

*Original article*

## Trends in the Incidence Rates of Cancer of the Tongue in the City of Belgrade

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### SUMMARY

Cancers of the oral tongue (OT) and floor of the mouth (FOM) are frequently grouped together as carcinomas of the tongue and floor of the mouth (OTFOM). The incidence rate of these cancers varies worldwide from 0.1/100,000 persons a year for females in Algeria, Chile and Korea to 7.4/100,000 persons a year for men in New Delhi, India. The aim of this study was to analyze the trends in age-standardized incidence rates of oral tongue cancer in the Belgrade population during the period of past 12 years. The data were obtained from the Serbian Cancer Registry (The Registry). Age-standardized incidence rates were calculated using the direct standardization method to the world standard population and presented as an incidence rate per 100,000 persons a year. Joinpoint regression analysis was used to analyze the trends and annual percentage change (APC). The results of the joinpoint regression analysis showed an increasing trend of OT cancers for both genders, with an APC of 4.1% among men and 1.7% among women. The incidence rate for FOM cancers increased, with an APC of 4.8% among men and 6.8% among women. Our results showed a continuously increasing incidence rate of oral tongue and floor of the mouth carcinoma in the capital of the Republic of Serbia.

*Key words:* tongue cancer, floor of mouth cancer, incidence

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## INTRODUCTION

Carcinomas of the tongue (CT) and carcinomas of the floor of the mouth (CFM) are usually described in the literature as a single entity – carcinomas of the tongue and floor of the mouth (CTFM). The incidence of these carcinomas throughout the world varies from 0.1/100,000 persons a year for women in Algeria, Chile and South Korea, to 7.4/100,000 for men in the New Delhi region in India (1, 2). It has been estimated that almost 485,000 new cases of carcinoma of the tongue and floor of the mouth are diagnosed worldwide, and that these cancers are the cause of death of over 260,000 people per year (3). Carcinomas of the tongue and floor of the mouth are the eight most common cause of cancer-related deaths in the USA, with 8,000 deaths a year on the average (4) and the 5-year survival rate of 39% (5). Carcinomas of the tongue are the most common intraoral carcinomas among Europeans and in the USA population, accounting for 40-50% of all oral carcinomas (6). Carcinomas of the tongue and floor of the mouth are most commonly planocellular, with lateral parts of the tongue being the most common sites of malignant transformation (7). Tobacco consumption (most commonly smoking) and alcohol intake are among the most important risk factors for the development of these carcinomas (8-10). Any separation of the effects of these two risk factors is quite complicated, since the individuals who drink larger quantities of alcohol are mostly smokers as well. Human papilloma virus (HPV) and genetic predisposition have also been mentioned in the relevant literature as the risk factors for these carcinomas (11-13). The reported high mortality and morbidity rates of these malignancies are a serious health problem in most countries throughout the world, and population registry studies may offer some important parameters for the institution of prevention measures and alleviation of this global health burden.

## AIMS

The aim of this study was to determine and analyze the trends of incidence of carcinoma of the tongue in the population of the capital of the Republic of Serbia in the studied period of 12 years.

## MATERIAL AND METHODS

The data about the diseases were obtained from the Central Serbia Cancer Registry. The sources of the Registry data had been the information about the patients with carcinoma of the tongue and floor of the mouth obtained from the institutes of oncology, oncological dispensaries, clinics, other inpatient and outpatient health care institutions, histopathological, hematological and other laboratories, from death certificates, health insurance organizations, and targeted investigations. All the cases of carcinoma of the tongue and floor of the mouth reported for the territory of Belgrade in the period from January 1, 1999 to December 31, 2010 were singled out from the Registry for the purpose of study. The carcinomas were classified in accordance with the International Classification of Diseases, 10th revision (ICD-10) as carcinomas of the tongue (ICD-10: C01-C02) and as carcinomas of the floor of the mouth (ICD-10: C04). Their oncological classification was performed in accordance with the International Classification of Diseases for Oncology, 3<sup>rd</sup> revision (ICDO-3). The tumors with the following ICDO-3 morphological codes were included in the study: 8000/3, 8010/3, 8020/3, 8021/3, 8032/3, 8033/3, 8050/3, 8051/3, 8052/3, 8070/3, 8071/3, 8072/3, 8074/3, 8075/3, 8076/3 and 8084/3.

