

# Malignant Skin Melanoma in Croatia

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## ABSTRACT

*Global heating and increased solar ultraviolet irradiance have caused an increase in number of many diseases, particularly skin malignant diseases. Aim of this study was to investigate the influence of climate changes on the health of the population of the Primorsko-goranska and Istria Counties. We gathered and analyzed data about the frequency of skin malignant melanoma in the period of eight years (1998–2005). The data were collected from the Croatian cancer registry. The incidence of malignant skin cancer was estimated overall, by age group and gender. We found that the incidence of the skin melanoma was approximately the same in both counties during the period 1998–2005. However, significant increase has been noted when compared to the situation in the period 1977–1996 ( $p=4.95 E-13$ ). The incidence of malignant skin melanoma has risen during the last ten years. It is differently distributed between gender and age groups in Primorsko-goranska and Istria County. It can be related to climate changes, but also to different ways of life between these two counties.*

**Key words:** skin melanoma, epidemiology, incidence, Croatia

## Introduction

Malignant skin melanoma (MSM), the fastest growing form of cancer in male and third fastest developing form of cancer in female population is occurring as a consequence of increased UV-B irradiance. In the past decades it has increased in number, particularly in Caucasian populations. Although in a different rate, particular areas and countries are recording an annual increase of 3% to 7%, so MSM is considered a public health problem to be monitored carefully<sup>1</sup>. Highest rates of incidence are recorded in Australia and New Zealand (37.7 in man and 29.4 in woman) as well as Northern America. In Europe, northern parts are marked with higher incidence (8.4 in man and 10.0 in woman) than southern parts (6.0 in men and 5.5 in women)<sup>2</sup>.

Over the past fifteen years the incidence of MSM in Croatia has constantly been rising, and since 2000 it has been considered one of the fifteen most common malignant diseases, still there have been a few projects researching it's frequency in our country<sup>3-5</sup>.

The aim of this study was to define the trend of MSM incidence in Croatia with special focus on Primorsko-goranska and Istria counties.

## Materials and Methods

The study is based on a database held by Croatian cancer registry which collects and classifies all cancer patients' data. We have only taken MSM patients into consideration. Data analyzed for entire Croatia was for the period from 1991–2005 and for Primorsko-goranska and Istria counties for the period 1998–2005<sup>6</sup>.

### Residents

Applying the correct number of residents into the study presented a methodological problem. Population censuses from 1991 and from 2001 differ methodologically. Population census from 1991 was based on the »de

jure« method with reference to the residents documented place of residence without considering their real presence at the time of the census making<sup>7</sup>. Taking international recommendations<sup>8</sup> into consideration, population census from the year 2001 was based on the »de facto« method with reference to all the residents living in one domicile at that time. To make the 1991 morbidity rates comparable to 2001 morbidity rates, our calculations were based on »real residential population« i.e. population working, paying taxes, using educational, social and municipal services and paying for them<sup>9</sup>. A significant in-country population shift during the warfare poses another problem for morbidity rate calculation between censuses. We used an approximation of resident population between censuses, made by our demographers, to make the calculations more valid<sup>7</sup>. For period after 2001 we used official annual assessments of total residential population in Croatia reduced by the population residing abroad<sup>10–14</sup>.

Data analysis and statistical analysis

Applying the number of residents according to stated criteria and the number of »sick« stated in the Croatian cancer registry, we calculated MSM incidence rates. 95% confidence interval CI was joined to each rate. Poisson distribution binominal approximation was used when the number of cases was under 100 or normal distribution approximation when the number of cases was 100 or more according to literature recommendations<sup>15</sup>. Standardized rates were calculated using the direct standardization method applying standard residents of Europe<sup>16</sup>. Differences in incidence were tested by the  $\chi^2$ -test. Calculations were made by using statistical programs<sup>17,18</sup>. Statistical significance was set to  $p < 0.05$ .

