



## Mortality rate of lip, oral cavity and pharynx malignant tumors in Serbia within a period 1991–2009

Stopa mortaliteta od malignih tumora usne, usne duplje i ždrela u Srbiji u periodu 1991–2009. godine

Milena Ilić\*, Svetlana Radević†, Vladimir Stefanović‡, Tatjana Ćirković‡, Tamara Zurovac‡, Borivoje Savić§, Vladan Kovačević‡

\*Department of Epidemiology, †Department of Social Medicine, Faculty of Medicine, University of Kragujevac, Kragujevac, Serbia; ‡Dental Clinic, Military Medical Academy, Belgrade, Serbia; §Centre for Nuclear Medicine, Clinical Centre of Serbia, Belgrade, Serbia

### Abstract

**Background/Aim.** Lip, oral cavity and pharynx malignant tumors account for 3.7% of all cancer deaths worldwide, with significant geographic variations in frequency and distribution. The aim of this descriptive epidemiologic study was to analyze the mortality rate of lip, oral cavity and pharynx malignant tumors in Serbia proper within a period 1991–2009. **Methods.** Mortality rates standardized directly using the world population as the standard were used in data analysis. Linear trend and regression analyses were used to analyze rate trends in mortality. **Results.** The Serbian population demonstrated an increase in the mortality of lip, oral cavity and pharynx malignant tumors ( $y = 3.32 + 0.03x$ ;  $p = 0.002$ ; average annual percent change = + 0.8). The male population showed a significant increase in mortality trend ( $y = 5.90 + 0.03x$ ;  $p = 0.020$ ; % change = + 0.9), while the female population did not show a significant increase in mortality. The male/female cancer mortality ratio was 5.5:1. Mortality rates for lip, oral cavity and pharynx cancer increased with age in both genders, with rates being the highest in the population aged 85 and older. Increasing trends of lip, oral cavity and pharynx cancer mortality were observed in males aged 50–54; the average annual percent change was + 7.4 % (95% CI, 6.2–9.0). The population of both genders aged 55–59 demonstrated an increase in lip, oral cavity and pharynx cancer mortality, the increase being + 1.8% (95% CI, 1.4–2.2) in men and + 34.3% (95% CI, 28.4–40.2) in women. **Conclusion.** The increasing trend in lip, oral cavity and pharynx cancer mortality points to the necessity to investigate etiology and improve primary and secondary prevention measures.

