Industrial pollution and cancer in Spain: An important public health issue.

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Title page

Title: Industrial pollution and cancer in Spain: an important public health issue

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Abstract

Cancer can be caused by exposure to air pollution released by industrial facilities. The European Pollutant Release and Transfer Register (E-PRTR) has made it possible to study exposure to industrial pollution. This study seeks to describe the industrial emissions in the vicinity of Spanish towns and their temporal changes, and review our experience studying industrial pollution and cancer. Data on industrial pollutant sources (2007-2010) were obtained from the E-PRTR registries. Population exposure was estimated by the distance from towns to industrial facilities. We calculated the amount of carcinogens emitted into the air in the proximity (<5km) of towns and show them in municipal maps. We summarized the most relevant results and conclusions reported by ecological E-PRTR-based on studies of cancer mortality and industrial pollution in Spain and the limitations and result interpretations of these types of studies. There are high amounts of carcinogen emissions in the proximity of towns in the southwest, east and north of the country and the total amount of emitted carcinogens is considerable (e.g. 20 Mt of arsenic, 63 Mt of chromium and 9 Mt of cadmium). Although the emissions of some carcinogens in the proximity of certain towns were reduced during the study period, emissions of benzene, dioxins+furans and polychlorinated biphenyls rose. Moreover, the average population of towns lying within a 5km radius from emission sources of carcinogens included in the International Agency for Research on Cancer list of carcinogens was 9 million persons. On the other hand, the results of the reviewed studies suggest that those Spanish regions exposed to the pollution released by certain types of industrial facilities have around 17% cancer excess mortality when compared with those unexposed. Moreover, excess mortality is focused on digestive and respiratory tract cancers, leukemias, prostate, breast and ovarian cancers. Despite their limitations, ecological studies are a useful tool in

environmental epidemiology, not only for proposing etiological hypotheses about the risk of living close to industrial pollutant sources, but also for providing data to account for situations of higher mortality in specific areas. Nevertheless, the reduction of emissions should be a goal, with special relevance given to establishing limits for known carcinogens and other toxic substances in the environs of population centers, as well as industry-specific emission limits.

Key words**:** epidemiology, cancer, industrial pollution, mortality.

1. Introduction

Cancer was the second leading cause of death behind cardiovascular diseases and caused over 8.7 million deaths globally in 2015 (Global Burden of Disease Cancer Collaboration et al., 2017). In scientific circles, there is a consensus that "environment" (construed in its widest sense as lifestyle, habitat and setting, occupation and diet) is implicated in the etiology of many types of cancer (Tomatis et al., 1990). In a stricter sense, many authors consider the term "environmental" to cover only those exposures that are present in the daily life of persons and defy individual control. In other words, they only consider those that correspond to habitat and setting—air (both indoor and outdoor), water and soil pollution—although occupational exposures could also be included in this category.

Specifically, air pollution, which is a complex mixture of different gaseous and particulate components, varies greatly by locality and time. In recent years and in urban

settings in particular, there has been an increase in traffic-related air pollution (with emissions of products generated by the combustion engine, including volatile organic compounds, nitrogen oxides, and fine particulate matter) along with the ensuing consequences on ozone levels. In addition, there are also emissions of industrial origin, rendering it difficult to study their respective health effects separately, perhaps because of the lack of information on specific emissions of each source.

Additionally, there is a biological rationale for numerous components of the air pollution mix, including benzo[a]pyrene, benzene, some metals, particles (especially fine particles), and possibly ozone, having a carcinogenic potential (Boffetta and Nyberg, 2003). In fact, recently, in October 2013, outdoor air pollution and particulate matter in outdoor air pollution were classified by the International Agency for Research on Cancer (IARC) as Group-1 carcinogens (Loomis et al., 2013). This decision was based on a review of the evidence provided by hundreds of epidemiological population-based studies and on experimental results of carcinogenicity in animals. In adults, for example, it is estimated that 1–2% of lung cancer cases are associated with the presence of a high concentration of these compounds (Alberg and Samet, 2003). The proposed mechanism is as follows: exposures to outdoor air pollution or particulate matter in polluted outdoor air are associated with increases in the type of genetic damage shown to be predictive of cancer in humans (Straif et al., 2013).

