DOI:https://doi.org/10.37699/2308-7005.2.2020.21

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TENDENCIES OF THE MORTALITY RATES FROM ESOPHAGEAL CANCER IN THE EU COUNTRIES AND UKRAINE

Summary. In this article the problems of the prevalence of esophageal cancer and the distribution of mortality rates from this disease are considered in EU countries. The rates of mortality from esophageal cancer are analyzed by statistical methods and time series analysis. A study is carried out of the features of the tendencies of mortality rates from esophageal cancer in six EU countries and in Ukraine. It is emphasized that 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 should be took into account for development of the programmes for the prevention of prevalence of esophageal cancer. By means of the models for time series analysis we forecast the rates of mortality from esophageal cancer for six countries of EU and for Ukraine, which can be used for the development of the national strategies to reduce the prevalence and mortality from esophageal cancer.

Key words: *epidemiology, esophageal cancer, rates of mortality, time series analysis, forecast.*

Introduction

Esophageal cancer has ranks in the top of 15 main causes of death connected with malignant tumors in the world. According to reports more than 450 000 people worldwide have this diagnosis and the occurrence of this disease is increasing rapidly [1, 2]. 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 [2, 5, 11].

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 [2, 7, 11, 12]. 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 of 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 [1, 2, 4, 6, 8, 9, 12].

Based on an analysis conducted in Ireland in 1994–2009 of 331 cases of esophageal cancer, the following anatomic localisations have been observed: in 23 % of male and 18 % of female – in the lower part of the esophagus; in 6 % of male and 10 % of female – in the middle part of the esophagus; in 2 % of male and 3 % of female – in the upper part of the esophagus and 10 % in both groups with non-specific localisation [2].

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 [2, 4, 6, 7, 8, 9, 12].

Other scientists note that several environmental risk factors are associated with esophageal cancer, which many researchers believe may result from chronic irritation of the esophagus. Over time, persistent inflammation can cause the cells that line the esophagus to undergo cancerous changes and form tumors, which can potentially invade the underlying connective tissue (submucosa) and muscle layer [12].

According to the different numerous studies researchers believe this chronic irritation could ultimately cause esophageal cancer because: it can eventually cause genetic mutations in the esophageal cells; the genetic mutations can change the way that the esophageal cells normally grow, making them divide and multiply at a much faster rate than normal; the rapidly growing cells can eventually form a cancerous tumor, which will steadily grow as more cells accumulate in the mass; the cancerous cells can eventually invade other nearby structures, such as the lymph nodes, blood vessels in the chest and other organs such as the lungs, liver or stomach [9, 12].

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 [1, 12, 13]. 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 [2, 10, 12].

The purposes of research. Materials and methods

The purposes of research were: to analyse the distribution of the mortality rates in EU countries; to analyse the tendencies in some EU countries and Ukraine for long-term period and predict expected values of mortality rates from esophageal cancer for next time period; to formulate some recommendations for the prevention of esophageal cancer in communities.

As materials we used review of scientific articles, reports, results of the reports and case studies, as well as Eurostat and WHO database contained data about mortality rates from esophageal cancer in the different countries. For the quantitative study of the data the methods of mathematical statistics and time series analysis were used.

The main results and discussions

In our research we studied the features of the distribution of mortality rates from esophageal cancer in EU countries during long-term period of 1994-2010. It is should be noted that these data were available in Eurostat, even on NUTS2 level, but later data concerning the dynamics of the number of death from this malignant neoplasm are presented only in database of WHO [11].

At first we suggested the hypothesis about normal distribution of mortality rates from esophageal cancer in EU countries. For this study we analysed the basic indicators for descriptive statistics, such as: mean, median, quartiles, standard deviation, skewness and kurtosis. Our results of the calculation are presented in table 1.

As it is seen from the table 1, the minimum value of mortality rate from esophageal cancer was 0,5 (Cyprus), and the maximum value of mentioned indicator was 12,3 (the United Kingdom). The median and mean were relatively close each other and made 4,45 and 4,91 respectively. The skewness was positive and it means that the distribution has asymmetrical character.

