Dioxin Emissions from a Solid Waste Incinerator and Risk of Non-Hodgkin Lymphoma

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Background: It is not clear whether low environmental doses of dioxin affect the general population. We previously detected a cluster of patients with non-Hodgkin lymphoma around a French municipal solid waste incinerator with high dioxin emissions. To explore the environmental route suggested by these findings, we carried out a population-based case-control study in the same area.
Methods: We compared 222 incident cases of non-Hodgkin lymphoma diagnosed between 1980 and 1995 and controls randomly selected from the 1990 population census, using a 10-to-1 match. Dioxin ground-level concentrations were modeled with a second-generation Gaussian-type dispersion model, yielding four dioxin exposure categories. The latter were linked to individual places of residence, using Geographic Information System technology.
Results: The risk of developing non-Hodgkin lymphoma was 2.3 times higher (95% confidence interval = 1.4–3.8) among individuals living in the area with the highest dioxin concentration than among those living in the area with the lowest dioxin concentration. No increased risk was found for the intermediate dioxin exposure categories. Adjustment for a wide range of socioeconomic characteristics at the block group level did not alter the results.
Conclusion: Although emissions from incinerators are usually not regarded as an important source of exposure to dioxins compared with other background sources, our findings support the hypothesis that environmental dioxins increase the risk of non-Hodgkin lymphoma among the population living in the vicinity of a municipal solid waste incinerator.

Key Words: case/control study, dioxins, geographic information system, incineration, non-Hodgkin lymphoma, waste management

(*Epidemiology* 2003;14: 392–398)

Dioxin is the name given to two classes of organochlorine compounds, 75 polychlorinated dibenzo-*p*-dioxins (PCDD) and 135 polychlorinated dibenzofurans (PCDF). Seventeen tetrachloro-substituted congeners are toxic, with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) being the most potent. Environmental contamination by dioxin can happen by several routes: combustion (waste incineration, burning of various fuels, other high temperature sources such as cement kilns); metals smelting, refining and processing (iron ore sintering, steel production, scrap metal recovery); chemical manufacturing (chlorine bleached wood pulp, chlorinated phenols, chlorinated aliphatic compounds); biologic and photochemical processes (action of micro organisms on chlorinated phenolic compounds); and reservoir sources (soils, sediments, biota, water).

The U.S. Environmental Protection Agency[1] and the International Agency for Research on Cancer[2] have classified 2,3,7,8-TCDD as a human carcinogen. Non-Hodgkin lymphomas and soft-tissue sarcomas have been associated with occupational or accidental exposures to chemicals contaminated with dioxins.[3–7] Aside from the studies involving heavy exposures in industrial settings, few studies have looked at the impact of environmental exposure to dioxins on the health of the general population.[8] Dioxin emissions from municipal solid waste incinerators are one of the major sources of dioxins and therefore are an exposure source of public concern.

Our team recently examined the spatial distribution of non-Hodgkin lymphomas and soft-tissue sarcomas around a French solid waste incinerator with high dioxin emission levels.[9] Some legal guidelines for incinerator emissions had not been followed at this location. For example, in 1997, dust and hydrogen emission levels were higher than prescribed and exhaust gases were not maintained at temperatures of

Editor's note: An invited commentary on this article appears on page 384.

Submitted 26 July 2002; final version accepted 25 March 2003.

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This research was supported by the Health and Rural Environment Research Group (EA 2276), University of Franche-Comté, France.

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1044-3983/03/1404-0392
DOI: 10.1097/01.ede.0000072107.90304.01

more than 850°C for the legal time (>2 seconds), allowing dioxins to be emitted. The first time that the dioxin concentration of an exhaust gas was ever measured (in December 1997) it was found to be 16.3 ng international toxic equivalency factor (I-TEQ)/m^3, whereas the European guide value is 0.1 ng I-TEQ/m^3.

Using a spatial scan statistic, we found evidence for clusters of non-Hodgkin lymphoma and soft-tissue sarcoma in the area that contains the solid waste incinerator. Standardized incidence ratios were 1.3 (95% confidence interval [CI] = 1.1–1.4) for non-Hodgkin lymphoma and 1.4 (CI = 1.1–1.9) for soft-tissue sarcoma.

