The Regional Differences in Mortality Attributable to Tobacco in the Czech Republic in 2017

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BACKGROUND: Smoking, as the leading cause of premature death, has many negative consequences and represents an economic burden across the globe. There are several diagnoses caused wholly or partially by tobacco use. The groups of diagnoses that are mainly related to tobacco use are neoplasms and diseases of the circulatory and respiratory system. **AIMS:** This study aims to examine whether the probability of dying because of neoplasms and circulatory diseases is higher in the case of tobacco smokers compared to non-smokers. Supposing that there are economic differences between the regions of the Czech Republic, the differences between regions in terms of the number of deaths attributable to selected groups of diagnoses was examined. The differences between groups of regions based on the number of deaths related to neoplasms and diseases of the circulatory system were analysed. **METHODS:** To compare the probability of dying, the relative risks in the Czech Republic from 1994 to 2017 were calculated. Cluster analysis was conducted to compare the regions of the Czech Republic with regard to the number of deaths attributable to smoking. The comparisons are made within two disease categories. **RESULTS:** The results show the differences in regional mortality attributable to tobacco use in the Czech Republic. The probability of dying of a disease diagnosed as a smoking-related neoplasm is higher in comparison to that of death from a disease diagnosed as a smoking-related disease of the circulatory system. The level of deaths as a result of smoking differs between the genders. **CONCLUSION:** Our findings demonstrate a relationship between smoking as a death risk factor and neoplasms and diseases of the circulatory system. The specificity of diagnoses might be the reason for the greater disparities in the mortality connected to neoplasms.

Keywords | Czech Republic – Attributable Fractions – Tobacco – Regional Cluster Analysis – Avoidable Mortality – Diseases of the Circulatory System – Neoplasms

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1 INTRODUCTION

Tobacco smoking is one of the leading risk factors linked with avoidable mortality and premature deaths (Doll et al., 2005; Reitsma et al., 2017). Each year eight million deaths are caused by tobacco use, out of which seven million are caused directly by smoking, and the rest are caused indirectly; that covers those people who were exposed to cigarette smoke even though they did not smoke themselves (WHO, 2019c). Even though smoking ranks second in terms of risk, smoking (or tobacco consumption) is declining worldwide (WHO, 2019b). According to a study by Stanaway et al. (2018), the rate of deaths caused by smoking has decreased worldwide, from 146 deaths per 100 thousand in 1990 to 90 per 100 thousand in 2017. Central European countries rank among the states with the highest prevalence of tobacco use in the European region (WHO, 2019a).

In the Czech Republic, smoking accounted for 18.8% (17.7–19.9%) of the total deaths in 2017 (GBD, 2017; Sovinová et al., 2007). As with alcohol, tobacco use is subject to several risks, which increase the overall number of avoidable deaths. The results of national population-based prevalence studies revealed a high rate of tobacco smoking that varied between 28% and 32% in the decade leading up to 2013 (Sovinová et al., 2014). However, the implementation of essential tobacco control measures (Kulhánek & Kostelecká, 2020) based on the WHO Framework Convention on Tobacco Control contributed to the slightly decreasing trend of tobacco use in the Czech Republic. For example, in 2016, Decree No. 261/2016 Coll., on tobacco products, introducing a combined health warning on tobacco packages, came into force. In 2017, what was termed the smoke-free law (Law No. 65/2017 Coll., on the protection of health from the harmful effects of drugs) prohibiting smoking in indoor public spaces (such as bars, pubs, and restaurants) was adopted and helped to reduce daily tobacco consumption and increase motivation to quit smoking (Kulhánek et al., 2019). Furthermore, the excise duty on tobacco increased sharply in 2020. These legislative changes resulted in a decline of the prevalence of tobacco use among the Czech adult population to 24.9% in 2019 (Csémy et al., 2020). The most significant decrease has been observed in the youngest target group (15–24 years).

