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Cardiac Problems and Concentration of Ambient Nitrogen Dioxide

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Abstract

Background: Environmental epidemiology studies report an association of cardiac health conditions with concentration of ambient air pollutants. As high level of air pollution increases the health risk.

Aim: To estimate the association in the form of the parametric concentration-response shapes.

Methods: A case-crossover technique is applied to realise the statistical models. The concentration of air pollution is transformed and submitted into the model. The parameters of the concentration-response function are estimated to satisfy the goodness of fit criterion. Emergency department (ED) visits for cardiac health problems are used as health outcomes. Nitrogen dioxide is used as ambient air pollution exposure.

Results: Positive statistically significant associations were obtained between the numbers of ED visits and the concentration of nitrogen dioxide lagged by 0, 1, 2, and 3 days. Odds ratios are growing with increased concentration levels and are between 1.03 and 1.10.

Conclusion: A concentration-response function allows summarizing the associations between cardiac problems and ambient nitrogen dioxide.

Keywords: Air pollution; Cardiac condition; Case-crossover; Concentration; Nitrogen dioxide

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Introduction

In this work, a new approach is described to represent the associations between the exposure to ambient air pollution and health conditions. Air pollution health effects are usually analyzed as a long-term or short-term exposure study. Here, we consider short-term exposure to ambient nitrogen dioxide (NO_2). Cardiac related health problems are used as health outcomes. In this presentation, we estimate the association between daily concentration of nitrogen dioxide and these health conditions.

Our goal is to obtain the association as an algebraic function that represents the concentration-response shape. The study is conducted for the concentrations of nitrogen dioxide lagged from 0 to 4 days.

We assume that for each used lag the concentration-response functions may have different shapes. These shapes are controlled and fully determined by the estimated parameters. The models used allow estimating an optimal set of such parameters. The criteria applied provide a measure of goodness of fit for the constructed models.

The results on the association may be reported as the concentration-response function for each individually considered lag. The next step further is to execute a sort of meta-analysis using the created algebraic functions. In this work we estimate a global concentration-response function which summarizes the results. As a final result,a single concentration-response function is constructed based on a series of such functions generated by the lags considered.

Methods

Here we illustrate the proposed approach using emergency department (ED) visit data. The health problems related to this study were identified by applying the International Classification of Diseases 9th Revision (ICD-9) codes. The visits were coded according to the discharge diagnosis using ICD-9 codes by medical records staff. The study was conducted using the data for the period from April 1992 to March 2002 (3,652 days) in Edmonton, Canada [1]. The accessed health database contains almost 3 million records of ED visits with various information, including date and time of visits, ICD-9 codes for each visit, age and sex of individuals.

In the study we used health outcomes related to cardiac conditions identified by the following ICD-9 codes: angina/myocardial infarction (ICD-9:410-414); dysrhythmia/conduction disturbance (ICD-9:426, 427), and heart failure (ICD-9:428). For illustrative purposes, we considered them all together as one common cardiac health problem. We used the daily concentration average of nitrogen dioxide as ambient air pollution exposure [1]. The estimation of the daily concentration levels of ambient nitrogen dioxide is based on measurements from 3 monitor stations in Edmonton.

Here we consider the following model:

log(RR)=Control(z)+Covariates

where z is the concentration of air pollutant and RR is the relative risk. Control is a function of z, and Covariates are usually weather variables and/or others. As a basis of the statistical method we are use a time-stratified case-crossover (CC) technique [2,3]. In the constructed models Covariates are temperature and relative humidity and are represented in the form of natural splines with three degrees of freedom.

The function Control(z) is constructed as a product of two functions, f(z) and LWF, where f(z) is the transformation function (here we used three transformation functions of the form:

f(z)=z, log(z) and sqrt(z)).

LWF is a logistic weighing function. This function has the following form:

LWF(z)=1/(1+exp{(mu-z)/(r*tau)})

where mu and tau are the parameters and r is the concentration range [4,5]. In the standard approach of realizing the CC method, the function Control(z)=z=concentration (here z=NO_2). In the proposed technique we transform the concentration z, say by log(z) or just z, or other functions, and we use the logistic weighing function to control shapes of the response along the concentration levels. For a given transformation f(z), and the parameters mu and tau, the statistical method used (here the CC method) estimates the coefficient Beta (the coefficient for the Control term) and provides the quality of goodness of fit for the model [5]. The quality of the approximation is measured by the AIC value [6]. The optimal values for the parameters mu and tau can be determined by minimization of the AIC value. The proposed approach can be called controlled case-crossover (CCC) method.

The standard CC method traditionally gives the relative risk calculated as exp(Beta*z). The presented CCC method gives the risk as RR(z)=exp(Beta*Control(z)). The logistic function used in the model, LWF, allows adapting to various shapes of the concentration-responses. The CCC method usually results with better fit than the standard CC method. The presented technique estimates the best model according to the criteria used and provides the coefficient Beta and its standard error (SE).

We realized our calculations with three transformation functions f(z). We used two values of the parameter tau; 0.1 and 0.2. The transformed concentration, represented in the form of the product (f(z)*LWF(z,mu,tau,f(z)) is submitted to the CC model. Among the constructed models we chose one which gives the best fit using the AIC value as a criterion. In this way the function f(z) and the value of mu and tauare determined. Knowing all the parameters, we can easily construct the concentration-response function. Here, the values of this function are interpreted as odds ratio (OR), and the function has the following form:

OR(z)=exp(Beta*f(z)*LWF(z))=exp(Beta*Control(z)).

As the Control function may have various forms, including different types of the transformation function f(z), it is reasonable to considered a common Control function.

