Available online at www.sciencedirect.com

ScienceDirect

Procedia Economics and Finance 24 (2015) 93 – 100

Procedia Economics and Finance

www.elsevier.com/locate/procedia

International Conference on Applied Economics, ICOAE 2015, 2-4 July 2015, Kazan, Russia

Epidemiology and Forecast of the Prevalence of Esophageal Cancer in the Countries of Central and Eastern Europe

Valery Boyko[a], Nadiya Dubrovina[b]*, Petro Zamyatin[a], Russell Gerrard[d], Sergey Savvi[a], Vjacheslav Lazirskiy[a], Vitaly Ghydetskyy[a], Alexander Sinelnikov[c], Denis Zamiatin[a],Olena Kolesnikova[e], Evgeniy Shaprynskyy[f]

[a]GI "Zaitcev V.T. Institute of General and Urgent Surgery of NAMS of Ukraine", Balakirev driveway, 1a, Kharkov, 61018, Ukraine
[b]University of Economics,Dolnozemska cesta 1,Bratislava, 85235,Slovakia
[c]*Lake Erie College of Medicine (LECOM),5000 Lakewood Ranch Blvd., Bradenton FL 34211,USA*
[d]*Cass Business School, City University London, 106 Bunhill Row,London EC1Y 8TZ, UK*
[e]*GI "MalayaL.T. Therapy National Institute of NAMS of Ukraine", Postysheva 2a,Kharkov 61039,Ukraine*
[f]*Vinnitsa National Pirogov Memorial Medical University, Vinnitsa, Ukraine*

Abstract

In this article the problems of the prevalence of esophageal cancer and the spatial distribution of mortality rates from this disease are considered using as examples the NUTS 2 regions in six countries of Central and Eastern Europe (Austria, Germany, the Czech Republic, Poland, Slovakia and Hungary). The rates of mortality from esophageal cancer are analyzed by statistical methods and by spatial econometrics. A study is carried out of the features of the spatial distribution of the rates of mortality from esophageal cancer. It allows us to determine more and less epidemiologically affected regions and to carry out more detailed studies on the link between the mortality rates from esophageal cancer and various factors, such as the environmental situation, socio-demographic characteristics of the population, culture and nature of nutrition, the general health status of the population, the availability of resources and the level of healthcare in the region. By means of the multifactor regression model we forecast the rates of mortality from esophageal cancer, taking into account characteristics of the countries, the dynamics of the number of patients with diseases of the esophagus and the general time trend.

Selection and/or peer-review under responsibility of the Organizing Committee of ICOAE 2015.

Keywords: epidemiology; esophageal cancer; rates of mortality; spatial analysis; forecast

* Nadiya Dubrovina. Tel.:+421 908-228-798; fax:+421-2/6729-1124
E-mail address: nadija@mail.ru

Selection and/or peer-review under responsibility of the Organizing Committee of ICOAE 2015.
doi:10.1016/S2212-5671(15)00622-X

1. Introduction

Esophageal cancer ranks sixth in the world among the main causes of death connected with malignant tumors. More than 450 000 people worldwide have this diagnosis and the occurrence of this disease is increasing rapidly (Cancer Trends, 2011). Standardized rates of the frequency of incidence of esophageal cancer and the rates of mortality from this cause differ significantly by countries and regions. High rates of incidence of esophageal cancer are registered in southern and eastern Africa, the USA, Singapore and other countries forming the so-called “Asian belt” (Turkey, the northeast of Iran, Kazakhstan, the northern and central regions of China). In the EU countries the highest standardized rates of incidence of esophageal cancer are registered in Great Britain, Ireland, the Netherlands, Belgium, Denmark, France, Hungary and Lithuania (Kollarova et al, 2007, Pennathur et al, 2013).

Two histological types of esophageal cancer – squamous carcinoma and adenocarcinoma – are predominant, and there are notable trends of prevalence of one type of carcinoma over another in different countries and continents, arguing different aetiology of incidence of these types of carcinoma and different habitude of certain populations and races to these types of carcinoma (Lepage et al, 2008, Pennathur et al, 2013). Other types of esophageal cancer (melanoma, leyosarcoma etc.) occur quite rarely.