2 LITERATURE REVIEW

According to the observation study of Doll, Peto, Boreham, and Sutherland (2005), the life expectancy of smokers is ten years shorter than that of non-smokers. As stated by Mehta and Preston (2012), the contribution of smoking to national mortality patterns is not decreasing. To reduce the increasing mortality related to smoking, it is necessary to reduce the prevalence of smoking. Lochen et al. (2017) state that occasional smoking is not a healthier alternative to continuous smoking. There is a need for information for the general public and healthcare workers about the harms of occasional smoking. As shown by the results of Lubin et al. (2016), smoking fewer cigarettes per day for a longer period was more deleterious than smoking more cigarettes per day for a shorter period. Since there are many types of diseases related to tobacco, authors tend to analyse groups of diseases, or they select specific diagnoses (Jones et al., 2017; Hackshaw, Morris, Boniface, Tang, & Milenković, 2018).

In epidemiology, the relationship between variables is quantified by the effect size measures such as the relative risk, odds ratio, correlation coefficient, and mean. Mean value indicators are most often used to monitor the differences between the two groups being compared. In the case of a correlation coefficient, it is possible to examine what proportion of the change in a given variable (dependent variable) is caused by an explanatory variable (independent variable). The group of correlation indicators also includes what is called the coefficient of determination, which is the power of the Pearson correlation coefficient. In the case of the relative risk and odds ratio, it is possible to compare the effect of the risk factor on the phenomenon being studied and compare it between two groups (Richardson, 1996). As stated by Newcombe (2012), effect size indicators are divided into absolute and relative. Mean value indicators belong among the absolute indicators. The odds ratio and relative risk are relative indicators. In the case of relative risks and odds ratio authors (Kraemer et al., 2003; Henson, 2006; LeCroy & Krysik, 2007) consider whether the risk factor affects the phenomenon under observation or not.

Gavurová and Kubák (2017) analysed how sociodemographic indicators, e.g. age, region, gender, and marital status, influence the odds ratio of dying as a result of coronary disease. Coronary disease is associated with smoking. Therefore the effect of smoking on the outbreak of coronary disease is also considered in this study. As the study of Gavurová and Kubák also showed, the territory proved to be an essential variable in relation to coronary disease, and it is necessary to study and compare the level of deaths attributable to tobacco regionally. This was also the case in the study by Boffett et al. (2008), where the authors examine the relationship between territory and diseases caused by smoking. The authors showed the dependence between regions and the outbreak of diseases related to smoking and so the next part of the work examines the mortality caused by tobacco for two categories of diseases from the perspective of the regions of the Czech Republic that fill the scientific gap in the problem of smoking. As studies concerning the same problem that compare the genders in the Czech Republic are still lacking, this study fills this gap as well.

3 METHODOLOGY

In this study, data from the Registry of Deaths of the Czech Republic is used. This data was provided by the Institute of Health Information and Statistics of the Czech Republic as part of the research project Grant No. A-86-19. The Registry of Deaths contains information about individual deaths. Each death in the registry is described by the following attributes: gender, age at death, the primary cause of death (ICD-10), the external cause of death (ICD-10), the

Neoplasms		Diseases of the coronary system	
ICD–10 code	**Diagnosis group name**	**ICD–10 code**	**Diagnosis group name**
C00–C09	Malignant neoplasms of lip, oral cavity, and pharynx	I20–I25	Ischaemic heart diseases
C10–C14	Malignant neoplasms of lip, oral cavity, and pharynx	I26–I28	Pulmonary heart disease and diseases of pulmonary circulation
C15–C26	Malignant neoplasms of digestive organs (includes diagnoses: C15, C16, C18–C20, C21, C22, C25)	I47	Other forms of heart disease – paroxysmal tachycardia
C30–C39	Malignant neoplasms of respiratory and intrathoracic organs (includes diagnoses: C32, C33, C34)	I48	Other forms of heart disease – atrial fibrillation and flutter
C51–C58	Malignant neoplasms of female genital organs (includes diagnoses: C51.9, C53, C54, C55)	I49	Other forms of heart disease – other cardiac arrhythmias
C60–C63	Malignant neoplasms of male genital organs (includes diagnoses C60.0, C60.1, C60.2, C60.9)	I50	Other forms of heart disease – heart failure
C64–C68	Malignant neoplasms of urinary tract	I51	Other forms of heart disease – complications and ill-defined descriptions of heart disease
C92.0	Acute myeloblastic leukaemia	I60–I62	Cerebrovascular diseases – haemorrhage
D00	Carcinoma in situ of oral cavity, oesophagus, and stomach (includes diagnosis: D00.1)	I63–I66	Cerebrovascular diseases – infarction
D01.9	Carcinoma in situ of other and unspecified digestive organs – digestive organ, unspecified	I67–I69	Other cerebrovascular diseases
D02.0	Carcinoma in situ of the middle ear and respiratory system – larynx	I70–I79	Diseases of arteries, arterioles, and capillaries
D06	Carcinoma in situ of cervix uteri		
D09.0	Carcinoma in situ of other and unspecified sites – bladder		

