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Sci Total Environ. 2010 Jul 15;408(16):3102-12

which has been published in final form at

<https://doi.org/10.1016/j.scitotenv.2010.03.051>

Mortality due to tumours of the digestive system in towns lying in the vicinity of metal production and processing installations

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Abstract

Background: Releases to the environment of pollutants from industrial metal production and processing installations can pose a health problem to humans, owing to the toxic substances that such emissions contain.

Objectives: To investigate whether there might be excess mortality due to tumours of the digestive system among the population residing near Spanish metal production and processing installations included in the European Pollutant Emission Register.

Methods: Ecological study designed to examine mortality due to malignant tumours of the digestive system (oral cavity and pharynx, oesophagus, stomach, pancreas, liver, gallbladder, and colon-rectum) at the municipal level, over the period 1994-2003. Population exposure to pollution was estimated on the basis of distance from town of residence to the pollution source. Using mixed Poisson regression models, we analysed: risk of dying from cancer in a 5-kilometre zone around installations by year of commencement of operations; effect of pollution discharge route (air or water) and type of industrial activity; and risk gradient within a 50-kilometre radius of such installations.

Results: Excess mortality (relative risk, 95% confidence interval) was detected in the vicinity of pre-1990 installations for colorectal cancer (1.05, 1.02-1.08 in men; 1.04, 1.00-1.07 in women) and liver cancer (1.06, 1.00-1.12 in men), with this risk being concentrated in installations that released pollution to air. On stratifying by type of industrial activity, statistically significant associations were also observed between the remaining tumours and certain metal production and processing activities. There was also a gradient effect in the proximity to a number of installations.

Conclusions: The results support the existence of an association between risk of dying due to some tumours of the digestive system and residential proximity to the Spanish metal production and processing installations studied.

Key Words: digestive tumours; metallurgical installations; metalworking fluids; industrial pollution; mortality; focused clustering

Introduction

Residential proximity to industrial point sources of air and water pollution is a potential source of exposure to known or suspected carcinogens. Metal production and processing installations constitute an industrial sector that warrants special attention by reason of its pollutant emissions. Human exposure to metals is common, due to their wide use in industry and long-term environmental persistence. Historically, the heaviest metal exposures occurred in the workplace or in environmental settings situated close to industrial sources (Hayes, 1997). These types of industries, which include non-ferrous and ferrous metal smelters, emit inorganic arsenic and other metals, such as chromium, cadmium, lead and nickel, regarded as known or possible carcinogens. Furthermore, fumes in the iron and steel foundry industry are known to emit other carcinogenic substances, such as polycyclic aromatic hydrocarbons (PAHs) (Humfrey et al., 1996), while chemical exposures in the primary aluminium industry are known to include numerous toxic substances (Benke et al., 1998). In addition, metalworking fluids (MWFs) -a group of chemical substances which epidemiological evidence has shown to be carcinogenic in humans (Savitz, 2003)- are used in installations for surface treatment of metals and plastic materials, as well as to cool and lubricate metalworking processes. It would thus seem altogether appropriate to assess the possible relationship between such installations and the frequency of cancer in their environs. Among the tumours that have been associated with carcinogens emitted by these industries are those of the digestive system (oral cavity and pharynx, oesophagus, stomach, pancreas, liver, gallbladder and colon-rectum) (Clapp et al., 2005; Siemiatycki et al., 2004).

In Spain, tumours of the digestive system represented one third of cancer-related deaths in 2007, with colorectal cancer being the second most frequent site with 13,516 deaths. This same year there were 5,747 deaths due to stomach cancer, 4,976 due to pancreatic cancer, 4,544 due to liver cancer, 2,204 due to oral and pharyngeal cancer, 1,777 due to oesophageal cancer and 1,305 due to gallbladder cancer, in both sexes (Instituto Nacional de Estadística, 2010). These tumour sites share common risk factors, such as tobacco, alcohol (colon-rectum, oral cavity and pharynx, oesophagus,

