

Epidemiological estimation incidence and mortality from cancer of the larynx in Ukraine and Europe

To Cite:

Olha M, Oleksandr P, Zhanetta C, Anzhela B. Epidemiological estimation incidence and mortality from cancer of the larynx in Ukraine and Europe. Medical Science, 2021, 25(114), 1963-1970

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Peer-Review History

Received: 20 June 2021

Reviewed & Revised: 23/June/2021 to 29/July/2021

Accepted: 31 July 2021

Published: August 2021

Peer-review Method

External peer-review was done through double-blind method.

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ABSTRACT

Background: Cancer incidence among the world's population has a steady upward trend. Malignant tumours of the larynx are the most frequent in the structure of oncological morbidity of otolaryngological organs and occupy a leading position. Smoking and alcohol are the major behavioural risk factors. In 95% of cases of laryngeal cancer, tumours are squamous. **Methods:** Using statistical and medico-epidemiological methods, the analysis of the database of the National Cancer Registry of Ukraine for 2010-2020 and information on "Notification of a patient with a first-time diagnosis of cancer or other malignant neoplasm" (form № 090 / r). **Results:** The dynamics of incidence and mortality from laryngeal cancer by sex and age in Ukraine and Europe region in the period 2010-2020 was analyzed. **Conclusion:** The incidence and mortality rate of laryngeal cancer among men has been declining since the late 1990s, while for women, these rates remain virtually unchanged.

Keywords: laryngeal cancer, incidence, mortality, epidemiology

1. INTRODUCTION

The most common malignant tumour of the upper respiratory tract is cancer of the larynx. According to the National Cancer Registry of Ukraine, the proportion of laryngeal cancer is about 5.06-5.5% per 100 thousand of the population among all oncological diseases, and early stages (T1 and T2) are detected in 30-40% of patients with newly diagnosed laryngeal cancer (Bray *et al.*, 2018). In the structure of oncological diseases of otolaryngological organs, laryngeal cancer occupies from 38 to 65% (Bray *et al.*, 2018). According to IARC, more than 151,000 new cases of laryngeal cancer are registered every year in the world, and more than 70,000 people die from them (Ferlay *et al.*, 2018). In recent years, the incidence of laryngeal cancer in the world has begun to rise slightly and amounted to 2.2 per 100,000 populations, primarily associated with the pandemic Covid 19. Moreover, in developed countries, compared with developing countries, the incidence rates were more than 2.5 times higher (4.7 per 100,000 and 1.7 per 100,000 populations, respectively).



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The highest incidence and mortality of larynx cancer are observed in European countries (52,000 new cases per year), which is probably due to the influence of harmful factors (namely smoking) and coverage of preventive examinations of almost 98% of the population and is about 2-5% of all laryngeal cancers, with a much higher incidence in men (90%) than in women (Nocini *et al.*, 2020). The annual incidence in men in southern and northern Europe is 18 and 6 per 100 thousand populations, respectively. In women, the incidence rate is not higher than 1.5 per 100 thousand per year.

The main risk factors for larynx cancer (Zuo *et al.*, 2017) are smoking and drinking alcohol of any type. Also, when considering the etiology of laryngeal cancer should take into account the various anatomical parts of the larynx. When smoking tobacco, the risk of affecting the vocal folds and glottis prevails, is more significant while alcohol for affecting the supraglottic space (Saedi *et al.*, 2009). Back in 2010, a large population-based case-control study in southern Europe found that more than 90% of current laryngeal cancer cases could have been prevented by quitting smoking and alcohol (Marron *et al.*, 2010). Smoking is associated with a high risk of disease, but the combination of smoking and alcohol significantly increases this risk, and the abandonment or even reduction of only one of these factors (such as alcohol) can prevent a quarter of cases.