Table 1 | Selected tobacco-related death diagnoses

region where the deceased lived, marital status, etc. For the purposes of this study, registered deaths during the period 1994–2017 were analysed.

As presented in *Table 1*, two categories of deaths caused by smoking-related diseases were selected for the purposes of this study: neoplasms and diseases of the coronary system. The category of neoplasms includes diagnoses such as Malignant neoplasms of lip, oral cavity, and pharynx (C00–C09), Malignant neoplasms of lip, oral cavity, and pharynx (C10–C14), Acute myeloblastic leukaemia (C92.0), etc. The category of diseases of the coronary system includes Ischaemic heart diseases (I20–I25), Pulmonary heart disease and diseases of pulmonary circulation (I20–I25), etc. Those categories were selected on the basis of their significant causation by smoking (Fenoglio et al., 2003; Park et al., 2014; Jones et al., 2017; Webster et al., 2019). As presented in the study of Jassem (2019), at least 30% of all cancer deaths are attributable to smoking. According to the WHO (2020), smoking is the single greatest avoidable risk factor for cancer mortality. Moreover, several authors (such as Lederle et al., 2003; Benjamin et al., 2017) emphasize the significance of the relation between smoking and diseases of the coronary system.

On the basis of previous studies (e.g. Zabransky et al., 2011; Collins & Lapsley, 2002; Park et al., 2014; Krueger et al., 2016), the fractions attributable to tobacco were identified. To calculate the number of deaths related to tobacco, we multiply the number of deaths linked to specific diagnoses by the corresponding fraction attributable to tobacco.

3.1 The relative risk of tobacco

To decide whether the likelihood of dying (because of the category of disease (previously described in *Table 1*) is higher in the case of smokers or non-smokers, we calculated the relative risks. Smoking was defined as a risk factor of death. The relative risks were calculated for the entire Czech population, stratified by gender and year of death. The relative risks, defined by Hackshaw et al. (2018), were calculated according to the formula below:

$$RR = \frac{a/(a+b)}{c/(c+d)}$$

where

- RR – the relative risk,
- a – the number of cases in which a person dies of a selected disease and their death is connected to smoking,

– b – the number of cases in which a person dies of diseases except for a selected disease, but their death is still connected to smoking,
– c – the number of cases in which a person dies of a selected disease, but their death is not connected to smoking,
– d – the number of cases in which a person did not die of a selected disease and their death is not connected to smoking.

According to the study of Sauerbrei and Blettner (2009), the confidence interval (CI) for the relative risks is calculated as follows:

$$CI\ \ 95\% = \ln(RR) \pm 1.96\sqrt{\frac{(e-a)/a}{e} + \frac{(f-c)/c}{f}}$$

– e – the sum of the number of cases in which a person dies of a selected disease and their death is connected to smoking and the number of cases in which a person dies of diseases except for a selected disease, but their death is still connected to smoking,
– f – the sum of the number of cases in which a person dies of a selected disease, but their death is not connected to smoking, and the number of cases in which a person did not die of a selected disease and their death is not connected to smoking.

To determine the statistical significance in the case of relative risks, we consider these hypotheses:

H0: the relative risk is not statistically different from 1
H1: the relative risk is statistically different from 1

If the confidence interval contains 1, there is no dependence between the risk factor and the phenomenon being investigated (we cannot reject the null hypothesis), and so it can be said there is no difference between the groups under comparison (those who were exposed to smoking and those who were not exposed to smoking).