### Key words:

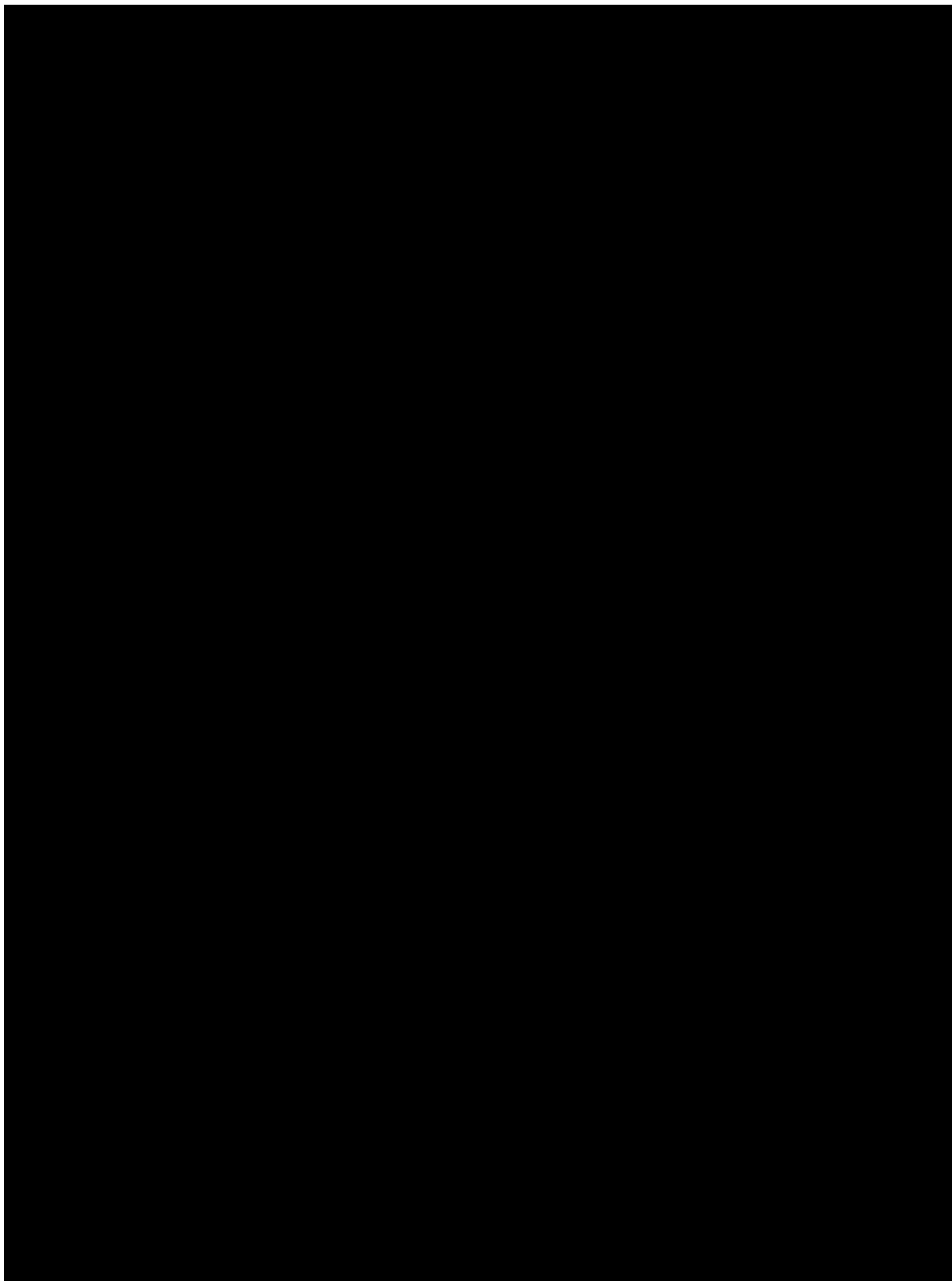
mouth neoplasms; pharyngeal neoplasms; serbia; mortality; risk factors.

### Apstrakt

**Uvod/Cilj.** Maligni tumori usne, usne duplje i ždrela uzrok su 3,7% svih smrtnih slučajeva od raka u svetu, sa značajnim geografskim varijacijama u učestalosti i distribuciji. Cilj ove deskriptivne epidemiološke studije bila je analiza mortaliteta od malignih tumora usne, usne duplje i ždrela u Srbiji u periodu od 1991. do 2009. godine. **Metode.** U analizi podataka korišćene su standardizovane stope mortaliteta, dobijene metodom direktne standardizacije sa populacijom sveta kao standardom. Linearni trend i regresiona analiza korišćeni su za analizu trenda mortaliteta. **Rezultati.** U populaciji Srbije zabeležen je porast mortaliteta od malignih tumora usne, usne duplje i ždrela ( $y = 3,32 + 0,03x$ ;  $p = 0,002$ ; prosečna godišnja procentualna promena = + 0,8). Kod muškaraca je zabeležen značajan trend porasta mortaliteta ( $y = 5,90 + 0,03x$ ;  $p = 0,020$ ; % promena = + 0,9), dok kod žena nije utvrđen značajan porast mortaliteta. Odnos mortaliteta među polovima (muškarci/žene) bio je 5,5 : 1. Stope mortaliteta od malignih tumora usne, usne duplje i ždrela povećavale su se sa starošću kod oba pola, pri čemu su stope bile najviše u populaciji starijih od 85 i više godina. Trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela uočen je kod muškaraca starosti 50–54 godine: prosečna godišnja procentualna promena iznosila je + 7,4% (95% IP = 6,2–9,0). U populaciji oba pola u uzrasnoj grupi 55–59 godina zabeležen je trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela, pri čemu je porast iznosio + 1,8% (95% IP = 1,4–2,2) kod muškaraca i + 34,3% (95% IP = 28,4–40,2) kod žena. **Zaključak.** Trend porasta mortaliteta od malignih tumora usne, usne duplje i ždrela ukazuje na neophodnost etioloških istraživanja i unapređenja mera primarne i sekundarne prevencije.