The link between laryngeal cancer and asbestosis is controversial. It should be noted that this relationship is enhanced by exposure to tobacco smoke. Reviews (Serra-Majem, 2016) highlight that in many cohorts with exposure to asbestos on workers' health, the risk of lung cancer was twice as high, and there is also a risk of developing laryngeal cancer: the relative risk ranges from 1.14 to 3.75. Other occupational carcinogenic agents include nickel and mustard gas, isopropyl alcohol and its vapours (Dal Maso *et al.*, 2016). Tumours arise from colonies of cells that have undergone specific genetic changes. A significant proportion of human head and neck tumours have been proven to be caused by changes in common oncogenes, such as p16, p53, PTEN, Rb, or proto-oncogenes: cyclin D1, pb3, and EGFR. In the case of laryngeal cancer D1 Rb, cyclin, EGFR may play a large role in terms of carcinogenesis.

All laryngeal papillomas are caused by human papillomavirus - genomic sequences of types bi 11. These types of human papillomaviruses are also known to cause oropharyngeal papillomas. Spontaneous malignant transformation of papillomas is a rare event, certainly less frequent than the risk observed in papillomas of the genital tract. The cofactors in these cases are not yet clearly defined: smoking is known to be one of these cofactors, but what explains the occurrence of cancer in non-smoker; X-ray therapy used in 1930 to treat laryngeal papilloma's caused about one third of the laryngeal carcinomas subsequently observed in these patients. Carcinomas in papilloma patients are fuelled by a similar genomic sequence of human papillomavirus type 6 or 11 found in papilloma's, but possibly the malignant potential of the tumour is associated with molecular rearrangements. Although up to 15% of laryngeal carcinomas do contain human papillomavirus DNA, these cases tend to have a low level of p53 mutation compared to tumours that do not contain human papillomaviruses. This feature supports the idea that squamous cell carcinoma in collaboration with the human papillomavirus may represent a separate category (Ang *et al.*, 2009).

We should also not forget about Epstein-Barr virus, a member of the family of human herpes viruses, which is associated with a number of lymphoproliferative diseases, some histological variants of cancer of the stomach, lungs, salivary, parotid, breast (Leoncini *et al.*, 2015), which is also very important in the emergence of viral carcinogenesis of the upper respiratory tract, one of which is laryngeal cancer. In this case, the transforming activity of a number of proteins of the Epstein-Barr virus was shown, one of the manifestations of which is the ability to inactivate the p53 gene. A significant role in the process of epithelial cell malignancy is played by the latent membrane protein of the Epstein-Barr virus (LMP-I).

The literary sources available to us practically do not cover the viral carcinogenesis of laryngeal cancer: there is no clear data on the role of the Epstein-Barr virus in the pathogenesis of RH, the mechanisms of tumour cell transformation have not been identified, as well as the contribution of factors that can contribute to oncogenes, in particular, the Epstein virus -Barr-associated chronic inflammatory processes in the mucosal epithelium, its immunosuppressive effect upon infection of the host organism. However, data were obtained on the modifying effect of carcinogenic environmental factors on the sensitivity of epithelial cells to infection with the Epstein-Barr virus (Herrero *et al.*, 2013).

Many epidemiological studies have shown (Ghosh *et al.*, 2016) that risk factors for laryngeal cancer associated with eating foods rich in fruits and vegetables and regular consumption of vitamins such as carotenoids, retinol and vitamin C can reduce the risk of laryngeal cancer. It has also been found that the simultaneous abuse of tobacco and alcohol acts synergistically and increases the risk of laryngeal cancer.

2. MATERIALS AND METHODS

According to the majority of epidemiologists, who have studied the features of the spread of malignant tumours in various regions of the world, the main source of information for determining the incidence of cancer is the materials of the state registration of cases

and causes of death. Analyzed the database of the National Cancer Registry of Ukraine for 2010-2020 and information on "Notification of a patient with a first-time diagnosis of cancer or other malignant neoplasm" (form № 090 / r), and data from the Statistics Committee of the Ministry of National Economy of Ukraine on the number and sex and age composition of the population for 2010-2020.

Used methods: epidemiological, medical and statistical.

3. RESULTS AND DISCUSSION

Analysis of the incidence and epidemiological characteristics of laryngeal cancer was conducted in different regions of the world, taking into account various causal factors: the relationship of the disease with genetic, hormonal, biochemical factors, nutritional factors, morphometric factors, previous pathology, socio-demographic and other geographic factors. Numerous searches for the causes and mechanisms of development of laryngeal cancer have not yet yielded answers and epidemiological data on the study of the role of the above factors in the etiologic of laryngeal cancer are contradictory. In European countries, laryngeal cancer is still one of the most common malignancies (about 52,000 new cases per year), with 90% of all cases occurring in men. The incidence in men in southern and northern Europe is between 18 per 100,000 and 6 per 100,000, respectively. About half of all cases of morbidity occur in Asian countries (Fig.1).

