



Pleural mesothelioma in Poland: Spatial analysis of malignant mesothelioma prevalence in the period 1999-2013

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Abstract

Malignant mesothelioma (MM), a rare and very deadly tumour, can be due to asbestos exposure. To better understand the cause of incidence of MM, spatial autocorrelation analysis with reference to the quantity of asbestos-cement products in use and the localisation of former asbestos manufacturing plants was applied. Geostatistical analysis shows that strong spatial clustering of MM incidence (referring to the general population as well as females and males separately) during the period 1999-2013 in the administrative units of Poland (provinces and counties). Incidence hotspots were found to be concentrated primarily in southern Poland but also seen in the county of Szczecin, which stands out in local autocorrelation analysis in north-western Poland. High incidence rates were discovered, in particular with reference to counties around former plants manufacturing

asbestos-containing products, mainly asbestos-cement manufacturers. The highest frequency of MM incidence rate was found in within a 55 km radius of plants in or near the towns Trzebinia, Ogrodzieniec and Szczucin in the South, where asbestos-cement products had been manufactured for close to 40 years. Areas with significantly high incidence rates were also discovered in the provinces of Śląskie, Małopolskie and Świętokrzyskie in southern Poland.

Introduction

Asbestos is the collective name for group of naturally occurring fibrous minerals: chrysotile, amosite, crocidolite, tremolite, anthophyllite and actinolite (Ross *et al.*, 2008). Due to its unique set of physical and chemical properties, asbestos had many industrial applications worldwide (Virta, 2003; Wilk *et al.*, 2014). The negative effects of asbestos and asbestiform fibres on human health are a consequence of inhalation of such fibres present in the air (Ledda *et al.*, 2018). Exposure to asbestos fibres refers to the occupational, the para-occupational and the environmental aspect. Occupational exposure is mainly related to work extracting asbestos in mines or with the production of asbestos-containing products, as well as in connection with dismantling, repair and maintenance of these products (McDonald *et al.*, 1997). Environmental exposure to the pathogenic effect of asbestos fibres mostly affects people living near asbestos mines, asbestos manufacturing and processing plants, or people living in highly urbanized areas where asbestos can be a factor initiating cancer (Britton, 2002; Harper *et al.*, 2015; Ledda *et al.*, 2016).

Malignant mesothelioma (MM) is a rare and very deadly tumour, a neoplasm typically originating in the mesothelial cells lining the body's serous cavities, mainly the pleura and the peritoneum (Huncharek, 1992; Agudo *et al.*, 2000; Neyens *et al.*, 2017). The number of MM cases depends on the type of asbestos used, and it typically increases along with the use of the crocidolite (McDonald and McDonald, 1978). The mesothelioma risk has been found to be much higher when exposure included crocidolite or amosite rather than chrysotile alone (McDonald and McDonald, 1996). Crocidolite is thus considered the most potent fibre type with respect to the pathogenesis of mesothelioma (Schneider *et al.*, 2008). Research has confirmed MM incidence after the exposure to asbestos (Newhouse and Thompson, 1965; Magnani *et al.*, 1995; Rogers and Nevill, 1995; Howel *et al.*, 1997; Rees *et al.*, 1999; Kielkowski *et al.*, 2000; Magnani *et al.*, 2000; Burdorf *et al.*, 2004; Maule *et al.*, 2007), whereas other types of tumours (Botha *et al.*, 1986; Stayner *et al.*, 1996) or other asbestos-related

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diseases (Mossman and Gee, 1989) were much less frequent. The estimation of the number of cases of other asbestos-related diseases, such as lung cancer, is extremely difficult, and therefore the attempts have been made to assess the asbestos-related lung cancer incidence rate on the basis of the number of MM cases in the general population (McDonald *et al.*, 1997; Nurminen and Karjalainen, 2001; Brüske-Hohlfeld *et al.*, 2000; McCormack *et al.*, 2012).