There is also evidence that exposure to elevated $PM_{2.5}$ after hepatocellular carcinoma diagnosis may shorten survival, with larger effects at higher concentrations (Deng et al., 2017), and that exposure to outdoor air pollution is associated with bladder cancer including occupational and residential exposure to traffic or traffic emissions

(Loomis et al., 2013). More recently Goldberg MS et al (Goldberg et al., 2017) have shown that ambient NO_2 and ultrafine particles may increase the risk of incident postmenopausal breast cancer. Because millions of people are exposed to high levels of air pollution and the dimensions of the problem are not yet fully known (Loomis et al., 2013), this is a major public health problem.

In the context of one source of air pollution, industrial activity, public Pollutant Releases and Transfers Registers (PRTRs) provide information about releases to air, water, and soil from a broad variety of productive activities (Wine et al., 2013), based on the principle of the right to public access to environmental information. This can be very useful for assessing population exposure to industrial pollution. It should be noted that some industrial facilities have introduced technical improvements in their production processes in recent years and, thus, achieved reductions in their pollutant emissions. Nevertheless, large quantities of toxic substances have been indiscriminately released for many years, which may have had and/or may still have an impact in the medium-to-long term health of the population exposed to such pollution. Several studies have determined that residential areas in the vicinity of industrial pollution foci are higher-risk cancer areas for adults (Bulka et al., 2013; Cambra et al., 2013; García-Pérez et al., 2015b; Morton-Jones et al., 1999; Pascal et al., 2013).

In Spain, the combination of the application of the European Directive on Integrated Pollution Prevention and Control (IPPC) and the subsequent creation of the European Pollutant Emission Register (EPER) and European Pollutant Release and Transfer Register (E-PRTR; http://prtr.ec.europa.eu/) has provided data which has made it possible to ascertain the importance of exposure to industrial pollution across a

country and to initiate a line of work aimed at revealing the consequences of such exposure on population health, specifically in cancer mortality (Fernández-Navarro et al., 2012; García-Pérez et al., 2009, 2013, 2015b, López-Abente et al., 2012b, 2012a). These ecological studies, despite their limitations, could be a useful and inexpensive tool for proposing etiological hypotheses. They allow us to identify plausible ecological associations between cancer mortality and exposure to industrial pollution to be studied more deeply in order to perform preventive measures in the environmental and/or public health context.

This report seeks to (1) describe the population exposure to carcinogens released from industrial facilities in Spain, based on the emissions to air recorded in the aforementioned registers, (2) describe our experience studying industrial pollution and cancer mortality in Spain, and (3) discuss the challenges posed by this type of study and the interpretation of the results.

2. Methods

Data on industrial pollutant sources for the period 2007-2010 were obtained from the E-PRTR and IPPC registries and supplied by the Spanish Ministry of Agriculture, Food & Environment (Ministerio de Agricultura, Alimentación y Medio Ambiente). This database contains information regarding 6,850 facilities identifying, among other variables, the industrial activity and the installation's geographical location by reference to its coordinates. Additionally, it includes information about the emissions of 105 pollutants, some of them carcinogens. There were no equivalent quality data