Squamous esophageal carcinoma is the most prevalent carcinoma of the esophagus worldwide and it is the most frequent in some Asian countries, in Kazakhstan, in northern and southern Africa, and in northern and central China. In these countries the rate of incidence of esophageal carcinoma is more than 100 cases per 100 thousand population. In the economically developed countries of Europe, in the USA, in Australia and Singapore, with a so-called “Western lifestyle,” adenocarcinoma of the esophagus is more prevalent, or else both types of esophageal carcinoma occur with equal frequency. The rates of incidence of esophageal cancer differ by age and gender groups. The risk of occurrence of this disease increases with age, and esophageal cancer occurs more frequently in males than in females (Ribeiro, 1996, Castellsague and Lagergren, 1999, Wu, 2001, Mayne, 2002, Lindblad, 2005, Yao, 2006).

Among the main reasons giving rise to a risk of esophageal cancer, the following are noted: smoking and overuse of alcohol; obesity; overconsumption of smoked and fried red meat products, preserved products, marinated or spicy food; insufficient consumption of fruits and vegetables; use of too hot food and drinks; intoxication with pesticides or nitrates; use of corns, affected with mold fungi; environmental pollution; work with petroleum products.

Factors contributing to the growth of squamous esophageal carcinoma are: achalasia, mutations of enzymes assisting in the metabolism of alcohol; intoxication with caustic soda; irradiation of the chest; non-epidermolytic palmoplantar keratoderma. Among the factors affecting the growth of esophageal adenocarcinoma, the following are noted: symptomatic gastro-esophageal reflux; Barret’s esophagus; irradiation of the chest; the use of drugs assisting in the relaxation of the lower esophageal sphincter; hereditary factors (Castellsague and Lagergren, 1999, Wu, 2001, Mayne, 2002, Polednak, 2003, Reid, 2010).

Research carried out in different countries has indicated that the prognosis of the course of esophageal cancer is unfavorable, because the disease is predominantly diagnosed in the later stages (Polednak, 2003, Pennathur, 2008, 2013). Even if cancer is diagnosed in the early stages and a surgical operation is possible, the survival rate is much less than in the case of other types of cancer. Thus, the survival potential of patients with esophageal cancer in economically developed countries with a high standard of living and high consumption of healthcare is 15% to 25% over a 5-year time horizon, while in countries with transitional economies and a low standard of living and healthcare, this probability is 5% to 10%, and sometimes even less (Pennathur, 2008, 2009, 2013). Despite certain progress and positive results in the detection and treatment of esophageal cancer, mortality rates remain high in the USA and in the EU (Polednak, 2003, Lepage, 2008, Pennathur, 2013).

A number of epidemiological studies related to the analysis of the prevalence of esophageal cancer in the Czech Republic and Hungary are presented in the studies of H. Kollarova, L. Mahova, L. Gersheni, Sh .Tulassaya *et al.* (Dušek, 2005, Kollarova, 2007). At the same time, there is scientific interest in a study of the epidemiological features of esophageal cancer in the countries of Central and Eastern Europe (CEE), which makes a comparative analysis of morbidity and mortality rates in different CEE countries taking into account the prevailing trends and which constructs predictions based on the application of mathematical and statistical methods and models.

2 Purpose, materials and methods of the study

The following purposes were set in the study: to investigate the rates of incidence of the esophageal cancer and the corresponding rates of mortality using the example of six CEE countries (Austria, Germany, the Czech Republic, Poland, Slovakia and Hungary); to explore the features of the spatial distribution of mortality from esophageal cancer for the regions of these countries; and to obtain predicted values of mortality, based on existing trends and characteristics of these countries. The materials on which the research is based are: Eurostat data, containing the rates of morbidity and mortality from different causes in the EU countries and in the regions of NUTS2; and results arising from the analysis of various reports of scientists engaged in problems of oncologic diseases. The methods of analysis of time series, methods of spatial econometrics and statistics were used for the study, presented here. Statistica and R were used for information processing and the required calculations.

3. The results of statistical and econometrical study

The problem of the increasing growth rate of the spread of oncologic diseases is one of the most important for national healthcare systems in the countries of Central and Eastern Europe (CEE). The rates of mortality and morbidity caused by esophageal cancer for six countries of Central and Eastern European (Austria, Germany, the Czech Republic, Poland, Slovakia and Hungary) are analysed in our study. The selection of these countries is interesting from the standpoint of studying the epidemiological characteristics of the extension of esophageal cancer using the methods of spatial statistics (Kopczewska, 2006), as well as a comparative analysis of the situation in countries with different levels of socio-economic development and healthcare. The results of mathematical and statistical analysis of the distribution of mortality from esophageal cancer by NUTS2 regions of six CEE countries from 2001 to 2010 were carried out.