Results

During the period 1989–2006 there were 5.916 new MSM patients recorded, 2.910 men and 3.006 women respectively. Average annual number of new 197 MSM pa-

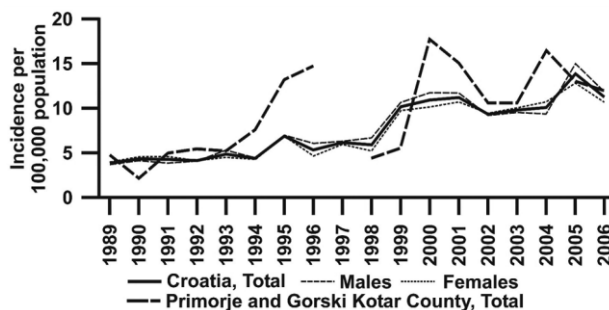


Fig. 1. Annual MSM incidence in Croatia for the period 1989–2006; men and women rates; also shows annual MSM incidence for both gender combined in the County of Primorje and Gorski Kotar during the same period of which 1991–1997 period relates to an earlier study of MSM in that county.

tients recorded for the period from 1989–1993 has risen to 435 new patients recorded for the period of 1999–2003 and finally to 496 for the period of 2004–2006 as shown in Figure 1.

Increasing of crude and standardized incidence rates for the named period is shown in Table 1. Specific incidences by age and sex in 1989–1993 compared to 1999–2003 are shown in Figure 2.

During the 1989–2006 period the incidence of MSM in the age group 0–19 years slightly differed, while in older age groups (20–59 years and 60 years and over) there was a significantly increasing. An overall increasing of 150.6% (6.8% yearly) was found in men aged 20–60 years ( $\chi^2=127.6754$ ,  $df=1$ ,  $p=1.32E-29$ ) and almost the same rate (148.4%; 6.7% yearly) in men aged 60 years and over ( $\chi^2=120.6226$ ,  $df=1$ ,  $p=4.62E-28$ ). In women aged 20–60 years the overall increasing amounted to 133.5% or 6.2% yearly ( $\chi^2=116.7265$ ,  $df=1$ ,  $p=3.30E-27$ ) and in 60 years old and over amounted to 141.5% or 6.2% yearly ( $\chi^2=123.5571$ ,  $df=1$ ,  $p=1.05E-28$ ). Details are presented in Table 2 and Figure 3.

TABLE 1  
INCREASE OF MSM ALL AGES INCIDENCE IN CROATIA

	Total		Males		Females	
	Incidence (95% CI LL, UL)		Incidence (95% CI LL, UL)		Incidence (95% CI LL, UL)	
Crude						
1989–1993	4.35	(4.08–4.63)	4.29	(3.91–4.71)	4.41	(4.04–4.81)
1994–1998	5.80	(5.48–6.13)	6.15	(5.68–6.55)	5.48	(5.06–5.93)
1999–2003	10.34	(9.92–10.79)	10.64	(10.02–11.30)	10.07	(9.49–10.69)
2004–2006	11.80	(11.21–12.42)	12.14	(11.29–13.06)	11.48	(10.68–12.34)
Standardized						
1989–1993	4.10	(3.85–4.37)	4.44	(4.05–4.86)	3.95	(3.62–4.31)
1994–1998	5.14	(4.86–5.43)	5.86	(5.42–6.34)	4.69	(4.33–5.07)
1999–2003	8.79	(8.43–9.17)	9.87	(9.30–10.49)	8.16	(7.66–8.66)
2004–2006	9.65	(9.17–10.15)	10.71	(9.95–11.52)	8.99	(8.36–9.66)

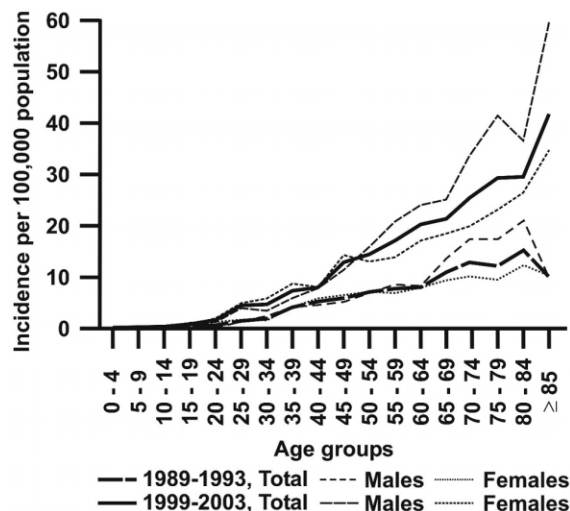


Fig. 2. Specific incidence of MSM in Croatia by age and sex in 1989–1993 and 1999–2003.