These results suggested an airborne route of dioxin exposure, which is at variance with the common assumption that intake from food accounts for over 90% of the burden of dioxins in the general human population.[2] This assumption may not hold for people living in the vicinity of a solid waste incinerator, however.[1] Possible exposure pathways include direct exposure (vapor inhalation or dermal absorption) and, more likely, the consumption of plant products or poultry from contaminated areas.

To address this issue further, we carried out a population-based case-control study on the population living around this solid waste incinerator, focusing on non-Hodgkin lymphoma (which is more frequent than soft-tissue sarcoma, thus improving the precision of the estimates). We had information on non-Hodgkin lymphoma incidence and census data which could be geocoded. A dioxin dispersion model made it possible to link ground-level dioxin concentrations to individual addresses (using Geographic Information System [GIS] technology).

METHODS

Selection of Cases and Controls

The most likely cluster in our previous study consisted of the cantons of Audeux and Besançon. Detailed census data (needed to sample population controls) were available only for the city of Besançon, with an average population during the study period of 114,000 inhabitants. We therefore limited our study to this zone, excluding 29,000 inhabitants of Audeux. Besançon is the regional capital, with a stable urban population (113,000, 113,000 and 117,000 inhabitants in 1982, 1990 and 1999, respectively), spread over 65 km^2.

The municipal solid waste incinerator under investigation is located 4 km west of the city center. Combustion chambers 1 and 2 (each with a capacity of 2.1 metric tons per hour) were put into service in 1971. In 1976, a third combustion chamber was opened (with a capacity of 3 metric tons per hour). In 1998, approximately 67,000 metric tons of waste were processed. Combustion chamber 1 (the most polluting) was shut down on December 31, 1998.

We obtained non-Hodgkin lymphoma incidence data for 1980–1995 from the Doubs cancer registry. The period we studied is before the first public concern about putative effects of municipal solid waste incinerators. This registry was established in 1976 and is complete for non-Hodgkin lymphoma cases, as ascertained by the ratio of the number of deaths to the number of cases registered during 1983–1987, which at 47% (for the Doubs region) is very similar to those reported in other Western countries.[10] Virtually all cases were histologically verified (97% among men and 99% among women). We collected data concerning the patients' address at diagnosis, date of birth, gender, cancer diagnosis and age at diagnosis from their medical records. *International Classification of Disease for Oncology* (ICD-O) morphology codes were 9590/3-9595/3, 9670/3-9723/3 and 9761/3.

We selected controls from a reliable and accessible database, the population census. Because of French privacy laws and confidentiality requirements the only individual data available to researchers are sex, age categories (0–19, 20–39, 40–59, 60–74 and 75+ years), and residence in a given block. The block is the smallest level of geographic resolution in the French census database and is defined only in densely populated areas. Each block is typically a quadrangle bounded by four streets. First described in the 1990 census, there are 705 blocks in Besançon, averaging 161 inhabitants.

We randomly selected population-based controls, according to a 10-to-1 matching procedure. Matching criteria were sex and age, producing 10 strata. To adjust for differences between the index case diagnosis year (1980–1995) and 1990 (year of census), cases were matched to controls based on the age they would have been in 1990.

Risk factor data were limited to what was available through the census either on an individual level or on a block group level. The 705 blocks of the study area are combined into 52 groups for analysis of socioeconomic status measures (educational, occupational, household-based indicators).

Data Analysis

We used residential address geocoding to pinpoint the location of case residences.[11] A municipal GIS analyst matched a file containing participants' addresses (street and number) against a street network file, using Star GIS software (Star Informatic, Liege, Belgium). The geographic coordinates of these exact locations were expressed in the Lambert two French-plane coordinate system.

To estimate dioxin exposure, we took advantage of a study performed in 1999 to support an environmental impact statement for a new combustion chamber. The work was carried out by Aria Technologies, Colombes, France, using APC3 software. APC3, a second-generation Gaussian-type dispersion model, allowed the three-dimensional modeling of the transport and dispersion of dioxin emissions. The model took into account meteorological data (5 years of data for windspeed, wind direction, pressure, temperature and atmospheric stability), surface topography and obstacle descriptions, stack characteristics and dioxin emission rate from the solid waste incinerator. It assessed average concentrations in hundreds of meteorological conditions (one Gaussian plume for each particular meteorological condition). The respective contours of these modeled ground-level concentrations (0.0001 pg/m^3, 0.0002 pg/m^3, 0.0004 pg/m^3, 0.0016 pg/m^3) were digitized and transferred onto the surface of the map (Fig. 1).