liver and pancreas), ionising radiation (colon-rectum, oesophagus, stomach, liver and pancreas) and type of diet (colon-rectum, oral cavity and pharynx, stomach and pancreas) (Blot et al., 2006; Clapp et al., 2005; Crew and Neugut, 2006; Giovannucci and Wu, 2006; Hsing et al., 2006; London and McGlynn, 2006; Lowenfels and Maisonneuve, 2006; Mucci and Adami, 2002). Insofar as occupational exposure is concerned, some studies have detected an increased risk of tumours of oesophagus, colon-rectum, stomach and pancreas among workers exposed to MWFs and mineral oils, and particularly among workers involved in grinding operations (Calvert et al., 1998; Mirer, 2003; Tolbert, 1997). There are also studies that have associated: exposure to heavy metals with tumours of stomach, pancreas and liver; exposure to organic solvents with tumours of rectum, oesophagus, stomach, liver and pancreas; and exposure to reactive chemicals with tumours of oral cavity and pharynx, liver and pancreas (Blair and Kazerouni, 1997; Clapp et al., 2005; Landrigan et al., 2000; Lynge et al., 1997; Siemiatycki et al., 2004).

The European Pollutant Emission Register (EPER) (EPER, 2009), a public inventory of industries set up by the European Commission under the terms of Directive 96/61/EC, is a valuable resource for monitoring industrial pollution, and enables the possible association between residential proximity to these pollutant installations and risk of cancer mortality to be studied (Garcia-Perez et al., 2009; Monge-Corella et al., 2008; Ramis et al., 2009). One of the EPER's industrial groups encompasses metal production and processing installations, with data on the pollutants released and the geographical co-ordinates of each installation.

This paper sought to ascertain whether there was excess mortality due to tumours of the digestive system among the population residing in the vicinity of Spanish metal production and processing installations which report their emissions to the EPER.

Materials and methods

An ecological study was designed to examine mortality due to tumours of the digestive system at a municipal level (8073 Spanish towns), over the period 1994-2003. Separate analyses were performed for the overall population and for each sex.

Observed municipal mortality data were drawn from the records of the National Statistics Institute for the study period, and corresponded to deaths coded as: malignant neoplasm of lip, oral cavity, and pharynx – codes 140-149 (International Classification of Diseases/ICD-9) and C00-C14 (ICD-10); malignant neoplasm of oesophagus – codes 150 (ICD-9) and C15 (ICD-10); malignant neoplasm of stomach – codes 151 (ICD-9) and C16 (ICD-10); malignant neoplasm of pancreas – codes 157 (ICD-9) and C25 (ICD-10); malignant neoplasm of liver and intrahepatic bile ducts – codes 155 (ICD-9) and C22 (ICD-10); malignant neoplasm of gallbladder and extrahepatic bile ducts – codes 156 (ICD-9) and C23-C24 (ICD-10); and malignant neoplasm of colon, rectum, and anus – codes 153-154,159.0 (ICD-9) and C18-C21, C26.0 (ICD-10). Expected cases were calculated by multiplying the specific rates for Spain as a whole, broken down by age group (18 groups), sex, and five-year period (1994-1998, 1999-2003), by the person-years for each town, broken down for the same strata. For calculation of person-years, the two five-years periods were considered, with data corresponding to the 1996 municipal roll and 2001 census being taken as the estimator of the population.

Population exposure to industrial pollution was estimated by reference to the distance from the centroid of town of residence to the industrial facility. Data on industries were obtained from the EPER-Spain (Ministerio de Medio Ambiente y Medio Rural y Marino, 2007). We selected the 118 Integrated Pollution Prevention and Control (IPPC) category-2 metal production and processing installations that reported their releases to air and water in 2001, along with the previously validated geographic coordinates of their respective locations. These installations included: production of pig iron or steel (17 installations) – category 2.2; hot-rolling mills (steel) (5 installations) – category 2.3.a; galvanizing (3 installations) – category 2.3.c; ferrous metal foundries (18 installations) – category 2.4; production

of non-ferrous crude metals (7 installations) – category 2.5.a; smelting of non-ferrous metals (19 installations) – category 2.5.b; and surface treatment of metals and plastic materials using an electrolytic or chemical process (49 installations) – category 2.6. Data on date of commencement of industrial activity were obtained from official websites of the metal industries.

