Ovarian cancer cases attributable to asbestos exposure: an ecological analysis in Lombardy, Italy 2000-2018

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Introduction

Asbestos is one of the most severe and widespread occupational carcinogens worldwide. Exposure to asbestos causes malignant mesothelioma (MM), cancer of the lung, larynx, and ovary [1].
The causal association of ovarian cancer and asbestos exposure, stated since 2009 on the basis primarily of five cohort studies [2].

Aim

We formulate a trivariate Bayesian spatial shared model to estimate the latent contribution of asbestos exposure on the occurrence of ovarian cancer at small geographical scale, including a third disease, breast cancer, which is not related to asbestos but shares other risk factors (including reproductive and lifestyle determinants) with ovarian cancer, to stabilize the estimates.
This study aimed to estimate cases and attributable fractions of ovarian cancer associated with asbestos exposure.

Methods

We adopt a Bayesian framework and rely on the literature's evidence; our theoretical assumption is that correlation among different diseases depends on shared risk factors [3]. From a modelling perspective, such correlation is captured by spatially structured random shared terms. We assumed that pleural and ovarian cancers share asbestos exposure; breast and ovarian cancers share other risk factors linked to lifestyles and reproductive life.
We analyzed deaths, extracted by the Statistical Service of the Italian National Institute of Health, with the following ICD codes: ovarian cancer (ICD-9: 183.0, ICD-10: C56); pleural cancer (including pleural cancer, ICD-9: 163 and ICD-10: C38.4 and pleural mesothelioma ICD-10: C45.0); and breast cancer (ICD9: 174, ICD10: C50) at municipality level in Lombardy Region for the period 2000-2018.
Expected cases were calculated by indirect internal standardization [4]. We described the spatial pattern of mortality for the tree diseases separately using Besag, York, and Mollié model [5].
We specify a Bayesian spatially structured trivariate model with shared and disease-specific components. We assume that breast cancer has a specific spatial pattern with a large-scale trend caught by specific clustering random terms –an urban/rural gradient - and spatially unstructured hot spots corresponding to high urbanized areas caught by the specific heterogeneity random terms [6]. Our model specifies specific heterogeneity random terms for within-area clustering for pleural and ovarian cancer due to specific hidden confounders. These choices are based on epidemiological knowledge about potential within area clustering

for pleural cancer and ovarian cancer – localized prevalence of risk factors not explained by shared components - and both within area clustering and large-scale spatial gradient for breast cancer – as results of localized and large scale socio-economic gradients [7,8].
We modelled the attributable risk of ovarian cancer resulting from asbestos exposure by the classic formula based on relative risks omitting the clustering component shared with pleural cancer to the risk of ovarian cancer.

Results

The number of deaths for pleural cancer among women in the period 2000–2018 in Lombardy Region (Italy) was 2,070 (SMR 0-22.14). We retrieved 10,462 deaths for ovarian cancer (SMR Range 0 -19.15) and 37,621 deaths for breast cancer (SMR range 0-6.12).
The geographical pattern for pleural cancer was very strong. In addition, well-known asbestos-polluted industrial areas were clearly identified [9,10]. The spatially structured pattern for ovarian and breast cancer was less pronounced.
We found shared dependencies between ovarian and pleural cancer, which capture risk factors common to the two diseases (asbestos exposure), and a spatially structured clustering component shared between ovarian and breast cancer, capturing risk factors unrelated to asbestos. We reported in Figure 1 the attributable fractions of ovarian cancer by municipality. Two areas are identified, the Broni area and the area around Iseo Lake where Sarnico is located [9,10].

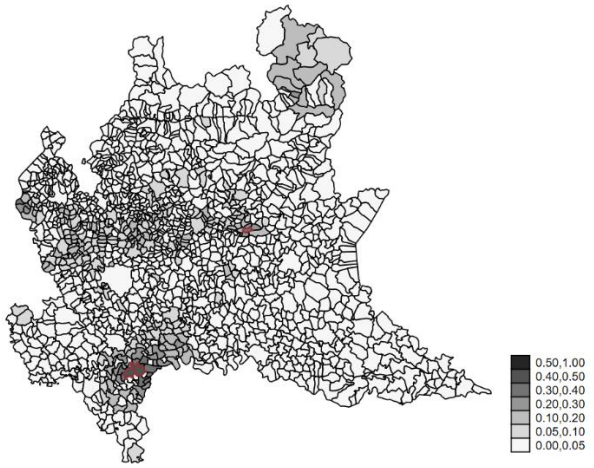

Figure 1. Attributable risks proportion of ovarian cancer by municipality

We estimated that 574 ovarian cancer cases (95% Credibility Interval 388-819) were attributable to shared asbestos exposure (attributable risk 5.5% 95% Credibility Interval 3.7-7.8). The highest attributable fractions were for Broni and Stradella (46%, 6 deaths out of 13 cases in each municipality), followed by 36% for Sarnico (3.6 deaths out of 10).

Discussion

We found evidence of a shared risk factor between ovarian and pleural cancer mortality at a small geographical level highlighting the sharing of geographical patterns between ovarian and pleural cancer in areas with known asbestos exposure sources.

Analyses suggest that the ovarian cancer mortality in Broni, Stradella and Sarnico is a combination of a low prevalence of risk factors for ovarian cancer and a high prevalence of asbestos exposure.
This study is subject to at least the following limitations. First, the mortality municipality may not reflect past asbestos exposure because of migration. Second, while mortality is a good proxy for MM incidence due to poor survival, it may be a suboptimal surrogate for ovarian and breast cancer.

Conclusion

The model used in the present paper could be helpful to estimate the burden of asbestos-related diseases with low etiologic fraction attributable to asbestos, such as ovary cancer. Findings may then be used to target interventions of prevention, health and compensation assistance.

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