This model was originally developed to predict the future impact of dioxin emissions, both from an old (but renewed) combustion chamber and from a new oven with up-to-date pollution controls. It was not possible to assess past exposure because past dioxin emission rates had not been collected. However, dispersion modeling is heavily influenced by factors that are stable over time (mean meteorological conditions, terrain elevations and stack height). Thus, we assumed that contour shapes, as derived from the prediction model, were reliable estimates of past dioxin deposition profiles and we used dioxin ground-level concentrations as relative figures rather than absolute figures to estimate past exposure. Hence, in the remaining part of this paper, the contours are classified as very low (modeled ground-level dioxin concentration <0.0001 pg/m^3 zone), low (modeled ground-level dioxin concentration 0.0001–0.0002 pg/m^3 zone), intermediate (modeled ground-level dioxin concentration 0.0002–0.0004 pg/m^3 zone) and high (modeled ground-level dioxin concentration 0.0004–0.0016 pg/m^3 zone) exposure areas.

We overlaid a map of case residences onto the digital dioxin concentration map to obtain a field—for risk—classification for each cancer patient. In the same way, we attributed a dioxin concentration category to each of the 705 city blocks and 52 block groups (provided half or more of their area was within a given contour).

We used conditional logistic regressions to calculate odds ratios (ORs) and 95% CIs for each level of dioxin

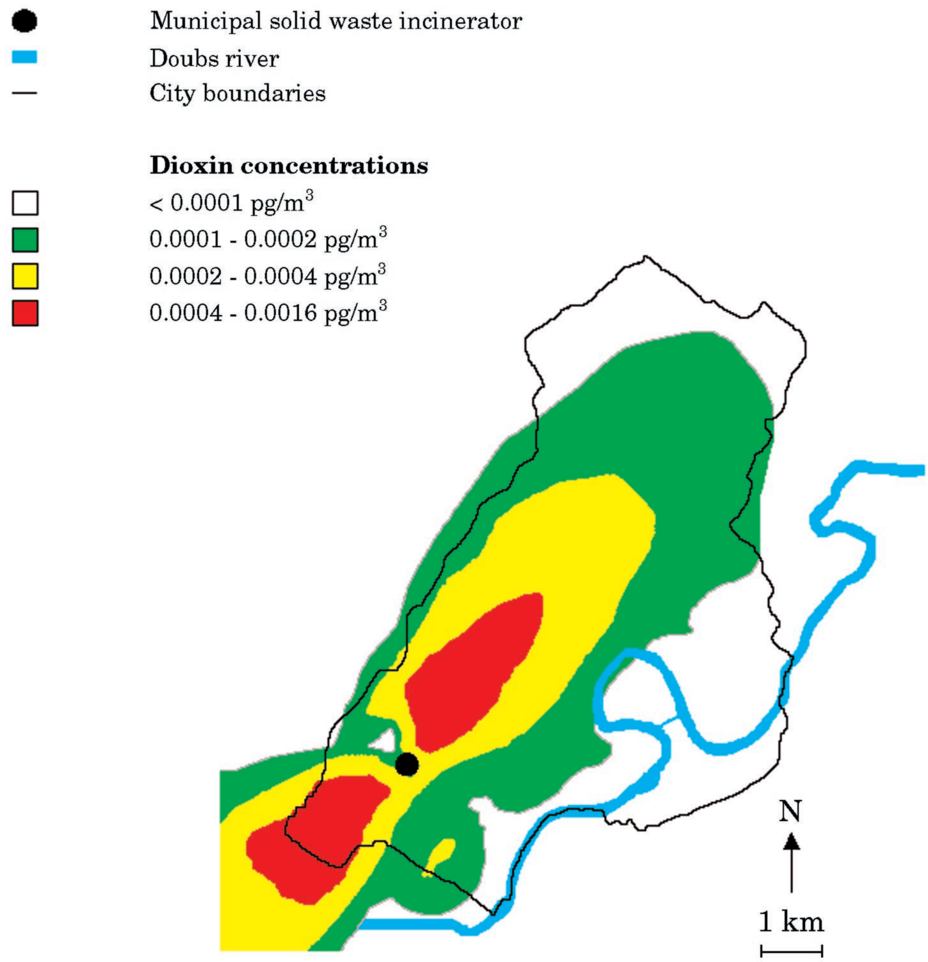

FIGURE 1. Modeled average ground-level dioxin concentrations around the municipal solid waste incinerator of Besançon, France.