In a first phase, we conducted an initial exploratory "near vs. far" analysis to estimate the relative risks (RRs) of towns situated at a distance of less than 5 kilometres from metal production and processing installations. The exposure variable was coded as a "dummy" with the following three levels:

- 1) exposed group ("near"), i.e., towns having their municipal centroid at a distance ≤ 5 km from a metal production and processing installation;
- 2) intermediate group, i.e., towns at a distance ≤ 5 km from any industrial installation other than production and processing of metals; and,
- 3) unexposed group ("far"), i.e., towns having no EPER-registered industry within 5 km of their municipal centroid (reference level).

RRs and their 95% confidence intervals (95% CIs) were estimated on the basis of a Poisson regression model (Breslow and Day, 1987), using expected cases as offset for the total population, men, and women, and the Spanish rates as reference. Estimations were adjusted for the following standardised socio-demographic indicators, chosen for their availability at a municipal level: population size; percentage of illiteracy, farmers and unemployed; average persons per household according to the 1991 census; and, mean income as a measure of income level (Ayuso Orejana et al., 1993). In addition, mixed models were fitted (Gelman and Hill, 2007), including province as a random effects term, to enable geographic variability to be taken into account and unexposed towns belonging to the same geographic setting to be considered as the reference level, something that is justified by the geographic differences observed in mortality attributable to these tumours (Lopez-Abente et al., 2006).

In order to take the minimum tumour latency periods into account, the analysis was replicated, by confining the above model to the 105 industries that entered into operation prior to 1990. Furthermore, separate analyses were performed for industries that had released some type of pollutant to air (61 installations) and for those that had released pollutants solely to water (44 installations). Similarly, in order to stratify the risk by type of industrial activity, we created a variable of interest coded as a "dummy" with various levels:

- 1) group 1, i.e., towns lying at ≤ 5 km from more than one IPPC category-2 metal installation (multiple pollution sources);
- 2) group 2, i.e., towns lying at ≤ 5 km from a single IPPC category-2.2 or -2.3.a metal installation (steel production and hot-rolling mills);
- 3) group 3, i.e., towns lying at ≤ 5 km from a single IPPC category-2.3.c metal installation (galvanizing);
- 4) group 4, i.e., towns lying at ≤ 5 km from a single IPPC category-2.4 metal installation (ferrous metal smelters);
- 5) group 5, i.e., towns lying at ≤ 5 km from a single IPPC category-2.5.a or -2.5.b metal installation (non-ferrous metal smelters and producers);
- 6) group 6, i.e., towns lying at ≤ 5 km from a single IPPC category-2.6 metal installation (surface treatment using an electrolytic or chemical process);
- 7) intermediate group, i.e., towns lying at ≤ 5 km from any industry other than metal production and processing; and,
- 8) unexposed group, i.e., towns having no EPER-registered industry within a radius of 5 km from the centroid (reference level).

Finally, in view of that fact that the characteristics of the respective metal installations vary (years of operation, type and amount of emissions), a "near vs. far" analysis was performed in the case of towns belonging to groups 2-6 ("individual" metal pollution sources) with each installation that

commenced operations prior to 1990 being analysed individually (38 installations). Moreover, the analysis was confined to an area of 50 km surrounding each complex, so as to have a local comparison group. To take into account the problem of multiple comparisons, p-values were also suitably adjusted by controlling for the expected proportion of false positives (False Discovery Rate), using the method proposed by Benjamini (Benjamini and Hochberg, 1995; Benjamini and Yekutieli, 2001). The risk gradient in the vicinity of each facility was likewise studied, with distance from town to installation as an explanatory variable, categorised in concentric rings (0-5, 5-10, 10-20 and 20-30 km; and 30-50 km as reference). This was included in all models as both a categorical and a continuous variable, thereby making it possible for: the effect of the respective distances to be estimated by the former; the existence of radial effects to be ascertained by the latter (rise in RR with increasing proximity to an installation); and, by applying the likelihood ratio test, the statistical significance of such distance-related effects to be computed. RR estimates were adjusted for the above-mentioned socio-demographic variables, and towns that had some EPER-registered industry other than production and processing of metals within a radius of 5 km of the municipal centroid were excluded.