As followed from the statistical analysis, the average rate of mortality from esophageal cancer is 4.71 per 100 thousand population for the entire sample, containing data on 84 NUTS2 regions of six CEE countries in 2001, but there is quite a high (about 27.61%) value of the coefficient of variation, indicating heterogeneity of rates across countries and regions. Thus, for the data of the year 2001, the minimum mortality rate from esophageal cancer was 2.1 per 100 thousand population in the Czech Republic (Prague region), and the maximum rate was 7.7 per 100 thousand population in Hungary (northern Hungary region). The coefficients of variation of mortality from esophageal cancer differ significantly across countries. Thus, in 2001, the lowest rate of the coefficient of variation in mortality from esophageal cancer was in Hungary (14.721%), and the highest one in Austria (37.77%).

In 2001 in Austria, the lowest rate of mortality from esophageal cancer was registered in the region of Upper Austria (2.5 per 100 thousand population) and the highest in the region of Burgenland (7.5 per 100 thousand population).

In the Czech Republic in 2001 the lowest rate of mortality from esophageal cancer was observed in the region of Prague (2.1 per 100 thousand population) and the highest in the region of Central Moravia (4.6 per 100 thousand population).

In Germany in 2001 the lowest rate of mortality from esophageal cancer was observed in Lower Bavaria (4.2 per 100 thousand population), and the highest in Chemnitz (7.2 per 100 thousand population).

In Hungary in 2001 the lowest rate of mortality from esophageal cancer was in the region of Southern Alföld (Southern Great Plain) (5.7 per 100 thousand population), and the highest in Northern Hungary (7.7 per 100 thousand population).

In Poland in 2001, the lowest rate of mortality from esophageal cancer was in the Subcarpathian Voivodeship (2.2 per 100 thousand population), and the highest value of this index was noted in Opole Voivodeship (5.1 per 100 thousand population).

In Slovakia in 2001, the lowest rates of mortality from esophageal cancer were observed in the Bratislava region (3.7 per 100 thousand population), and the highest one – in the region of Western Slovakia (6.4 per 100 thousand population).

In 2010 the average rate of mortality from esophageal cancer was 5.217 per 100 thousand population, demonstrating a growth in the average rate. In addition, the value of the coefficient of variation of mortality from esophageal cancer for the entire sample increased to 30%. At the same time, a decrease in the values of the coefficients of variation was observed for individual countries. Thus, the lowest values of the coefficients of variation in mortality from esophageal cancer were observed in the Czech Republic (12.242%) and Hungary (16.418%), while the highest one – in Austria (26.43%). In 2010 the lowest rate of mortality from esophageal cancer was noted in the Subcarpathian Voivodeship in Poland and was 2.0 per 100 thousand population, and the highest (10.1) was registered in the region of Trier (Germany).

In 2010 in Austria the lowest mortality rate from esophageal cancer (3.0 per 100 thousand population) was observed in several regions (Tyrol, Salzburg, Carinthia), and the highest was observed in Burgenland (6.0 per 100 thousand population).

In the Czech Republic in 2010 the lowest mortality rate from esophageal cancer was registered in Prague (3.8 per 100 thousand population) and the highest (5.4 per 100 thousand population) was observed in the region of Central Moravia.

In Germany in 2010 the lowest rate of mortality from esophageal cancer was in Lower Bavaria (3.7 per 100 thousand population), and the highest in Trier (10.1 per 100 thousand population).

In Hungary in 2010 the lowest rate of mortality from esophageal cancer was observed in the region of West Dunantul (5.1 per 100 thousand population), and the highest in Northern Hungary (7.7 per 100 thousand population).

In Poland in 2010 the lowest rate of mortality from esophageal cancer was registered in Subcarpathian Voivodeship (2.0 per 100 thousand population), and the highest in Podlachian Voivodeship (4.6 per 100 thousand population).

In Slovakia in 2010 the lowest rate of mortality from esophageal cancer was in Eastern Slovakia (3.9 per 100 thousand population), and the highest in Central Slovakia (6.1 per 100 thousand population).

