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The influence of benzene air pollution on leukemia incidence and mortality rates

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Abstract. The following study identifies areas where adverse conditions related to benzene pollution are concurrent with leukaemia incidence and mortality (C91–C95). Moreover, it determines the similarities between benzene and leukaemia levels, as well and rules defining their co-occurrence. The analysis covered the period of 2015–2017. Data were obtained from Dane.gov.pl (number of leukaemia cases), the Polish National Cancer Registry website (number of deaths), the Local Data Bank of the Central Statistical Office (population data) and the Chief Inspectorate of Environmental Protection and the Air Quality Portal (data on air quality). Based on the conducted analysis, it was concluded that the following poviat towns have an unfavourable epidemic situation related to leukaemia: Kielce (incidence), Rzeszów (incidence), Elbląg (mortality); meanwhile, high leukaemia incidence and mortality co-occurred with high average benzene concentration in 2015–2017 in the following poviat towns: Kielce, Rybnik, Płock and Rzeszów. It was found that leukaemias belonging to the three-character ICD-10 categories C94, C95 and C92 show the highest rate of co-occurrence with benzene concentration. In addition, two main rules for the co-occurrence of benzene pollution and leukaemia were identified. It was also noted that it is necessary to continue the research for a longer time period, especially in the poviat towns of Kielce and Rzeszów.

Key words:
medical geography,
leukaemias,
air pollution,
multidimension scaling,
k-means clustering,
Poland

Introduction

The relations between benzene and the occurrence of leukaemias are discussed in the literature. Research on these relations is part of a broader trend that has been focusing on the search for any connection between air pollution and cancer incidence and mortality (Chen et al. 2016; Su et al. 2019; Bai et al. 2020). Additional analyses and meta-analyses were also carried out with the purpose of studying the risk of cancer being caused by benzene (Atabi and Mirzahosseini 2013; Dimitriou and Kassomenos 2019, 2020; Sakizadeh 2019; Teras et al. 2019) and finding any connections between benzene (present not only in the air) and leukaemia incidence and mortality, especially in children (Best et al. 2001; Pyatt and Hays 2010; Filippini et al. 2015; Janitz et al. 2017; Raaschou-Nielsen et al. 2018).

It is also worth mentioning that a number of studies took into account workplace exposure to benzene and its subsequent impact on leukaemia occurrence (Vlaanderen et al. 2012; Rushton et al. 2014; Stenehjem et al. 2015; Linet et al. 2019).

The aim of this study is to identify areas at risk of adverse conditions related to benzene pollution being concurrent with leukaemia incidence and mortality. The indirect goal is to determine the similarities between benzene and leukaemia levels and the rules defining their co-occurrence. In the scope of its subject matter the study analysed the values of benzene concentrations and the following leukaemias, referred to in accordance with the current nomenclature, codes and classification of ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th revision) (ICD-10 codes presented in brackets):

- "lymphoid leukaemia (C91);
- myeloid leukaemia (C92);
- monocytic leukaemia (C93);
- other leukaemias of specified cell type (C94);
- leukaemia of unspecified cell type (C95)" (ICD-10).

The selection of leukaemias in the ICD-10 was made on the basis of a publication by Cieślik (2011).

The analysis covered the period 2015–2017. The choice of the time range was related to the availability of leukaemia data (most recent data from 2017), the completeness of the daily benzene measurement data and the type of measuring station.

Methods and data sources

Data on the number of C91–C95 leukaemia cases from the period 2015–2017 (separate for women and men) was obtained from Dane.gov.pl (Otwarte Dane 2020), while the data on the number of deaths (separate for women and men) was obtained from the Polish National Cancer Registry website (Wojciechowska and Didkowska 2020). The total number of cases and deaths was calculated based on the above-mentioned data. In addition, raw total incidence and mortality rates, as well as separate rates for women and men, were calculated for the averages from the period 2015–2017. Data on the population numbers of women, men and total was obtained from the Local Data Bank of the Central Statistical Office (BDL GUS 2020).