MSM incidences by counties in the period 2000–2001 are shown in Figure 4.

The highest rates were found in the counties of Primorje and Gorski Kotar, Varaždin and Istria and the lowest rate in the county of Virovitica and Podravina. Coastal counties shared a significantly highest rate than continental counties did: 11.0 (95% IP 10.0–12.1) vs. 9.7 (95% IP 9.0–10.4);  $\chi^2=4.7620$ ,  $df=1$ ,  $p=0.0291$ .

During the period 1998–2006 311 MSM cases were registered in the County of Primorje and Gorski Kotar (147 men and 164 women) and 206 in the County of Istria (100 men and 106 women) what represent respec-

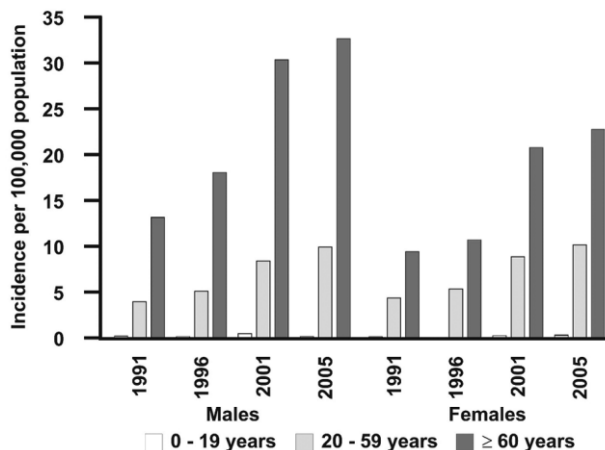


Fig. 3. Increase of MSM incidence in major age groups by years.

tively 7.9% and 5.3% of all the cases registered in Croatia in the same time period.

Annual incidences for both counties in the 1998–2006 period are presented in Figure 5 and 6.

The mean inconsiderable annual incidence during the period of 1998–2006 for MSM in Primorje and Gorski Kotar County was 11.7 (95% CI 10.5–13.1) and 11.1 (95% CI 9.6–12.7) in the County of Istria while standardized in both counties were 9.3. There were no differences between sexes.

In the above mentioned period the incidence of for MMK in Primorje and Gorski Kotar County was insignificantly higher in women by comparison with men and it amounts 11.8 (95% CI 10.5–13.1), respectively 11.6 (95%

TABLE 2  
INCIDENCE OF MSM IN CROATIA BY MAJOR AGE GROUPS DURING 1989–2006

Age / Periods	Total		Males		Females	
	Incidence (95% CI LL. UL)		Incidence (95% CI LL. UL)		Incidence (95% CI LL. UL)	
0–19						
1989–1993	0.17	0.08–0.31	0.20	0.07–0.43	0.14	0.04–0.35
1994–1998	0.09	0.03–0.21	0.14	0.04–0.37	0.04	0.00–0.21
1999–2003	0.36	0.21–0.57	0.47	0.24–0.82	0.25	0.09–0.53
2004–2006	0.21	0.08–0.46	0.14	0.02–0.50	0.29	0.08–0.75
20–59						
1989–1993	4.15	3.80–4.53	3.96	3.48–4.50	4.34	3.84–4.90
1994–1998	5.22	4.82–5.65	5.10	4.54–5.72	5.33	4.77–5.96
1999–2003	8.62	8.09–9.18	8.38	7.65–9.19	8.85	8.10–9.67
2004–2006	10.02	9.30–10.80	9.91	8.90–11.04	10.13	9.11–11.25
≥ 60						
1989–1993	10.87	9.90–11.93	13.15	11.47–15.07	9.42	8.29–10.71
1994–1998	13.60	12.54–14.74	18.06	16.14–20.19	10.69	9.50–12.02
1999–2003	24.62	23.23–26.10	30.36	27.94–32.99	20.77	19.13–22.56
2004–2006	26.75	24.91–28.74	32.66	29.48–36.18	22.77	20.59–25.18