The age-standardized rate (ASR) of incidence was calculated using the direct standardization method, and the world population was taken as a standard population. The incidence was presented as an incidence rate per 100,000 people in a year. The method of regression analysis with joinpoints was used to analyze the changes in incidence trends and the annual rate of change.

## RESULTS

During the studied period, the total of 638 people with carcinoma of the tongue and floor of the mouth (484 men and 154 women) were reported to the Registry. Table 1 describes the distribution of the patients with carcinoma of the tongue and floor of the mouth in the population of Belgrade by the factors of tumor site, and patient age and gender. Among the affected, there were 76% of men and 24% of women. The relative male-to-female ratio for these carcinomas was 3.1:1. Most of these cancer patients were in their 6<sup>th</sup> and 7<sup>th</sup> decades of life, and less than 4% of the total number

were those below 39 years of age. The age-standardized incidence rate (related to the world population as a whole) of carcinoma of the tongue and floor of the

mouth by the factors of gender, year of diagnosis, and tumor site is presented in Table 2.

**Table 1.** Distribution of patients with carcinoma of the tongue and floor of the mouth by the factors of tumor site, patient gender and age

	<b>Tongue</b> Number of cases (%)	<b>Floor of the mouth</b> Number of cases (%)	<b>Total</b> Number of cases (%)
<b>Gender</b>			
Male	281 (75)	203 (77)	484 (76)
Female	95 (25)	59 (23)	154 (24)
<b>Age</b>			
< 39	18 (5)	6 (2)	24 (4)
40 - 49	39 (10)	27 (10)	66 (10)
50 - 59	136 (36)	77 (33)	213 (33)
60 - 69	108 (29)	76 (29)	184 (29)
70 <	75 (20)	76 (29)	151 (24)
<b>Total</b>	<b>376 (100)</b>	<b>262 (100)</b>	<b>638 (100)</b>

**Table 2.** Standardized incidence rate of carcinoma of the tongue and floor of the mouth in Belgrade by the factors of gender and year of diagnosis

<b>Year of diagnosis</b>	<b>Men</b>		<b>Women</b>	
	CT - ASR	CFM - ASR	CT - ASR	CFM - ASR
1999	1.55	1.06	0.63	0.18
2000	2.15	2.09	0.61	0.42
2001	1.73	1.49	0.69	0.21
2002	1.95	1.25	0.39	0.31
2003	1.34	0.77	0.52	0.17
2004	1.34	0.85	0.59	0.18
2005	1.48	1.23	0.52	0.41
2006	2.22	1.16	0.24	0.31
2007	2.17	0.79	0.34	0.16
2008	1.79	1.52	0.54	0.28
2009	2.86	2.27	0.65	0.78
2010	3.02	1.86	0.76	0.33
All years	1.97	1.39	0.54	0.31

CT- carcinoma of the tongue, CFM – carcinoma of the floor of the mouth, ASR- Age-standardized incidence rates

The ASR for the studied period of time (1999-2010) and for all carcinomas of the tongue and floor of the mouth was 1.97 for men and 0.54 for women per

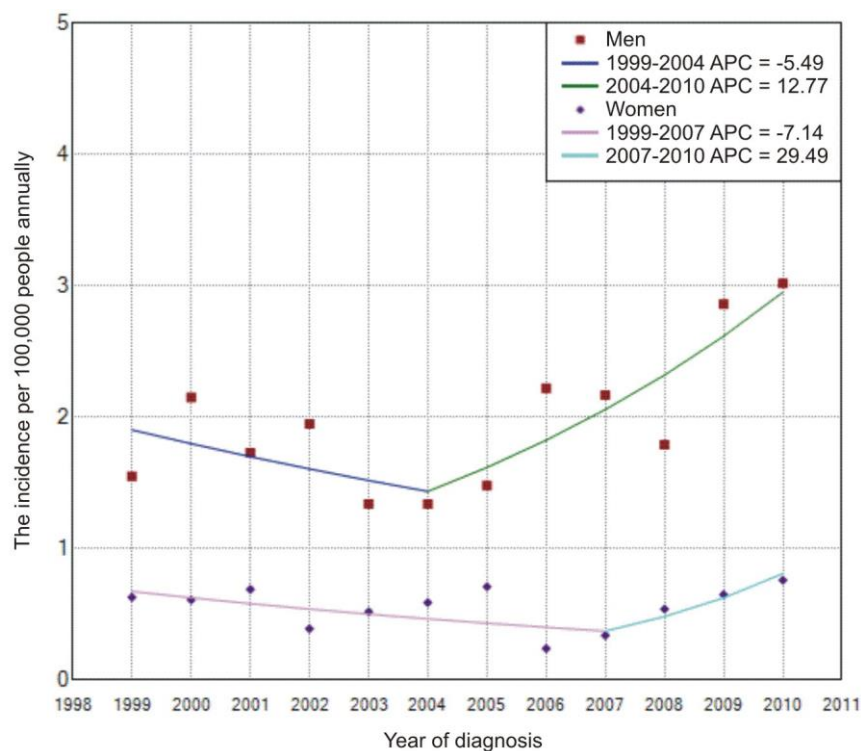
100,000 people a year. The ASR for carcinoma of the tongue in men increased from 1.55/ 100,000 people a year in 1999 to 3.02 in 2010, while in women the rate

