Ovarian cancer mortality and industrial pollution

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Abbreviations:

EDCs: Endocrine disrupting chemicals

IPPC: Integrated Pollution Prevention and Control

E-PRTR: European Pollutant Release and Transfer Register

NSI: National Statistics Institute

RRs: Relative risks

IARC: International Agency for Research on Cancer

WHO: World Health Organization

UNEP: United Nations Environment Programme

PACs: Polycyclic aromatic chemicals

Non-HPCs: Non-halogenated phenolic chemicals

POPs: Persistent organic pollutants

95% CrIs/CIs: 95% credible/confidence intervals

BYM: Besag, York and Mollié

SMRs: Standardized Mortality Ratios

INLAs: Integrated nested Laplace approximations

DIC: Deviance information criterion

PM_{10}: Particulate matter

PAHs: Polycyclic aromatic hydrocarbons

Abstract

We investigated whether there might be excess ovarian cancer mortality among women residing near Spanish industries, according to different categories of industrial groups and toxic substances. An ecologic study was designed to examine ovarian cancer mortality at a municipal level (period 1997-2006). Population exposure to pollution was estimated by means of distance from town to facility. Using Poisson regression models, we assessed the relative risk of dying from ovarian cancer in zones around installations, and analyzed the effect of industrial groups and pollutant substances. Excess ovarian cancer mortality was detected in the vicinity of all sectors combined, and, principally, near refineries, fertilizers plants, glass production, paper production, food/beverage sector, waste treatment plants, pharmaceutical industry and ceramic. Insofar as substances were concerned, statistically significant associations were observed for installations releasing metals and polycyclic aromatic chemicals. These results support that residing near industries could be a risk factor for ovarian cancer mortality.

Capsule abstract:

Our results support that residing in the vicinity of pollutant industries could be a risk factor for ovarian cancer mortality.

1. Introduction

In 2012, ovarian cancer was the seventh leading tumor, in terms of new cases and deaths, in women worldwide, and the highest mortality rates were registered in the more developed regions, as Europe and Northern America (IARC, 2015). In Spain, there were 2050 ovarian cancer deaths in 2012 accounting to 5% of all cancer-related deaths in women (Carlos III Institute of Health, 2015). According to EUROCARE-5 (EUROpean CAncer REgistry based study on survival and care of cancer patients) project, relative survival in Spain at five years of diagnosis is 36.8%, figure similar to the European average (De Angelis et al., 2014; Istituto Superiore di Sanità, 2015).

Insofar as the etiology of this cancer is concerned, well-established risk factors are age, family history of ovarian cancer, and infertility, whereas increasing parity, oral contraceptive use, hysterectomy or tubal ligation decrease risk (Hankinson and Danforth, 2006; Lukanova and Kaaks, 2005). Other known environmental exposures include ionizing radiation and asbestos (Hankinson and Danforth, 2006). Lastly, limited evidence exists linking ovarian cancer with pesticides, primarily from women reporting personal use of the herbicide atrazine (Clapp et al., 2005; Dich et al., 1997).

Despite ovarian cancer is primarily a disease of the industrialized world (Mattison and Thorgeirsson, 1978) few factors associated with the industrial processes that contribute to its etiology have been identified (Schwartz and Sahmoun, 2014). Some occupational studies have found associations between women working in graphics and printing industries and increased risks of ovarian cancer (Shen et al., 1998). However, there are no epidemiologic studies that have analyzed the risk of ovarian cancer in populations near industrial plants. Many types of industries release known or suspected carcinogens (Garcia-Perez et al., 2007; Samet and Cohen, 2006), as well as endocrine disrupting chemicals (EDCs), substances that alter functions of the endocrine system and are related with the increase in incidence of ovarian cancer. Accordingly, it would seem necessary to assess the relationship between facilities that release these types of toxic emissions and the frequency of ovarian cancer in their environs.

In this context, the aims of this study were to: (1) assess possible excess mortality due to ovarian cancer among the Spanish women residing in the environs of industrial installations included in the Integrated Pollution Prevention and Control (IPPC) Register and the European Pollutant Release and Transfer Register (E-PRTR); and, (2) analyze this risk according to the different categories of: a) industrial groups, b) installations releasing carcinogenic substances; and, c) installations releasing EDCs.

2. Materials and methods

We designed an ecologic study to evaluate the association between ovarian cancer mortality and proximity to industrial installations at a municipal level (8,098 Spanish towns), over the period 1997-2006.