### Ključne reči:

usta, neoplazme; farinks, neoplazme; srbija; mortalitet; faktori rizika.



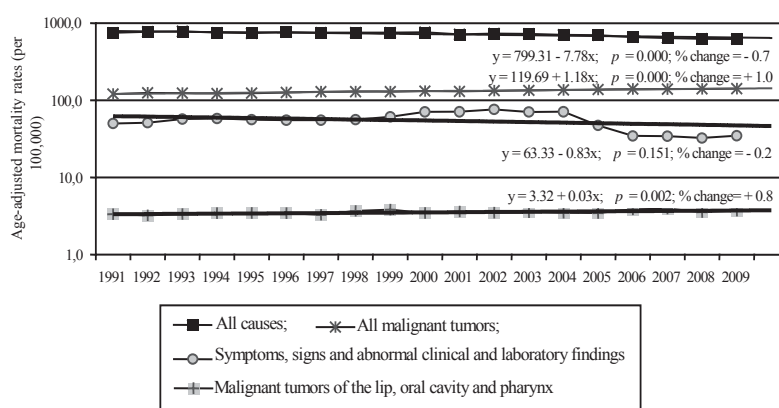


Fig. 1 – The mortality rates of the chosen causes in Serbia, excluding the Province of Kosovo, in 1991–2009

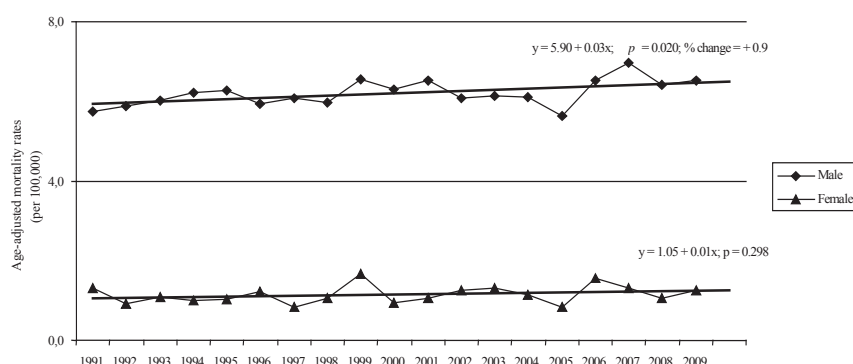


Fig. 2 – The mortality rates of malignant tumors of the lip, oral cavity and pharynx by gender in Serbia, excluding the Province of Kosovo, in 1991–2009

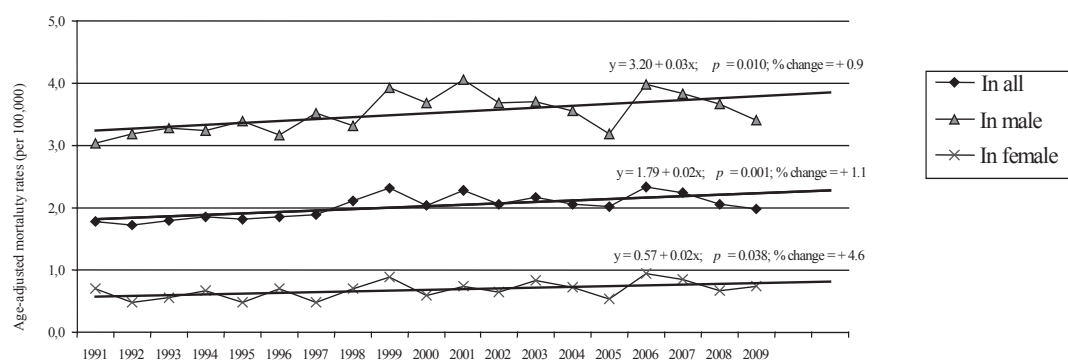


Fig. 3 – The mortality rates of malignant tumors of the lip and oral cavity by gender in Serbia, excluding the Province of Kosovo, in 1991–2009