Data on air quality was taken from the database of the Chief Inspectorate of Environmental Protection and found via the Air Quality Portal (GIOŚ 2019). The stations for further analyses were selected based on the level of data completeness (set at 99.8% for daily data) and the type of the measuring station (urban background stations). On the basis of the collected data, the monthly, annual, and long-term averages for benzene concentration were calculated and presented in $\mu g \cdot m^{-3}$.

The study makes use of the *k*-means clustering to identify areas at risk of adverse conditions related to leukaemia incidence and mortality, and the multidimensional scaling method was used to find the similarities between benzene and leukaemia levels and the rules of their co-occurrence.

The *k*-means algorithm used in the cluster analysis is an algorithm used to find points that will play the role of cluster centres, while a given observation closest to a given cluster centre belongs to this cluster (Gągolewski et al. 2016). The *k*-means clustering in research on air pollution has been used by Kingsy et al. (2016), Keller et al. (2017) and Zhou et al. (2017).

Multidimensional scaling is a method with the primary goal of showing the hidden structure of objects through the content of established dimensions (respondents' similarities and preferences) and showing the relationships between objects in *r*-dimensional space (Zaborski 2012). When assessing the results of multidimensional scaling, the STRESS adjustment value is used, which, if it amounts to less than 0.02, it might be claimed that representation is faithful, and if the value is greater than 0.2, it should be concluded that the matching is very weak (Pekasiewicz and Szczukocka 2017). The possibility of applying multidimensional scaling in population health studies has been mentioned by Lopes et al. (2016), Canser et al. (2018) and Scepanovic et al. (2019).

The analysis with the use of *k* -means clustering and multidimensional scaling (PROXSCAL) was performed in the PS IMAGO PRO 6.0 program based on the IBM SPSS Statistics analytical engine. Grouping with the use of the *k*-means clustering was performed for an arbitrarily determined number of groups, n=3. Multidimensional scaling was based on the Euclidean distance measure. Inkscape 1.0.1 was used for the graphic processing of the results.

Table 1. Final cluster centres

Sex	Variable according to the ICD-10 code (2015–2017)	Incidence Cluster number			Mortality Cluster number		
		1	2	3	1	2	3
Women	C91	0.21	0.91	0.54	0.27	0.19	0.42
	C92	0.21	0.31	0.46	0.45	0.26	0.63
	C93	0.00	0.05	0.04	0.03	0.02	0.00
	C94	0.03	0.05	0.03	0.05	0.00	0.00
	C95	0.00	0.02	0.00	0.03	0.02	0.05
Men	C91	0.55	1.16	0.67	0.71	0.36	0.34
	C92	0.14	0.52	0.25	0.39	0.38	0.80
	C93	0.03	0.09	0.05	0.08	0.06	0.06
	C94	0.03	0.04	0.06	0.06	0.02	0.06
	C95	0.00	0.00	0.05	0.00	0.02	0.06
Number of poviats		2	2	3	2	4	1

Source: Own study based on Otwarte Dane (2020), Wojciechowska and Didkowska (2020) and BDL GUS (2020)

Results and discussion

With the use of *k*-means clustering, three separate groups of poviats were distinguished that differ in raw incidence rates, and three separate groups that differ in raw mortality rates (Table 1).

In terms of the value of raw incidence rates, group 2 is characterised by the most unfavourable epidemic situation, especially in terms of "lymphoid leukaemia (C91)", among women and men alike (Table 1). This group includes the poviat town of Kielce (Table 2), where the highest annual benzene concentrations were recorded in all analysed years (Table 3). The poviat town of Rzeszów also belongs to group 2, and it is characterised by a high increase in benzene concentration between 2015 and 2017.