2.1 Mortality data

Observed municipal mortality data were drawn from the records of the National Statistics Institute (NSI) for the study period, and corresponded to deaths coded as malignant neoplasm of ovary and other uterine adnexa, codes 183 (International Classification of Diseases-9th/ICD-9) and C56, C57(ICD-10). Expected cases were calculated by taking the specific rates for Spain as a whole, broken down by age group (18 groups: 0-4, …, 80-84 years, and 85 years and over) and five-year period (1997-2001, 2002-2006), and multiplying these by the person-years for each town, broken down by the same strata. Person-years for each quinquennium were calculated by multiplying the respective populations by 5 (with data corresponding to 1999 and 2004 being taken as the estimator of the population at the midpoint of the study period).

2.2 Industrial pollution exposure data

Women exposure to industrial pollution was estimated by taking the distance from the centroid of town of residence to the industrial facility. In Spain, municipal centroids are computed by taking only the inhabited area of the designated town into account, and are situated in the center of the most populous zone where the town hall and the main church tend to be located. We used the industrial database (industries governed by IPPC and facilities pertaining to industrial activities not subject to IPPC but included in the E-PRTR) provided by the Spanish Ministry for Agriculture, Food & Environment in 2009. Bearing in mind the minimum induction period for ovarian cancer, generally 10 years (UNSCEAR, 2006), we selected the 1970 installations which released emissions into air, water, land, or generated toxic waste in 2009, and came into operation prior to 1993 (10 years before the mid-year of the study period). Therefore, the facilities were still running to date 2009, i.e., at least, they have worked 17 years. The year of commencement of the respective industrial activities was provided by the industries themselves.

In order to document the location and characteristics of the facilities, Supplementary Data, Figures S1 and S2 show the geographic distribution of the 1970 installations studied, by industrial group, and the distribution of the years of commencement of operations, by industrial group, respectively. The men year of commencement of operations for industries as a whole was 1964.

Each of the installations was classified into one of the categories of industrial groups listed in Supplementary Data, Table S1. These groups were formed on the basis of the similarity of their pollutant emission patterns.

Owing to the presence of errors in the initial location of industries, the geographic coordinates of the industrial locations recorded in the IPPC+E-PRTR 2009 database were previously validated: every single address was thoroughly checked using Google Earth, the Spanish Agricultural Plots Geographic Information System (Spanish Ministry of Agriculture and Food and Environment, 2015),

the "Yellow pages" web page, and the web pages of the industries themselves, to ensure that location of the industrial facility was exactly where it should be.

2.3 Statistical analysis

Four types of analysis were performed to assess possible excess ovarian cancer mortality in towns lying near ("near") versus those lying far ("far") from pollutant industries, known as a "near vs. far" analysis. In all cases, several distances of 2, 3, 4 and 5 km were taken as the area of proximity ("exposure") to industrial installations:

1) in a first phase, we conducted a "near vs. far" analysis to estimate the relative risks (RRs) of towns situated at each one of the above-defined distances from industries as a whole (all sectors). The variable, "exposure", was coded as: a) exposed or proximity area ("near"): towns at ≤2, 3, 4 and 5 km from any facility; and, b) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group);

2) in a second analysis, we analyzed the risk according to the different categories of industrial groups defined in Supplementary Data, Table S1. To this end, we created a variable of "exposure" for each industrial group in which the exposed area was stratified into the following levels: a) exposed or proximity area ("near"): towns at ≤2, 3, 4 and 5 km from any installation belonging to the industrial group in question; b) intermediate area: towns lying at the above-defined distances from any industrial installation other than the group analyzed; and, c) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group);

3) in the third analysis, we assessed the relationship between ovarian mortality cancer and municipal proximity to industries releasing substances classified by the International Agency

for Research on Cancer (IARC) as carcinogenic (Group 1), probably carcinogenic (Group 2A) and possibly carcinogenic (Group 2B) to humans. To this purpose, we created a variable of "exposure" for each carcinogenic group in which the exposed area was stratified into the following levels: a) exposed or proximity area ("near"): towns at ≤ 2, 3, 4 and 5 km from any installation releasing pollutants including into the carcinogenic group in question; b) intermediate area: towns lying at the above-defined distances from any industrial installation other than the carcinogenic group analyzed; and, c) unexposed area ("far"): towns having no (IPPC+E-PRTR)-registered industry within each one of the above-defined distances of their municipal centroid (reference group); and,