increased from 0.63 in 1999 to 0.76 in 2010. The ASR for carcinoma of the floor of the mouth for men rose from 1.06 in 1999 to 1.86 in 2010, and for women from 0.18 to 0.33 in the same period. The join-point regression analysis demonstrated an increasing ASR trend for carcinoma of the tongue (ICD-10: C01-C02) in both genders in the period 1999-2010, with the annual percentage change

(APC) of 4.1% (95% CI: -3.1; 11.8) for men, and 1.7% (95% CI: -11.5; 16.9) for women (Table 3). The ASR trend increase for carcinoma of the tongue was statistically significant in men in the period 2004-2010 (APC, 12.8%; 95% CI: 1.4; 25.4), while it was without any statistical significance in women in the period 2007-2010 (APC, 29.5%; 95% CI: -23.9; 120.4) (Graph 1).

**Table 3.** Annual percentage of change (APC) standardized incidence rates of carcinoma of the tongue in Belgrade, 1999-2010

Gender	Period	APC	95 % CI	P - value
Men	1999-2010	4.1 %	-3.1-11.8	0.3
	1999-2004	-5.5 %	-17.9-8.8	0.37
	2004-2010	12.8 % <sup>^</sup>	1.4-25.4	0.03
Women	1999-2010	1.7 %	-11.5-16.9	0.8
	1999-2007	-7.1 %	-17.3-4.3	0.18
	2007-2010	29.5 %	-23.9-120.4	0.29



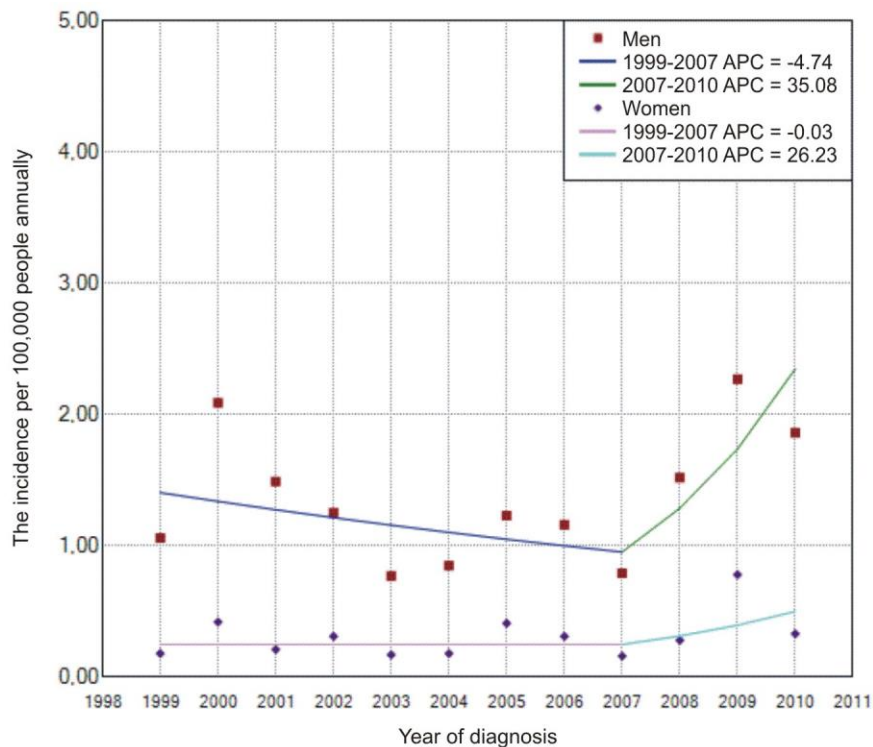
**Graph 1.** Joinpoint analysis of the standardized incidence rate of carcinoma of the tongue in Belgrade, 1999-2010, with the annual percentage of change (APC)