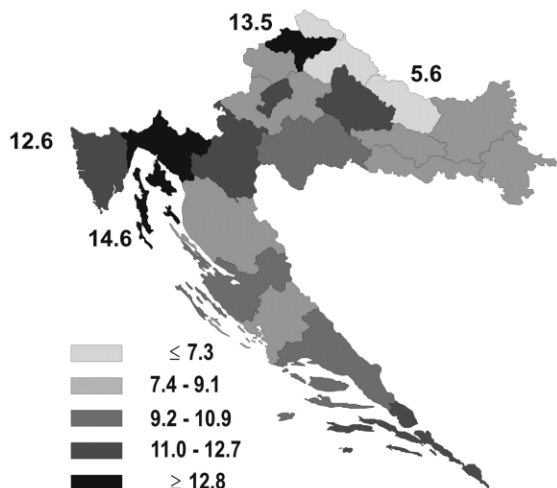


Fig. 4. Incidence of MSM in Croatia by counties in 2000–2002.

IP 9.9–13.7). Standardized incidences in women amount 9.3 (95% IP 7.9–10.9) and in men they are 9.8 (95% IP 8.3–11.5).

In Istria County the incidence of MMK is almost the same in men and women – 11.1 (95% IP 8.0–13.6), respectively 11.0 (95% IP 9.1–13.4). The same is valid for the standardized rates: 9.7 (95% IP 8.1–11.9), respectively 9.1 (95% IP 7.5–11.1).

It is interesting to note that in Primorje and Gorski Kotar County the mean annual incidence of 9.2 noted in the period from 1998–2000 period increased significantly to 13.9 in the period from 2004–2006 ( $\chi^2=8.4497$ ;  $df=1$ ,  $p=0.0037$ ) while in Istria County in the same time periods the mean annual incidences were quite similar: 11.2 and 12.0. Specific incidences in both counties are shown in Figure 7 and 8.

Older age groups show greater incidences in both counties. In Primorje and Gorski Kotar county men develop MSM more frequently than women yet from 45 years of age, and in Istria County after 60 years of age. No statistically significant change in MSM incidence be-

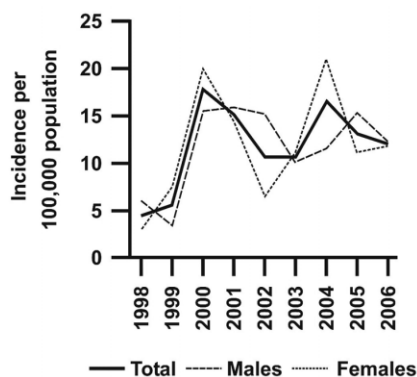


Fig. 5. Annual MSM incidence in Primorje and Gorski Kotar County for the period 1998–2006.

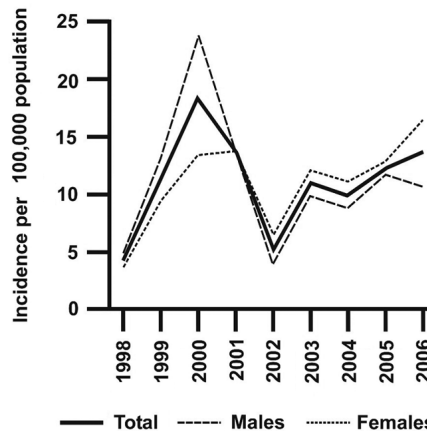


Fig. 6. Annual MSM incidence in Istria County for the period 1998–2006.

tween age groups was recorded during the period 1998–2001 and 2003–2005.

### Discussion

We are aware of the shortcomings of this research considering Primorsko-goranska and Istria county, short period of 8 years for gathering data, respectively. In fact, in this study also, different incidence intensity could be proved only by comparing average annual incidences of two distant time periods, for example incidences relating to Croatia in whole. According to publications statements, global warming of our planet started in the middle of the seventies and it is approximated to 0.50 °C annually<sup>19,20</sup>. Meteorological data is systematically monitored from 1861 in Croatia and ultraviolet irradiance from the end of the nineties<sup>21</sup>. UV irradiance monitoring of only over the past decade was a limitation for correlating the MSM incidence with the intensity of UV irradiance. That there is a rise in skin changes, and particularly MSM, we

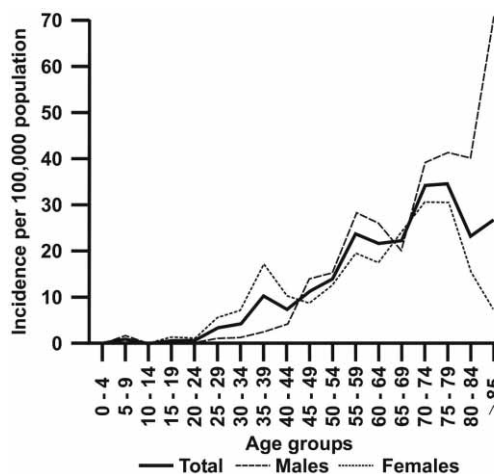


Fig. 7. Specific incidence of MSM by age and sex in Primorje and Gorski Kotar County for the period 1998–2006.