In Fig. 1 the empirical histogram of distribution of the mortality rates from esophageal cancer is given and expected frequencies for normal distribution were calculated and shown on the plot.

As we can see from the Fig.1 there are some differences in the values for the empirical and theoretical normal (or Gauss) distribution. To confirm it we applied Kolmogorov-Smirnov test for normality and null hypothesis about normal distribution was rejected at level $p<0,01$. It means that to need more detail study the features of mortality from esophageal cancer in certain countries of EU, because the differences in the values of these indicators may be explained by: socio-economic factors; pollution of environment from chemical industry, mining, agriculture, construction, etc.; national and race structure of population, the national traditions in

Table 1

Descriptive statistics of sample for mortality rates from esophageal cancer in EU countries from 1994-2010

	Mean	Confid.for mean		Median	Min	Max	Lower Quartile	Upper Quartile	Std. Dev.	Skewness	Kurtosis
		-95 %	+95 %								
MRE_EU	4,91	4,71	5,12	4,45	0,5	12,3	3,7	5,95	2,18	1,29	2,35

Source: own calculations in Statistica

diet, life style, etc.; living standards; capacities of the national health systems and efficiencies of their functions in screening and treatment of oncology diseases.

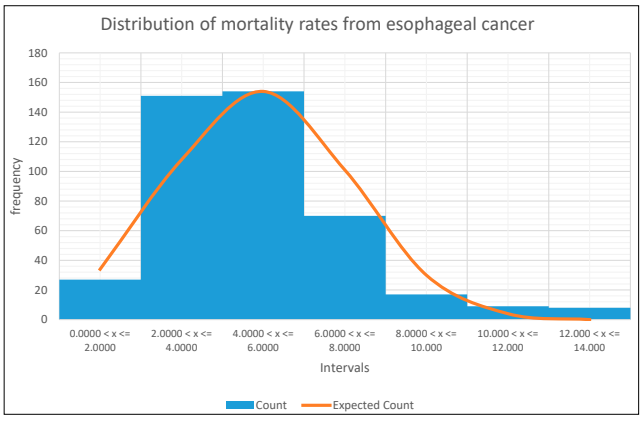

Fig. 1. Histogram of the empirical distribution of mortality rates from esophageal cancer in EU countries for 1994-2010

Source: own elaboration in Excel and Statistica

Thus, we selected six EU countries like Austria and Germany from the core of well-developed countries of EU and former socialist countries such as Czech Republic, Hungary, Poland and Slovakia. As well we analysed situation of the mortality rates from esophageal cancer in Ukraine. The tendencies of these indicators are given in Fig. 2.

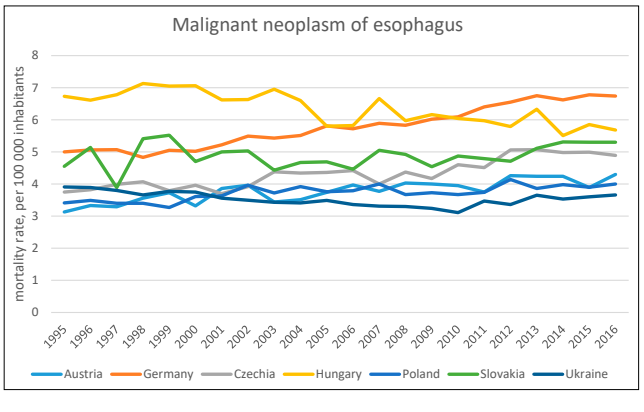

Fig. 2. Tendencies of the mortality rates from esophageal cancer for some EU countries and Ukraine

Source: own elaboration in Excel

These countries were selected for the comparative analysis due to their socio-economic conditions, geographical positions and common borders, differences in capacity and funding national healthcare systems. In addition, it is important to compare the situation in Ukraine with her neighbours like Slovakia, Poland and Hungary.

As we can see from the Fig. 2 the tendencies of the mortality rates vary in countries presented for the analysis. The higher values were observed in Hungary, but in recent years the decreasing is noted for the mortality rates from esophageal cancer in this country. But, in Germany the opposite situation is revealed, during last years the mortality rates from esophageal cancer are going up.