Poland is perceived as one of the countries where the detection rate of MM is one of the lowest in Europe (Bianchi and Bianchi, 2014). Compared to other European countries, where a similar amount of asbestos fibres were imported, about 3–4 times fewer cases of MM are diagnosed in Poland. In countries where preventive scientific programmes are undertaken, the results obtained form the basis of an assessment of the population's health situation and production of epidemiological estimates (Krówczyńska and Wilk, 2018a). No epidemiological studies in Poland have been carried out and this makes it impossible to verify any hypothesis related to the incidence of MM (Szeszenia-Dąbrowska, 1996), or to develop a strategy to reduce the asbestos exposure (Świątkowska, 2009). An important part of health needs assessments is the identification in areas at high risk for a disease (Osei and Duker, 2008). Spatial autocorrelation, *i.e.* the occurrence of one phenomenon in a given spatial unit causing an increase or decrease in the probability of its occurrence in neighbouring units (Janc, 2006; Wang *et al.*, 2016), may be used to identify spatial patterns.

In Poland, starting from the 1920s until the total national asbestos ban in 1997, imported fibres were used for the manufacturing of the asbestos-containing products. The most intensive development of asbestos-containing products manufacturing was in the 1970s. Twenty-eight plants across the country used asbestos fibres for industrial manufacturing (Wilk *et al.*, 2014). Over 90% of asbestos used in production was chrysotile, with less than 10% of crocidolite and amosite, which was used for the manufacture of pressure pipes until the 1980s (Dyczek, 2006). An estimated of 8.2 million tons of asbestos-cement products are still in use in Poland (Wilk *et al.*, 2017). Safe removal of all asbestos-containing products used in Poland is supported by the GeoAzbest database (GeoAzbest, 2017), which was developed during the implementation of the national asbestos abatement plan (Krówczyńska and Wilk, 2016). The incidence of MM is closely correlated to the concentration of asbestos fibres in the air (Ledda *et al.*, 2018). The quantity and quality of asbestos-containing products still in use, as well as the level of the environmental pollution, are the factors influencing the MM incidence (Carbone and Bedrossian, 2006). Although the production of asbestos-containing products has been banned for more than 20 years in Poland, the population is still exposed to the environmental effects of the inhalation of asbestos fibres present in the air (Krówczyńska and Wilk, 2018a). An analysis of the actions taken in the area of the asbestos exposure, including health protection, as part of the National Asbestos Abatement Programme in Poland, in 2004–2013 have been presented by Krówczyńska and Wilk (2018b).

The purpose of the study was to provide better comprehension of the incidence of MM and its geographic distribution in Poland in order to find a rational basis for a national policy development with reference to prevention and monitoring of potential cases of MM, in particular due to the environmental asbestos exposure.

Materials and Methods

Data sources

The subject of the study undertaken were the MM cases registered under code C45 of the 10th Revision of International Statistical Classification of Diseases and Related Health Problems. General and local spatial autocorrelation methods were used for the spatial correlation testing (Tobler, 1970). The total number of MM cases in Poland in 1999–2013 were derived from the National Cancer Register (Wojciechowska and Didkowska, 2016). Collected data refer to the period of 1999–2013 and are classified by county and gender. Calculations were performed for males and females as well as for the general population. The information on the territorial division of Poland by province and county was acquired from the Polish National Geodetic and Cartographic Documentation Centre (Państwowy Rejestr Granic – PRG, 2017), while the data on the quantity and locations of asbestos-containing products in use were derived from the GeoAzbest web service provided in the Asbestos Database (Krówczyńska *et al.*, 2014). The localisation of asbestos manufacturing plants, types of production undertaken and localization were collected during field surveys (Wilk *et al.*, 2014).

Methods

General spatial autocorrelation

Moran's I autocorrelation coefficient (Moran, 1950; Li *et al.*, 2007) was used to measure the correlation between neighbouring outputs in 380 counties in Poland, and was calculated as follows (Eq. 1):

$$I = \frac{n \sum_{i=1}^n \sum_{j=1}^n w_{ij} (x_i - \bar{x})(x_j - \bar{x})}{(\sum_{i=1}^n \sum_{j=1}^n w_{ij}) \sum_{i=0}^n (x_i - \bar{x})^2}, i \neq j \quad \text{Eq. 1}$$

where n is the number of study areas (counties), w_{ij} an element of a weight matrix of links between object i and j (MM cumulated incidence in i or j county), x_i and x_j variable values in i and j spatial unit (MM prevalence rate) and the arithmetic mean of the variable for all units.

