Reviewer's report

Title: Lung cancer mortality in towns near paper, pulp and board industries in Spain

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Reviewer: Denis Zmirou-Navier

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General comments:

This paper relates lung cancer mortality over the period 1994-2003 in 8073 Spanish cities to distance to 18 paper and board industries which have reported their emissions to the EPER (European Pollutant Emission Register) database in 2001. This work illustrates, according to the authors, how this EPER database may be used to assess the health impact of industrial activities using a small scale ecological approach. EPER collects information on 50 pollutants whose emissions are to be declared by industries when pollutant-specific threshold levels are exceeded. SMRs (Standardized Mortality Ratios) have been calculated, using age and sex-specific rates for whole Spain, across two five-year periods (1994-1998 and 1999-2003), to compute expected number of deaths. The choice of paper and board industries as the “exposure” parameter is justified by occupational epidemiology studies that tend to show excesses of cancers (including lung cancers) in this sector.

Although, as a whole, no excess risk is shown across the 18 plants, analysis of 2 particular plants suggests, according to the authors, significant trends of lung cancer SMRs among males with distance, not among females.

This paper is closely related to a preceeding work published in this journal (Description of industrial pollution in Spain; BMC Public Health 2007, 7:40 (21 March 2007). However interesting in principle, this paper is affected by severe limitations that preclude its publication in the present form. The authors are invited to liaise with environmental epidemiologists to circumvent some of these limitations.

Major Compulsory Revisions

- Surprisingly, the Material and Methods section states (page 5, paragraph 2) that exposure was indexed as a 3 levels variable: (a) towns whose centroïd is less than 2km from the plants (“exposed group”); (b) “intermediate group”: towns at distance less than 2 km from any air polluting industry other than paper, pulp and board; (c) towns having no EPER-registered industry within a 2 km radius of the municipal centroïd. Firstly, based on this categorization, this so called “intermediate group” might include cities located close to petroleum or chemical plants, for example, a situation which would yield a considerable degree of exposure misclassification. Further, this categorization is actually not used, in my
understanding, in the results section that essentially rests on increasing distances of cities to paper, pulp and board plants only. No mention is made to other, more appropriate, exposure metrics that might have been accommodated. For instance, in combination with distance, the analysis might have considered the emission levels (not presented in table 1 but whose data are available from the EPER database for the regulated pollutants that are exhibited in the table).

- Despite the fact that the overall analysis did not show associations between cancer risks and short distance (<2 km; table 2) to the plants, the authors focus on two particular plants (nº 3730 and 2761) and proceed to analyse the risk trend with increasing distances (<5km, 5-10, 10-15, 15-20, 20-50 km; table 3). Why plant 3730 when table 2 does not show an increased risk? The distance split is not justified and the authors should explain on what basis they hypothesize that carcinogens emitted by the plants may disperse over such long distances, 15, 20 km and further). This lack of justification also lends some doubt on the fact that many cut off values were tested, raising a serious concern about the issue of multiple testing, an issue which is not even alluded to in the discussion. Even if there were no true association, multiplying the number of tests, as one may think the authors did, will inevitably result in spurious “significant” statistical associations. Further, they tend to over-interpret p values (table 3), not looking carefully to the consistency of the trend. Finally, one might expect comments on the observation of associations found among men exclusively, but not among females. Regarding an environmental route of exposure, this is somehow intriguing.

Minor Essential Revisions

- Background section (end of second paragraph p 3): surprisingly, no reference is made to traffic-related emissions as a possible contributor to the risk of lung cancer in urban areas. The authors should relate more critically cancer risks to the pollutants that are declared in the EPER database (SO2, NOx, PM and others not mentioned) (last paragraph page 3 and first paragraph p 4), an idea that is (wrongly) exposed again in their conclusion, when suggesting SO2 emissions might partly explain cancer risk excesses in the vicinity of industrial plants, a statement that is based on old animal experiments.

- Because industrial plants tend to aggregate in some locations, had the authors shown associations of cancer risks with distance, this would not have allowed them to conclude that paper, pulp and board industries would be the causal factors. So that their claim that “introduction of province as a random effect term partly solves this problem” (of confounding) is inaccurate (p8, 3rd paragraph).

Discretionary Revisions: None

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being
published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests