

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

## Trends in incidence of non-melanoma and melanoma skin cancers in central Serbia

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## SUMMARY

**Introduction/Objective** The incidence of both melanoma and non-melanoma skin cancers (NMSC) has been increasing over the past decades worldwide. NMSC is the most common cancer in white population and melanoma is one of the deadliest cancers today.

The objective of the paper was to determine trends in age-standardized incidence rates of NMSC and melanoma in central Serbia from 1999 to 2013.

**Method** A descriptive epidemiological study was done. Data about incidence for NMSC and melanoma were obtained from the Serbian Cancer Registry and data about population originating from 1991, 2001, and 2011 censuses. Crude incidence rates were calculated per 100,000 inhabitants. Direct method of standardization was performed with the world population as the standard. Trend lines were estimated using linear regression.

**Results** During a 15-year period, the total number of new NMSC cases was 41,719 [21,690 (52%) in men and 20,029 (48%) in women]. There were 5,781 new cases of melanoma [2,969 (51.4%) in men and 2,812 (48.6%) in women]. A significantly increasing incidence trend for NMSC both in men ( $y = 0.617x + 24.29$ ,  $R^2 = 0.500$ ) and women ( $y = 0.672x + 0.670$ ,  $R^2 = 0.670$ ) was determined. In the same period, a statistically significant increase of incidence trend for melanoma was determined in men ( $y = 0.111x + 3.708$ ,  $R^2 = 0.384$ ) and in women ( $y = 0.098x + 3.375$ ,  $R^2 = 0.409$ ). NMSC was registered in persons of all ages. NMSC incidence increased rapidly in persons older than 50 years. Melanoma predominates in children and adolescents and is registered more frequently than NMSC in persons below 60 years of age.

**Conclusion** Our findings showed significantly increasing trend of age-standardized incidence rates for both NMCC and melanoma. In the observed period, there were 7.2 times more new cases of NMSC than melanoma in the population of central Serbia. There were more registered new cases of NMSC and melanoma in men than in women. Screening of skin cancers and earlier diagnosis may improve treatment and prognosis.

**Keywords:** non-melanoma skin cancers; melanoma; trend; incidence

## INTRODUCTION

Skin cancer represents the most common type of malignancy in the white population [1]. They are often classified as non-melanoma skin cancers (NMSC) and melanoma [2]. Melanoma and NMSC are the most common types of skin cancers with documented increasing incidence in the several past decades [3, 4].

Unlike other cancers, the incidence of NMSC is not well documented. Many cancer registries do not register all primary NMSC. Small forms of NMSC and recurrent cases are not registered [5]. NMSC are sometimes treated without histological confirmation, and some cancer registries do not attempt to register cases of NMSC. Overall, this leads to under-reporting of the true burden of NMSC on the health system [6, 7].

The World Health Organization (WHO) estimates two to three million cases of NMSC per year which are most likely to be under-reported [8]. NMSC is associated with high morbidity

and costs, few cancer deaths overall, and decreased quality of life [9, 10].

There are wide variation in incidence rates of NMSC among different countries and continents. The highest incidence rates of NMSC are registered in Sweden (estimated incidence of 23.9 in 2012; for Switzerland and Great Britain, higher than 16.9 per 100,000 for 2012). Balkan countries, central Serbia, Moldova, and Bosnia and Herzegovina are standing at the lower incidence levels (< 5.3 per 100,000 for 2012) [11].

New Zealand and Australia have the highest incidence and mortality rates from NMSC and melanoma in the world. The incidence of NMSC is 18–20 times higher than the incidence of melanoma [12].

About 90% of NMSC are associated with exposure to ultraviolet (UV) radiation from the sun and especially with the exposure to the UVB radiation. The most important risk factors in the development of melanoma are as follows: the number of common nevi and atypical nevi, skin phenotype, a family history of melanoma

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(in 8–12% of patients), actinic damage,  $\geq 65$  years of age, history of sunburns and intermittent sun exposure (especially in childhood), geographic localization [13].

The incidence of melanoma in Europe varies considerably between countries. The lowest rates are observed in East and South-East Asia, and in South Asia [14].

The objective of the paper was to determine and analyze trends in age-standardized incidence rates of NMSC and melanoma skin cancers in central Serbia in the 1999–2013 period.

## METHODS

A descriptive study was performed. Data were obtained from the Serbian Cancer Registry and were analyzed for central Serbia, which included the territory of Serbia excluding the territory of the Autonomous Province of Vojvodina and the Autonomous Province of Kosovo and Metohija [15]. Cancer diagnosis was coded according to the Tenth Revision of International Classification of Diseases – ICD-10th (code C43 for melanoma and code C44 for NMSC) [16].