In addition *Getis-Ord general G* statistics (Getis and Ord, 1992; Ord and Getis, 1995) was used (Eq. 2):

$$G = \frac{\sum_{i=1}^n \sum_{j=1}^n w_{ij} x_i x_j}{\sum_{i=1}^n \sum_{j=1}^n x_i x_j}, i \neq j \quad \text{Eq. 2}$$

where x_i , x_j are variable values in spatial units i and j , w_i and w_j weigh of links between units i and j , and n the number of spatial units.

The feature that differentiated the research objects was the severe prevalence rate of MM. The reason for the application of the raw prevalence rate of MM was the lack of data about MM cases and incidence by age (Eq. 3).

$$SS = \frac{\sum_{j=1}^n k_j}{\sum_{j=1}^n p_j} \times 100,000 \quad \text{Eq. 3}$$



where n is the number of years in the period analysed, k_j the number of MM incidence among the population tested within the given period i , and p_j the number of people in the tested population in the middle of period j .

Local spatial autocorrelation

The statistical measures of the *Getis-Ord Gi* statistic (Ord and Getis, 1995) were used to determine the local pattern ($Gi(d)$) indicating points of high MM risk (Eq. 4).

$$G_i(d) = \frac{\sum_{j=i}^n w_{ij}(d)x_j}{\sum_{j=i}^n x_j} \quad \text{Eq. 4}$$

where w_{ij} is the weight of links between objects i and j (MM incidence frequency or aggregated number of registered MM cases in i or j county), x_j the variable value in the unit j , and d the maximum distance within which the clusters are expected to occur.

In order to identify statistically significant hotspot and coldspot clusters the Local Moran's I statistic was applied (Anselin, 1995) (Eq. 5).

$$I_i = \frac{n^2}{\sum_i \sum_j i j} x_i \frac{(x_i - \bar{x}) \sum_j w_{ij} (x_j - \bar{x})}{\sum_j (x_i - \bar{x})^2}, \quad i \neq j \quad \text{Eq. 5}$$

where n is the number of study areas (counties), w_{ij} the weight matrix of links between objects i and j (MM frequency or cumulated incidence in i or j county).

Fixed distance band was then applied for calculations of the spatial autocorrelation (Moran's I) and Getis-Ord General G Statistic (G). Each county was analysed in the context of neighbouring features. Peak values $Z(I)$ and $Z(G)$ were applied to set out distance buffers from the asbestos-manufacturing plants. The distance of 55 km was applied as a threshold value for all analyses and clusters (Table 1).

The same threshold value (55 km) was applied to set out distance buffers from asbestos manufacturing plants. ArcGIS software version 10.5 (<http://www.esri.com/en/arcgis/products/arcgis-pro/overview>) was used for mapping.

Results

The MM incidence rate in Poland was seen to increase (Figure 1). The highest number of cases was registered in 2013 in each group: 210 cases among male population and 116 cases among female population. However, the number of cases decreased in 2000 and 2008. The spatial differentiation of MM incidence rates refers to three groups: the general population, females only and males only (Figure 1).

The highest rate of MM per 100,000 inhabitants of an administrative unit occurred in southern Poland (Figure 2).

The incidence of MM in the general population was found to be concentrated in southern Poland, and to lesser extent, in northern Poland. The highest values of MM incidence rate were discovered in the following 12 counties: Szydłowiecki, Parczewski, Chrzanowski, Dąbrowski, Olkusi, Tarnów, Buski, Świnoujście,

