Menne B (2004) The effect of temperature on food poisoning: a time-series analysis of salmonellosis in ten European countries. Epidemiol Infect 132:443–453
- Mackey BM, Kerridge AL (1988) The effect of incubation temperature and inoculum size on growth of salmonellae in minced beef. Int J Food Microbiol 6:57–65
- Mathsoft (1999) S-PLUS 2000 guide to statistics, vol 1. Data Analysis Products Division, Mathsoft, Seattle, WA
- Ramsay TO, Burnett R, Krewski D (2003) Exploring bias in a generalized additive model for spatial air pollution data. Environ Health Perspect 110:1283–1288
- Statistics Canada (2002) Population and dwelling counts, for Canada, Provinces and Territories, 2001 and 1996 censuses. Statistical Reference Centre, Ottawa, ON, http://www12.statcan.ca/english/census01/products/standard/popdwell/Table-PR.cfm)
- Ulm K, Salanti G (2003) Estimation of the general threshold limit values for dust. Int Arch Occup Environ Health 76:233–240
- Woods SN (2004) Stable and efficient multiple smoothing parameter estimation for generalized additive models. J Am Stat Assoc 99:673–686