TABLE 1. Socioeconomic Characteristics (Defined at the Block Group Level) of Dioxin Exposure Zones

	Very Low (N = 11)	Low (N = 21)	Intermediate (N = 14)	High (N = 6)
Persons with a high school diploma (%)	34	30	27	28
Women in labor force (%)	47	49	48	55
Workers in labor force (%)	17	24	26	23
Unemployed in labor force (%)	13	15	15	13
Single woman as head of household (%)	7	8	11	9
Owner-occupied houses (%)	35	32	29	36
Number of persons per dwelling (mean)	2.2	1.9	2.2	2.2
Single-family houses (%)	35	14	12	30

exposure estimated from the dispersion model. A set of dummy variables was generated for this categorical scale variable using the lowest category as the reference group. Models were run with Egret for Windows software (CYTEL Software Corporation, Cambridge, MA).

Multilevel models were run to explain the outcome (case/control status) defined at the individual level, while introducing risk factors at the individual level (dioxin exposure) and the block group level (socio-economic characteristics). MlwiN software (Institute of Education, London, United Kingdom) was used to carry out these analyzes.

RESULTS

As expected, the risk of airborne dioxin exposure was not distributed evenly throughout the population. The distribution of dioxin fall-out was characterized by a skewed distance distribution, following a northeast to southwest direction, with peaks at varying distances on both sides of the incinerator (Fig. 1). The asymmetry of the distribution is caused by the foot-hills of the Jura mountains, which channel the wind preferentially in two directions. Socioeconomic characteristics (education, occupational social class and household-based indicators), defined at the block group level, did not vary with dioxin exposure category (Table 1).

During the 16-year study period, 225 non-Hodgkin lymphoma cases were diagnosed, corresponding to a mean age-standardized (world) incidence rate of 14.9 per 100,000 for the 1980–1995 time period. The age-standardized (world) incidence rate for France as a whole was estimated at 7.8 per 100,000 in 1995.[12] Address matching was successful for 222 cases (three medical records had incomplete address information). Eighty percent of non-Hodgkin lymphoma cases occurred within the 1990 ± 5 year time range and the proportion of males was 51%. The age distribution was slightly skewed toward young ages (lower quartile: 49 years; median: 66 years; upper quartile: 77 years).

The distribution of these cancer patients by dioxin exposure categories is displayed in Table 2. The conditional logistic regression analysis showed that individuals living in the highest exposed zone were 2.3 times more likely (CI = 1.4–3.8) to develop non-Hodgkin lymphoma than were individuals living in the very low emission area, with no increased risk for the other dioxin risk categories (Table 2).

The results of an analysis restricted to the non-Hodgkin lymphoma cases diagnosed between 1985 and 1995 were very similar: ORs were 1.3 (CI = 0.8–2.0), 1.0 (CI = 0.6–1.6) and 2.1 (CI = 1.1–3.7), for the low, intermediate and high dioxin exposure categories, respectively.

Adjustment for a wide range of block group characteristics (those reported in Table 1), introduced in turn in a 2-level hierarchical model, did not alter the results. Inclusion of socioeconomic status measures resulted in ORs ranging from 0.9 to 1.0, 0.9 to 1.0 and 2.1 to 2.4, for the low, intermediate and high dioxin exposure categories, respectively.

DISCUSSION

We found a 2.3-fold risk for non-Hodgkin lymphoma associated with residence in areas classified as highly exposed to dioxin emitted from a municipal solid waste incinerator (as estimated by an airborne dispersion model), com-

TABLE 2. Association of Non-Hodgkin Lymphoma with Dioxin Exposure Categories,* City of Besançon, France, 1980–1995

Dioxin Exposure	Non-Hodgkin Lymphoma Cases	Controls	OR (95% CI)
Very low†	42	441	1.0
Low	91	952	1.0 (0.7–1.5)
Intermediate	58	681	0.9 (0.6–1.4)
High	31	146	2.3 (1.4–3.8)

* From Aria Technologies modelling (with APC3 software).
† Reference category.

pared with very low exposure areas; the low and intermediate exposure categories did not exhibit an excess risk.

The strengths of this study are as follows. First, it was a population-based design. Cases were actively identified through multiple sources within a defined geographic area and controls were randomly selected from the same study area as the cases. The 10-to-1 matching procedure produced fairly precise relative risk estimates, as reflected by the narrowness of the corresponding confidence intervals (Table 2).