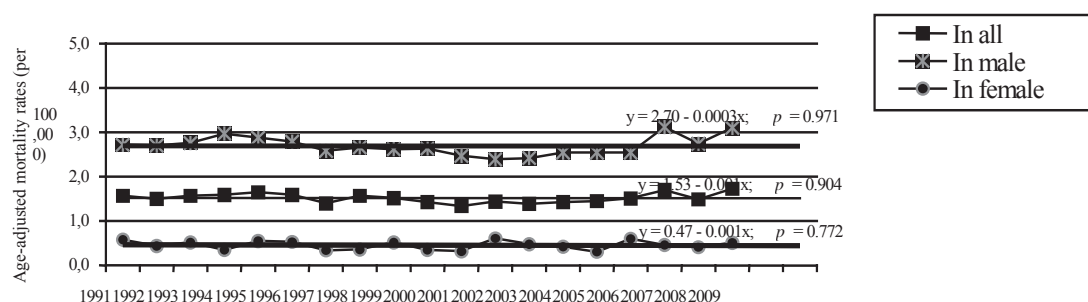


Fig. 4 – The mortality rates of malignant tumors of the pharynx by gender in Serbia, excluding the Province of Kosovo, in 1991–2009



crease of nearly 16% in women<sup>9,13</sup>. However, in some countries, such as Hungary, Romania, Slovakia and Czech Republic, an increase in oral and pharynx cancer mortality in both men and women is recorded. Oral cancer mortality in men has been declining since the late 1980s in most western countries, although some persisting upward trends were recorded in Denmark, United Kingdom, England and Wales, and Scotland. These trends should be essentially interpreted in terms of patterns and changes in exposure to alcohol and tobacco in Central and Eastern Europe<sup>4,9</sup>.

For the youngest age categories in the Serbian population, mortality rates were generally less than 1 per 100,000 individuals per year; however, after about the third decade of life, rates began to increase notably, with the sharpest increases seen for males. Lip, oral cavity and pharynx cancer mortality rates in 11 countries (USA, Asian and European countries, and Australia) during the period 1990–2006, were from 3 to 10 times higher in males than in females<sup>5</sup>. The reason for this may be that men had been more likely to use tobacco and alcohol in the past<sup>4,7,10</sup>. Among females, few differences in mortality rates were observed for all the countries studied with the exception of China (Hong Kong)<sup>5</sup>. Although the age-standardized rates in China (Hong Kong) have evidently decreased over the period, they were still 5 times higher for both genders.

Oral cavity cancer mortality rates ranged from 12.1 per 100,000 among males and 5.9 among females in Melanesia, 6.3 among males and 3.6 among females in South-Central Asia, to less than 1 for both genders in North America, Northern and Western Europe, and Australia/New Zealand<sup>1,3</sup>. The highest pharyngeal cancer mortality rates in 2008 were recorded in South-Central Asia and Southern Africa (7 per 100,000 among males and approximately 2 per 100,000 among females). The lowest pharyngeal cancer mortality rates (1 per 100,000) for both genders were recorded in North America, Northern and Western Europe, and Australia/New Zealand. In India, among all malignant tumors, lip, oral cavity and pharynx cancer mortality rates have a leading position in the structure of mortality when considering the entire population (9.7 per 100,000) and the male population alone (14.4), while they rank number 3 in female population (5.4)<sup>1,3</sup>. In India, pharyngeal cancer death was more frequent than oral cavity cancer death in men (7.6 versus 6.8), while in women oral cavity cancer mortality rates were twice as high as those of pharyngeal cancer.