Cancer reporting is mandatory by Serbian legislation. The Serbian Cancer Registry was established in 1970. After a successful reorganization during 1996–1998, which substantially improved data quality, the Registry became a member of the International Agency for Research on Cancer and the European Network of Cancer Registries [17].

## Statistical analysis

Crude and age-standardized incidence rates were calculated. Method of direct standardization was performed [18]. Population of the world was used as the standard. Data about population of central Serbia were obtained from 1991, 2002, and 2011 censuses. For the inter-census period, the data were obtained from the estimates published by the Statistical Office of the Republic of Serbia.

Trend lines were estimated using linear regression. The least-squares method was used to estimate the linear trends. Correlation coefficients were calculated, with a positive value indicating an increasing trend, while a negative value was indicative of a decreasing trend. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

A total of 47,500 new cases of skin cancers were registered in the 1999–2013 period. NMSC accounts for 87.8% of all registered new cases of skin cancers, and melanoma accounts for 12.2%. A total of 41,719 new cases of NMSC were registered (21,690 in men and 20,029 in women) during the observed period. Fifty-two percent of all registered cases were men, while 48% were women. The NMSC incidence ratio of men to women was 1.08:1.

The total number of new melanoma cases was 5,781 (2,969 in men and 2,812 in women). Of all registered mel-

**Table 1.** Annual age-standardized incidence rates for non-melanoma and melanoma skin cancers in men and women, central Serbia, 1999–2013

Year	Non-melanoma skin cancer age-standardized incidence rate (World)		Melanoma skin cancer age-standardized incidence rate (World)	
	Men	Women	Men	Women
1999	19.7	15.2	4.1	3.8
2000	26.6	19.5	4.4	3.7
2001	25.7	17.4	3.9	3.6
2002	26.1	18.2	3.6	3.9
2003	27.2	19.7	5.0	4.0
2004	30.7	24.3	3.7	3.6
2005	27.5	21.9	4.2	3.9
2006	35.4	27.7	3.4	3.0
2007	29.5	22.8	5.1	4.4
2008	33.5	25.4	4.7	4.7
2009	30.7	25.2	5.5	4.5
2010	30.8	25.3	5.5	4.4
2011	30.9	24.7	6.2	6.0
2012	30.7	24.2	5.1	4.7
2013	30.7	26.0	4.6	4.3

noma cases, 51.4% were men and 48.6% were women. The men to women incidence ratio for melanoma was 1.05:1.

On average, there were 7.2 times more new cases of NMSC than of melanoma.

Annual age-adjusted incidence rates for melanoma and NMSC are shown in Table 1.

The total number of new cases of NMSC in men was 7.8 times higher than the number of new melanoma cases in men. At the same time, there were 7.6 times more new cases of NMSC in women compared with the number of new melanoma cases in women.

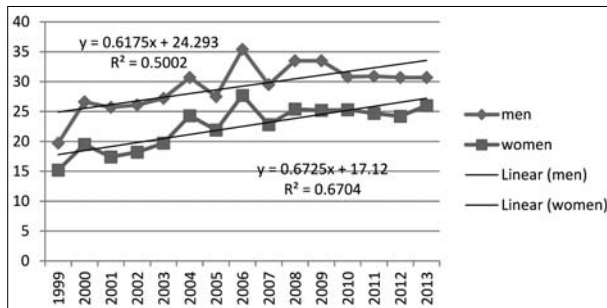
Annual age-standardized incidence rates for NMSC in men ranged from 19.7 (1999) up to 35.4 (2006). In women, annual age-standardized incidence rates for NMSC ranged from 15.2 (1999) up to 27.7 (2006).

The lowest annual age-standardized incidence rates for melanoma for both men and women were registered in 2006 (3.4 in men and 3.0 in women). The highest annual age-standardized incidence rates were registered in 2011 and amounted to 6.2 in men and 6 in women. The ratio of men to women was 1.05:1.

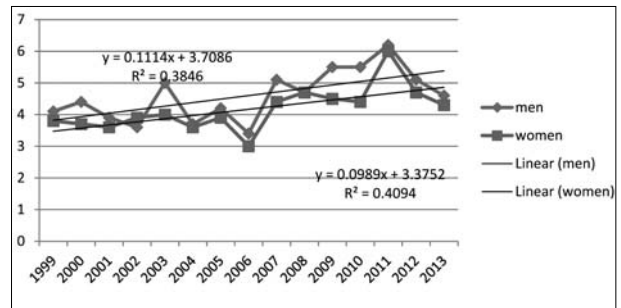
In the observed period, a statistically significant increasing incidence trend for NMSC was determined in both men ( $y = 0.617x + 24.29$ ,  $R^2 = 0.500$ ) and women ( $y = 0.672x + 0.670$ ,  $R^2 = 0.670$ ) (Figure 1).