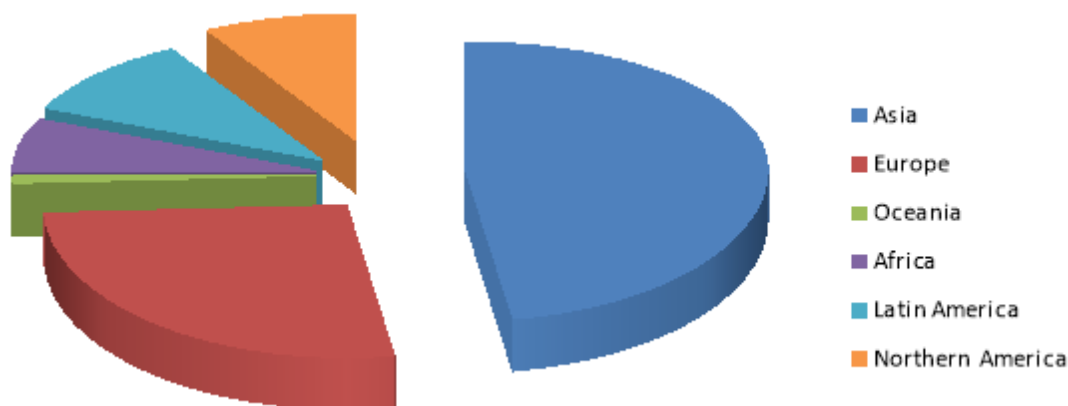


Figure 1 Distribution of laryngeal cancer in different parts of the world as estimated by IARC (Globocan 2018)

For women, the incidence rate does not exceed 1.5 per year per 100,000. The peak incidence occurs at the age of 70 years. Assessing the anatomical location of laryngeal cancer in different European regions, supraglottic cancer is more common in southern Europe than fold and subglottic cancer, while in northwestern Europe the situation is opposite, and this affects the overall survival of people diagnosed «Cancer of the Larynx». Squamous cell carcinoma is histologically determined in approximately 95% of all cases of laryngeal cancer. Over the past 15 years, levels have been broadly stable for both sexes, but the risk for future generations of men in England and Wales is expected to decrease, although the risk will increase in Scotland. Increases in incidence have been reported from Canada, Italy, Denmark, the United States, Australia, especially among women. For example, in Finland, a general decline in morbidity has been observed among men since the early 1970s (*Jasevi ien et al., 2003*). This was solely due to a decrease in the incidence of epiglottitis, which was most likely due to a sharp decrease in the number of smokers in Finland. The incidence of laryngeal cancer among European men increases with age, with most cases diagnosed in people aged 65 and over (about 45% of all cases), and the peak incidence occurs at 60 - 70 years at the rate of about 50 new cases per 100,000 population for a year. The prevalence of laryngeal cancer in 1992 (*Licitraa et al., 2003*) was 142 per 100,000 (271 in men and 22 in women). Most of them (76%) were long-term survivors, that is, people living with a diagnosis of 5 years or more. The relative survival rate from laryngeal cancer in adults was recorded in Europe in the period 1985-1989 and amounted to 62% over 5 years. The general progress in prognosis was in the period from 1978 to 1989, 5-year survival rate increased from 58 to 63%.

In the United States, approximately 11,300 cases of laryngeal cancer were reported in 2007 and approximately 3,660 deaths from this disease are predicted. The ratio of the incidence of men and women is 3.8 ÷ 1.1. For the most part, the epidemiological pattern and risk factors that contribute to laryngeal cancer are identical to those for other head and neck tumours. More than 90% of cancers occur in those over 40 years of age, and 85% to 95% of these are squamous cell carcinomas. Given the increased impact of risk factors, a higher incidence is observed in men, and due to the increase in the number of women who smoke over the past 60 years,

the gap has narrowed from more than 15–1 to about 4–1. In 2020, the highest incidence rates of laryngeal cancer were noted in Cuba, Macedonia, Uruguay, Brazil, Argentina, in the countries of Eastern and Western Europe: Hungary, Poland, Croatia, Portugal and the Latvia, Romania, Slovakia (Table 1).