To study the features of the tendencies of the mortality rates from esophageal cancer we used models of linear trend and exponential smoothing with linear trend adjustment (Holt's models).

The characteristics of linear trend models for the mortality rates from esophageal cancer are given in table 2.

Table 2

The characteristics of linear trend models for the mortality rates from esophageal cancer in different countries

Variable	Estimate of b	St. Error of b	t(20)	R coef-ficient	Std. Error of esti-mate
Austria					
Intercept	3,28	0,08	38,57	0,84	0,19
T (time variable)	0,04	0,01	6,83		
Germany					
Intercept	4,64	0,07	70,93	0,98	0,15
T (time variable)	0,1	0	19,69		
Czechia					
Intercept	3,61	0,09	38,63	0,89	0,21
T (time variable)	0,06	0,01	8,67		
Hungary					
Intercept	7,08	0,14	52,41	0,81	0,31
T (time variable)	-0,06	0,01	-6,13		
Poland					
Intercept	3,41	0,07	50,25	0,76	0,15
T (time variable)	0,03	0,01	5,29		
Slovakia					
Intercept	4,7	0,17	27,82	0,26	0,38
T (time variable)	0,02	0,01	1,21		
Ukraine					
Intercept	3,73	0,08	45,6	0,53	0,19
T (time variable)	-0,02	0,01	-2,79		

Source: own elaboration in Statistica

As we can see from the results of the calculations for the linear trend models and their comparative analysis with real data, the estimations for intercept were statistically significant at level $p<0.01$ and closed for real data for 1994. The estimations for slope or parameter for T (time variable equals 1 for 1995, 2 for 1996, etc.) were mostly statistical significant at level $p<0,05$ and have positive or negative values, that means increasing or decreasing tendencies for period of 1995-2010. In these models the value of the slope indicates annual change in the mortality rates from esophageal cancer. The estimations for the coefficients of correlation for linear trend models were high for Austria, Germany, Czech Republic, Hungary and Poland, but for Slovakia and Ukraine these estimations for the coefficient of correlation for linear trend models are essentially lower.

Thus, to take into account more complicated character of dynamics of the mortality rates from esophageal cancer we applied exponential smooth-

ing with trend adjustments or Holt's models. Their characteristics are presented in table 3.

As it is seen from this table these models are also good fitted the real data, for most models the mean absolute percentage error (m.a.p.e.) don't exceed 5 %, only for case of Slovakia the value of m.a.p.e. is slightly more than 6 %.

Thus, the models of linear trends as well as Holt's models can be used for forecast of the mortality rates from esophageal cancer for countries which we selected for our research. The results of the predictions for next 5-year period are given in table 4.

It is should be noted that our calculations were relatively closed for the results of the analysis pro-

Table 3

The characteristics of Holt's models

Country	S0	T0	Alpha (α)	Gamma (γ)	Mean error	Mean absolute error	Mean percentage error	Mean abs. perc. error
Austria	3,102	0,0557	0,083	0	0	0,16	-0,081	4,283
Germany	4,959	0,0829	0,683	0	0	0,111	-0,103	1,947
Czechia	3,723	0,0543	0,095	0	0,007	0,17	-0,184	3,937
Hungary	6,755	-0,05	0,209	0	0,018	0,245	-0,025	3,884
Poland	3,396	0,0281	0,008	0	0,009	0,116	0,103	3,099
Slovakia	4,532	0,0357	0	0	-0,061	0,302	-1,794	6,326
Ukraine	3,916	-0,012	0,731	0	-0,001	0,091	-0,083	2,591

Source: own elaboration in Statistica

Table 4

Predicted values of mortality rates from esophageal cancer for some EU countries and Ukraine for period of 2017-2021