There was a significant increasing incidence trend for melanoma in both men ( $y = 0.111x + 3.708$ ,  $R^2 = 0.384$ ) and women ( $y = 0.098x + 3.375$ ,  $R^2 = 0.409$ ) (Figure 2).

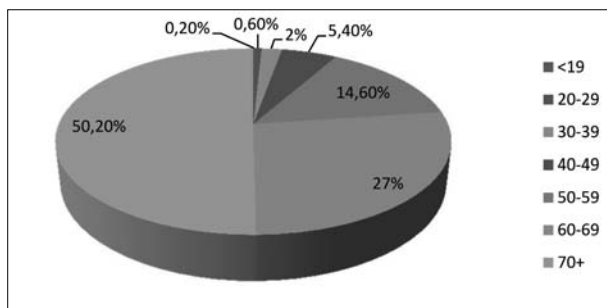
During the observed period, NMSC was registered in all age groups. There were 0.2% of new cases in persons below 19 years of age, 0.6% for persons 20–29 years old, 2% for persons 30–39 years old, 5.4% for persons 40–49 years old, 14.6% for persons 50–59 years old, 27% for persons 60–69 years old, and 50.2% for 70-year-olds and older. The number rapidly increases after 50 years of age. More than 50% of newly diagnosed cases were 70 years old or older (Figure 3).



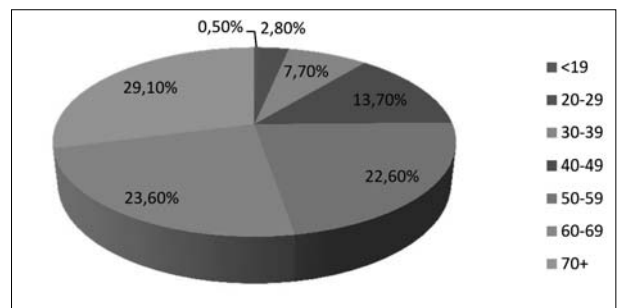
**Figure 1.** Linear trends for NMSC in men and women, based on age-standardized incidence rates, central Serbia, 1999–2013



**Figure 2.** Linear trend for melanoma based on age-standardized incidence rates in men and women, central Serbia, 1999–2013



**Figure 3.** The percentage of new cases of non-melanoma skin cancers according to the age groups, central Serbia, 1999–2013



**Figure 4.** The percentage of new cases of melanoma by age groups, central Serbia, 1999–2013

Melanoma was continuously registered after the age of five years. In children and teenagers (< 19) there were 31 (0.5%) new cases. Incidence rates increased with age: 2.8% for the 20–29 age group, 7.7% for 30–39, 13.7% for 40–49, 22.6% for 50–59, 23.6% for 60–69, and 29.1% for the 70+ age group. A rapid increase of new melanoma cases was registered after 30 years of age. The highest number of new melanoma cases was registered at the age of 70 years and older (Figure 4).

## DISCUSSION

According to our findings, incidence trends of NMSC and melanoma increased statistically significantly in both men and in women. There were more new cases of NMSC and melanoma registered in men than in women. In the observed period, there were 7.2 times more new cases of NMSC than of melanoma in the population of central Serbia.

Our findings showed that NMSC accounts for the majority of skin cancers in the population of central Serbia. According to our results, during a 15-year period, NMSC were registered in all ages, predominantly in older age groups.

Melanoma predominated in children and in young adults. It was more frequent in persons of both sexes below 60 years of age. In the older age groups, NMSC was more frequent than melanoma, especially in persons older than 70 years. Men are exposed to a greater melanoma incidence risk. Melanoma is registered in children older than five years [18].

The incidence of NMSC in Albania shows an increasing trend over the past decade, with men being more often af-

ected by this health condition [19]. Some of the countries neighboring Serbia have the following incidence rates: Montenegro – 2.6 per 100,000, Greece – 2 per 100,000, and Albania – 1.7 per 100,000 [19]. NMSC is the second most common cancer in both men and women in the city of Belgrade [20].

Age-standardized incidence rates for both skin cancers are increasing in Iran, and they are higher in men than in women [21]. Increasing of age-standardized incidence rates for NMSC was determined in both men and women in the city of Belgrade in the 1999–2011 period [2].

Both skin cancers have a wide age distribution and the incidence increasing with age, with it being higher in men than in women. Some studies have shown results about increasing age-standardized incidence rates in older age groups [2, 18, 22–25]. In 1999, melanoma was occurring slightly more in women than in men in central Serbia [15].