4) lastly, we assessed the relationship between ovarian mortality cancer and municipal proximity to industries releasing EDCs classified into one of the following 8 categories defined by the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) (WHO/UNEP, 2015): a) "*Metals*": metals and organometallic chemicals; b) "*Pesticides*": current-use pesticides, including herbicides, insecticides and fungicides; c) "*PACs*": polycyclic aromatic chemicals; d) "*Non-HPCs*": non-halogenated phenolic chemicals; e) "*Plasticizers*": plasticizers and other additives in materials and goods; f) "*POPs*": persistent organic pollutants not included in any of the above sections; g) "*Other persistent*": other persistent and bioaccumulative chemicals; and, h) "*Other solvents*": other solvents not included in any of the above sections. To this end, we created a variable of "exposure" for each category of EDCs, analogous to the third analysis.

For all the above analyses, we used two statistical approaches based on log-linear models to estimate the RRs and their 95% credible/confidence intervals (95% CrIs/CIs), assuming that the number of deaths per stratum followed a Poisson distribution:

a) a Bayesian conditional autoregressive model proposed by Besag, York and Mollié (BYM) (Besag et al., 1991), with explanatory variables:

$O_i \sim Poisson\ (\mu_i)$, with $\mu_i = E_i\lambda_i$

$$\log(\lambda_i) = \alpha Expos_i + \sum_j \beta_j Soc_{ij} + h_i + b_i \Rightarrow \log(\mu_i)$$

$$= \log(E_i) + \alpha Expos_i + \sum_j \beta_j Soc_{ij} + h_i + b_i$$

$$Soc_{ij} = ps_i + ill_i + far_i + unem_i + pph_i + inc_i$$

$$i = 1, \dots, 8098\ towns, \quad j = 1, \dots, 6\ potential\ confounders$$

$h_i \sim Normal(\theta, \tau_h)$

$b_i \sim Car.Normal(\eta_i, \tau_b)$

$\tau_h \sim Gamma(1, 0.01)$

$\tau_b \sim Gamma(1, 0.001)$

b) a mixed Poisson regression model (Gelman and Hill, 2007):

$O_i \sim Poisson\ (\mu_i)$, with $\mu_i = E_i\lambda_i$

$$\log(\lambda_i) = \alpha Expos_i + \sum_j \beta_j Soc_{ij} + p_i \Rightarrow \log(\mu_i) = \log(E_i) + \alpha Expos_i + \sum_j \beta_j Soc_{ij} + p_i$$

$$Soc_{ij} = ps_i + ill_i + far_i + unem_i + pph_i + inc_i$$

$$i = 1, \dots, 8098\ towns, \quad j = 1, \dots, 6\ potential\ confounders$$

with λ_i being the RR in town i, the number of observed deaths in town i (O_i) being the dependent variable, and the number of expected deaths in town i (E_i) being the offset, in both cases. All estimates for the variable of "exposure" ($Expos_i$) were adjusted for the following standardized, sociodemographic indicators (Soc_{ij}), chosen as potential confounders directly from the 1991 census for their availability at a municipal level, potential explanatory ability vis-à-vis ovarian cancer mortality

pattern (Lope et al., 2008) and because they have proven to be useful in other studies (Alavanja et al., 2005; Awadalla et al., 2007; Bristow et al., 2015; Garcia-Perez et al., 2013; Halbert et al., 2005; Shirley et al., 2014): population size (ps_i); percentage of illiteracy (ill_i), farmers (far_i) and unemployed ($unem_i$); average persons per household (pph_i); and mean income (inc_i) by the Spanish Market Yearbook, as a measure of income level (Ayuso Orejana et al., 1993). The variable of "exposure" and potential confounding covariates were fixed-effects terms in the models.

To enable the positive spatial autocorrelation problem to be assessed (which occurs when a set of spatial features and their associated data values tend to be clustered together in space), this was estimated by applying Moran's I statistic to the Standardized Mortality Ratios (SMRs) at a municipal level (Bivand et al., 2008). The BYM Bayesian autoregressive model takes this problem into account, thanks to the inclusion of two random effects components, namely: a spatial term containing municipal contiguities (b_i); and the municipal heterogeneity term (h_i). Integrated nested Laplace approximations (INLAs) (Rue et al., 2009) were used as a tool for Bayesian inference. For this purpose, we used R-INLA (The R-INLA project, 2015), with the option of "Laplace" estimation of the parameters. A total of 8098 towns were included, and the spatial data on municipal contiguities were obtained by processing the official NSI maps.