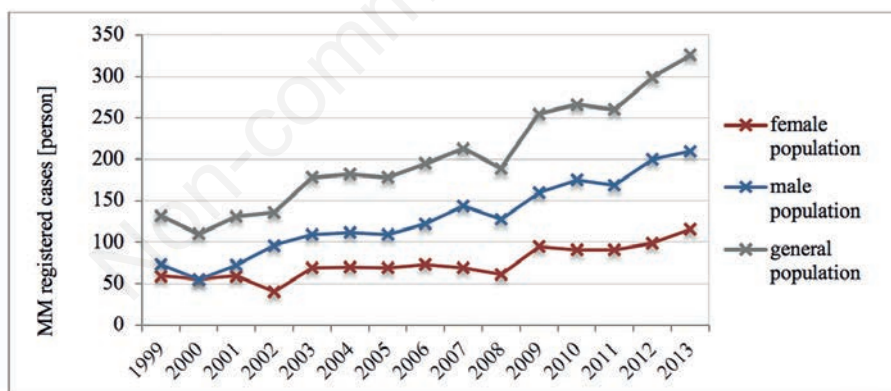


Figure 1. The number of malignant mesothelioma (MM) cases in Poland per sex and per year.

Table 1. Moran I statistic (Z(I)) and Getis and Ord (Z(G)) varying with the distance.

TARGET DISTANCE (km)	45	50	55	60	65	70	75	80	85	90	95	100
All Z(I)	8.73	8.69	8.9	8.86	9.12	9.68	10.03	9.67	10.13	10.58	10.88	11.12
All Z(G)	8.3	8.52	8.8	8.56	8.86	9.18	9.9	9.63	9.95	10.39	10.53	10.55
Women Z(I)	6.02	5.1	5.15	5.05	4.57	4.67	5.28	4.82	4.9	5.2	5.27	5.6
Women Z(G)	5.8	5.1	5.17	4.79	4.46	4.41	5.37	5.07	5.16	5.42	5.41	5.6
Men Z(I)	9.67	10.38	10.69	11.17	11.86	12.7	12.85	12.74	13.41	13.83	14.27	14.47
Men Z(G)	9.26	10.18	10.73	10.75	11.61	12.19	12.64	12.52	12.94	13.42	13.67	13.64

Ruda Śląska, Kłobucki, Zawierciański, and Świnoujście.

In the designated buffers around the asbestos manufacturing plants there were 44 out of 49 counties designated as hotspot (High-High) areas, and 45 out of 47 counties designated as hotspot areas both with 99% confidence level (Figure 3).

The spatial distribution for the male cases is similar to that of the general population, while the female population differed signif-

icantly since higher values were denoted in counties located in northern Poland. However, in Dąbrowski County in southern Poland, the MM incidence rate was significantly higher compared to the rest of the country, irrespective of gender (Figure 4). There was also a difference with reference to the positive autocorrelation of the frequency of the accumulated MM incidence rates in that the highest statistically significant level of autocorrelation for the