The high homogeneity of the data and the reduction of variations in the values between regions can be explained by the pursuit of a committed policy in the area of cancer prevention carried out at the regional level, particularly in disadvantaged areas. For example, in 2001 the mean rate of mortality from esophageal cancer was markedly higher in Hungary, but in 2010 this striking difference against the background of the other countries is absent.

Using spatial econometrics tools in R, the maps were constructed for the analysis of spatial features of the distribution of the rates of mortality from esophageal cancer; in this case the NUTS2 regions of the six CEE countries were split into four groups according to their values.

The first group includes regions where the rates of mortality from esophageal cancer do not exceed the lower quartile; the second group includes regions where the rates are in the range from the lower quartile to the median; the third group includes regions where the rates are greater than the median, but less than the upper quartile; the fourth group includes regions where the rates are greater than the upper quartile.

Based on a visual analysis of the maps it is evident that the most disadvantaged areas, with quite high mortality rates from esophageal cancer, are represented by clusters of regions in northwestern Germany and in Hungary. To justify the existence of a nonrandom distribution of groups of regions, characterized by different rates of mortality from esophageal cancer, the values of the coefficients of spatial correlation known as Moran's I and Geary's C were calculated. From the statistical significance of the Moran and Geary coefficients, as calculated by the authors, a moderate positive spatial autocorrelation is observed for the data of 2001 and of 2010. That is, based on the spatial analysis of the distribution of the rates of mortality from esophageal cancer, we can conclude that, in general, regions with higher mortality rates from esophageal carcinoma are surrounded by similar regions, i.e., regions with relatively high rates, and, vice versa, regions with lower rates of mortality from esophageal cancer are surrounded by regions with low values of these rates.

The methods of spatial statistics allow us to analyze various local clusters of regions and to explore the spatial régimes where the qualitative change from one group of regions to another takes place. There are four types of spatial régimes: "HH" – regions with quite high rates, surrounded by regions with high rates; "HL" – regions with high rates, surrounded by regions with low rates; "LL" – regions with low rates, surrounded by regions with relatively low rates; "LH" – regions with low rates, surrounded by regions with high rates (see Kopczewska, 2006). Fig. 1 shows the spatial régimes characterizing the features of distribution of mortality rates from esophageal cancer in the regions of CEE countries.

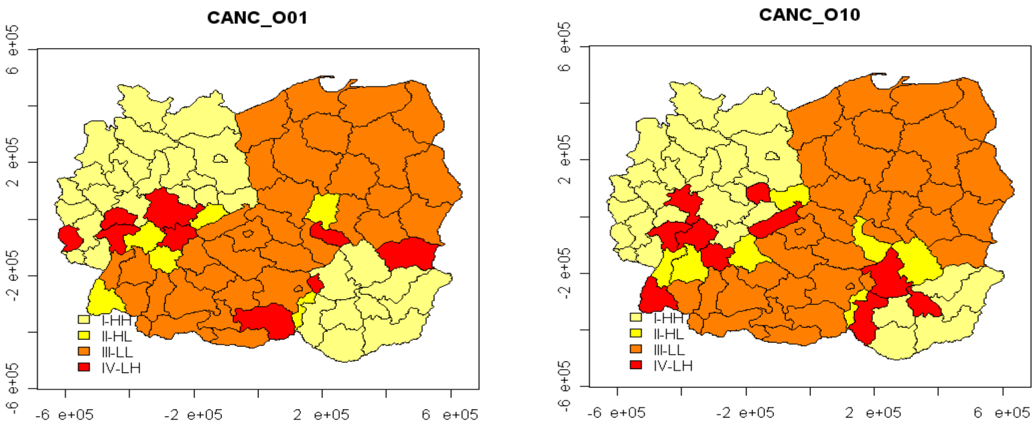

Fig. 1. Spatial regimes of distribution of mortality rates from esophageal cancer per 100 thousand population for the NUTS2 regions of CEE countries in 2001 and 2010
Source: Eurostat data, processed by N. Dubrovina in R.

Based on an analysis of maps for these régimes built in R, we can see that the northwestern and central regions of Germany, and certain regions of Hungary, are characterized as régimes of “HH” type, i.e. where regions with quite high rates are surrounded by regions with similarly high rates. At the same time, “LL” régimes, i.e. where regions with low rates are surrounded by regions with relatively low rates, are characteristic for the majority of regions in Poland, the Czech Republic and Austria. Transient regimes occur in certain central and southern regions of Germany or in frontier regions of other countries.

To investigate the dynamics of rates of mortality from esophageal cancer in CEE countries, it is advisable to analyze trend models.

A linear trend equation has the form (1):

$$\hat{y}_{t,k} = a_k + a_{1,k} \cdot t\,, \tag{1}$$

where the $\hat{y}_{t,k}$ are the forecast values of rates of mortality from esophageal cancer (per 100 thousand) in year t for country k, a_k and $a_{1,k}$ are estimates of the model parameters of a linear trend for the rates of mortality from esophageal cancer in the country $\boldsymbol{k}$, and t is the time factor.

Data on rates of mortality from esophageal cancer (per 100 thousand population) in CEE countries during the period of 2000–2010 were used for the construction of models of linear trends.

The estimation of the a_k parameter can be interpreted as an initial level of the rate of mortality from esophageal cancer in the moment of time $t = 0$ (for the year 2000) for country $\boldsymbol{k}$, and $a_{1,k}$ is an annual rate of change of the rate of mortality from esophageal cancer in country $\boldsymbol{k}$. The variable t takes the value 1 for the year 2001, 2 for the year 2002 etc. The estimates a_k and $a_{1,k}$ of the unknown parameters for the linear trend model are found with the help of least squares method.

As seen from the results of trend analysis, the trends in the rates of mortality from esophageal cancer in Austria, the Czech Republic, Germany and Hungary are described quite well by linear models, as argued by sufficiently high coefficients of correlation.

This trend is observed most clearly for Germany, where the coefficient of correlation, 0.955, is close to 1. Different estimates of the a_k parameter are observed for different countries, revealing the presence of initial differences between countries. The estimates of $a_{1,k}$ are positive for Austria, the Czech Republic and Germany, indicating an annual growth of the rates of mortality from esophageal cancer, while the estimate of a_k is negative in Hungary, indicating that the rates of mortality from esophageal cancer are tending to decrease.

No linear trends were observed in the rates of mortality from esophageal cancer in Poland and Slovakia during the period 2000–2010, as indicated by the fact that the estimates of the $a_{1,k}$ and the relevant values of the coefficients of correlation are close to 0.

The analysis of interdependencies of the trends in the rates of mortality from esophageal cancer, carried out on the basis of matrices of correlations between the trends in CEE countries, demonstrated that the trends in these rates are the most interconnected in Germany and Austria (coefficient of pair correlation is 0.684), and also in the Czech Republic and Germany (coefficient of pair correlation is 0.517).

The trends in the rates of mortality from esophageal cancer have a significant inverse relationship in Austria, the Czech Republic and Germany in comparison with the trend in Hungary, as indicated by the negative values of the correlation coefficient. The trends in the rates of mortality from esophageal cancer are weakly dependent or independent for other groups of the countries.

To assess the forecast of the rates of mortality from esophageal carcinoma in the population, we constructed a multivariate linear model, using categorical variables, reflecting the country and the time factor, and taking into account the current trend and the number of patients with esophageal diseases (per 100 thousand population).

This model is represented by the following equation (2):

$$deathr\_o(t) = b_0 + b_1 \cdot disch\_0 + b_2 \cdot t + c_1 \cdot d\_cz + c_2 \cdot d\_hu + c_3 \cdot d\_au + c_4 \cdot d\_pl + c_5 \cdot d\_sl + \varepsilon \,, \quad (2)$$

where $deathr\_o(t)$ is a model rate of mortality from esophageal cancer (per 100 thousand population) at the moment of time t; $disch\_0$ is an index of the number of patients with the diseases of esophagus (per 100 thousand of population); $d\_cz, d\_hu, d\_au, d\_pl, d\_sl$ are categorical variables indicating the country (the Czech Republic, Hungary, Austria, Poland and Slovakia); $b_0, b_1, b_2, c_1, c_2, c_3, c_4 \cdot, c_5$ are estimates of parameters multiplying these factors, and ε is a random value.

All categorical variables take the value 1 or 0. There is no categorical variable for Germany to avoid multicollinearity, i.e., all the categorical variables take the value zero to indicate Germany. The time variable t takes the value 1 for 2001, 2 for 2002, etc.