Furthermore, the mixed Poisson regression model includes province as a random effects term (p_i), to enable geographic variability and extra-Poisson dispersion to be taken into account and unexposed towns belonging to the same province to be considered as the reference group in each case, something that is justified by the geographic differences observed in mortality attributable to ovarian cancer in Spain (Lope et al., 2008).

Additionally, we used the deviance information criterion (DIC) to assess the goodness of fit of the statistical models (Ando, 2007).

Finally, we performed an additional analysis to assess the risk gradient in the vicinity of installations, described in detail in Supplementary Data, Appendix A.

3. Results

From 1997 to 2006 there were 18046 deaths due to ovarian cancer in Spain. Table 1 shows the RRs and 95%CrIs/CIs for ovarian cancer in towns near pollutant industries, by industrial group, estimated using BYM and Poisson mixed regression models. Firstly, it is important to emphasize that the estimations yielded by both models are practically identical in all distances analyzed. Moreover, DICs were very similar in both BYM and Poisson mixed models (data not shown), and thus the use of either of the two models is justified. On the other hand, spatial autocorrelation in the distribution of ovarian cancer mortality was not detected (Moran's I test statistic=0.00180327, p-value=0.8134).

For all sectors combined, statistically significant excess risks were observed for the BYM model in distances of 5 km (RR=1.07), 4 km (RR=1.06) and 3 km (RR=1.05). Insofar as the specific industrial groups were concerned, attention should be drawn to the significant excess risks found for the following (BYM model): 'Refineries and coke ovens' (RRs=1.20 in 5 km, 1.22 in 4 km, and 1.30 in 3 km), 'Fertilizers' (RRs=1.17 in 5 km, 1.16 in 4 km, 1.24 in 3 km, and 1.22 in 2 km), 'Glass and mineral fibers (RR=1.15 in 5 km), 'Paper and wood production' (RRs=1.12 in 5 km, and 1.12 in 4 km), 'Disposal or recycling animal waste' (RR=1.12 in 5 km), 'Food and beverage sector' (RRs=1.10 in 5 km, and 1.07 in 4 km), 'Urban waste-water treatment plants' (RRs=1.09 in 4 km, and 1.10 in 3 km), 'Hazardous waste' (RR=1.10 in 5 km), 'Pharmaceutical products' (RR=1.10 in 5 km), 'Ceramic' (RRs=1.08 in 5 km, and 1.10 in 4 km), 'Organic chemical industry' (RRs=1.08 in 5 km, and 1.07 in 4 km), and 'Inorganic chemical industry' (RR=1.08 in 5 km). It is also noteworthy to note that there are marginal results (considerably high excess risks close to the statistical significance) in the environs of industrial groups 'Mining industry' (RR=1.38, 95%CrI=0.99-1.84 in 2 km) and 'Production of carbon or electro-graphite' (RR=1.29, 95%CrI=0.99-1.66 in 5 km).

Table 2 shows the RRs and 95%CrIs/CIs for ovarian cancer in towns at ≤5 km from industries releasing pollutants grouped by carcinogenic substances and EDCs, estimated using BYM models. The choice of this distance was based on the sensitivity analysis for 2, 3, 4 and 5 km showed in Table 1. With respect to the groups of substances defined as carcinogens by the IARC, the results showed statistically significant excess risks in all categories (RRs=1.07 for facilities releasing Group 1 carcinogens, 1.08 for Group 2A carcinogens, and 1.06 for Group 2B carcinogens). Insofar as the different groups of substances classified as EDCS by WHO and UNEP were concerned, excess risks were concentrated in the surroundings of installations releasing metals (RR=1.07), and PACs, POPs and other solvents (RRs=1.05 in all cases).

Table 3 shows carcinogenic pollutants and EDCs released by facilities, amounts in Tn and number of industrial facilities reporting these releases, and RR of dying from ovarian cancer in towns at ≤5 km from industries releasing these substances, estimated using BYM models. The results showed statistically significant excess risks in women residing near pollutant industries that released ethyl benzene, dichloromethane, and mercury and compounds (RR=1.09 in all cases), tetrachloroethylene, nickel and compounds, and chromium and compounds (RR=1.08 in all cases), arsenic and compounds, cadmium and compounds, lead and compounds, and particulate matter (PM_{10}) (RR=1.07 in all cases), and dioxins+furans and polycyclic aromatic hydrocarbons (PAHs) (RR=1.05 in both cases).