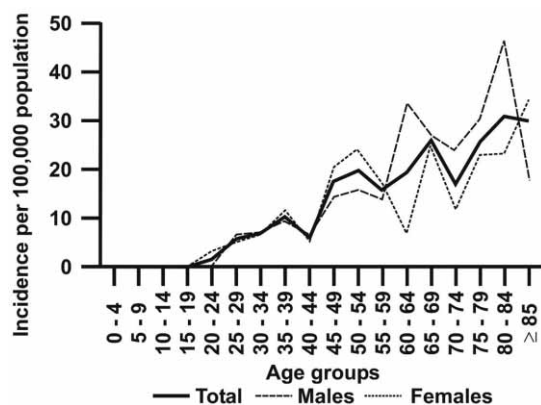


Fig. 8. Specific incidence of MSM by age and sex in Istria County for the period 1998–2006.

are instructed by studies and publications conducted worldwide<sup>22,23</sup> and inland<sup>24,5,25</sup> Longitudinal skin melanoma monitoring by Zamolo et al.<sup>5</sup> during the 20 year period prove incidence increase from 4.8 to 7.2. Our research states that values recorded over the past decade are even higher, and demonstrate statistically significant difference compared to the former values, showing similarity with those registered in Scandinavia and Western Europe<sup>1,2</sup>. Average age of melanoma occurring is mid forties<sup>26,27</sup> which we confirmed in our study. Moreover, it is familiar that men are more liable to MSM than women in that age. The fact that it occurs yet after 45<sup>th</sup> year of age in Primorsko-goranska County and not be-

fore 60<sup>th</sup> year of age in Istria County indicates the possible greater exposure of women to UV irradiation by working with men together in the field. Before 20 years of age melanoma is occurring only sporadically. All that indicates that influence of causal factors cumulates by age, according to literature, respectively<sup>27</sup>.

## Conclusion

Influenced by climate changes, the incidence of malignant melanoma rises in Croatia. In Istria and Primorsko-goranska Counties, annual incidences of malignant melanoma morbidity are even higher, and this has especially been the case during the last decade. We have noticed a difference in morbidity between gender morbidity in these two Counties, as well as the age at the melanoma occurs, which is at least by some part conditioned by the way of life in these two Counties. Therefore, we can conclude that the intensity and the nature of climate influence on malignant melanoma morbidity is changing according to geographic regions, amount of exposure to climate changes, social capability of adaptation to stated changes, liability of particular populations and particular characteristics of each individual.

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## MALIGNI MELANOM KOŽE U HRVATSKOJ

### SAŽETAK

Globalno zagrijavanje i povećano solarno ultraljubičasto zračenje su uzrokovali povećani broj mnogih oboljenja, pogotovo malignih kožnih oboljenja. Cilj ove studije je bio istraživanje utjecaja klimatskih promjena na zdravlje populacije Primorsko-goranske i Istarske županije. Sakupili smo i proanalizirali podatke o učestalosti malignog melanoma kože u periodu od osam godina (1998.–2005.). Podaci su preuzeti iz Hrvatskog registra za rak. Incidencija malignog melanoma kože je procjenjena skupno te po dobnim i spolnim skupinama. Uočili smo da je incidencija malignog kožnog melanoma približno ista u obje županije tijekom perioda 1998.–2005. godina. Međutim, značajan porast je zapažen u usporedbi sa periodom 1977.–1996. godina ( $p=4,95 E-13$ ). Incidencija malignog melanoma kože je u porastu zadnjih deset godina. Distribucija incidencije među dobnim i spolnim skupinama u Primorsko-goranskoj i Istarskoj županiji je značajno drugačija. To se može objasniti klimatskim promjenama te različitim stilom života u ove dvije županije.