Table 1 Morbidity and mortality rates per 100,000 populations from laryngeal cancer among men and women in Europe and Ukraine

Countries	Incidence			Mortality		
	male	female	Both sexes (ASR new)	male	female	Both sexes (ASR new)
Netherlands	10,1	6,3	8,2	1,8	1	1,4
Hungary	19,6	6,3	12,4	10,9	2,4	6,3
France	14,7	6,1	10,2	3,5	1	2,2
Belgium	12,7	5,9	9,2	3,5	1,4	2,5
Germany	11	5,7	8,3	3,2	1	2,1
Denmark	8,8	5,5	7,1	3	1,3	2,1
Ireland	10,8	5,2	7,9	3	0,9	1,9
Czechia	11,8	5,2	8,4	4,5	2	3,2
Poland	18,3	5,1	11,3	9,2	2	5,4
Sweden	6,2	4,8	5,5	1,8	1,3	1,5
Spain	12,8	4,6	8,6	3	1,1	2,0
Austria	9,3	4	6,5	4,7	1,2	2,3
Finland	6,9	3,9	5,4	2,3	1,3	1,8
Italy	6,7	3,6	5,1	2,4	0,9	1,6
Slovenia	11,4	3,4	7,4	2,5	0,8	1,7
Slovakia	21,4	3,4	11,9	9,1	1,5	5,1
Estonia	9,3	3,3	5,9	6,2	0,7	3,1
Bulgaria	9,6	3,2	6,2	3,8	0,8	2,2
Croatia	13,5	3,2	8,1	5,1	1	2,9
Portugal	17,0	3	9,6	5,8	0,8	3,1
Luxembourg	14,1	2,8	8,5	1,3	1	1,2
Malta	4,3	2,6	3,4	2,2	1,6	1,9
Lithuania	13,2	2,6	7,2	11	1,5	5,6
Latvia	24,7	2,3	11,9	10	1,3	5,0
Romania	19,4	2,2	10,3	9,6	0,8	5,0
Greece	7,2	1,7	4,3	2,3	0,5	1,3
Cyprus	4,6	1,5	3,0	1,5	0,3	0,9
Ukraine	10	1,1	5,2	7,8	0,6	4,0

Compared to European countries, the incidence of laryngeal cancer in Ukraine is on average 5.2 per 100,000 populations (for men - 10.0, and for women - 1.1 per 100 thousand populations, respectively). In the United States, Ireland, Venezuela, Germany, Denmark, Spain, France, Israel, Jordan, and most other Central European, Scandinavian, and Arab countries, the incidence varies at relatively high levels. The average level is registered in Australia, Canada, Great Britain, Iceland, Mexico, Papua New Guinea, Mozambique, Zambia, and Angola. Low incidence is observed in most countries in Africa, China, Japan, Norway, Finland, and Sweden.

There are significant differences in 5-year survival for laryngeal cancer between European countries: Eastern Europe and France have low survival rates (less than 55%). In the Netherlands, Sweden and Germany, overall survival was higher (more than 70%). The prognosis for laryngeal cancer varies considerably according to the location of the tumour, which affects the early onset of symptoms and, consequently, the early diagnosis and possibility of radical resection. Geographical differences in survival may be

largely due to different combinations of specific components. Cancer of the laryngeal fold has a more optimistic prognosis of 5-year survival in comparison with supraglottic, subglottic and laryngeal cartilage tumours, which are extremely rare. In addition, a link was found between well-being and survival for laryngeal cancer: the survival rate for low-income men is, on average, 13% lower than for wealthy men; there is no such difference for women.

Comparing mortality rates in European countries (Table 1), the highest levels of laryngeal cancer were recorded in Hungary, Poland, Slovakia, Lithuania, Latvia and Romania, where the mortality of men is about 5 times higher than the corresponding figure of the female population. In Ukraine, the mortality rates from laryngeal cancer are also quite high, which is explained by the low level of primary cancer prevention. In our study, we also analyzed the dynamics of morbidity and mortality (Table 2, Fig. 2) from laryngeal cancer in 2010-2020 in Ukraine among men and women.