Results

From 1994 to 2003 there were 113,512 deaths in Spain due to colorectal cancer, 62,185 due to stomach cancer, 38,227 due to pancreatic cancer, 23,251 due to liver cancer, 21,875 due to oral and pharyngeal cancer, 17,823 due to oesophageal cancer and 13,865 due to gallbladder cancer, in both sexes.

Table 1 shows the RRs and their 95% CIs for towns with metal production and processing installations at a distance of less than 5 km, estimated by Poisson mixed regression models for the seven tumours under study. As can be seen, the "near vs. far" analysis covering all metal installations and those that commenced operations prior to 1990 showed a slight statistically significant excess

risk of dying due to liver and colorectal cancer in towns in the vicinity of these installations, both overall and for males (in the case of colorectal cancer there was also a significant excess risk for women). When this risk was stratified by pollution discharge route (air or only water), in liver cancer the significant excess risk was concentrated exclusively in installations that released some type of pollutant to air, whereas in colorectal cancer the statistically significant excess risk appeared in both types of installations, for the overall population and males alike, but was nevertheless greater in installations with releases to air. It should also be noted that, in the case of women, there was a significant excess risk of both tumours associated with this latter type of installation.

Table 2 shows the RRs of towns lying at less than 5 km from pre-1990 metal production and processing installations that released pollution to air, by type of industrial activity, for the seven tumours under study. In cancer of oral cavity and pharynx, a statistically significant excess risk was observed for women in towns exposed to multiple pollution sources. In oesophageal cancer, the highest RR (1.81) was found among women in towns lying close to ferrous metal foundries. Insofar as tumours of stomach and pancreas were concerned, the significant excess risk was concentrated in the surroundings of installations for surface treatment using an electrolytic or chemical process, among males and the overall population respectively. For liver cancer, which already registered a statistically significant excess risk in the analysis shown in Table 1, the risk was concentrated in the environs of galvanizing installations and non-ferrous metal producers and smelters, among men and women alike. Gallbladder cancer displayed a significant excess risk for males in towns lying in the vicinity of installations for surface treatment. Lastly, for colorectal cancer there was a significant excess risk in both sexes in the vicinity of almost all types of industrial activities studied, with the single exception of the ferrous metal group. The sex-specific analysis showed that, among men, the excess was concentrated in the surroundings of galvanizing, non-ferrous metals and surface treatment installations, whilst among women this was found in the vicinity of steel, non-ferrous metal and surface treatment installations.

With regard to metal production and processing installations that released pollution solely to water (data not shown), there was an elevated, statistically significant excess risk (3.81) for cancer of oral cavity and pharynx among women in towns lying in the vicinity of ferrous metal installations, though with only 3 cases observed. Attention should be drawn to the fact that among males, liver cancer displayed an RR of 1.59 in towns neighbouring galvanizing complexes, and gallbladder cancer displayed an RR of 2.10 for non-ferrous metal installations. In the case of colorectal cancer, a significant excess risk was observed in the environs of multiple pollution sources (1.09) for men, and in the environs of ferrous metal (1.80) and non-ferrous metal installations (1.35) for women.

Table 3 shows the RRs for the environs of "individual" metal pollution sources that commenced industrial activity prior to 1990, and for ever-decreasing radiuses within a 50-kilometre area surrounding each complex. The data are shown for complexes which yielded statistically significant results in the "near vs. far" and/or risk gradient analyses, for one or more of the tumours studied. Of the 26 installations shown in the table, a total of 8 (the geographical locations of which are depicted in Figure 1) registered significant results for two or more tumours. In general, excess risks and significant test for trend appeared in both men and women.