152 from previous years because reporting pollutant emissions to these registers had been
153 voluntary prior to 2007. However, as in the previous industrial registers, the emissions
154 had been annually reported by the industries themselves.
155
156 Population exposure to industrial pollution was estimated by referencing the
157 distance from town centroids to industrial facilities. All the geographic coordinates of
158 the industries registered were validated using orthophotos and detailed information
159 obtained with the aid of the new tools provided by the Internet and Google Earth (with
160 aerial images and street view application). Some of these validation procedures have
161 been described elsewhere (García-Pérez et al., 2008).
162
163 We calculated the total annual amount of emissions (expressed in tonnes) for
164 each of the carcinogens classified as recognized and suspected by the IARC (Group 1,
165 2A and 2B), that had been emitted by industrial facilities into the air in the proximity
166 (defined as less than 5 km) of population centers in the period 2007-2010. Moreover,
167 we also calculated the percentage change from 2007 to 2010 of the total annual amount
168 for each of the carcinogen emissions.
169
170 Furthermore, we also determined the total amount of emissions to air of
171 carcinogens classified as recognized and suspected by the IARC (Group 1, 2A and 2B)
172 released by the industrial facilities in the 2007-2010 period in the proximity of towns in
173 Spain (5km) by industrial group. These groups were formed based on similarities in
174 their pollutant emission patterns (García-Pérez et al., 2015c).
175

176 The "exposed" population was estimated as the annual average resident
177 population of any town situated less than 5 km from the emission sources of each
178 substance. We chose the distance of 5 km because it was the distance that achieved the
179 best balance between identifying the risk and obtaining a sufficient number of observed
180 deaths to provide enough statistical power in the majority of our group´s ecological E-
181 PRTR-based studies of cancer mortality and industrial pollution in Spain.
182
183 Additionally, to describe the spatial distribution of the municipal exposure to the
184 recognized carcinogens by the IARC (Group I) released to air, the total amount was
185 plotted on a map by municipality for each year.
186
187 We also summarized the most relevant results and conclusions reported by
188 ecological E-PRTR-based studies of cancer mortality and industrial pollution in Spain
189 based on the data recorded by our group from 2007 to 2010. In these studies, based on
190 spatial epidemiology techniques, relative risks (RRs) of dying from cancer between
191 exposed and non-exposed municipalities were estimated using mixed Poisson regression
192 models or Bayesian conditional autoregressive models proposed by Besag, York and
193 Mollié (Besag et al., 1991) with explanatory variables. And the industrial pollution
194 exposure was defined as the proximity of population centroids to pollutant sources,
195 considering towns without any nearby pollutant industry as the reference for
196 comparison purposes.
197
198 In the Poisson mixed effects model, province was included as a random effects
199 term to enable geographic variability and to account for extra-Poisson dispersion.
200 Unexposed towns belonging to the same geographic setting (province) were considered

as the reference group in each case. In the BYM Bayesian autoregressive models, on the other hand, the random effects terms included two components: a spatial term containing municipal contiguities and the municipal heterogeneity term in order to control for the possible spatial effects of dependence and heterogeneity.

All estimates were adjusted for the following standardized sociodemographic indicators: population size, percentage of illiteracy, percentage of farmers, and percentage of unemployed, average persons per household and mean income as reported. They were chosen as potential confounders for their availability at a municipal level, potential explanatory ability vis-à-vis certain geographic mortality patterns and because they have proven to be useful in other studies: population size, percentage of illiteracy, percentage of farmers, and percentage of unemployed, and average persons per household according to the 1991 census; and mean income as reported by the Spanish Market Yearbook.

In this manuscript, only excess risks of cancer mortality observed in these studies in either sex not explained by random chance are shown. Finally, we also summarized some relevant considerations about the interpretation of the results. All statistical analyses and maps were performed using R Software.

3. Results

3.1. Population exposure to industrial pollution

According to the results shown in Table 1, though the amounts discharged in the proximity of towns centers have in many instances been reduced, emissions of benzene, polycyclic aromatic hydrocarbons (PAHs), dioxins+furans and polychlorinated biphenyls (PCBs) nevertheless rose.

It should also be noted that heavy metals had been emitted into the air near population centroids in considerable quantities, e.g., 20 metric tonnes (Mt) of arsenic, 63 Mt of chromium, 9 Mt of cadmium and 210 Mt of nickel, during the 2007-2010 period.