In addition to group 2, in terms of raw incidence rates, group 3 should also be mentioned. Group 3 is characterised by a high value of the final cluster centre in terms of "myeloid leukaemia (C92)" among women and among men in terms of "other leukaemias of specified cell type (C94)" and "leukaemia of unspecified cell type (C95)". The following poviat towns were classified in group 3: Rybnik, Elbląg and Gdańsk. Rybnik is the second town directly behind Kielce in terms of high average (2015–2017) benzene concentration, though it is also a town that recorded a decrease in benzene concentration between 2015 and 2017 (Table 3). Elbląg, on the other hand, recorded the highest increase in benzene concentration between 2015 and 2017. The situation in Gdańsk in terms of benzene pollution might be considered stable. Taking into consideration the above-mentioned characteristics, group 3 might be considered to be potentially at risk of an unfavourable epidemic situation.

In terms of the value of separated groups of raw mortality rates (Table 1), the poviat town of Elbląg is characterised by an unfavourable epidemic situation, in particular in terms of "myeloid leukaemia (C92)", both among women and men (Group no. 3). Group 1 is characterised by an unfavourable situation in terms of "lymphoid leukaemia (C91)" among men. Towns of Kielce and Płock were classified as part of group 1 (Table 2). Płock is characterised by the third highest average (2015–17) concentration of benzene, preceded by Kielce and Rybnik. However, it should be noted that in the case of Kielce and Płock, there

Table 2. Cluster affiliation

Poviat town (TERYT*)	Poviat town	Incidence	Mortality
		Cluster number	
1462	Płock	1	1
1863	Rzeszów	2	2
2261	Gdańsk	3	2
2465	Dąbrowa Górnicza	1	2
2473	Rybnik	3	2
2661	Kielce	2	1
2861	Elbląg	3	3

*Explanation: TERYT – "National Official Register of the Territorial Division of the Country" TERYT GUS (2021)
Source: Own study based on Otwarte Dane (2020), Wojciechowska and Didkowska (2020) and BDL GUS (2020)

Table 3. Benzene concentrations in the air for analysed stations in 2015–2017

Poviat town (TERYT*)	Poviat town	Station code	2015	2016	2017	2015–2017
1462	Płock	MzPlocMiReja	1.55	1.69	1.17	1.47
1863	Rzeszów	PkRzeszRejta	1.24	1.32	1.47	1.35
2261	Gdańsk	PmGdaKacze02	0.87	1.02	0.89	0.92
2661	Dąbrowa Górnicza	SkKielJagiel	0.54	0.77	1.20	0.84
2465	Rybnik	SlDabro1000L	2.26	2.36	1.66	2.09
2473	Kielce	SlRybniBorki	3.84	4.62	3.22	3.89
2861	Elbląg	WmElbBazynsk	0.94	1.03	1.23	1.07

*Explanation: TERYT – "National Official Register of the Territorial Division of the Country" TERYT GUS (2021)
Source: Own study based on GIOŚ (2019)

Table 4. Converted Euclidean distances for benzene and C91–C95 leukaemias

Incidence							Mortality						
Variable according to ICD-10 code (2015–17)	C91	C92	C93	C94	C95	Benzene	Variable according to ICD-10 code (2015–17)	Benzene	C91	C92	C93	C94	C95
C91	0						Benzene	0					
C92	0.72	0					C91	1.28	0				
C93	0.71	0.91	0				C92	1.22	0.71	0			
C94	1.14	0.80	0.94	0			C93	1.39	0.75	1.06	0		
C95	1.00	0.73	1.14	1.25	0		C94	1.38	0.36	0.80	0.54	0	
Benzene	1.36	0.89	1.29	0.70	1.06	0	C95	0.83	1.02	0.66	1.20	1.09	0

Source: Own study based on Otwarte Dane (2020), Wojciechowska and Didkowska (2020), BDL GUS (2020) and GIOŚ (2019) was a decrease in benzene concentration between 2015 and 2017 (Table 3).

The results of multidimensional scaling are presented in Table 4 and Figure 1. In the case of incidence–benzene, the following values were obtained: STRESS-I = 0.08990, STRESS-II = 0.30983 and S STRESS = 0.02150. In the case of mortality–benzene, these values were 0.07907, 0.22115 and 0.01471, respectively. In both cases, the values indicate exceptionally low matching, but they may indicate the phenomenon of co-occurrence analysed in this article.