According to the updated data of the National Cancer Registry of Ukraine in 2020, 1,845 new cases of malignant laryngeal neoplasms were registered, the total gross incidence of laryngeal cancer reached 5.2 per 100 thousand population, i.e. compared to 2010 decreased slightly by 0.4%, with why for the female population it increased by 0.5%, and for the male - on the contrary decreased by 1.4%. The peak incidence of laryngeal cancer in 2010-2020 occurred in 2019 - 6.5 per 100 thousand people (for women - 1.6, men - 12.2 per 100 thousand people), which is likely to increase associated with the pandemic of Covid 19.

Table 2 Distribution of morbidity and mortality from laryngeal cancer in Ukraine by sex and age groups in 2020

Age groups	Morbidity		Mortality	
	male	female	male	female
<30	0,1	0,2	-	-
30-39	0,6	0,3	0,1	0,1
40-49	5,7	0,2	2,4	0,1
50-59	24,7	0,3	11,1	0,2
60-69	42,4	1,1	26,7	0,4
≥70	32,2	1,1	36,9	0,4
Number of cases is an absolute number	1763	82	1025	31
Rough figure	10,6	0,4	7,8	0,6
Standardized indicator	7,1	0,2	6,2	0,2
Error	0,2	0,0	0,1	0,0

As can be seen from Table 2, a high proportion of patients (for both sexes) was established at the age of 60-69 years (43.5%), a similar picture was in men (42.4%), and in women, a high proportion of cancer incidence did not decrease. and in the age group 70 and older (1.1%). In general, the ratio of men to women was $21.5 \div 1$. In all age groups, this ratio was higher in the direction of men, with the greatest differences in the ratio of men and women found at 50-59 and 60-69 years, respectively.

Of course, the occurrence of laryngeal tumours, and subsequent morbidity and mortality from them are largely related to the age of the population, as one of the most important risk factors for laryngeal cancer is age. Thus, among persons under 30 years of age, the incidence rate of the entire population with laryngeal cancer was $0.02 \pm 0.004 \text{ ‰}$; at 30-39 years, the incidence rate increased 20 times compared with the group under 30 and reached $0.4 \pm 0.1 \text{ ‰}$; then at 40-49 years, the incidence increased 6.3 times compared with the data of 30-39 years reaching $2.5 \pm 0.2 \text{ ‰}$. In 50-59 years, the incidence rate of $10.1 \pm 0.8 \text{ ‰}$ was 4 times higher in the previous one. At the age of 60-69, the maximum incidence rates were set at $17.6 \pm 1.1 \text{ ‰}$, and at the age of 70 and older, they left 15.0 ± 0.9 .

The number of deaths from cancer in 2020 was 1053 people, with a rough mortality rate of 4.0 per 100 thousand populations, which is 0.8% higher than in 2013, including 0.4% for women and by 1.1% in men. As with the incidence, the peak mortality from laryngeal cancer, occurred in 2019 - 4.4 per 100 thousand population (for men - 8.6, for women - 0.7 per 100 thousand population). Analyzing the first diagnosed tumors of the larynx and subsequent mortality from them in Ukraine in 2013-2020 by sex (Fig. 3), it is seen that for the female population these figures are slightly higher in 2020 compared to 2013, with a gradual increase from 2013 to 2018 and later with a sharp jump in 2019 (by 37.5% in terms of morbidity, by 28.6% in terms of mortality) and a slight decrease in 2020 (by 31.2% and 14.3%, respectively).