When carcinomas of the floor of the mouth were analyzed separately, an increasing ASR trend was observed for the whole studied period (1999-2010), with the annual percentage of change of 4.8% (95% CI: -8.2; 19.6) for men and 6.6% (95% CI: -13.2; 30.9) for women (Table

4). The increase of the incidence trend was highest for men from 2004 to 2010 (APC, 35.1%; 95% CI: -18.6; 124.3) and for women from 2007 to 2010 (APC, 26.2%; 95% CI: -42.5; 177) (Graph 2).

**Table 4.** Annual percentage of change (APC) standardized incidence rates of carcinoma of the floor of the mouth in Belgrade, 1999-2010

Gender	Period	APC	95 % CI	P - value
Men	1999 - 2010	4.8 %	-8.2 - 19.6	0.5
	1999 - 2004	-4.7 %	-14.7 - 6.4	0.3
	2004 - 2010	35.1 %	-18.6 - 124.3	0.2
Women	1999 - 2010	6.6 %	-13.2 - 30.9	0.5
	1999 - 2007	0 %	-15.7 - 30.9	0.5
	2007 - 2010	26.2 %	-42.5 - 177	0.5



**Graph 2.** Joinpoint analysis of the standardized incidence rate of carcinoma of the floor of the mouth in Belgrade, 1999-2010, with the annual percentage of change (APC)

A comparative representation of the trend of the incidence of carcinoma of the tongue and floor of the mouth throughout the world in the periods 1998-2002 and 2003-2007 is laid out in Table 5.

**Table 5.** Standardized incidence rate of carcinoma of the tongue worldwide

Year Country/Gender	Period I (1998-2002)		Period II (2003-2007)		Men, trend PI/PII	Women, trend
	Men	Women	Men	Women		
<b>AFRICA</b>						
Algeria	0.2	0.1	0.2	0.1	≈	≈
Egypt	0.9	0.5	0.6	0.6	↓	↑
Libya	0.4	0.4	0.4	0.2	≈	↓
Malawi	0.7	0.2	0.3	0.4	↓	↑
Zimbabwe	0.6	0.5	0.9	0.4	↑	↓
<b>CENTRAL AND SOUTH AMERICA</b>						
Argentina	1.5	0.7	1.6	0.5	↑	↓
Brazil	4.7-6.4	0.7-1.3	4.2-5.6	1.2-1.5	↓	↑
Chile	0.4	0.1	0.2	0.2	↓	↑
Colombia	1	0.9	1.3	0.6	↑	↓
Costa Rica	0.8	0.4	0.9	0.6	↑	↑
Ecuador	0.3	0.6	0.6	0.5	↑	↓
<b>NORTH AMERICA</b>						
Canada	1.5-2.4	0.3-1.7	1.6-2.7	0.6-1.4	≈	≈
USA	0.7-4.6	0.5-1.5	1.2-4.3	0.6-1.5	≈	≈
<b>ASIA</b>						
China	0.5-1.9	0.2-1.0	0.7-2.2	0.2-1.1	↑	≈
India	3.2-6.1	1.6-2.6	3.0-7.4	1.7-3.5	↑	↑
Israel	0.8	0.5	0.9	0.6	↑	↑
Japan	1.0-1.9	0.7-1.0	1.1-2.6	0.5-1.4	↑	↑
South Korea	0.7-1.5	0.1-0.5	0.9-1.4	0.3-0.8	≈	↑
Kuwait	0.6	0.9	0.7	0.5	≈	↓
Singapore	1.7	0.7	1.5	0.6	↓	↓
Thailand	0.9-4.4	0.7-0.9	1.3-3.7	0.4-0.9	≈	≈
Turkey	0.7	0.5	0.8	0.5	↑	≈
<b>OCEANIA</b>						
Australia	1.8-6.1	0.7-1.6	2.2-4.0	0.7-2.3	↓	↑
New Zealand	1.4	0.7	1.9	0.9	↑	↑
<b>EUROPE</b>						
Austria	2.1-2.4	0.3-1.3	1.5-2.4	0.9-1.0	≈	≈
Belarus	2.4	0.2	3	0.2	↑	≈
Bulgaria	1.9	0.2	1.9	0.4	≈	↑
Croatia	3.7	0.5	3.7	0.5	≈	≈
Cyprus	1	0.7	0.9	0.5	↓	↓