Benzene shows the greatest similarity between level of concentration and incidence of "other leukaemias of specified cell types (C94)" and "myeloid leukaemia (C92)", and between level of concentration and mortality of "leukaemia of unspecified cell type (C95)" and also "myeloid leukaemia (C92)" (Table 4). It is important to indicate that the relationships of benzene with the occurrence of myeloid leukaemia, especially its acute form, are mentioned in the general oncological literature (Natelson 2007; Kata and Kyrcz-Krzemień 2011; Fenga et al. 2016). In addition, it should be emphasised that currently the stance of the International Agency for Research on Cancer (IARC) on the subject is that the evidence (in humans) supporting the relationship between benzene and leukaemia is sufficient for acute non-lymphoid leukaemia, including acute myeloid leukaemia, but that the evidence is limited for chronic lymphoid leukaemia, chronic myeloid leukaemia, acute myeloid leukaemia in children, non-Hodgkin lymphoma and multiple myeloma (IARC 2020).

On the other hand, the similarities between benzene and myeloid leukaemia, especially its acute form, obtained in this research have been confirmed by other studies conducted around the world. An increased risk of acute myeloid leukaemia related to the concentration of benzene in the air has been found in the southern and central parts of the city of Tehran (Massaeli et al. 2018). During the studies conducted in Denmark, a pattern of higher risk of developing acute myeloid leukaemia (AML) in children (associated with the concentration of benzene in the air in their place of residence) was discovered, but not in cases of acute lymphocytic leukaemia (ALL) (Raaschou-Nielsen et al. 2018). However, some interesting results were obtained in the USA. Although the studies did not show a statistically significant relationship between acute myeloid leukaemia and benzene, the results for the main sources of benzene emissions (industrial, mobile on-road and area, other) suggest at least a 26% higher risk of acute myeloid leukaemia when

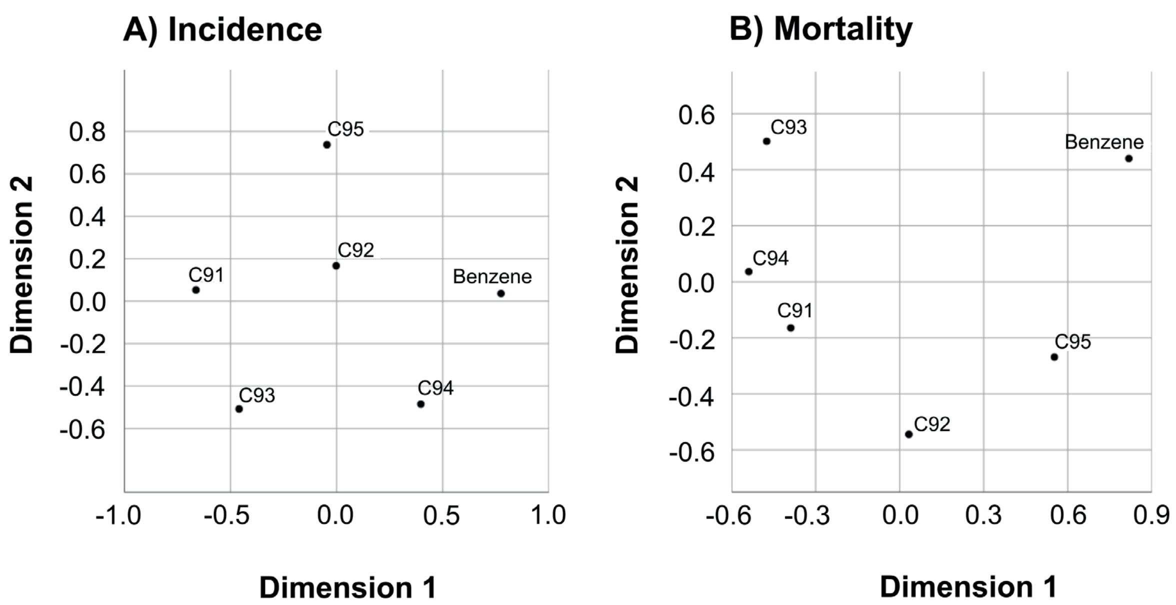

Fig. 1. Two-dimensional common space for incidence and mortality of leukaemia (C91–C95) and air pollution with benzene
Source: Own study based on Otwarte Dane (2020), Wojciechowska and Didkowska (2020), BDL GUS (2020) and GIOŚ (2019)

comparing the highest to the lowest tertile (Teras et al. 2019).