Predictions	2017	2018	2019	2020	2021
Austria					
Lower boundary	4,12	4,15	4,18	4,21	4,24
Predicted value by linear trend model	4,29	4,34	4,38	4,43	4,47
Upper boundary	4,47	4,53	4,58	4,64	4,7
Predicted value by exp.smoothing with linear trend (Holt's model)	4,38	4,44	4,5	4,55	4,61
Germany					
Lower boundary	6,76	6,85	6,94	7,02	7,11
Predicted value by linear trend model	6,89	6,99	7,09	7,19	7,29
Upper boundary	7,03	7,14	7,25	7,35	7,46
Predicted value by exp.smoothing with linear trend (Holt's model)	6,86	6,94	7,02	7,11	7,19
Czechia					
Lower boundary	4,84	4,89	4,94	4,99	5,03
Predicted value by linear trend model	5,03	5,1	5,16	5,22	5,28
Upper boundary	5,23	5,31	5,38	5,46	5,53
Predicted value by exp.smoothing with linear trend (Holt's model)	4,99	5,04	5,09	5,15	5,2
Hungary					
Lower boundary	5,35	5,26	5,18	5,1	5,02
Predicted value by linear trend model	5,63	5,56	5,5	5,44	5,37
Upper boundary	5,91	5,86	5,82	5,78	5,73
Predicted value by exp.smoothing with linear trend (Holt's model)	5,69	5,64	5,59	5,54	5,49
Poland					
Lower boundary	3,9	3,92	3,94	3,96	3,97
Predicted value by linear trend model	4,04	4,07	4,1	4,13	4,15
Upper boundary	4,19	4,22	4,26	4,3	4,33
Predicted value by exp.smoothing with linear trend (Holt's model)	4,04	4,07	4,1	4,13	4,16
Slovakia					
Lower boundary	4,71	4,7	4,69	4,68	4,67
Predicted value by linear trend model	5,06	5,08	5,09	5,11	5,12
Upper boundary	5,41	5,45	5,49	5,53	5,57
Predicted value by exp.smoothing with linear trend (Holt's model)	5,35	5,39	5,43	5,46	5,5
Ukraine					
Lower boundary	3,16	3,13	3,11	3,08	3,05
Predicted value by linear trend model	3,33	3,32	3,3	3,28	3,26
Upper boundary	3,5	3,5	3,49	3,49	3,48
Predicted value by exp.smoothing with linear trend (Holt's model)	3,62	3,61	3,6	3,59	3,58

Source: own elaboration in Statistica

vided in other article (V. Boyko et al., 2016) and where the predicted values obtained for 2014-2016 were closed to their real data observed later [1]. Also in the mentioned research the regional characteristics were studied and spatial effect was revealed, that is important to provide further investigations for factors which have significant impact on the mortality rates from the esophageal cancer in the different regions or territories in selected countries.

In our research we can see that according official data from WHO Ukraine has relatively low level of the mortality rates from esophageal cancer, but the question is in the problem of possible differences between "official" data and real situation, for example, what is "true" registration of deaths caused by esophageal cancer; how often to meet bad diagnostics and recognition of some cases; what is about artificial attempts to "improve" the real situation, etc. In addition, due to serious problems in healthcare and poor funding of this system in Ukraine, a lot of patients don't have need access to modern medical services like diagnostics of diseases or screening oncology, or treatment. Besides, in Ukraine the national cancer register should be modernised and accumulate all information about patients with oncology. The modern treatment, palliative care, rehabilitation should be accessible for all population in Ukraine.

Conclusions

The national programmes and strategies for the prevention of the esophageal cancer should be developed and complex of government and public activities including avoiding exposure to certain substances that are present in some workplaces and other environments should be implemented. It is important to inform population to avoid exposure to certain environmental factors that are believed to contribute to the risk of esophageal cancer, such as: tobacco smoke; asbestos; certain mineral spirits, paints and varnishes; toluene, a hydrocarbon present in coal and petroleum; synthetic adhesives, such as formaldehyde resins, epoxy resins, polyvinyl acetate resins and hot melts; sulphuric acid, a substance used in the manufacture of certain fertilizers, soaps and rayon; as an electrolyte in batteries; and in the purification of petroleum products; perchlorethylene, a common dry-cleaning solvent; carbon black and other polycyclic aromatic hydrocarbons, which are contained in chimney soot, printing ink and certain rubber products.