Finally, Supplementary Data, Table S2 shows the RRs of dying from ovarian cancer in towns for ever-decreasing radiuses within a 50-kilometer area surrounding each facility, by industrial group (risk gradient analysis), and we detected statistically significant radial effects in all sectors as a whole, especially near 'Refineries and coke ovens', 'Fertilizers', 'Urban and waste-water plants', and 'Tanning of hides and skins'.

4. Discussion

To our knowledge, this is the first study that analyzes the risk of dying from ovarian cancer in the vicinity of industrial plants, according to different industrial groups and pollutants, and taking a

national industrial register into account. In general, the results indicate an association between risk of dying due to ovarian cancer and proximity to Spanish industries with pollutant emissions, inasmuch as both models detected higher mortality due to this tumor for various industrial and toxic substances groups, and the risk gradient analysis detected statistically significant radial effects.

With respect to the results broken down by industrial group, attention should be drawn to the RRs registered for women in towns lying near refineries and coke ovens, fertilizers plants, glass and mineral fibers production, paper and wood production, disposal or recycling animal waste, food and beverage sector, urban waste-water treatment plants, hazardous waste treatment plants, production of pharmaceutical products, ceramic industry, organic chemical industry, inorganic chemical industry, mining industry and production of carbon or electro-graphite. Insofar as carcinogens and EDCs were concerned, attention should be drawn to facilities releasing carcinogens, metals, PACs, POPs and other solvents.

In relation to the industrial groups of our study, some studies have focused attention into the pulp and paper industry: (Schwartz and Sahmoun, 2014) observed a significant correlation between ovarian cancer incidence per state and pulp and paper manufacturing industry in the United States. Pulp and paper industry release toxic substances, including asbestos (Korhonen et al., 2004), a known risk factor for ovarian cancer, and this could be related to the significant excess risks found in our study for women living in the vicinity of paper and wood production industries.

As regards other industrial activities, one of the most noteworthy results of our study is the high excess risk found in the proximity (≤2 km) of mining industries, a finding that does not appear in the other distances. Although the percentage of women working in the Spanish extractive industries is very low (2.7% in 1989 (National Statistics Institute, 2015)), it is probably that this excess affects, principally, to women working in these facilities (that tend to live near the plants). In this sense, the

results of a study about cancer occurrence among European mercury miners revealed three deaths from ovarian cancer among female workers, likely representing an excess (Boffetta et al., 1998).

Lastly, some occupational studies about women working in the petroleum industry found high SMRs for ovarian cancer (Huebner et al., 2010; Lewis et al., 2000). In our study, 'Refineries and coke ovens' was the industrial group that showed the highest statistically significant excess risks.

On the other hand, we have analyzed the risk associated with proximity to facilities releasing specific substances, both carcinogens and EDCs, and the results reported in our study show significant excess risks between 5% and 9% in many pollutants. With respect to substances classified as carcinogenic to humans by IARC, some occupational studies have found elevated risks for ovarian cancer in women exposed to PAHs (Hartge and Stewart, 1994) and aromatic hydrocarbon solvents (Vasama-Neuvonen et al., 1999), a finding that could be related to the significant excess risk observed by us in women living near industries releasing PAHs. Another carcinogenic pollutant that has been studied by its possible relationship with ovarian cancer is cadmium: whereas the results from an American study suggested associations between ovarian cancer and cadmium exposure (Adams et al., 2012), other study suggested that dietary cadmium exposure is not likely to have a substantial role in ovarian cancer development (Julin et al., 2011). In our study, we have found an increase excess risk in towns near facilities releasing cadmium. Insofar as dioxins exposure is concerned, some animal models have been demonstrated its carcinogenicity in the ovary (Davis et al., 2000), and a study about the industrial accident in Seveso (Italy) in relation to young people exposed to dioxins in the residential community observed two ovarian cancers versus none expected (Pesatori et al., 1993). This could be related to the significant excess risk found by us. With respect to exposure to ECDs, associations between atrazine and ovarian tumors have been observed in some studies (Dich et al., 1997). Nevertheless, we did not find any excess risk in relation to this pesticide in our study.