The analyses in the above table were performed separately for each of the pre-1990 installations (both "individual" and multiple pollution sources), as were the corrections using multiple comparisons (see Supplementary Material).

Figure 2 depicts the geographical location of those metal production and processing installations in Table 3 which registered significant results for a single tumour.

Discussion

Our results indicate a slight excess risk of dying from liver cancer among men, and from colorectal cancer in both sexes, in the vicinity of Spanish metal production and processing installations, regardless of whether these are studied jointly or after eliminating the most recent

installations, the possible influence of which is arguable bearing in mind the minimal latency periods of solid tumours. Moreover, on stratifying the risk by pollution discharge route and type of industrial activity, associations were observed between the remaining tumours studied and residential proximity to certain types of installations, namely:

- a) between "installations for surface treatment using an electrolytic or chemical process" which release pollution to air, and tumours of stomach (men), pancreas (total population), gallbladder (men) and colon-rectum (both sexes);
- b) between "non-ferrous metal production and smelting installations" that release pollution to air and tumours of liver and colon-rectum (both sexes), and between those that release pollution to water only and tumours of gallbladder (men) and colon-rectum (women);
- c) between "galvanizing installations" that release pollution to air and tumours of liver (both sexes) and colon-rectum (men), and between those that release pollution to water only and liver cancer (men);
- d) between "ferrous metal smelting installations" that release pollution to air and oesophageal cancer (women), and between those that release pollution to water only and colorectal cancer (women); and,
- e) between "hot-rolling steel mills" that release pollution to air and colorectal cancer (women).

It is important to mention here that, in the individualised analysis, there were quite a few industries that registered statistically significant results in both sexes, in the "near vs. far" and risk gradient analyses, for one or more of the seven tumours studied, and for those of the colon-rectum, stomach and liver in particular.

A further noteworthy aspect of the results is the fact that, in tumours of liver and colon-rectum, significant excess risks affected both sexes, which might be indicative of a pathway of environmental exposure. In tumours of stomach and gallbladder, however, the significant results solely affected men, thus being indicative of a possible occupational-exposure pathway. Owing to a lack of data, we were unable to control for occupational exposures that might account for this difference between men and

women. Lastly, it should also be noted that, for oesophageal cancer, the highest excess risks were exclusively in evidence for women.

Despite suffering from some limitations, the hypothesis that some excess cancer mortality may, in part, be due to pollutant emissions of industrial origin has gathered strength in recent years. Specifically, a series of studies has been published reinforcing the idea of a possible association between residential proximity to industrial complexes and an increased risk of various tumours, such as those of lung, larynx, bladder, non-Hodgkin's lymphoma, prostate and colon-rectum (Casella et al., 2005; Garcia-Perez et al., 2009; Parodi et al., 2005; Ramis et al., 2009; Tsai et al., 2009; Viel et al., 2008). Although occupational studies serve to formulate hypotheses and guide research into many carcinogenic risk factors (Firth et al., 1999; Rotimi et al., 1993; Sim et al., 2009), the association between industrial emissions and digestive tumours in the population can be studied via other types of designs, such as the one described in this study. One advantage of the design chosen is its high power, owing to the inclusion of a greater number of subjects. Another advantage lies in the fact that the analysis can be repeated in future for the purpose of monitoring and controlling for the effects of environmental pollution on health.

This study likewise has some limitations. Working with small areas means that the data display great random variability, an aspect that could affect women in the results obtained for some tumour sites, though the small study area reduces any possible ecological bias associated with the nature of the study *per se*.

In an attempt to reduce possible biases deriving from confounding variables not included in the study, mixed models were fitted with "province" as the random effects term, something that constitutes a more conservative option. Another point to be borne in mind is that some installations for which significant excess risks were observed, are situated in areas with numerous industries releasing pollution into the environment. This is why risk was stratified by type of industrial activity and a distinction drawn between "multiple and individual metal pollution sources", with in-depth analysis

of the installations belonging to this latter group, in which towns are exposed to a single metal-sector pollution source.