A proper statistically significant model was constructed (Table 1) and the estimates of parameters were found using the program Statistica.

Table 1. The results of the estimates of model parameters

Factors	Estimates of parameters	Standard deviation of the estimates of parameters	t- value	Level of statistical significance
	B, C	St. Err. of B or C	t(44)	p-value
Intercept	4.409997	0.493997	8.927182	1.96E-11
DISCH_O	0.013669	0.006406	2.133889	0.038464
T	0.027689	0.012899	2.146637	0.037374
D_CZ	-0.84348	0.2856	-2.95336	0.005029
D_HU	0.909695	0.226868	4.009805	0.000232
D_AU	-2.35028	0.241078	-9.74905	1.45E-12
D_PL	-1.3718	0.274598	-4.99567	9.78E-06
D_SL	-0.19713	0.340853	-0.57835	0.565978

Source: Eurostat data, processed by N. Dubrovina in the program Statistica.

Fisher’s test value was 98.15 at a level $p < 0.001$ for the given model. The value of the multiple correlation coefficient was 0.969 and the coefficient of determination was 0.939 for the constructed model. The Durbin-Watson test statistic was 2.11, indicating the absence of autocorrelation of errors. High values of the coefficients of correlation and determination indicate quite a good fit for the model, suggesting the possibility of using it as a basis for forecasts.

All parameter estimates appear statistically significant by Student's t-test at $p < 0.05$, except the categorical variable for Slovakia. The positive estimate of the parameter for $disch\_0$ shows that the rate of mortality from esophageal cancer increases with the increase of the number of patients with diseases of the esophagus. The positive value for the coefficient of the time factor t means that an annual growth of the rates of mortality from esophageal cancer is detected for the CEE countries examined. The different values of the coefficients of the categorical variables demonstrate the differences in mortality from esophageal cancer by countries and indirectly indicate the efficiency of the health system, its policies, aimed at a prevention and treatment of esophageal cancer.

The estimates of the relevant categorical variables are negative for Austria, the Czech Republic and Poland, i.e., *ceteris paribus,* the rates of mortality from esophageal cancer will be lower, due to ongoing activities, effectiveness of treatment and other factors. Although a negative value is obtained for the categorical variable for Slovakia, it is close to 0 and is not statistically significant.

A positive statistically significant estimate of the coefficient of the categorical variable is obtained for Hungary, confirming the previous summaries, that higher rates of mortality from esophageal cancer are observed in Hungary.

On the basis of the constructed model (2), forecast rates of mortality from esophageal cancer were obtained for the CEE countries examined for 2014-2015 (Table 2).

Table 2. Forecast rates of mortality from oesophageal cancer per 100 thousand population in CEE countries

Country	Year	Forecast	Lower confidence limit	Upper confidence limit
Austria	2014	4.02	3.766	4.273
	2015	4.051	3.778	4.323
The Czech Republic	2014	4.447	4.176	4.718
	2015	4.471	4.178	4.764
Germany	2014	5.704	5.348	6.06
	2015	5.732	5.355	6.109
Hungary	2014	6.172	5.792	6.552
	2015	6.171	5.752	6.589
Poland	2014	4.129	3.867	4.39
	2015	4.176	3.893	4.458
Slovakia	2014	4.921	4.616	5.226
	2015	4.941	4.611	5.272

Source: the calculations by the authors in the program Statistica

The forecast is constructed on the basis of the characteristics of individual countries, the number of patients with esophageal diseases and a common trend reflecting the growth of the rate of mortality from esophageal cancer.

It should be noted that the forecast, constructed with the use of a multifactor model, is more reliable because it takes into account the complex influence of different factors, rather than just the time factor, as in the trend model. Furthermore, the use of the complete set of quantitative factors and categorical variables (qualitative factors) in one model allows us to use the entire set of observations, improving the statistical reliability of the model itself and of the forecast obtained from the model.