Some potential explanations for this apparent differences among the countries may be discrepancies in the disease early detection and availability of the improved treatment methods. However, numerous epidemiological studies indicated that the increase was attributed primarily to changes in the patterns of smoking and alcohol use (especially among women) in recent decades; in addition, nutritional, lifestyle and other factors<sup>3,14</sup>. The difference in rates between black and white population is attributable to racial differences in patterns of alcohol intake, especially among current smokers, as well as to higher risks associated with alcohol intake among blacks<sup>7,10,15</sup>. A Swedish population-based case-control study showed that risk factors for oral

and oropharyngeal squamous cell carcinoma were poor oral hygiene, dental status (defective and missing teeth), oral mucosal lesions, alcohol and tobacco use, human papilloma virus (HPV) infection, and lifestyle-related factors<sup>16</sup>. The findings in England and Wales<sup>17</sup> about a positive correlation between liver cirrhosis and intraoral cancer suggested that rising alcohol consumption is more closely related to increasing intraoral cancer incidence and mortality than smoking, most notably among younger males since the early 1970s.

In India<sup>14</sup>, tobacco chewing emerged as the strongest risk factor for oral cancer, while the strongest risk factor for pharyngeal cancer was tobacco smoking in current smokers. Oral tobacco products (snuff or chewing tobacco) are related to cancers of the cheek, gums, and inner surface of the lips. In Southeast Asia, South Asia, and some other areas of the world, many people chew betel and/or gutka<sup>18,19</sup>. Several studies have found that a diet low in fruits and vegetables is related to an increased risk of oral cavity and oropharyngeal cancers<sup>20,21</sup>.

The rising rate of HPV related cancers is thought to be due to changes in sexual practices in recent decades, particularly to the increase in oral sex<sup>22</sup>. The International Agency for Research on Cancer conducted a multicenter case-control study of oral cavity and oropharyngeal cancer in nine countries, where HPV DNA was detected in biopsy specimens of 3.9% of oral cavity cancers with valid polymerase chain reaction (PCR) results and 18.3% of oropharyngeal cancers<sup>23</sup>.

Mortality rates in the Republic of Serbia for which symptoms, signs and ill-defined states were indicated as causes of death suggest that caution must be present when interpreting statistical data on mortality in international comparisons. However, it is not likely that these had a significant impact on the increasing trend of lip, oral cavity and pharynx cancer mortality, for which the increasing trend ( $y = 3.31 + 0.02$ ;  $p = 0.033$ ) was also observed for the 1991–2003 period, when mortality rates of undefined death causes also demonstrated a considerable increasing trend ( $y = 47.23 + 1.93$ ;  $p = 0.000$ ).

A similar increasing trend of the mortality of lip, oral cavity and pharynx malignant tumors (average annual percent change = + 0.8) and the mortality of all malignant tumors (average annual percent change = + 1.0) in Serbia can be only partially explained by the lack of organized programs for primary and secondary prevention, especially during the recent decades which characterised the economic sanctions against Serbia, the war and the 1999 NATO bombing of Yugoslavia. Other than, it was not possible to give specific information about internally displaced persons and refugees, although they may have a different exposure, which could be of great importance for understanding the trends in mortality of malignant tumors. Despite changes in recent years, the most significant exposures to risk factors for malignant tumors in Serbia are still higher than in developed countries. The prevalence of smokers in the adult population has decreased from 40.5% in 2000 to 33.6% in 2006, while a third of young people in the 15–19 age group consumed alcoholic beverages<sup>24</sup>. In Serbia,