This study uses distance to the pollution source as a proxy of exposure, assuming an isotropic model, something that could introduce a problem of misclassification, since real exposure is critically dependent on prevailing winds, geographical landforms and releases into aquifers. A further possible bias in the allocation of exposure is the use of centroids as co-ordinates to pinpoint the entire population of a town, when, in reality, the population may be fairly widely dispersed. Nevertheless, these problems would be posed in all cases, limiting the capacity to find positive results but not invalidating the associations found.

Another critical decision when analysing the risk of towns situated "near" pollution sources is the choice of radius. The choice of 5 km around metal production and processing installations is in line with the characteristics of such plants, many of which extend over large surface areas and release discharges to the local water, with the pollution so emitted achieving a wide radius of spread.

Although the industries analysed in this study reported pollution data in 2001, the date of commencement of their industrial activity was nevertheless taken into account for analytical purposes: the great majority began operations prior to the 1960s, so that the surrounding populations could have been exposed to their emissions for long periods of time, a fact that is coherent with the latency periods described for solid tumours.

Of all the industrial groups registered in the EPER-Spain, metal production and processing installations are the principal emitters to air of cadmium, hydrogen cyanide, CO, chromium, copper, lead, perfluorocarbons, tetrachloroethylene and zinc, and the principal emitters to water of benzene, toluene, ethylbenzene, xylenes, cyanides, dichloromethane, phenols, fluorides, PAHs and nickel.

The presence of metal production and processing installations, which encompass several types of industrial activities, arouses social alarm due to the health problems that may be generated in their workers and environs, and the financial consequences stemming from a possible administrative intervention. According to the International Agency for Research on Cancer (IARC),

exposure circumstances such as aluminium production and iron and steel founding are recognised as carcinogenic to humans, as are a number of substances released by such installations, including arsenic, benzene, cadmium, chromium, dioxins, asbestos, formaldehyde, radon, silica, crystalline, soots, coal-tar pitches and some PAHs. Other substances are either: probable carcinogens, such as tetrachloroethylene, trichloroethylene, acrylamide and nitrosamines; or possible carcinogens, such as lead, nickel, furans, ethylbenzene, hexachloroethane and welding fumes (IARC, 2009; Tossavainen, 1990). Additionally, chemical exposures entailed in the alumina and primary aluminium industry include many toxic substances, such as diesel fumes, solvents, oils, sulphur dioxide, copper dust and silica dust (Benke et al., 1998). Moreover, installations for surface treatment of metals and plastic materials (many of which belong to the automobile sector) use MWFs, a range of oils and other chemical substances, which are used to cool and/or lubricate metal workpieces when they are being machined, ground, milled, etc., and are known to be carcinogens in humans (Savitz, 2003). There is substantial evidence to show that some MWFs have been associated with increased risk of certain cancers, including tumours of the digestive system. Although measures have been taken in recent decades to reduce these exposures in the occupational sphere, e.g., removal of PAHs from MWFs began in the 1950s, and U.S. Environmental Protection Agency (US-EPA) regulations in the 1980s were directed at reducing nitrosamine exposures, there is nonetheless insufficient data to conclude that these changes will have eliminated all carcinogenic risks (DHHS (NIOSH), 1998). Lastly, it should be stressed that effluents from the metals industries are genotoxic: they induce cytogenetic damage, mutations, and DNA damage in repair processes (Houk, 1992).

A number of studies have associated residential proximity to metal production and processing installations with lung cancer (Brown et al., 1984; Pershagen, 1985; Smith et al., 1987). In the case of tumours of the digestive system, Casella observed an association between municipal proximity to a steel production plant and excess risk of colorectal and bowel cancer in women (Casella et al., 2005). Furthermore, some studies have reported statistically significant excess risks in metal industry workers, due to tumours of stomach (Rockette and Arena, 1983; Rotimi et al., 1993; Sim et al., 2009),

pancreas (Rockette and Arena, 1983; Rotimi et al., 1993), liver (Adzersen et al., 2003) and oesophagus (Firth et al., 1999). Firth also detected a significant excess mortality when he studied all the tumours of the digestive system as a whole (Firth et al., 1999). Insofar as occupational exposure to MWFs is concerned, a number of studies have linked this to tumours of the digestive system, particularly those of pancreas, rectum and stomach (Bardin et al., 1997; Calvert et al., 1998; Malloy et al., 2007; Mirer, 2003).