Ecologic studies, such as that reported here, are proposing new hypothesis and lines of research with respect to population exposure to industrial pollution. In this regard, one of the principal strengths of our study resides in the completeness of its exploratory analysis, which consisted of an in-depth examination of ovarian cancer mortality with reference to 27 industrial groups and 50 pollutant substances. Another strength was its use of different methodological approaches to perform the statistical analysis: one, based on a hierarchical spatial model at a municipal level, with inclusion of explanatory variables (BYM model), in which the use of spatial terms in the model, not only meant that it was less susceptible to the presence of the ecological fallacy (Clayton et al., 1993), but also ensured that the geographic heterogeneity of the distribution of mortality was taken into account; and the other, based on a Poisson mixed regression model, was justified by its ease of adjustment and shorter computation times. In our study, the non-presence of spatial autocorrelation at a municipal level could be indicating that the spatial term in the BYM model does not substantially improve the model fit (this fact was checked comparing DICs in models with and without this spatial term, data not shown). However, the inclusion of the spatial term, together with heterogeneity term, always improves the fit model, and therefore, these random effects should be taken into account. On the other hand, the method of estimation afforded by INLA amounts to a qualitative leap in the use of hierarchical models with explanatory variables (Rue et al., 2009). A consideration to bear in mind is that spatial models are more restrictive to detect potential statistical associations and robust to possible risk factors not included (residual confounding) than standard Poisson regression models (Garcia-Perez et al., 2013). An example of the above mentioned can be seen in our results on "Refineries and coke ovens" in 2 km: whereas the mixed model provided statistically significant results, the model BYM did not show a statistically significant association.

Further advantages of the study are: its high statistical power, thanks to the inclusion of a great number of reported deaths, a factor that enables it to identify excess mortality of a lower magnitude, in

line with the expected effects of environmental exposures; and elimination for study purposes of those installations that had come into operation most recently, and whose possible influence on tumor development is debatable if the minimum latency period is taken into account.

Aside from the limitations inherent to all ecologic studies, in our case mention should also be made of the following: the inclusion of many variables in the models that could make the analyses very susceptible to type I error; the assumption that exposed and unexposed areas have a homogeneous behavior in risk in the models; the non-inclusion of possible confounding factors that might be associated with distance (though adjustment for socioeconomic variables goes some way to mitigating this lack of information, since many life-style-related risk factors, such as type of diet, show a distribution correlated with socioeconomic status (Prattala et al., 2009)); the use of distance from town of residence to industrial centers as a "proxy" of population exposure to industrial pollution, based on the assumption of an isotropic model, since real exposure may depend on prevailing wind patterns or geographical landforms (though this would limit the capacity for detecting positive results, without invalidating the associations found); and the use of mortality rather than incidence data, due to the absence of a national population-based incidence register.

A further possible bias in the allocation of exposure is the use of municipal centroids as coordinates to pinpoint the entire population of a town, when, actually, the population may be fairly dispersed (e.g., in highly populated cities). In our case, however, this would amount to a non-differential bias (it would affect towns in both exposed and unexposed areas) which would limit the capacity to find positive results and, in turn, render the estimators of real risk greater than those found.

A critical decision when analyzing the risk of towns "near" pollution sources is the choice of radius. We have used several distances (2, 3, 4 and 5 km) that coincide with that used by other authors (Cambra et al., 2013; Huang and Batterman, 2000; Lopez-Abente et al., 2012; Lopez-Cima et al., 2013; Pascal et al., 2013; Yang et al., 2003) and could be justified because, in these types of studies, if some

increase in risk were to be found, it would most likely be in areas neither too close nor too far from pollutant sources. Moreover, the choice of 5 km has provided satisfactory results in the statistical analyses in similar ecologic studies (Federico et al., 2010; Garcia-Perez et al., 2013).

In general, our results are noteworthy by virtue of the magnitude of the RR, since in ecological studies, effect estimators for the exposures like environmental pollution tend to be very low.

5. Conclusion

Our results support that residing in the vicinity of pollutant industries could be a risk factor for ovarian cancer mortality, inasmuch as both models used in the study detected higher mortality due to this tumor for various industrial and toxic substances groups.

The findings support the need for more detailed exposure assessment and health risk analysis of certain toxic substances in population near industrial facilities.

Acknowledgments:

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