Also the improvement of the diagnostics and treatment of esophageal cancer should be essential part of the national programmes and strategies. Esophageal cancer surgery is a common type of treatment and can eliminate most (or all) of the cancerous cells from the body, although radiation therapy or chemotherapy may be recommended after the operation to ensure that any remaining cells are destroyed. Sometimes, radiation therapy or chemotherapy are recommended prior to surgery in an attempt to shrink the tumor and make surgery easier.

In treating esophageal cancer, surgery is most often recommended when the cancer is at an earlier stage and has not spread to other parts of the body. Because it is more common for esophageal cancer to be diagnosed after it has reached advanced stages, surgery is not typically the primary treatment method. In some instances, surgery might be used not with an intention to completely eradicate the cancer, but rather to prevent or relieve symptoms it may cause and improve a patient's quality of life.

REFERENCES

1. Boyko V, Dubrovina N, Zamiatin P, et al. Epidemiology and Forecast of the Prevalence of Esophageal Cancer in the Countries of Central and Eastern Europe. J. Adenocarcinoma. 2016, 1:2. doi: 10.21767/2572-309X.100010
2. Cancer Trends No.8. Cancers of oesophagus and stomach. March 2011. Available from: www.ncri.ie
3. 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.
4. Duљek L, Muћnk J, Kubбsek M, Kortнkovб J, Žaloudнk 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.
5. 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.
6. Lagergren J, Bergstrцm R, Lindgren A, Nyrйn O. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N. Engl. J. Med. 1999; pp. 25–31.
7. 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.
8. 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.
9. 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.
10. Polednak AP. 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.
11. WHO statistics database. Available at: http://apps.who.int/healthinfo/statistics/mortality/whodpms/params_ex.php; https://moffitt.org/cancers/esophageal-cancer/faqs/what-environmental-factors-contribute-to-your-risk-of-esophageal-cancer/

ТЕНДЕНЦІЇ РІВНЯ СМЕРТНОСТІ ВІД РАКУ СТРАВОХОДУ В КРАЇНАХ ЄС ТА УКРАЇНІ

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Резюме. У цій статті розглядаються проблеми поширеності раку стравоходу та розподілу смертності від цієї хвороби в країнах ЄС. Темпи смертності від раку стравоходу аналізуються статистичними методами та аналізом часових рядів. Проведено дослідження особливостей тенденцій смертності від раку стравоходу у шести країнах ЄС та в Україні. Підкреслюється, що слід враховувати різні фактори, такі як екологічна ситуація, соціально-демографічні характеристики населення, культура та характер харчування, загальний стан здоров'я населення, наявність ресурсів та рівень охорони здоров'я в регіоні, треба враховувати розробку програм профілактики поширеності раку стравоходу. За допомогою моделей аналізу часових рядів ми прогнозуємо показники смертності від раку стравоходу для шести країн ЄС та для України, які можуть бути використані для розробки національних стратегій зменшення поширеності та смертності від раку стравоходу.

Ключові слова: *епідеміологія, рак стравоходу, показники смертності, аналіз часових рядів, прогноз.*

ТЕНДЕНЦИИ СМЕРТНОСТИ ОТ РАКА ПИЩЕВОДА В СТРАНАХ ЕС И УКРАИНЕ

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Резюме. В данной статье рассматриваются проблемы распространенности рака пищевода и распределения показателей смертности от этого заболевания в странах ЕС. Показатели смертности от рака пищевода анализируются статистическими методами и анализом временных рядов. Изучены особенности тенденций смертности от рака пищевода в шести странах ЕС и в Украине. Подчеркивается, что следует принимать во внимание различные факторы, такие как экологическая ситуация, социально-демографические характеристики населения, культура и характер питания, общее состояние здоровья населения, доступность ресурсов и уровень здравоохранения в регионе. во внимание при разработке программ по профилактике распространенности рака пищевода. С помощью моделей для анализа временных рядов мы прогнозируем показатели смертности от рака пищевода для шести стран ЕС и для Украины, которые можно использовать для разработки национальных стратегий по снижению распространенности и смертности от рака пищевода.

Ключевые слова: *эпидемиология, рак пищевода, показатели смертности, анализ временных рядов, прогноз.*