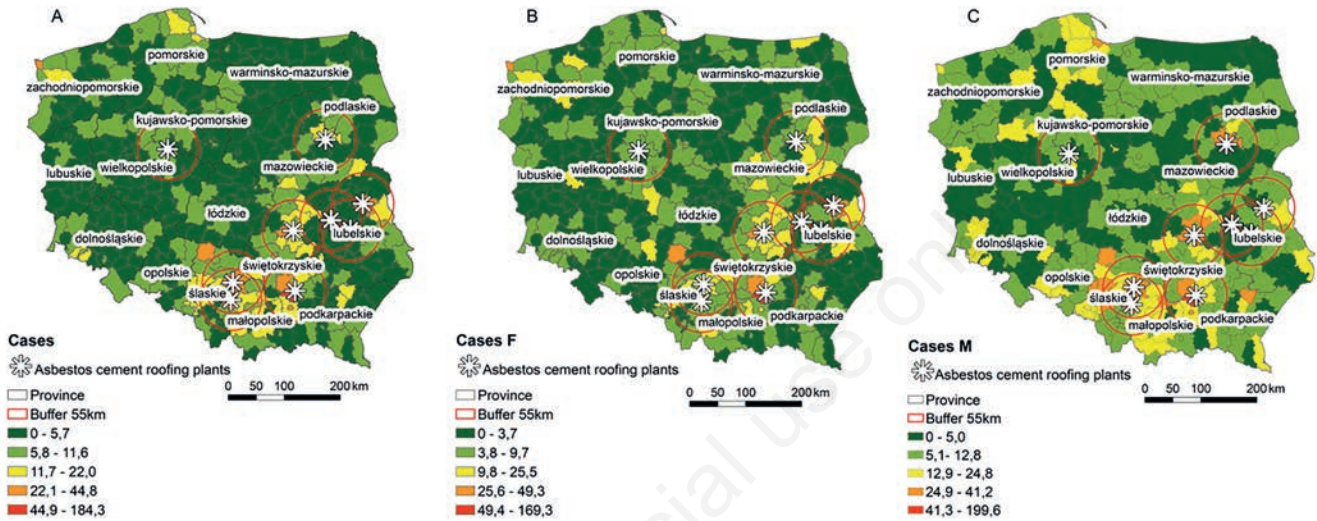


Figure 2. Raw malignant mesothelioma incidence ratio per county. (A) General population cases: 1. Szydłowiecki, 2. Parczewski, 3. Chrzanowski, 4. Dąbrowski, 5. Olkusi, 6. Tarnów, 7. Buski, 8. Świnoujście, 9. Ruda Śląska, 10. Kłobucki, 11. Zawierciański, 12. Gliwice. (B) Females cases: 1. Szydłowiecki, 2. Parczewski, 3. Dąbrowski, 4. Buski, 5. Świnoujście, 6. Kłobucki. (C) Male cases: 1. Ostrowski, 2. Radomski, 3. Szydłowiecki, 4. Chrzanowski, 5. Dąbrowski, 6. Olkusi, 7. Proszowicki, 8. Tarnów, 9. Leżajski, 10. Buski, 11. Tychy, 12. Gdańsk, 13. Kłobucki, 14. Gliwicki, 15. Mikołowski, 16. Tarnogórski, 17. Zawierciański, 18. Chorzów, 19. Gliwice, 20. Mysłowice.

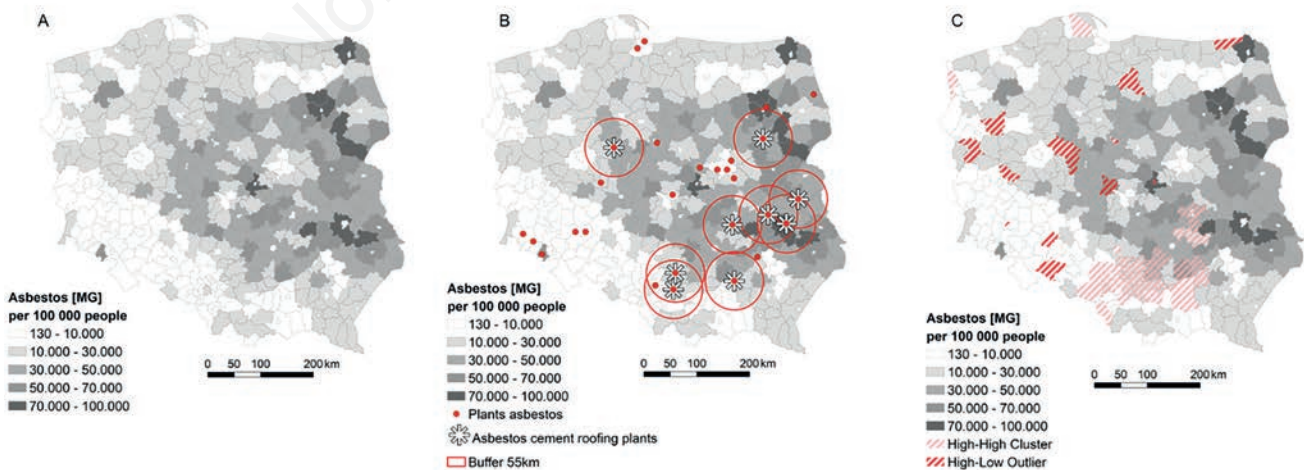


Figure 3. The amount of asbestos-cement products per 100,000 inhabitants. (A) The amount of asbestos-cements products used per 100,000 inhabitants in counties; (B) the amount of asbestos-cement products used per 100,000 inhabitants in counties with the reference to the localisation of asbestos manufacturing plants; (C) the amount of asbestos-cement products used per 100,000 inhabitants in counties with designated hotspot areas.