Second, we were able to use dioxin exposure data based on sophisticated methods for modeling of emissions.[13] The modeled ground-level concentrations represented the best available surrogates for past dioxin exposure measurements from the same source, given that no earlier measurements had been taken.

Third, this GIS-based case-control study improved upon the conventional case-control design. This study was based on a complete directory of Besançon city residents (census data), with a modest but relevant and reliable list of characteristics available at low cost. The amount of information does not increase proportionally with the size of the control group; a ratio of around 4 or 5 is usually considered to be a good trade-off. However, when the cost of additional information is negligible, a high control/case ratio is justified.[14] We decided a priori on a ratio of 10, which was kept constant across the strata. This considerably enhanced the precision and thereby improved the efficiency of the study.

Fourth, we carried out a sensitivity analysis based on multilevel modeling. More complex in theory and practice, it can demonstrate the independent effects of area characteristics and individual factors.

However, our methodology also presented some limitations. First of all, we lacked actual exposure data regarding biota in the contaminated area and exposed humans. In 1998, concentrations of dioxins in cow's milk from farms located within a 3-km radius of the incinerator were requested by public health authorities. Only four farms met the criterion, and one of these farms was not involved in cattle breeding. Dioxin concentrations (in ng I-TEQ/kg of fat) and distances between the farms and the plant were as follows: 1.03 (0.9 km), 0.59 (1.5 km) and 0.58 (2.0 km). However, the sampling frame was questionable as only one farm (with the highest dioxin level) was located under the plume of the incinerator's stacks.

To circumvent this lack of actual exposure data, we used dispersion modeling as a proxy for dioxin exposure, assuming that residents within a given contour were homogeneously exposed. When interpreting the results it is important to remember that this model was developed for regulatory purposes rather than as a means of assessing exposure to air pollution.[15] Furthermore, its representativeness of exposure over time had to be assumed in this study of long-term effects, because no data concerning dioxin emission levels are available for the period before 1997. Residence location as a surrogate of exposure cannot distinguish contributions from the direct and the indirect exposure pathways (*eg*, from air to soil and home-grown produce). We lacked the necessary household and soil measurements to confirm the validity of the dispersion model. Moreover pollutant-specific deposition modelings are interrelated and thus pollutant effects are difficult to separate. Emissions of dust and hydrogen chlorine, which were also above the legal limits, could be important if these exposures are associated with occurrence of non-Hodgkin lymphoma (but, to our knowledge, no such associations have been described).

This study is of mixed individual/ecological design with case residences linked to the dispersion map by exact address whereas control residences are at the block level. Thus, although census blocks have a limited area (decreasing the distance between actual and surrogate locations) and were assigned one of four exposure levels prior to control sampling, the possibility of some differential exposure misclassification cannot be ruled out.

Controls were residents in 1990, whereas cases were diagnosed between 1980 and 1995, introducing a time lag in the sampling for some matched sets. We believe that the shortness of this time lag did not affect the coverage of the target population. First, restricting the analysis to cases diagnosed between 1985 and 1995 did not alter the results. Second, the population of Besançon appears to be stable over time for the age groups considered; 86% of the people over 40 years of age who lived in Besançon in 1999 were already residing in the city in 1990. Third, if some housing development occurred during this short time period, there is no reason to believe that it was related to dioxin risk categories, for which modeling was performed in 1999. We conclude that the effect (if any) of such a short time lag would be to bias the odds ratios towards 1.0.

The lack of information pertaining to residence history and time-activity patterns limited our ability to ascertain the duration of exposure. Considering the long exposure-to-effect interval, some subjects might have lived elsewhere at the times of relevant exposure or have been lightly exposed to dioxins from the incinerator. However, this potential misclassification is likely to be random with respect to disease status, resulting in a bias of our risk estimates towards the null.[16]

Regarding other occupational or environmental sources of exposure to dioxins, there are no adjacent industrial sources of combustion-effluents; highly polluting industries were replaced 2 decades ago by small-scale advanced technologies. Before that time, the main factory (producing synthetic textiles) was located 5 km east of the city center, in the very low dioxin exposure area. No cement kilns, iron or steel works, or foundries were located in this area. Other potential thermal and combustion sources, such as automobile exhausts and home heating, result in diffuse, nonspatially organized emissions. Alternatively, there is mounting evidence implicating phenoxy herbicides in the etiology of non-Hodgkin lymphomas. In general, but not consistently, positive associations have been found between occupational exposure to herbicides and non-Hodgkin lymphoma in case-control studies, whereas results from follow-up studies are less suggestive of an association.[17] In any case, Besançon is highly urbanized with few pastures (only four farms within a 3-km radius of the MSW incinerator). Thus, in our opinion, neither other factories nor farmland are likely to affect the interpretation of these results.