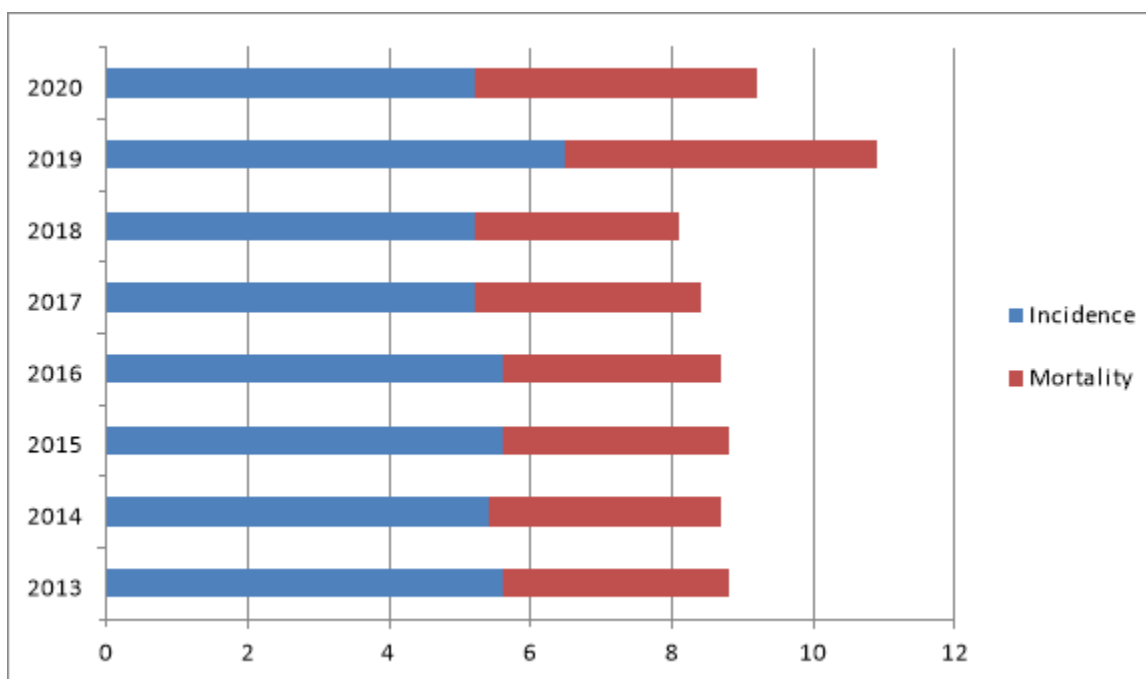


Figure 2 Incidence and mortality from laryngeal cancer in Ukraine for 2013-2020

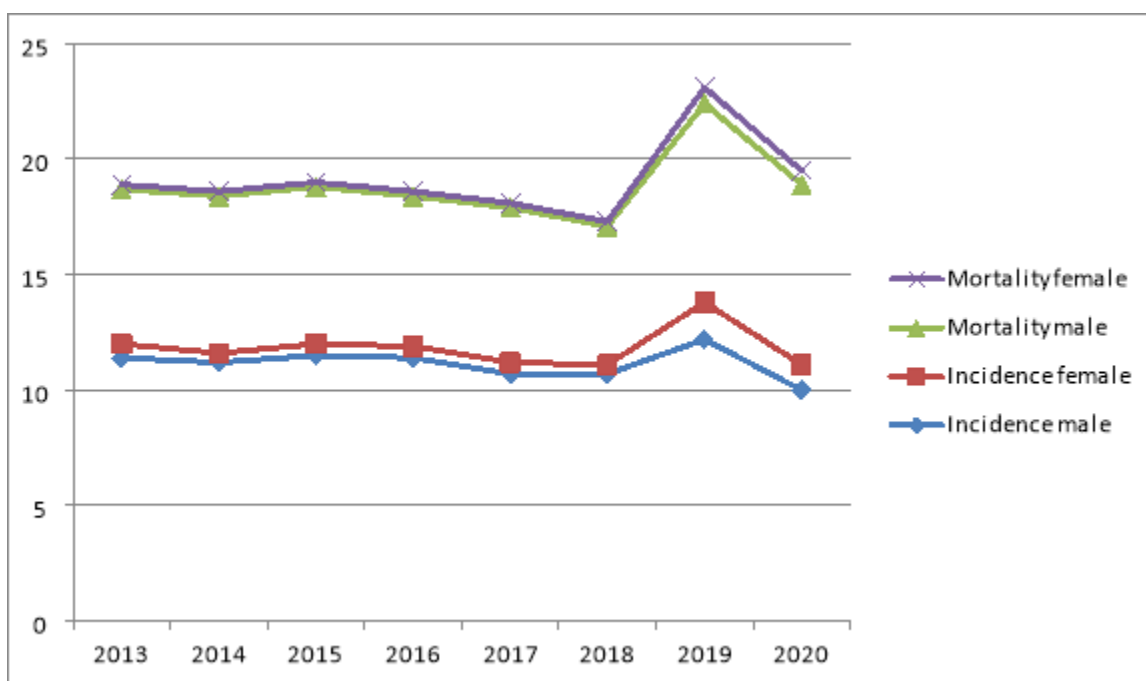


Figure 3 The incidence and mortality of laryngeal cancer among male and female population of Ukraine 2013-2020