Czech	2.5	0.4	2.6	0.6	↑	↑
Denmark	1.8	0.7	2	0.9	↑	↑
Estonia	2.8	0.6	2.7	0.6	↓	≈
Finland	1.5	0.8	1.4	1.1	↓	↑
France	3.1-7.0	0.6-1.6	2.9-4.9	0.5-1.6	↓	≈
Germany	2.1-3.4	0.5-1.1	2.7-3.4	0.7-1.2	≈	≈
Iceland	0.9	0.6	1.4	0.6	↑	≈
Italy	0.6-3.4	0.3-0.9	1.0-3.8	0.3-1.2	↑	↑
Latvia	2.2	0.3	1.9	0.3	↓	≈
Lithuania	2.6	0.3	2.7	0.3	↑	≈
Malta	1.2	0.5	1.3	0.5	↑	≈
Netherlands	1.6	1	1.9	1.1	↑	↑
Norway	1.5	0.7	1.5	0.7	≈	≈
Poland	1.0-2.0	0.2-0.4	1.1-1.7	0.2-0.3	↓	≈
Russia	2.8	0.5	2.7	0.6	↓	↑
Slovakia	4.9	0.4	4.8	0.5	↓	↑
Slovenia	3.2	0.5	2.4	0.4	↓	↓
Spain	2.2-4.3	0.5-1.0	1.8-3.6	0.4-1.1	↓	≈
Sweden	1.1	0.7	1.3	0.8	↑	↑
Switzerland	2.0-3.4	0.4-2.2	2.1-5.0	0.4-1.6	↑	↓
UK	1.5-2.6	0.6-1.1	1.8-2.9	0.9-1.2	↑	↑

↓ - decreasing trend, ↑ - increasing trend, ≈ - trend without significant oscillations

## DISCUSSION

The ratio of the affected men and women in our study agrees with most of the available literature data (7, 14, 15). Such a gender ratio is almost certainly the result of a greater exposure of men to the proposed risk factors for the disease. The most important risk factors for the onset of carcinoma of the tongue and floor of the mouth are excessive tobacco use and alcohol consumption (16). Carcinomas of the tongue and floor of the mouth most commonly occur at an advanced age of life. In our study, most of the affected were in their sixties; these malignancies are very rarely encountered in persons before their fourth decade of life. Most authors worldwide have reported the frequency of these cancers to be highest in those over 60 years of age, and mostly among tobacco and alcohol users (15, 17-19). The appearance of these carcinomas in individuals below 40 years of age has not usually been associated with the risk factors characteristic of more advanced ages (such as smoking, excessive alcohol consumption). Among the patients below 40

years of age, there have been individuals who never smoked or drank alcohol, or the periods of exposure to these harmful agents was too short for these malignancies to appear (20-22). The prognosis of these cancers in younger individuals is usually much worse compared to the elderly (23).

The standardized incidence rate for carcinoma of the tongue in men in our study (1.97/100,000 persons a year) was similar to the rates obtained for some of the European cities and regions (Western Austria, Vorarlberg; Bulgaria; Hamburg, Germany; Umbria, Italy; Krakow, Poland; Granada, Spain; Martinique, France; regions in Italy), Canada (British Columbia, Alberta), and some parts of England (1, 2). The standardized incidence rate for carcinoma of the tongue in women (0.54/100,000 persons a year) was similar to the rates reported in Northern Italy (Romagna and Modena), Martinique in France, Bulgaria, and Spain (the province of Navara) (1, 2). According to the Globocan surveys, the highest incidence of carcinoma of the tongue in men has been reported for the region of New Delhi, India; it was

7.4/100,000 persons a year in the period 2003-2007 (1, 2). In the same period, high incidence rates were reported in other parts of India as well (Trivandrum, 6.8; Chennai, 5.9; and Karunagappally, 5.7/100,000 persons a year) (1, 2). The highest incidence of carcinoma of the tongue in women was reported in the period 2003-2007, again in India, ranging from 1.7-3.5/100,000 persons a year, depending on the regional cancer registries (1, 2).