This study was also limited by the scarcity of covariates (only age and gender), which could potentially confound the relationship between dioxin exposure from the municipal solid waste incinerator and non-Hodgkin lymphomas. However, most reports of mortality and incidence data for lymphomas show no clear association with social class.[18] In our study, the similarities across block groups characterized by differing exposure levels are reassuring. Still, the possibility that there are other differences between subjects living in the highest exposure zone and those with lower exposures cannot be ruled out. For example, the percentage of subjects with a high school diploma is similar, but income may vary, or there may be differences at the high or low end of the education scale.

Thus, for all the above-mentioned reasons, we cannot firmly exclude the possibility that residual confounding affected the reported odds ratios.

We found that the risk of non-Hodgkin lymphoma incidence was elevated in the highest dioxin concentration category, suggesting a possible threshold effect. However, as we used a ranking system rather than actual measurements to classify exposure levels we cannot be more precise about this threshold level.

Other researchers have concluded that the health risks caused by dioxin emissions from incinerators are relatively unimportant compared with other background sources of dioxins.[19,20] Deml et al[21] found no indication of an enhanced body burden of dioxins and furans in nonoccupationally exposed persons living in the vicinity of a municipal waste incinerator. Dioxin and furan emissions in their study resulted in values of about 2 ng I-TEQ/m^3, which is much lower than levels from the Besançon incinerator (16.3 ng I-TEQ/m^3). Gonzales et al[22] showed that blood dioxin levels did not depend on the distance of residence from a Spanish incinerator with similarly low dioxin stack emissions (2.5 ng I-TEQ/m^3).

In a cancer risk assessment of dioxin and furan emissions from a municipal solid waste incinerator, Nessel et al[23] estimated the lifetime total cancer risk as 2.5×10^{-6} in the highly exposed scenario, compared with 1.8×10^{-7} in the common scenario (representative of the general population), which is a 10-fold difference. They nevertheless concluded that the relatively low magnitude of these risks suggests that the dioxin and furan emissions from this incinerator should not be of public health concern. Yoshida et al[24] showed that life-time cancer risk for residents living within 1 km of a municipal solid waste incinerator (and perhaps because of dioxin exposure), were twice as high as those of the general population, but considered these results sufficient to guarantee safety. In a recent quantitative risk assessment, Ma et al[25] found that the carcinogenic risk of dioxins (all cancers) ranged from 1×10^{-6} (under the exposure scenario of insufficient local food production for residents' consumption) to 7.1×10^{-5} (under the exposure scenario of sufficient local food production), for the most polluting of nine Taiwanese incinerators (6.67 ng I-TEQ/m^3).

However, our findings are in line with the results provided by Bertazzi et al[26] on the 20-year mortality of the Seveso population. People in the Seveso cohort had mean TCDD blood lipid concentration of 136 ng TCDD/kg, which falls between the typical occupational dioxin levels ($>$ 1,000 ng TCDD/kg) and background levels (2–3 ng TCDD/kg).[27] Allowing for a latency time window of 15–20 years, results for non-Hodgkin lymphomas clearly did stand out, according to Bertazzi et al,[28] with a relative risk of 2.8 (CI = 1.1–7.0).

In summary, we find an increased risk of non-Hodgkin lymphoma in the highest exposure zone around a municipal solid waste incinerator that emitted high levels of dioxins. This finding, together with the non-Hodgkin lymphoma mortality excess reported by Bertazzi et al[26,28] around Seveso, lends support to the hypothesis that airborne dioxin exposure may be a public health concern.

ACKNOWLEDGMENTS

We thank François Tourneux and Annibale Biggeri for their technical assistance. We are grateful to Robert Schwint (former mayor of Besançon) for allowing the support of the GIS municipal staff (Roland Draussin and Jean-Pierre Guivier) and for transmitting the dioxin diffusion model.

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