These findings could be partially explained by exposure to UV radiation. The “pollutants” that are most detrimental to the skin are UV radiation, polycyclic aromatic hydrocarbons, volatile organic compounds (benzene), heavy metals, and ozone. The genotoxicity of UV light is well-documented (type of lesion or mutation, etc.) and its carcinogenic effect is clearly demonstrated in vivo in men. Some epidemiological studies describe the carcinogenicity of certain pollutants such as arsenic or lead on the skin cancers [26].

Both epidemiological surveys and experiments with animal models suggest that UVA, and perhaps the visible light, may induce melanomas. It is known that the Japanese have a much lower incidence of skin cancer than Caucasians; the dramatic rise in skin cancer in Japanese Americans in Hawaii exposed to high-intensity irradiation raises concerns [27].

Development of skin cancers is a long process that may take decades. Evidence suggests that childhood and adolescence are critical periods in the etiology of skin cancer [28].

Skin cancers that are the most common are also preventable [5, 22, 27, 28]. Studies measuring the effect of public education programs show a substantial change in attitudes and behavior in the sunlight, particularly in younger age groups. Behaviour change might also be achieved through direct and indirect routes [29].

Primary prevention is more beneficial and effective in children, not only due to the particular importance of sunlight exposure during this period, but because this is when individuals are more open to changes and adopt new attitude and behavior [30].

In Serbia, skin cancers are expected to increase. Many persons are adopting the western life style with more UV light exposure during outdoor recreational activities. Our population is getting older, and an increase of new skin cancer cases is expected in the future.

There are some important limitations to this investigation – the data on histology of skin cancers and on body localization of skin cancers are missing.

## CONCLUSION

There were continuous increasing trends of age-standardized incidence rates for NMSC and melanoma in both men and women. Age-standardized rates were much higher in men than in women. NMSC and melanoma have a wide age distribution and the age-standardized incidence rates increasing with age. In order to prevent skin cancers, it is necessary to promote education campaigns to limit uncontrolled sun exposure and to limit indoor tanning. Presented findings support the important role of primary prevention and early detection of NMSC and melanoma, at the earliest age. Screening of skin cancers leading to an earlier diagnosis may improve the treatment and prognosis.

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## Тренд инциденције немеланомског рака и меланома коже у централној Србији

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### САЖЕТАК

**Увод/Циљ** Инциденција рака коже је у сталном порасту последњих деценија у свету. Немеланомски рак коже је најчешћи рак у белој популацији, а меланом коже је један од најсмртоноснијих канцера данас.

Циљ рада био је да утврди трендове стандардизованих стопа инциденције немеланомског рака коже и меланома у популацији централне Србије у периоду од 1999. до 2013.

**Методе** Примењена је дескриптивна студија. Подаци о инциденцији рака коже добијени су из Регистра за рак у централној Србији. Подаци о становништву су из пописа становништва 1991, 2001, 2011. године. Рачунате су нестандардизоване стопе инциденције на 100.000 становника, а затим су стандардизоване методом директне стандардизације. Стандардизација је извршена према стандардној популацији света. Рачунат је линеарни тренд.

**Резултати** У посматраном периоду регистровано је укупно 41.719 новооболелих од немеланомског рака коже – 21.690 (52%) мушкараца и 20.029 (48%) жена. Регистровано је 5.781 новооболелих од меланома коже – 2.969 (51,4%) мушкараца и 2.812 (48,6%) жена. Утврђен је значајан пораст трен-

да стандардизованих стопа инциденције немеланомског рака коже и код мушкараца ( $y = 0,617x + 24,29$ ,  $R^2 = 0,500$ ) и код жена ( $y = 0,672x + 0,670$ ,  $R^2 = 0,670$ ). У истом периоду утврђен је статистички значајан пораст тренда стандардизованих стопа инциденције меланома коже код мушкараца ( $y = 0,111x + 3,708$ ,  $R^2 = 0,384$ ) и код жена ( $y = 0,098x + 3,375$ ,  $R^2 = 0,409$ ). Немеланомски рак коже регистрован је код особа свих узраста, а нагли пораст регистрован је код старијих од 50 година. Меланом коже је чешћи код деце и адолесцената и региструје се чешће од немеланомског рака код особа млађих од 60 година.

**Закључак** Резултати показују значајан пораст тренда инциденције немеланомског рака коже и меланома коже у централној Србији. Регистровано је значајно више новооболелих од немеланомског рака коже него од меланома и значајно више у мушкој него у женској популацији. Применом мера превенције и раног откривања и лечења рака коже може се смањити инциденција.

**Кључне речи:** немеланомски рак коже; меланом; инциденција