cumulative prevalence rate was denoted for the male cases (Table 2). MM hotspots with respect to all analysed cases were located in southern Poland *i.e.* in Kraków and Katowice, the capital cities of Małopolskie and Śląskie provinces, respectively. For the female cases in Katowice, the hotspots did not cover the metropolitan area, while those in Kraków were located east and northeast of the

city. For the male cases the hotspots cover the areas of Kraków and Katowice, and a part of the southern part of Świętokrzyskie and the western part of Podkarpackie (Figure 5). We identified 47 counties with higher MM incidence rate than normal (3 in Podkarpackie, 5 in Świętokrzyskie, 10 in Małopolskie and 29 in Śląskie); 15 counties for the female cases (3 in Podkarpackie, 6 in Małopolskie and

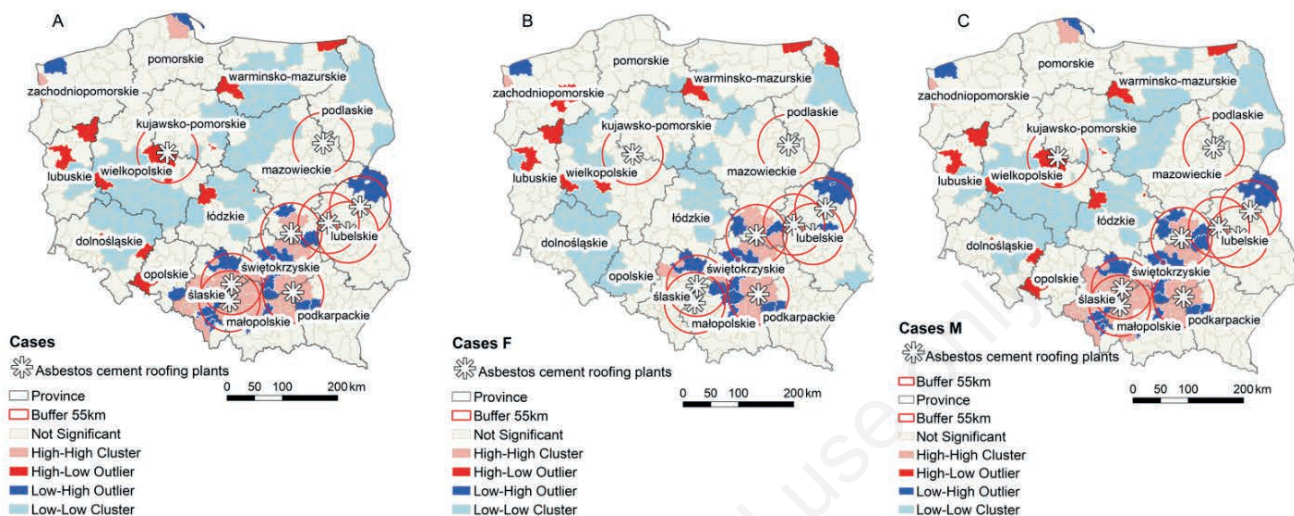


Figure 4. Local autocorrelation of malignant mesothelioma incidence rate per county. (A) General population cases; (B) Female cases; (C) Male cases.