When examining the total annual amount of emissions by industrial group (see Table 1 SM), one observes that emissions of PM10 can be found in any of the industrial groups. Emissions of dioxins+furans, on the other hand, are only found in a few groups like Combustion, Production and processing of metals or Organic chemical industry. In general, however, almost all industrial groups release more than one of the substances that have been analyzed.

3.2. Spatial distribution of exposure

The total amount of IARC Group-1 carcinogen emissions in each of the 8,098 Spanish municipalities by year is shown in Fig. 1. There were 1,390, 1,456, 1,505, and 1,481 exposed towns in 2007, 2008, 2009, and 2010, respectively, which had emissions of carcinogens in their vicinity. Most of them are the same towns in all the years of the study period.

It should also be noted that the towns where there have been emissions of carcinogens in their proximity are similar during the four-year period. Moreover, the total amount of carcinogen released in the towns is also similar, with high total amounts of carcinogen emissions found in the proximity of towns in the southwest, east and north of the country. Nevertheless, there were towns exposed to industrial pollution throughout the territory.

3.3. Exposed population

In relation to the "exposed" population, the average population residing less than 5 km from emission sources of IARC Group I carcinogenic substances was 9.6 million (see Table 1). If the radius of exposure were reduced to 2 km from emission sources, the average population figures would be 2 million (data not shown) for Group 1.

3.4. Cancer mortality and industrial pollution in Spain

Tables 2 and 3 show a summary of the results of ecological studies on mortality due to cancer and industrial pollution in Spain, by type of tumor and industrial sector, respectively. Exploratory studies of all cancers had been undertaken, both by the industrial sector (Table 2) and for specific tumors which displayed an association with proximity to pollutant sources in a variety of sectors (Table 3). Excess mortality shown was around 17% (median value of the RRs in those statistical significant associations in men and women) and centered on malignant tumors of the digestive system and respiratory tract, gallbladder cancer, leukemias, prostate, breast and ovarian cancers. Within each sector, there were groups in which excess mortality risk was concentrated

(e.g., the use of coal as fuel in power stations and lung and gallbladder cancer, or the extraction of anthracite, bituminous coal, and lignite in mines and colorectal cancer).

3.5. Interpretation of the results

The following are some relevant aspects in relation to the interpretation of the results:

a) The statistical significance of any findings does not imply a causal relationship due to the study design.

b) The magnitude of the association effects found is small and logical, in line with the environmental risks shown in other works.

c) Current industrial facilities are probably not comparable to the old ones at many levels. Thus, it is important to take into account the induction period of the exposure to the pollutants emitted by the facilities to ensure that they may have been involved in the generation of cancer. In the studies shown here, years of activity was used as a criterion for the inclusion of industries.

d) The exposure time is also very important to determine a causal effect. In the studies shown in this manuscript, where the causal effect is not assessed, the beginning years of the industrial facility activities were taken into account to control this exposure time.

e) The exposure dose (for example, the amount of emission released) has not been taken into account in any of the reviewed studies.

f) In the reviewed studies, many comparisons are made and the probability of false positives increases (positive relationships found that are really not). However, the number of statistically significant excess risks is much higher than the number we would expect to find at random and although there are mathematical methods to control

this problem of multiple comparisons, they have not been developed in the context of the Bayesian models performed.

g) The ecological fallacy is present in the studies that are shown because there is not any information about individual exposure to possible agents that cause the disease.

h) There are some uncontrolled variables (such as pollution from traffic, tobacco, natural radiation, etc.) in the studies that could be confounding the results.

4. Discussion

According to the E-PRTR-IPPC record of substances emitted during the 2007-2010 period in Spain, though there has been a reduction in the emission into air of many carcinogens there is still a high level of carcinogen emissions at sites lying very close to population centroids. However, detailed records of emissions into the air have only been kept during the four years in which reporting to the register has been compulsory, thus only a minimal period of the history of industrial emissions has been taken into account. There is no way of knowing whether the amount of pollutants released in previous years might have been similar to or higher than those for 2007.