For the estimated concentration-response functions corresponding to the used lagged concentration, we created their “summary”. We attempt to represent the association by one common function, of the following form:

G(z)=exp{T*log(1+z/A)/[1+exp((MU-z)/(r*tau))]}

where the parameters T, A, and MU are estimated using the least square approximation. The common function is estimated using a set of the concentration-response functions. In this work two such functions are obtained; one is based on the shapes generated for lags from 0 to 3, and the second on lags from 0 to 4. The same form of the function G(z) is fitted to the 95% confidence interval (CI) shapes.

Results

From the ED database in Edmonton we retrieved the following numbers of the ED visits: 35,216 (ICD-9:410 - 414), 26,825 (ICD-9:426, 427), and 17,149 (ICD-9:428). We considered them all together and in total we had 79,190 ED visits related to cardiac conditions.

Table shows the estimated parameters; the coefficient Beta, its standard error (SE), P-value, and the value of the parameter mu (Table 1). The results are shown for the used lags, from 0 to 4. These estimations are obtained using the standard case crossover method.

In this situation, for all considered lags the transformation function f(z)=log(z) and tau=0.1 were chosen among three tested variants of the transformation functions (z, log(z), sqrt(z), and tau=0.1 and tau=0.2) as the best candidates. For example, for lag 0 we estimated: Beta= 0.0311, standard error, SE=0.0113, mu= -2.6, and for lag 3, Beta= 0.0190, SE = 0.0076, mu= 9.0.

The results are positive statistically significant for the concentration lagged by 0 (same day), 1, 2, and 3 days. The figure illustrates the results (ORs and their 95% confidence intervals, CI) for exposure to nitrogen-dioxide and ED visits for the considered cardiac health condition (Figure 1).

The main result of the described technique is the ability to represent a odds ratio as the value of the flexible concentration-response function. Two situations are presented. A left panel of figure illustrates a summary function (G(z)) estimated on the basis of the concentration-response shapes obtained for lags from 0 to 3 (Figure 2). The associations for these lags are positive statistically significant. The function G(z) has the following parameters: A=1.2728, T=0.0276, and MU=2.0488. A right panel also includes the results for lag 4 (only positive). In this case, we have the function G(z) with the parameters: A=1.3169, T=0.0262, and MU=0.6834.

Discussion

We presented the methodology which allows to “summarizing” the concentration-response functions obtained from various sources. In our situation, these functions were estimated for different lags. In general, they can be from various studies conducted in different research centers. A similar idea was presented in for the longitudinal

Table 1. The parameters of the fitted models.

Log	Beta	SE	P-value	mu
0	0.0311	0.0113	0.006	-2.6
1	0.019	0.0076	0.012	9
2	0.0249	0.0107	0.021	-1.1
3	0.0291	0.0097	0.003	2
4	0.0183	0.0133	0.17	-58.7

Note: In all cases f(z)=log(z), tau=0.1. The risk is estimated as R=exp{Beta*log(z)/(1+exp[(mu-z)/rtau])}, rtau= tau*range.

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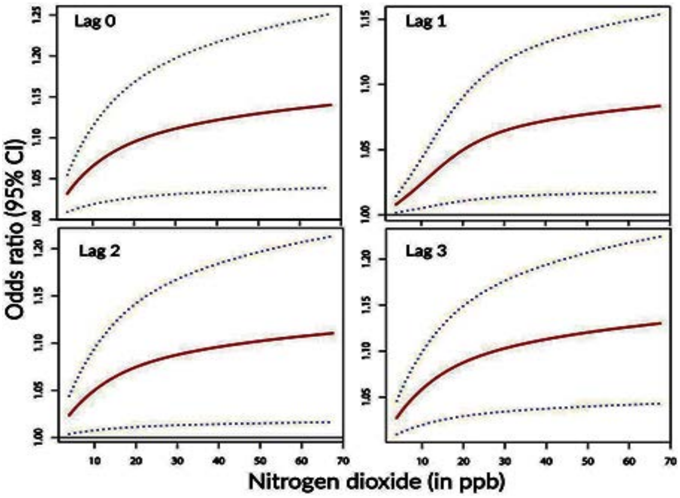

Figure 1: Concentration-response functions for nitrogen dioxide by lags (0-3). The ORs (in red) and their 95% CI (in blue) are shown.

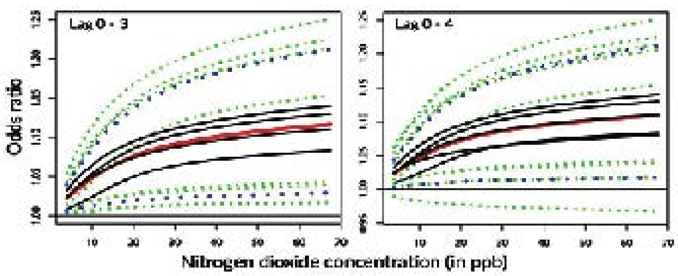

Figure 2: The association between concentration of NO_2 and the number of ED visits for cardiac condition. The ORs (black lines) and their 95% CIs (dotted green lines) are shown. The global estimation of ORs (red line) and global estimation based on 95% CIs (dotted blue) are represented based on lag 0-3 (left panel) and on lag 0-4 (right panel).

studies of mortality, where the concentration-response shapes from 41 cohorts from 16 countries were used to construct a global concentration-response function [7].

In our example, the technique used always indicated the same transformation function (here log(z)). Of course, various transformations f(z) can be realized and classified as the best choice. The function G(z) is constructed using values from the estimated shapes tabulated for the considered concentrations. These concentrations can be air pollutant levels or any air quality health index values [8].

The technique considered in this work is a relatively new methodology and needs more studies, theoretical and practical.

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