Conclusions

An analysis of the rates of mortality from esophageal cancer in different countries of Central and Eastern Europe confirms our conclusions that these values vary significantly by country and by region. Application of the methods of spatial statistics allows us to confirm the existence of a non-random element in the distribution of the rates of mortality from esophageal carcinoma in population by NUTS 2 region for six CEE countries. The clusters of similar regions and the clusters of regions with transitional régimes, i.e. those in which the situation is qualitatively different from the surrounding group of regions, were identified using cartographic output from spatial models. The study of the features of the spatial distribution of the rates of mortality from esophageal cancer allows us to determine more and less epidemiologically affected regions. We then carry out more detailed studies, related to the link between the rates of mortality from esophageal cancer and a variety of factors, such as the environmental situation, the socio-demographic characteristics of the population, the culture and nature of nutrition, the general health status of the population, the availability of resources and the level of healthcare in the region. A study of the trends in the rates of mortality from esophageal cancer revealed common tendencies in the level of CEE countries; a multifactor model, obtained through the use of the entire data set for the CEE countries, provided an opportunity to construct a more accurate forecast of the rates of mortality from esophageal cancer, taking into account characteristics of the countries, the dynamics of patients with the diseases of the esophagus and the general time trend.

References

Cancer Trends No.8. Cancers of oesophagus and stomach. March 2011. Available from: www.ncri.ie

Castellsague X, Munoz N, De Stefani E, Victora CG, Castelletto R, Rolon PA et al. Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in males and females. Int. J. Cancer. 1999; 82 (5). pp.57–64.

Dušek L, Mužík J, Kubásek M, Koptíková J, Žaloudík J, Vyzula R. The Czech national web portal of cancer epidemiology [online]. Masaryk University, [2005], 26.3.2007 [cit. 2007-3-26]. Incidence and mortality C15 – malignant neoplasm of esophageal, time trend 1977–2002. Available from: URL:http://www.svod.cz.

Kollarova H., Machova L., Horakova D., Janoutova G., Janout V. Epidemiology of esophageal cancer – an overview article. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2007, 151(1). Pp.17–28. 17.

Kopczewska K. Ekonometria i statystyka przestrzenna. Wydanie I, Warszawa, 2006. – 162 s.

Lagergren J, Bergström R, Lindgren A, Nyrén O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N. Engl. J. Med. 1999; pp. 25–31.

Lepage C, Rachet B, Jooste V, Faivre J, Coleman MP. Continuing rapid increase in esophageal adenocarcinoma in England and Wales. Am. J. Gastroenterol. 2008; pp.94–99.

Lindblad M, Rodriguez LA, Lagergren J. Body mass, tobacco and alcohol and risk of esophageal, gastric cardia and gastric non-cardia adenocarcinoma among males and females in nested case-control study. Cancer Causes Control 2005; 16(3):2. pp. 85–94.

Mayne S.T, Navarro S.A. Diet, obesity and reflux in the etiology of adenocarcinomas of the esophagus and gastric cardia in humans. J. Nutr. 2002;132 (11 Suppl): pp. 3467–3470.

Pennathur A, Farkas A, Krasinskas AM, et al. Esophagectomy for T1 esophageal cancer: outcomes in 100 patients and implications for endoscopic therapy. Ann. Thorac Surg. 2009; pp. 48–55.

Pennathur A, Luketich JD. Resection for esophageal cancer: strategies for optimal management. Ann. Thorac Surg. 2008; pp. 51–56.

Pennathur A., Gibson M., Jobe B., Luketich J. Oesophageal carcinoma. Lancet 2013; 381. pp. 400–412.

Polednak A.P. Trends in survival for both histologic types of esophageal cancer in US surveillance, epidemiology and end results areas. Int. J. Cancer 2003; pp. 98–100.

Reid B.J, Li X, Galipeau P.C, Vaughan T.L. Barrett's oesophagus and oesophageal adenocarcinoma: time for a new synthesis. Nat. Rev. Cancer 2010; pp. 87–101.

Ribeiro U. Jr, Posner M.C, Safatle-Ribeiro A.V, Reynolds J.C. Risk factors for squamous cell carcinoma of the esophagus. Br. J. Surg. 1996; 83(9):11. pp.74–85.

Wu AH, Wan P, Bernstein L. A multiethnic population-based study of smoking, alcohol and body size risk of adenocarcinomas of the stomach and esophagus (United States). Cancer Causes Control 2001; 12(8):7. pp. 21–32.

Yao P.F, Li G.C, Li J, Xia H.S, Yang X.L, Huang H.Y et al. Evidence of human papilloma virus infection and its epidemiology in esophageal squamous cell carcinoma. World J. Gastroenterol. 2006; 12(9):13. pp.52–57.