The reduction in the emission of many carcinogens reported for Spain, which has also been reported for other countries (Fauser et al., 2013), could be related to the period of economic crisis that Spain experienced during the 2008-2010 period (Fernández-Navarro et al., 2016) where surely many industries had to reduce their productions and consequently, they reduced their emissions. Moreover, as pointed out in the introduction section of this manuscript, some industrial facilities have introduced

technical improvements in their production processes in recent years and thus achieved reductions in their pollutant emissions.

In relation to the spatial distribution of exposure, there were towns exposed to industrial pollution throughout the whole territory, although there is a high level of the IARC Group I-carcinogens emissions in the proximity of several towns in the southwest, east and north of the country. These zones correspond to the most industrialized regions of Spain.

It should be noted that the registration of the amounts reported as having been emitted provides no way of validating the information for each of the installations, though it would seem logical to assume that, at the very least, these would represent the amounts really released. Moreover, although the emissions shown correspond to a very short and very recent period, they nevertheless involve hundreds of tonnes emitted into the air extremely close to population centers. Given their magnitude, these emissions could have important consequences on long-term malignant tumor incidence.

Upon examination of the different exploratory epidemiological studies of our group that have targeted specific industrial sectors or tumors, statistically significant excess mortality were found in populations residing close to emission sources. Certain industrial sectors seem to influence the excess risk detected for different tumor sites, as is the case of mining activity and hazardous waste. This latter sector encompasses heterogeneous subgroups with a great number of different emissions (incinerators, scrap metal + end-of-life vehicles, oil waste, solvents, and physical/chemical treatment). Furthermore, certain types of cancer sites, such as colon-rectum, pleural, ovary,

prostate, and breast, have been associated with residence in the proximity of facilities belonging to different industrial sectors, and more detailed study is thus required. Whereas some of these associations are supported by previous studies (e.g.: stomach cancer and mining (Wang et al., 2011; Weinberg et al., 1985), others are novel (e.g.: kidney cancer and scrap metal + end-of-life vehicles (García-Pérez et al., 2013) or ovarian cancer and fertilizers (García-Pérez et al., 2015a).

Additionally, the presence of excess risks in men and women supports the hypothesis of environmental exposure. In the case of lung cancer, excess risks are found among men, but not among women (mining, combustion, incinerators), which might point towards occupational exposures or an interaction between smoking and industrial air pollution. In this latter respect, most epidemiological studies on air pollution and lung or other cancers have addressed tobacco smoking as a potential confounding factor, which has been controlled for through stratification or modelling (Samet and Cohen, 2006). Some studies provide information on effect modification and, in general, point to the synergy between air pollution and smoking (Samet and Cohen, 1999), with the attributable risk for joint exposure being higher than 30%. Another possibility is that the results for lung cancer in women reflect the rural nature of the exposed towns: the prevalence of smokers in rural settings can be assumed to be lower than that in urban settings, thus giving rise to lower RR values in exposed areas. No data could be obtained on the prevalence of smoking by sex in the towns, which would have allowed us to control for this in the models. In Spain, the women cohorts who initiated smoking are all post-1940 (López-Abente et al., 1995).

In relation to other associations that suggest occupational exposures (found only in men or in women), the excess risk of colorectal cancer mortality found only in men in those municipalities in the proximity of metallurgical facilities is a good example according with the evidence. On the one hand, it has been suspected that exposures deriving from work in the metal industry might possibly be related to tumors of the digestive system (Firth et al., 1999). On the other hand, however, there is evidence to show that exposure to metalworking fluids is associated with colorectal cancer (Calvert et al., 1998).