3.2 Cluster analysis

Next, the calculation of the number of deaths in each region separately for 14 Czech regions and by gender was performed by means of cluster analysis. The cluster analysis was conducted regionally, using the number of deaths for each diagnosis (that is included in the selected diagnosis category). This cluster analysis aims to identify similar regions according to tobacco-related deaths. Hierarchical cluster analysis was implemented.

The distance between clusters, known as the Euclidean distance, was calculated according to the following formula:

$$d = \sqrt{\sum_{i=1}^{N} \left|P_i - Q_i\right|^2)}$$

– P,Q – Euclidean vectors

Later, a distance matrix was created (Maechler et al., 2019). It is computed by using the specified distance measure to compute the distances between the rows of a data matrix. The distances between clusters are recomputed at each stage by means of the Lance-Williams dissimilarity update formula according to Ward's minimum variance method. According to Chang et al. (2015), it is a convenient formulation that unifies the graph and the geometric methods. It is used as a generic equation for updating the dissimilarity matrix D at each iteration once the newly formed cluster $C_{(ij)} = C_i \cup C_j$ has been added to the dendrogram. The dissimilarity between C_{ij} and another cluster C_k is given by:

$$D(C_{(ij)}, C_k = \alpha_i D(C_i, C_k) + \alpha_j D(C_j, C_k) + \beta D(C_i, C_j) + \gamma \left| D(C_i, C_k) - D(C_j, C_k) \right|$$

The data analysis was conducted in SPSS Clementine and R-studio.

4 EMPIRICAL RESULTS

4.1 Relative risk calculation

As the focus of our interest was to determine whether the probability of dying because of the selected diagnoses category is greater in the case of smoking-related death compared to a non-smoking-related death, we calculated the relative risk (*Figure 1*). As none of the confidence intervals involves 1 (considering α=0.05), we reject the null hypothesis. It may be said that there is a difference between the groups under comparison.

In the case of neoplasms, we can see that in 1994 the relative risk was 2.53. After that, there was a slight decrease in the relative risks until 1996, followed by a continuous increase until 2017. In 1994, the probability of dying of a specified type of neoplasm was 2.53 times higher in the case of a smoking-related death compared to a non-smoking-related one. However, in 2017, the probability of dying

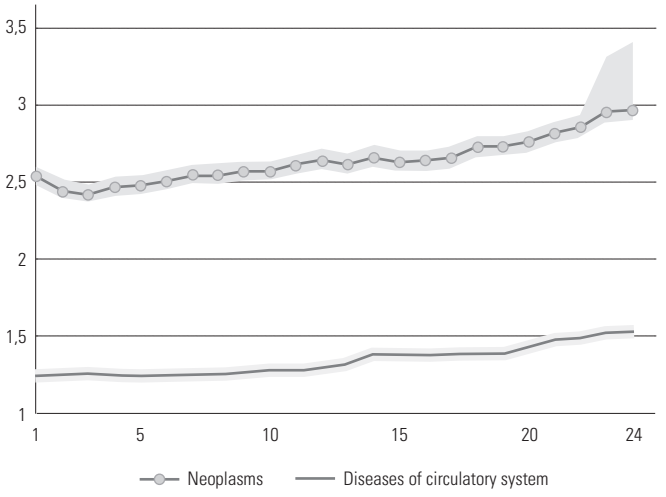

Figure 1 | Relative risks with corresponding confidence intervals
Source: authors' own calculations

was 2.96 times higher in the case of a death caused by a neoplasm attributable to smoking.

In 1994, in the case of cardiovascular disease, the probability of dying as a response to smoking was 1.27 times higher compared to a no-smoking death. The increase in the relative risk of coronary disease attributable to smoking was evident until 2017 as well. While in 1994, the relative risk of coronary disease attributable to smoking was 1.27, in 2017, it increased to 1.56.

On the basis of the results concerning the effect of smoking on deaths caused by neoplasms and diseases of the coronary system, there is evidence of a stronger association between smoking and neoplasms.

4.2 Neoplasms related to smoking

In this section, we present the comparison of clusters based on the number of deaths (neoplasms) related to smoking separately for women and men. This part takes into account the deaths from the Registry of Deaths caused by neoplasms as a side-effect of smoking in 2017.