The lowest incidence of carcinoma of the tongue in men worldwide was reported to be 0.2/100,000 persons a year in Setif, the capital of a province in East Algeria, and in Valdivia, Chile, in the period 2003-2007. A low incidence rate of these cancers was reported in Blantyre, Malawi (0.3); Cuenca, Equador (0.3); and Benghazi, Libya (0.4) (1, 2). The lowest incidence rate of carcinoma of the tongue in women was reported again in Setif, Algeria; Valdivia, Chile; provinces Ulsan and Jejudo, South Korea, each with 0.1/100,000 persons a year (1, 2).

The observed high incidence of carcinoma of the tongue in the population of India was most certainly the consequence of tobacco chewing, in both male and female populations. The study by Mowonge et al. in 2008 demonstrated a strong impact of tobacco chewing on the occurrence of all oral carcinomas, with a significantly stronger impact on female populations (24). Similar studies by other authors confirmed these findings (25, 26). Our own data suggested an increasing incidence trend for carcinomas of the tongue in the studied period (a yearly percentage of growth of 4.1% for men, and 1.7% for women), with the highest percentage of growth observed for men in the period 2004-2010. An increased incidence of carcinoma of the tongue in men from the period 1998-2002 to the period 2003-2007 was found in other European countries as well (Belarus, Czech Repub-

lic, Denmark, Iceland, Italy, Lithuania, Malta, Netherlands, Sweden, Switzerland, the UK), countries in the Central and South America (Brasil, Chile, Costa Rica), Asia (India, Israel, Japan, South Korea), and Oceania (Australia and New Zealand) (1, 2).

It is a generally known fact that the most important risk factors for carcinomas of the tongue and floor of the mouth (and for all oral cavity carcinomas for that matter) are excessive alcohol consumption, smoking, infection with human papilloma virus and immune system conditions (27-30). The concomittant action of these factors markedly elevates the risk of these carcinomas (16). The most probable reason for increased incidence rates of carcinomas of the tongue and floor of the mouth in our study was increased alcohol consumption in Serbia and an increased frequency of severe alcohol intoxication episodes, related to the situation in the country and socioeconomic issues in the last 10 years of the studied period, as indicated by other studies as well (31). The wars in the region certainly contributed to this increased incidence, creating various fears and immune system deficiencies in the affected populations.

## CONCLUSION

In the studied period of 12 years, the incidence rates of carcinoma of the tongue and floor of the mouth increased. The observed growing trends of incidence of these carcinomas necessitate the creation of prevention programs for the Republic of Serbia, since the high mortality and morbidity rates of these cancers represent a serious health problem, both in our country and abroad.



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## Trend u incidenciji karcinoma jezika i poda usne duplje na teritoriji grada Beograda

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### SAŽETAK

Karcinomi jezika (KJ) i karcinomi poda usta (KPU) se u literaturi najčešće opisuju kao jedan entitet – karcinomi jezika i poda usta (KJPU). Incidencija ovih karcinoma u svetu varira od 0,1/100.000 osoba godišnje za ženski pol u Alžiru, Čileu i Koreji, do 7,4/100.000 za muškarce u oblasti Nju Delhija u Indiji.

Cilj rada bio je odrediti i analizirati trend u incidenciji karcinoma jezika u populaciji glavnog grada Republike Srbije tokom dvanaestogodišnjeg perioda.

Podaci o oboljenjima su dobijeni iz Registra za rak centralne Srbije. Standardizovana stopa incidencije je izračunavana korišćenjem direktne metode standardizacije, a kao standardna populacija korišćena je populacija sveta. Za analizu promena trenda incidencije i godišnjeg procenta promene korišćena je metoda regresione analize uz pomoć tačkaka spajanja (eng. joinpoint regression analysis). Jointpoint regresiona analiza je pokazala povećanje trenda incidencije KJ kod oba pola u ispitivanom periodu, sa godišnjim procentom rasta od 4,1% za muškarce i 1,7% za žene. Incidencija KPU je rasla sa godišnjim procentom rasta za muškarce od 4,8% i za žene 6,6%. Stope incidencije karcinoma jezika i poda usta su u stalnom porastu u glavnom gradu Republike Srbije.

*Ključne reči:* karcinom jezika, karcinom poda usta, incidencija