One of the most interesting results of our study is the excess mortality due to tumours of liver and colon-rectum in the vicinity of galvanizing installations. The galvanizing sector is one of the industrial activities that releases dioxins to air (ATEG-Grupo Interlab, 2005) and is included in the Spanish National Dioxin and Furane Inventory (Martinez et al., 2008). Dioxins are recognised by the IARC as carcinogens in humans (IARC, 2009) and there are studies that have observed increased risks for all cancers combined, and for digestive system cancers in particular (IARC, 1997). Furthermore, human exposure to dioxins due to industrial or accidental exposure has been associated with alterations in liver enzyme levels in children and adults (IARC, 1997).

Another of the most noteworthy results is the excess mortality due to tumours of liver, gallbladder and colon-rectum found in the vicinity of non-ferrous metal production and smelting installations. One of the principal environmental challenges facing these types of installations, especially facilities producing copper, aluminium, lead, zinc, cadmium and alkaline metals, is the treatment and elimination of dioxins which are generated by the presence of small amounts of chlorine in secondary raw materials (Integrated Pollution Prevention and Control (IPPC), 2001). As mentioned above, these substances are carcinogens linked to tumours of the digestive system and could be related to the excess risk observed in our study. Finally, the point must be made that non-ferrous metals smelting installations release arsenic to air, a known carcinogen for liver cancer (Clapp et al., 2005).

In brief, it can be said that industrial emissions from metal production and processing installations comprise a complex mix of carcinogens and toxic substances released to air and water.

It is highly likely that chemical substances released to water pass into the soil and water catchment areas, and thence into the human food chain, where they cause damage to the digestive organs. With regard to substances released to air, on the one hand the population would be directly exposed to the polluted air, and on the other, the heavy metals would be deposited in plants, soil and water, and would then pass into the trophic chain affecting the population.

The fact that EPER data are available to the public means that emissions from these types of installations can be ascertained. Unfortunately, there are no data on the amounts of hazardous waste (such as MWFs and mineral oils) discharged by these industrial complexes, though the updating of the EPER in the form of the new European Pollutant Release and Transfer Register (E-PRTR) at the end of 2009 will provide a valuable tool for gathering information on this type of toxic waste.

Conclusion

The results of this study show: an association between residential proximity to metal production and processing installations as a whole and excess risk of mortality due to tumours of liver and colon-rectum; and an excess risk in the remaining tumours of the digestive system associated with certain types of industrial activity. Furthermore, in the environs of a number of "individual" pollution sources, excess risks were observed in the "near vs. far" analysis, along with statistically significant risk gradients. The ecological nature of the study may hinder interpretation of the results of association in terms of cause and effect.

At present, the study of cancer mortality in areas surrounding industrial pollution sources is beginning to assume growing importance, and industrial pollutant emission registers such as the EPER and E-PRTR afford a very useful tool for the surveillance and monitoring of the possible effects of industrial pollution on the health of the population.

Acknowledgements



This study was funded by a grant from Spain's Health Research Fund (*Fondo de Investigación Sanitaria - FIS 040041*) and formed part of the MEDEA project (*Mortalidad en áreas pequeñas Españolas y Desigualdades socio-Económicas y Ambientales – Mortality in small Spanish areas and socio-economic and environmental inequalities*).

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Figure legends

Figure 1: Geographical location of "individual" metal production and processing installations which commenced operations prior to 1990 and displayed statistically significant excess mortality in the "near vs. far" analysis and/or significant test for trend in the risk gradient analysis, for two or more tumours specified in the headline of each map.

Figure 2: Geographical location of "individual" metal production and processing installations which commenced operations prior to 1990 and displayed statistically significant excess mortality in the "near vs. far" analysis and/or significant test for trend in the risk gradient analysis, for a single tumour.