There is also some evidence indicating a potential environmental exposure (found in men and in women). This is the case for the association found between thyroid gland cancer mortality and underground coal mining facilities, for example. It should be noted that the best-evidenced etiologic factor implicated in thyroid cancer is ionizing radiation. McBride et al. (McBride et al., 1978) examined the uranium and thorium content of fly ash from coal-fired power plants in Tennessee and Alabama (USA). They estimated radiation exposure around the coal plants and compared it with exposure levels around a boiling-water reactor and pressurized-water nuclear power plants. The estimated radiation doses ingested by those living near the coal plants were equal to or higher than doses for those living around the nuclear facilities. This fact may support the idea of a possible association between coal mines and thyroid cancer. In addition, Lope et al. (Lope et al., 2006) found a clear pattern of excess thyroid cancer mortality in the north of Spain, where most of the country's coal mines are located, indicating that environmental factors might provide possible etiologic hypotheses to be kept in mind in future geographic studies.

In ecological cancer mortality studies where proximity of pollutant sources was considered an exposure, statistical associations were found which indicate the aforementioned excess mortality. These studies may display biases deriving from errors of classification of what is deemed to be exposure, and have been the subject of criticism (Cox et al., 2013). Unless the errors of classification of exposure are different for the groups being compared, these types of biases tend to mask the associations by shifting the relative risks towards unity (Copeland et al., 1977). In these kinds of studies, exposure is characterized by the distance of the centroids of population centers to the industrial pollutant sources, and is based on an isotropic model (homogeneous dispersion of pollutants around the source), with the result that neither meteorological variables (e.g., prevailing winds in terms of both direction and intensity) nor topographical variables are taken into account. Similarly, such studies also fail to take the mobility and movements of persons and individual exposures (smoking, diet, and occupation) into account.

Other limitations are related to the impossibility of estimating intensity, duration and variability of exposure. Populations residing in the proximity of pollutant industries could potentially be exposed to large amounts of toxic substances. However, it was not possible to estimate the intensity, duration or even the variability of exposure, due to a lack of knowledge about the dates when emissions began, the annual amounts involved, and the influence of meteorology on the dispersion and spread of pollutants. Moreover, the heterogeneity of the industrial facilities within the same industrial group or other non-industrial sources of carcinogenic pollutants were not taken into account, which are other possible sources of bias.

Due to the methodological shortcomings and limitations mentioned, these studies are considered exploratory and do not allow for causal associations to be established. However, although the magnitude of the effects (RR) shown is not very high and the excess risks tend to go no higher than 50%, the sheer size of the population that is potentially exposed has no possibility of minimizing the associated health impact, and it makes industrial pollution a serious problem.

It should also be noted that mortality rates used in these studies depend on survival, and therefore on advances in medical technology. Moreover, the mechanisms for disparities in cancer survival are multidimensional, and vary according to the type of cancer, the specific health care system involved. These mechanisms may pertain to screening, treatment, diagnostic conditions, access to specialized care, or follow-up modalities, possibly inducing spatial heterogeneities in cancer mortality. In Spain, for example, the 5-year survival rates for Colon and Pleural cancer are 57.1% and 3.3%, respectively (De Angelis et al., 2014; Francisci et al., 2015). Because the Spanish National Health Service ensures equity in access to health care, there is no reason to believe that there would be health care differences which might condition geographical disparities in mortality which would also be related to proximity to pollutant sources (López-Abente et al., 2007).

There were also several study limitations, one of which was the estimation of population exposure to industrial pollution by referencing the distance from town centroids to industrial facilities. We assumed an isotropic model of exposure. This could introduce a problem of misclassification, because real exposure is critically dependent on other variables, such as prevailing winds or geographic landforms. To address these

challenges, there are other methodologies for exposure evaluation (Nieuwenhuijsen et al., 2006). However, because we do not have relevant information for these models like meteorological data, we decided to use the distance for determining exposure.

A further possible bias lies in the use of centroids as coordinates for pinpointing the entire population of a town, when, in reality, the population may be fairly widely dispersed. We assumed that the whole municipal population was exposed to the same type and amount of pollutant substances. Nevertheless, the use of small areas as units reduces the risks of ecologic bias and misclassification stemming from these assumptions (Richardson et al., 2004).