Evaluating the relevant indicators among the male population we see a wave-like dynamics in terms of incidence: almost unchanged in 2013-2016 (on average by 0.9%), with a decrease in 2017-2018 (by 6.5%), an increase in 2019 (12.3%) and a sharp decline in 2020 (by 22%). A similar situation is observed with regard to mortality: from 2013 to 2015 - a slight increase (by 1.5%), in 2016 - a decrease (by 4.6%), in 2017 again an increase, a return to the value of 2013 (by 3%), in 2018 - a decrease (by 11.7%), in 2019 - an increase (by 30.2%) and in 2020 again a decrease (by 10.3%), which is most likely due to the unsatisfactory state of cancer care in Ukraine and low level of screening.

4. CONCLUSION

Recently, there has been an increase in the number of head and neck tumours diagnosed, especially among people with papillomavirus. The occurrence of laryngeal cancer largely depends on the socio-economic affiliation of the patient - the lower the social class to which a person belongs, the higher the chance of developing laryngeal cancer. They often abuse smoking and alcohol, which most likely reflects some difficulties with social integration. Because of its location, laryngeal cancer affects some of the basic life functions, including breathing, chewing, swallowing, and communication, thereby having a significant impact on quality of life. Early diagnosis improves outcomes and promotes survival, especially for early-stage tumours.

In men, laryngeal cancer is diagnosed much more often than in women: during life, each of the 180 men, but only one in 1,100 women suffers from laryngeal cancer. The average age of development of this cancer is 64 years for women and 66 years for men, which is earlier than the average age of cancer in general. The peak incidence of laryngeal cancer for women is 55 - 75 years, for men 65 - 75 years. High rates of morbidity and mortality from laryngeal cancer testify to the insufficient volume of medical and preventive measures carried out on the territory of Ukraine.

To change the situation, you must: improve the quality of clinical examination and medical examinations of patients; improve the oncological alertness of primary health care workers; improve the qualifications of doctors of medical and preventive institutions, specialists of examination rooms, feldsher and obstetric points; improve the medical literacy of the population through regular health education.

Declaration

The work is a fragment of the research project of the department of social medicine and public health of Bukovinian State Medical University - «Substantiation and development of medical and social technologies for the prevention of major non-infection diseases» (State Registration No. 0120U102625).

Acknowledgement

The authors are grateful to the Chernivtsi Public Health Center, the Chernivtsi Regional Information and Analytical Center for Medical Statistics, Engineering and Pharmaceutical Support of Regional Health Institutions, and the Chernivtsi Oncology Center.

Author Contributions

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

Funding

This study has not received any external funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Ethical approval

The study acquired the ethical approval from the Commission on Biomedical Ethics for compliance with moral and legal rules of medical research of Bukovynian State Medical University of the Ministry of Health of Ukraine, (letter number Nr. 2 from 18.02.2021 - project number 0120U102625).

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Ang KK, Harris J, Wheeler R, Weber R, Rosenthal DI, Nguyen-Tân PF, Westra WH, Chung CH, Jordan RC, Lu C, Kim H, Axelrod R, Silverman CC, Redmond KP, Gillison ML. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med* 2010; 363(1):24-35.
2. Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, Ferlay J. Cancer Incidence in Five Continents, Vol. XI. IARC Cancer Base No. 14. Lyon: International Agency for Research on Cancer; 2017.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Cancer Statistics 2018: GLOBOCAN estimates of

- incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; 68(6):394-424
4. Dal Maso L, Torelli N, Biancotto E, Di Maso M, Gini A, Franchin G, Levi F, La Vecchia C, Serraino D, Polesel J. Combined effect of tobacco smoking and alcohol drinking in the risk of head and neck cancers: a re-analysis of case-control studies using bi-dimensional spline models. *Eur J Epidemiol* 2016; 31(4):385-393.
5. Ferlay J, Colombet M and Bray F. Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9 [Internet]. Lyon, France: International Agency for Research on Cancer; 2018.
6. Fidler MM, Soerjomataram I, Bray F. A global view on cancer incidence and national levels of the Human Development Index. *Int J Cancer* 2016; 139(11): 2436- 2446.
7. Ghosh S, Ghosh S, Bankura B, Saha ML, Maji S, Ghatak S, Pattanayak AK, Sadhukhan S, Guha M, Nachimuthu SK, Panda CK, Maity B, Das M. Association of DNA repair and xenobiotic pathway genopolymorphisms with genetic susceptibility to gastric cancer patients in West Bengal, India. *Tumour Biol* 2016; 37(7):9139-9149.
8. Herrero R, Quint W, Hildesheim A, Gonzalez P, Struijk L, Katki HA, Porras C, Schiffman M, Rodriguez AC, Solomon D, Jimenez S, Schiller JT, Lowy DR, van Doorn LJ, Wacholder S, Kreimer AR; CVT Vaccine Group. Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica. *PLoS ONE* 2013; 8(7):e68329.
9. Jaseviciene J, Gurevicius R, Juozulynas A, Cicenias S. An evaluation of laryngeal cancer morbidity time trends in Lithuania. *Rocz Akad Med Bialymst* 2003; 48:85-89.
10. Leoncini E, Edefonti V, Hashibe M, Parpinel M, Cadoni G, Ferraroni M, Serraino D, Matsuo K, Olshan AF, Zevallos JP, Winn DM, Moysich K, Zhang ZF, Morgenstern H, Levi F, Kelsey K, McClean M, Bosetti C, Schantz S, Yu GP, Boffetta P, Lee YC, Chuang SC, Decarli A, La Vecchia C, Boccia S. Carotenoid intake and head and neck cancer: a pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Eur J Epidemiol* 2016; 31(4):369-383.
11. Licitra L, Bernier J, Grandi C, Locati L, Merlano M, Gatta G, Lefebvre JL. Cancer of the larynx. *Crit Rev Oncol Hematol* 2003; 47(1):65-80.
12. Marron M, Boffetta P, Zhang Z, Zaridze D, Wunsch-Filho V, Winn DM, Wei Q, Talamini R, Szeszenia-Dabrowska N, Sturgis EM, Smith E, Schwartz SM, Rudnai P, Purdue MP, Olshan AF, Eluf-Neto J, Muscat J, Morgenstern H, Menezes A, McClean M, Matos E, Mates IN, Lissowska J, Levi F, Lazarus P, LaVecchia C, Koifman S, Kelsey K, Herrero R, Hayes RB, Franceschi S, Fernandez L, Fabianova E, Daudt AW, Dal Maso L, Curado MP, Cadoni G, Chen C, CastellsagueX, Boccia S, Benhamou S, Ferro G, Berthiller J, Brennan P, Møller H, Hashibe M. Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *Int J Epidemiol* 2010; 39(1): 182-196.
13. Nocini R, Molteni G, Mattiuzzi C, Lippi G. Updates on larynx cancer epidemiology. *Chin J Cancer Res* 2020; 32(1): 18-25.
14. Saedi B, Razmpa E, Sadeghi M, Mojtahed M, Mojtahed A. The epidemiology of laryngeal cancer in a country on the esophageal cancer belt. *Indian J Otolaryngol Head Neck Surg* 2009; 61(3):213-217.
15. Serra-Majem, L. Head and neck cancer: smoking, drinking, eating and sexual practices. *Eur J Epidemiol* 2016; 31(4): 333-335.
16. Zuo JJ, Tao ZZ, Chen C, Hu ZW, Xu YX, Zheng AY, Guo Y. Characteristics of cigarette smoking without alcohol consumption and laryngeal cancer: overall and time-risk relation. A meta-analysis of observational studies. *Eur Arch Otorhinolaryngol* 2017; 274(3):1617-1631.