The optimal number of identified clusters was four. Within the clusters, regions are similar according to the number of deaths attributable to smoking (neoplasms). However, the variability of the economic level in those regions is evident.

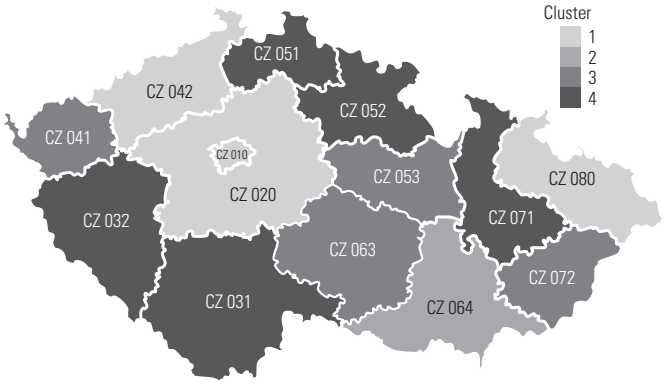

Figure 2 | Clusters of Czech regions with similar levels of deaths attributable to tobacco-related cancer in the case of women, 2017
Source: authors' own compilation

As presented by *Figure 2*, based on the results of the cluster analysis, we distinguish the following clusters, taking into account the number of women's deaths:

1. CZ 010 – Prague, CZ 042 – Ústí nad Labem Region, CZ 080 – Moravian-Silesian Region, CZ 020 – Central Bohemian Region;
2. CZ 064 – South Moravian Region;
3. CZ 041 – Karlovy Vary Region, CZ 053 – Pardubice Region, CZ 063 – Vysočina Region, CZ 072 – Zlín Region;
4. CZ 032 – Pilsen Region, CZ 051 – Liberec Region, CZ 052 – Hradec Králové Region, CZ 031 – South Bohemian Region, CZ 071 – Olomouc Region.

In this part, the results of the cluster analysis for men are shown. As in the case of women, there is variability among the economic levels within the clusters. On the other side, there are similarities when comparing the number of deaths attributable to smoking (men, neoplasms).

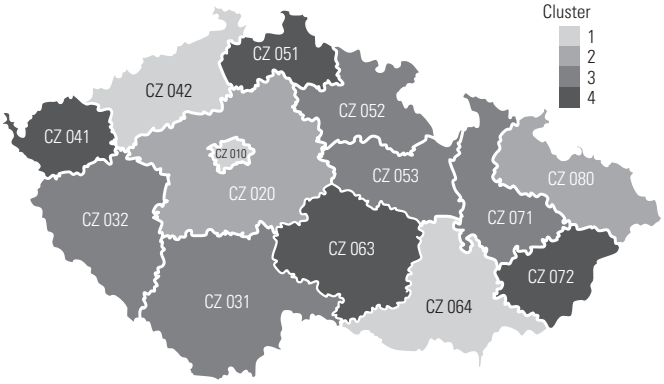

Figure 3 | Clusters of Czech regions with similar levels of deaths attributable to tobacco-related cancer in the case of men, 2017
Source: authors' own compilation

As in the case of women, the optimal number of cluster was four. *Figure 3* shows identified clusters that involve the Czech regions as follows:

1. CZ 010 – Prague, CZ 042 – Ústí nad Labem Region, CZ 064 – South Moravian Region;
2. CZ 080 – Moravian-Silesian Region, CZ 020 – Central Bohemian Region;
3. CZ 052 – Hradec Králové Region, CZ 053 – Pardubice Region, CZ 071 – Olomouc Region, CZ 031 – South Bohemian Region, CZ 032 – Pilsen Region;
4. CZ 041 – Karlovy Vary Region, CZ 063 – Vysočina Region, CZ 072 – Zlín Region, CZ 051 – Liberec Region.