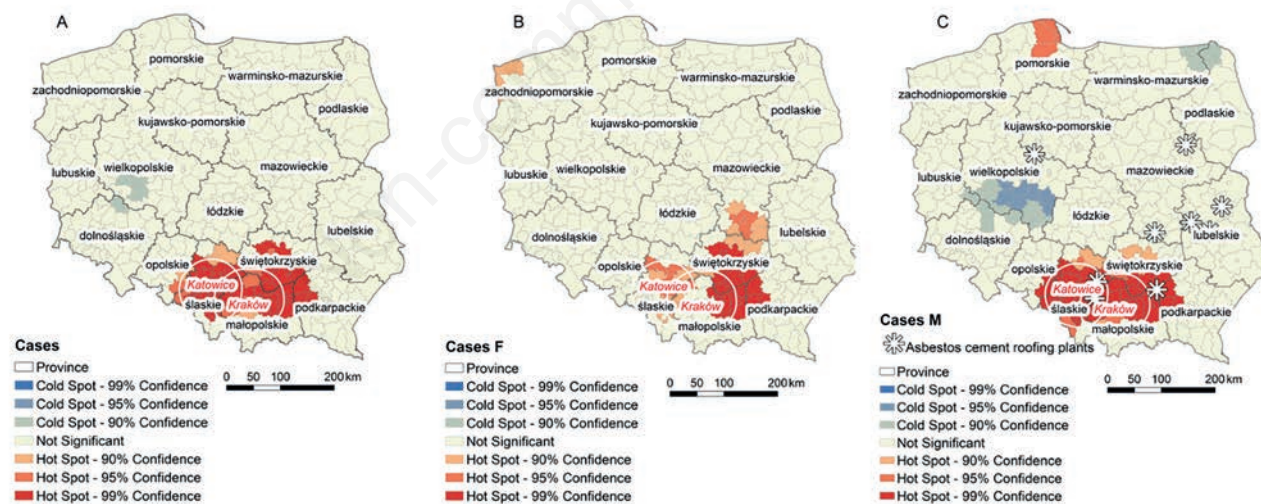


Figure 5. The hot spot analysis of malignant mesothelioma per county. (A) General population cases; (B) Female cases; (C) Male cases.

Table 2. Global Moran's *I* (I) and Getis and Ord (G) statistics for the MM rate in Poland.

Case description	I	Var (I)	Z (I)	P-value	G	Var (G)	Z (G)	P-value
Gen. cases	0.1447	0.00027	8.9260	0.000000	0.0036	0.000000	8.8049	0.000000
Females	0.0846	0.00029	5.1598	0.000000	0.0479	0.000012	5.1762	0.000001
Males	0.1964	0.00034	10.6995	0.000000	0.0036	0.000000	10.730	0.000000

6 in Świętokrzyskie) and 53 counties for the male ones (2 in Opolskie, 3 in Podkarpackie, 4 in Świętokrzyskie, 13 in Małopolskie and 31 in Śląskie). A coldspot was found for the male population in 7 counties in Wielkopolskie in western Poland.

Counties with high rates of MM incidence rate surrounded by counties with similar high MM incidence rates were designated similarly as hotspots in southern Poland. There was a clear border between the northern part of Małopolskie and Śląskie provinces in southern Poland designated by the Low-High counties. In the group of female cases, behind the designated border to the South, there were counties in which the studied phenomenon did not affect neighbouring ones. Moving North, we found numerous counties with low values of MM incidence rate, also surrounded by low values (Low-Low) of MM incidence rate, most frequently in the male case groups and in the general population.

In order to determine the impact of the quantity of asbestos-containing products still used (based on the number of inhabitants) in relation to the number of cases of MM, the Spearman rank correlation coefficient was calculated. It ranged from -0.2 to -0.25 for individual groups. This indicates a negative correlation between the number of products used per one inhabitant of the county and MM incidence rate.

Discussion

The incidence analysis does not give rise to cause-and-effect considerations but may be helpful for needs and planning in the health care system. The prevalence analysis makes it possible to determine the circumstances in which the development of the disease begins what is the promoting its development, *e.g.* environmental factors. An important part of health needs estimation starts with identification of high-risk areas to improve the level of health care (Osei and Duker, 2008). The use of spatial autocorrelation statistics for the analysis of spatial clusters enables the capture of spatial changes, which can indicate high-risk areas. The regions with higher MM incidence are particularly interesting from the epidemiological point of view, since clustering indicates the existence of environmental, industrial or quasi-industrial factors increasing the MM incidence rate. The results of local and global autocorrelation statistic indicate a statistically significant relationship of MM incidence in some provinces in Poland. Hotspots are concentrated in the southern part of the country besides the Szczecin County, which stands out in the local autocorrelation analysis in north-western Poland. High incidence rates were found in particular counties concentrated around several former asbestos manufacturing plants, mainly producing asbestos-cement. As seen in Figure 2, the highest incidence rates were recorded near seven out of eight asbestos-cement manufacturing plants (Parczew, Małkinia, Lublin, Końskowola, Wierzbica, Szczucin, Ogrodzieniec and Trzebinia), but only in the case of Trzemeszno, the correlation had not been registered.