Moreover, a critical decision was assessing only the emissions of industrial facilities into the air that were located in the proximity (less than 5 km) of population centers. This distance of 5 km was the best distance for detecting risks and having enough statistical power in the majority of the studies reviewed in this manuscript. In that way, the description of the emissions at this distance could be a good picture of the industrial pollution assessed in the studies performed.

Another limitation was only considering the emissions released to the air, instead of other routes of pollutant intake like drinking water, diet, or soil. However, we tried to give an overall picture of a more related route, perhaps with the distance used in the definition of exposure assuming isotropic models. On the other hand, because there are other non-industrial sources of carcinogens, exposure does not only depend on the industrial emissions.

Finally, it is important to stress that ecological studies using PRTRs are a useful tool, not only for proposing etiological hypotheses about the risk entailed in living close to industrial pollutant sources which regularly emit toxic substances into the environment, but also for providing data to account for situations of higher mortality in specific areas. Moreover, the limitations inherent in these types of studies may be offset by their viability, due to their low cost and usefulness in environmental epidemiology. It is currently very difficult to obtain individual exposure data in order to study cancer risk in the vicinity of industries, but it is equally true that the use of biomarkers (CDC, 2014) and new individual pollutant monitoring systems (Snyder et al., 2013) are both essential for progressing along this route.

It should be also noted that, apart from the EU, many other countries have PRTRs. Application of a comparative approach in the United States, Canada and Australia shows significant differences in PRTR systems across countries and suggests that the mere presence of a PRTR may not lead to reduced industrial emissions (Kerret and Gray, 2007). Even so, implementation of PRTRs can play an important role in improving the quality of the environment, if the population, investors and consumers recognize the environmental policy pursued by industries and their efforts to protect the environment.

Moreover, the mere presence of a registry with public information is an element of great importance for the control of industrial emissions, a mechanism which, until now, had been lacking in Spain for many highly toxic emissions. Seemingly "the damage is done" but, when one considers the great number of people exposed, a small

reduction in airborne pollutants could have a sizeable effect on the prevention of many cases of cancer and other diseases (Boldo et al., 2014).

5. Conclusions

Characterization of E-PRTR-IPPC reported emissions and the results of epidemiological studies based on registry data suggest that those who reside in towns situated near industrial pollutant sources have a greater risk of cancer mortality than those who live in non-industrialized areas, though it is difficult to separate the effect of industrial emissions from that of other types of exposure. Nevertheless, bearing in mind both that express recognition of the carcinogenicity of environmental pollution which includes industrial pollution and that the amount of carcinogens issued into the air by industries lying very close to population centers is considerable, reduction in pollutant emissions has to be seen as a mandatory goal.

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717 **Figure/table legends**

718

719 Figure 1. Total amount of IARC Group I carcinogen emissions in the proximity of the
720 8,098 Spanish towns by year in the 2007-2010 period.

721
722 Table 1. Emissions to air of carcinogens released by the industrial facilities (2007-2010)
723 in the proximity of towns in Spain (5km). Data expressed in tonnes per year (except for
724 dioxins and furanes which are expressed in Kg).

725

726 Table 2. Mortality relative risks (RR) and confidence intervals (95% CI) /credibility
727 intervals (95% CrI) from several cancers comparing mortality in towns situated at a
728 distance of less than 5 km from installations of different industrial sectors with mortality
729 in more remote municipalities without industries. Only RRs with intervals not including
730 1 in either men, women, or both are shown here.

731

732 Table 3. Mortality relative risks (RR) and credibility intervals (95% CrI) from pleural,
733 colorectal, prostate, breast and ovarian cancers comparing mortality in towns situated at
734 a distance of less than 2 km from installations of different industrial sectors with
735 mortality in more remote municipalities without industries. Only RRs with CrIs not
736 including 1 in either men, women, or both are shown here.

737