4.3 Diseases of the circulatory system related to smoking

Smoking is related to many types of diseases. This section presents a comparison of clusters to make a comparison

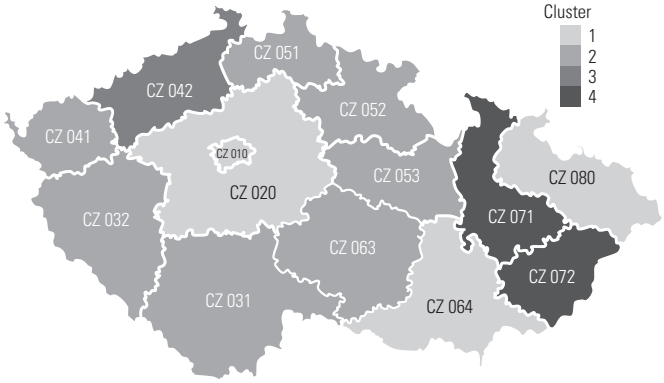

Figure 4 | Clusters of Czech regions with similar levels of deaths attributable to tobacco-related circulatory diseases in the case of women, 2017

of the regions of the Czech Republic according to the number of deaths (diseases of the circulatory system) related to smoking as well. *Figure 4* shows the clusters of regions based on women's deaths connected to diseases of the circulatory system attributable to smoking as follows:

1. CZ 010 – Prague, CZ 042 – Ústí nad Labem Region, CZ 064 – South Moravian Region;
2. CZ 080 – Moravian-Silesian Region, CZ 020 – Central Bohemian Region;
3. CZ 052 – Hradec Králové Region, CZ 053 – Pardubice Region, CZ 071 – Olomouc Region, CZ 031 – South Bohemian region , CZ 032 – Pilsen Region;
4. CZ 041 – Karlovy Vary Region, CZ 063 – Vysočina Region, CZ 072 – Zlín Region, CZ 051 – Liberec Region.

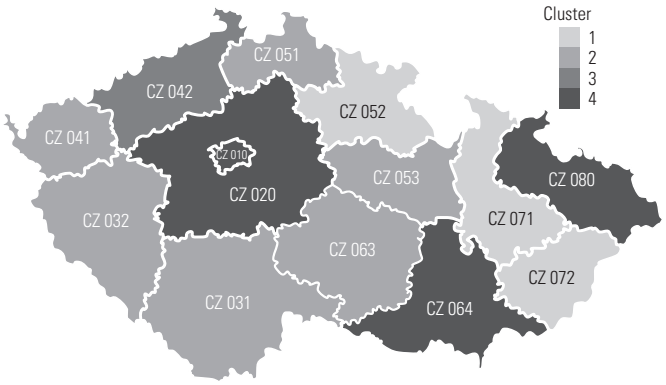

Figure 5 | Clusters of Czech regions with similar levels of deaths attributable to tobacco-related circulatory diseases in the case of men, 2017

Next, on the basis of the number of deaths related to tobacco and diseases of the coronary system, we continued by performing cluster analysis for men. The optimal number of clusters was estimated as four (*Figure 5*). The clusters contain the regions of the Czech Republic as follows:

1. CZ 052 – Hradec Králové Region, CZ 071 – Olomouc Region, CZ 072 – Zlín Region;
2. CZ 041 – Karlovy Vary Region, CZ 063 – Vysočina Region, CZ 051 – Liberec Region, CZ 031 – South Bohemian Region, CZ 032 – Pilsen Region, CZ 053 – Pardubice Region;
3. CZ 042 – Ústí nad Labem Region;
4. CZ 010 – Prague, CZ 080 – Moravian-Silesian Region, CZ 020 – Central Bohemian Region, CZ 064 – South Moravian Region.

5 DISCUSSION

As there are many diseases related to mortality attributable to the tobacco use, two disease categories were analysed in this study. The first category was neoplasms, which include the following diagnoses: Malignant neoplasms of lip, oral cavity, and pharynx (C00–C09), Malignant neoplasms of lip, oral cavity and pharynx (C10–C14). The category of diseases of the coronary system includes diseases related to cardiological issues, such as Ischaemic heart diseases (I20–I25), Pulmonary heart disease, diseases of pulmonary circulation (I20–I25), etc.

The calculated relative risks showed that the relationship between smoking and death is higher in the case of neoplasms than in diseases of the circulatory system. Although the relative risks were statistically significant, in the case of circulatory diseases, the probability of smoking-related deaths was less than two times higher. However, as we can see, the relative risks increase over time. That means the probability of the death of smokers compared to non-smokers is gradually increasing.