## R E F E R E N C E S

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011; 61(2): 69–90.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127(12): 2893–917.
3. Boyle P, Levin BE. *World Cancer Report*. Lyon: IARC Press; 2008.
4. Parkin DM. International variation. *Oncogene* 2004; 23(38): 6329–40.
5. Yako-Suketomo H, Matsuda T. Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center. *Jpn J Clin Oncol* 2010; 40(11): 1118–9.
6. Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Mortality from major cancer sites in the European Union, 1955–1998. *Ann Oncol* 2003; 14(3): 490–5.
7. Morse DE, Kerr AR. Disparities in oral and pharyngeal cancer incidence, mortality and survival among black and white Americans. *J Am Dent Assoc* 2006; 137(2): 203–12.
8. Garavello W, Bertuccio P, Levi F, Lucchini F, Bosetti C, Malvezzi M, et al. The oral cancer epidemic in central and eastern Europe. *Int J Cancer* 2010; 127(1): 160–71.
9. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Altekruse SF, et al. *SEER Cancer Statistics Review, 1975–2009 (Vintage 2009 Populations)*. Bethesda, MD: National Cancer Institute; 2009. Available from: [http://seer.cancer.gov/csr/1975\\_2009](http://seer.cancer.gov/csr/1975_2009) [updated 2012 August 20].
10. Tanaka S, Sobue T. Comparison of oral and pharyngeal cancer mortality in five countries: France, Italy, Japan, UK and USA from the WHO Mortality Database (1960–2000). *Jpn J Clin Oncol* 2005; 35(8): 488–91.
11. Jensen OM, Parkin DM, Lennan R, Muir CS, Skeet RG. *Cancer registration. Principles and Methods*. Lyon: IARC; 1991.
12. *World Health Organization*. WHO Statistical Information System. Geneva: World Health Organization; Available from: <http://www.who.int/whosis/whostat/>
13. Bosetti C, Bertuccio P, Levi F, Lucchini F, Negri E, La Vecchia C. Cancer mortality in the European Union, 1970–2003, with a joinpoint analysis. *Ann Oncol* 2008; 19(4): 631–40.
14. Znaor A, Brennan P, Gajalakshmi V, Mathew A, Shanta V, Varghese C, et al. Independent and combined effects of tobacco smoking, chewing and alcohol drinking on the risk of oral, pharyngeal and esophageal cancers in Indian men. *Int J Cancer* 2003; 105(5): 681–6.
15. Day GL, Blot WJ, Austin DF, Bernstein L, Greenberg RS, Preston-Martin S, et al. Racial differences in risk of oral and pharyngeal cancer: alcohol, tobacco, and other determinants. *J Natl Cancer Inst* 1993; 85(6): 465–73.
16. Rosenquist K. Risk factors in oral and oropharyngeal squamous cell carcinoma: a population-based case-control study in southern Sweden. *Swed Dent J Suppl* 2005; (179): 1–66.
17. Hindle I, Downer MC, Moles DR, Speight PM. Is alcohol responsible for more intra-oral cancer? *Oral Oncol* 2000; 36(4): 328–33.
18. Dikshit RP, Kanbere S. Tobacco habits and risk of lung, oropharyngeal and oral cavity cancer: a population-based case-control study in Bhopal, India. *Int J Epidemiol* 2000; 29(4): 609–14.
19. Moles DR, Fedele S, Speight PM, Porter SR and dos Santos Silva I. Oral and pharyngeal cancer in South Asians and non-South Asians in relation to socioeconomic deprivation in South East England. *Br J Cancer* 2008; 98(3): 633–5.
20. Riboli E, Norat T. Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk. *Am J Clin Nutr* 2003; 78(3): 559s–69s.
21. Tavani A, Gallus S, La Vecchia C, Talamini R, Barbone F, Herrero R, et al. Diet and risk of oral and pharyngeal cancer. An Italian case-control study. *Eur J Cancer Prev* 2001; 10(2): 191–5.
22. Termine N, Panzarella V, Falaschini S, Russo A, Matranga D, Lo Muzio L, et al. HPV in oral squamous cell carcinoma vs head and neck squamous cell carcinoma biopsies: a meta-analysis (1988–2007). *Ann Oncol* 2008; 19(10): 1681–90.
23. Herrero R, Castellsagué X, Pawlita M, Lissowska J, Kee F, Balaram P, et al. Human papillomavirus and oral cancer: the International Agency for Research on Cancer multicenter study. *J Natl Cancer Inst* 2003; 95(23): 1772–83.
24. *Republic of Serbia, Ministry of Health*. National health survey Serbia, 2006 – key findings. Belgrade: Ministry of Health; 2006.

Received on January 10, 2012.

Revised on May 18, 2012.

Accepted on May 21, 2012.

Copyright of Vojnosanitetski Pregled: Military Medical & Pharmaceutical Journal of Serbia & Montenegro is the property of Military Medical Academy INI and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.