The highest rate of MM incidence rate was obtained for Dąbrowski County in all surveyed groups (184 in the general population with 169 in women and 200 in men is the gender group studies), which is almost five times higher than in other counties. The asbestos-cement plant in Szczucin, Dąbrowski County operated in the period 1959-1999. About 1,000 products were manufactured there, mainly asbestos-cement pipes with large diameters, for which crocidolite was used, the consumption of which at the Szczucin plant is estimated at 70% of the total amount used in the

whole country (Kotela *et al.*, 2010). Szczucin municipality itself used asbestos-cement waste for pavement of streets, yards and sport facilities (Szeszenia-Dąbrowska *et al.*, 1998).

A group of plants manufacturing different asbestos-containing products in the vicinity of which counties with increased rates of MM cases are located; this included paper in Pilchowice, textiles in Gryfów Śląski and rubber in Lubawka and Gdańsk. The most common situation there was occupational and the para-occupational exposure to asbestos fibres. The incidence of MM is higher for male, than for the females, which confirms the results obtained by other researchers (Van den Borre and Deboosere, 2014). This is caused by the fact that most of asbestos industry employees were males (Fazzo *et al.*, 2012; Corfiati *et al.*, 2015). During the undertaken study the correlations between the crude female incidence rate and the crude male incidence rate amounted to 0.83, which is similar to the standardized incidence rate in France of 0.80 (Goldberg *et al.*, 2010). This regularity confirms the impact of occupational and para-occupational exposure to asbestos on the number of MM cases in the population (Goldberg *et al.*, 2010; Fazzo *et al.*, 2012; Corfiati *et al.*, 2015).

The production of asbestos-containing products was banned in Poland in 1997, but the general population is still exposed due to the presence and quality of asbestos-cement products used in buildings. In order to determine the impact of the quantity of asbestos-containing products still used (based on the number of inhabitants) in relation to the number of cases of MM, the Spearman rank correlation coefficient was calculated. This indicates a negative correlation between the number of products used per one inhabitant of the county and MM incidence rate.

The number of cases of MM cases caused by the environmental asbestos exposure may increase as safe use of the products has been established for 30 years, while the latency period of MM is very long, from 20 to 50 years (Szeszenia-Dąbrowska and Świątkowska, 2016). Secondly association with air pollution can still be a risk factor (Dockery *et al.*, 1993). The largest amount of asbestos products is used in eastern Poland (Lubelskie, Podlaskie, Świętokrzyskie and Podkarpackie), but air pollution assumes its lowest values there (Kobus *et al.*, 2015), while most counties with the highest quantity of the asbestos-cement product use per capita are rural counties in which access to health care system is weaker.

The risk of MM increases with the amount of dust in the air (Dockery *et al.*, 1993). Designated hotspots in Poland were compared with zones with high air pollution, as set out in a five-year assessment of air quality in zones in Poland. Areas with the highest risk of the air pollution with substances constituting health risk for people are located in Śląskie, Małopolskie and Świętokrzyskie (Kobus *et al.*, 2014). This may affect the MM incidence rate in Poland.

Conclusions

There is a relationship between the localisation of former asbestos manufacturing plants and designated areas of the increased risk of MM. Due to the biological reasons, it is reasonable to assume that different exposures to the same factor have an effect (Pira *et al.*, 2005), which may explain the higher incidence of MM cases in sites near former asbestos manufacturing plants and which areas also have the highest risk of air pollution with hazardous substances for people's health. When spatial patterns of MM cases do not fully relate to the amount of asbestos-containing



products still in use and the distance from former asbestos manufacturing plants, further research is necessary. Cases of morbidity and deaths related to the occupational exposure and other cases should be separated in order to determine the impact of the environmental exposure on the number of reported cases and deaths. Spatial regression model, which would allow the estimation of the impact of the asbestos fibres in the cases of MM as well as the estimation of the local (county) effects and the spatial correlation should be used in further research.

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