The low results of the obtained similarity can be explained by the research conducted by Carletti and Romano (2002) regarding the health risk caused by benzene pollution in an urban area (Naples). Based on these studies, it was concluded that only 9% of additive risk can be attributed to outdoor exposure (traffic and other external sources) (Carletti and Romano 2002).

In order to understand the low results of the similarity, it is important to take into account the phenomenon of tumour latency and exposure to a given factor (low dose and time). Studies show that in the period of 10–15 years after benzene exposure has stopped, the risk of developing leukaemia decreases or even disappears (Triebig 2010).

The obtained two-dimensional common space for leukaemia incidence and mortality (C91–C95) and air pollution with benzene indicates the presence of two rules (Fig. 1). The rule for co-occurrence is shown in dimension 2 (Fig. 1A). This rule can be interpreted as "environmental risk factors for leukaemia represented by benzene (environmental health risk factors)". Dimension 1 is not related to the co-occurrence phenomenon, but to the aetiology of the analysed leukaemias (Fig. 1A).

In the case of mortality (Fig. 1B), dimensions 1 and 2 can be treated as one rule: "air pollution represented by benzene, temporarily affecting the sick organism before death (environmental weakening of the patient's immunity to cancer)". In the relation between mortality and benzene, the phenomenon of co-occurrence is noticeable, but there is no strict cause-and-effect relationship.

Conclusions

As a result of the analysis with the use of k-means clustering, areas characterised by an unfavourable epidemic situation related to the incidence and mortality of leukaemia (C91–C95) were identified. In terms of incidence, this group includes the poviat towns of Kielce and Rzeszów, while Elbląg, Rybnik and Gdańsk are areas potentially at risk of an unfavourable epidemic situation. In terms of mortality, Elbląg is the area with the greatest unfavourable situation, and Kielce and Płock are potentially at the highest risk of developing into such areas.

The areas where adverse conditions related to benzene pollution (high average benzene concentration from 2015–17) and leukaemia incidence and mortality co-occur are the following towns: Kielce, Rybnik, Płock and Rzeszów. Among these areas, only Rzeszów noted an increase in benzene concentration between 2015 and 2017.

The study also involved an analysis based on the multidimensional scaling method, based on which it was found that the greatest similarity between benzene and leukaemia levels occurs for "other leukaemias of a specified cell type (C94)" (incidence) and for "leukaemia of unspecified cell type (C95)" (mortality). It should be emphasised, however, that "myeloid leukaemia (C92)" was second in terms of similarity between benzene and leukaemia levels, both in terms of incidence and mortality, which has been confirmed in the literature on the subject.

Based on a two-dimensional analysis of the common space for incidence and mortality of leukaemias (C91–C95) and benzene concentrations conducted as part of multidimensional scaling, two main rules for the co-occurrence of benzene and leukaemia were identified. The first can be described as: "environmental risk factors for leukaemia represented by benzene (environmental health risk factors)", and the second as: "air pollution represented by benzene, temporarily affecting the sick organism before death (environmental weakening of the patient's immunity to cancer)".

Taking into consideration the obtained results it might be concluded that it is necessary to continue the research for a longer time period, and in particular in the poviat towns of Kielce and Rzeszów.

Disclosure statement

No potential conflict of interest was reported by the authors.

Author contributions

Study design APi; data collection APi, APo; statistical analysis APi; result interpretation APi; manuscript preparation APi, APo; literature review: APi, APo.

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