Since we proved that the probability of death is rising, this study seems to contradict the OECD statement that the prevalence of smoking is declining. However, the apparent discrepancy might be explained by the results of Lubin et al. (2016). In their study, it was proved that smoking is more harmful in the case of smokers who smoke less but do so for a long time.

The results of the cluster analysis confirmed the similarities between the individual regions, despite the fact that in the clusters that were mentioned, there were regions that differ from each other in terms of economic indicators. These results thus provoke debate as to whether smoking is directly linked to economic indicators or not. In the case of smoking, we can consider that smoking will not depend on the economic status of the population but on other factors, which may include e.g. lifestyle or the age at which a person died. The results of a study by Gavurová and Kubák (2019) in which the authors examined the relationship between age and death confirm that the level of mortality associated with cardiovascular disease increases with age. Thus, in regions that are similar in terms of the number of tobacco-related deaths, it can be assumed that, although they are not economically similar, there is demographic similarity. That means that there might be a similarity in terms of age structure between the people living in these regions.

When the results of the cluster analysis of neoplasms were compared with the results of the cluster analysis of circulatory disease, there was more significant variability between the sexes in the case of neoplasms.

While in the case of neoplasms in women, Prague was in the same cluster as the Ústí nad Labem Region, Moravian-Silesian Region and Central Bohemian Region, in the case of men, Prague was in the same cluster as the South Moravian Region and Ústí nad Labem Region. In the case of women, the South-Moravian Region was in cluster 2. For women, the Karlovy Vary Region, Pardubice Region, Vysočina Region, and Zlín Region were in the same cluster. In the case of men, the Karlovy Vary Region was also in the same cluster as the Vysočina and Zlín regions but the Pardubice Region was missing. Instead of the Pardubice Region, the Liberec Region was in cluster 4. However, in the case of women the last cluster was formed by the Pilsen, Liberec, Hradec Králové, South Bohemian, and Olomouc regions. The third cluster in the case of men includes the Hradec Králové, Pardubice,

Olomouc, South Bohemian, and Pilsen regions. We explain these differences by the fact that in the case of cancer, different diseases affect different sexes. Thus, the differences are caused by specific diagnoses that might be related only to one gender, not to both of them. On the other hand, diseases of the circulatory system are connected to both genders in the same way.

By comparing the results of the cluster analyses of cardiovascular diseases associated with smoking, we see similarities, such as the fact that the Ústí nad Labem Region forms a separate cluster in the case of both women and men. Furthermore, in the case of men and the case of women, clusters 1 and 4 are the same, and include the Central Bohemian, Prague, South Moravian, and Moravian-Silesian regions. We also see similarities in the last two groups, where the Karlovy Vary Region, Pilsen Region, South Bohemian Region, Vysočina Region, Pardubice Region, and Liberec Region constitute the same clusters. While in the case of men, the Hradec Králové Region is in the same cluster as the Olomouc region and Zlín Region, in the case of women, this region belongs to the most numerous cluster.

6 CONCLUSION

This study confirms the assumption that the mortality of smokers is higher compared with the mortality of non-smokers. There is a relation between smoking as a death risk factor and neoplasms and diseases of the circulatory system. By comparison, it was found that in the case of the Czech Republic, the probability of a cause of death diagnosed as a smoking-related neoplasm is higher compared to one diagnosed as a smoking-related disease of the circulatory system.

Through the conducting of the cluster analysis, the regional differences among smoking-related deaths became evident. As the results show, the levels of deaths resulting from smoking are different between the genders. Greater disparities were revealed in the mortality connected to neoplasms, which might arise from the specificity of diagnoses. This specificity means that in the case of tumours, more diagnoses are typical of just one gender.

The present work helps provide public health professionals, policymakers, and other public authorities with a better understanding of the necessity of government intervention in tobacco prevention. It provides a platform and significant knowledge to evaluate better the efficiency of tobacco regulation across the regions of the Czech Republic.

Authors' contributions: BG prepared the econometric design of the study, AK performed the literature review and the data mining procedure. The data analysis was performed by MT and BG. BG, MT, and AK participated in the data interpretation. All the authors contributed to the draft and approved the final manuscript before its submission.

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