Agnes Stier *
Anna Paldy °

TEMPORAL CHANGES IN SKIN CANCER EPIDEMIOLOGY IN HUNGARY (2001-2015)

Abstract. Skin cancer, including the potentially fatal melanoma and the less harmful non-melanoma skin cancer (NMSC), traditionally affected Northern populations in Europe. Less attention was paid to the incidence in Central and Eastern Europe (CEE), including Hungary. Firstly, this paper aims to interpret the incidence and death rate of skin cancer in Hungary in the CEE region and neighbouring countries from available databases. Next, this paper also looks at the tendencies of skin cancer incidence between 2001 and 2015 by using age-standardised incidence rates, utilizing data from the National Cancer Registry. The third aim of the study is to depict the distribution of skin cancer using Bayesian smoothed indirectly standardised relative risks using data provided by the Rapid Inquiry Facility (RIF).
The CEE region is characterised by a relatively high death rate of melanoma meanwhile the incidence rate is the lowest in Europe. It was found that both melanoma and NMSC increased between 2001 and 2015, especially in the population aged 65 years and above. The distribution of melanoma and NMSC incidence somewhat follows the pattern of UV radiation in Hungary. However, there are areas where the incoming UV radiation is not particularly high and still belong to the highest quantile of skin cancer incidence. These areas require further analysis to study the underlying risk factors of the observed high incidences.

Keywords: skin cancer, melanoma, epidemiology, Hungary, temporal changes, spatial distribution.

1. Introduction

The incidence and mortality of the two distinct types of skin cancer, namely melanoma and non-melanoma skin cancer (NMSC), are at the extremes of the mortality measures. On the one hand, melanoma is a

* Semmelweis University Doctoral School of Health Sciences ° National Public Health Center

potentially fatal form of cancer, which often develops from a minuscule spot and is often diagnosed once it has spread in the body (Gordon, 2013; Matthews, Li and Qureshi, 2014). On the other hand, NMSC is regarded as a relatively harmless type, which rarely metastasises and, therefore, is associated with a low death rate.

The highest incidence of melanoma is recorded in Australia and New Zealand, the Nordic countries, and the Netherlands in Europe (Barbaric et al., 2016). Incidence rates were rising to a lesser extent in South-Eastern Europe (SEE) between 2000-2010, and death rates were even stabilising in some countries (Barbaric et al., 2016). Similarly to countries in the SEE region, the Central and Eastern European (CEE) incidence rate of melanoma was never remarkably high compared to Nordic countries. Thus, this region is often left out of the analysis. Ferlay et al. (2013) has shown that in 2012, 36% of the melanoma deaths in Europe occurred in the CEE region. This region includes the EU member states that joined the European Union in 2004 (Hungary, Czechia, Poland, Slovakia, Slovenia) and member states that joined in 2008 and 2013 (Bulgaria, Romania and Croatia). This article focuses on Hungary, which performs poorly in cancer outcomes and repeatedly tops the highest death rates among men and women in Europe (EUROSTAT, 2017). In 2014, 33 000 people succumbed to cancer, and projections suggest that this number has not improved by 2020 (European Commission, 2017; IARC, 2020). A large percentage of cancer cases and deaths were amenable in Hungary. Cancer incidence can be traced back to unhealthy lifestyle choices, social deprivation, and lack of effective and timely healthcare. (European Commission, 2017, 2019).

The risk of melanoma comprises inherited factors (genetic susceptibility), phenotypic characteristics (fair hair and skin), and exposure to risk factors. It is well known that the single most important environmental risk factor is the omnipresent UV radiation (Ortiz, Goodwin and Freeman, 2005). The Hungarian population receives a nearly equal solar exposure because the vast majority of the country is geographically flat, and the latitude changes are not significant. According to a recently published global radiation map produced by the Hungarian Meteorological Services, the highest global radiation is indicated in Csongrád –Csanád county districts in the Southern Great Plain, located in south-eastern part of Hungary, east to the Danube. In addition, around Lake Balaton, which is a freshwater lake in Transdanubia and at the same time the most popular vacation destination for the local population, a somewhat elevated global radiation was measured (Hungarian Meteorological Services, 2021).

The population was also not at high risk in the past since international leisure travel has not begun until the early 2000s. Since EU accession and the kick-off of low-cost airlines, exposure to high UV radiation during summer or winter holidays in lower latitudes or high altitudes ski resorts has increased. An increase in melanoma and NMSC incidence in Hungary can be read from the National Cancer Registry (National Institute of Oncology, 2020). NMSC worldwide is one of the most commonly diagnosed cancer. Its development is associated with improved survival and cumulative exposure that could also explain the increasing incidence (Ciążyńska et al., 2021).

Another possible explanation for the rising incidence of skin cancer could be the effects of socioeconomic factors and lifestyle (education, occupation, income) (Ortiz, Goodwin and Freeman, 2005). The socioeconomic factors contributing to cancer development has been intensively documented since the seminal works of McKie and Hole (1996) and Harrison (1998) (MacKie and Hole, 1996; Harrison et al., 1998).

Inspired by the neglected nature of skin cancer incidence in the CEE region, this research aims to examine the age-standardised incidence and death rates in Hungary relative to the international rates, using two different international databases, the Globocan and ECDC.

The research also looks at the temporal trends of age-standardised melanoma incidence and death rates in Hungary in men and women in different age groups (15-64 years and 65 or older) between 2001 and 2015. Similarly, the temporal trends of age-standardised incidence rates in Hungary are also in focus.

Finally, analysis of the spatial distribution is undertaken to study if skin cancer (melanoma and NMSC) incidence rate is equally distributed at the district level in Hungary.

2. Empirical background

It has been extensively documented that melanoma and non-melanoma skin cancer incidence are of concern worldwide, including the CEE region and Hungary. There are many factors behind the increase in incidence. In this section, the most well-described risk factors will be discussed.

From the 1960s and onwards, the release of chlorofluorocarbons, also known as CFCs, contributed most significantly to the increase of ultraviolet exposure. These substances react with ozone in the stratosphere, which protects against UV exposure (Lucas et al., 2006).

There was a concerted global effort to stop the emission of ozone-damaging substances, and as a result, the Montreal Protocol entered into force in 1987 (UNEP Ozone Secretariat, 2020). Since then, a regeneration of the ozone layer has commenced. Tóth et al. (2019) reviewed the ozone content and long-term UV radiation in Hungary. They showed that the minimal erythema dose (MED) increased between 1995 and 2018, captured in five UV measurement stations. The increase can be explained by the increasing optical density, which resulted from the modernisation of the socialist industry that began after 1989. The amount of UV radiation reaching the Earth's surface is a function of the regeneration of the ozone layer; however, other complex climatic events may slow down this process. For example, incoming Mediterranean air transporting low ozone content air may skew the picture of the healing process. All projections, fortunately, point toward a successful regeneration of the ozone layer (Tóth, Páldy and Antal, 2019).

IARC declared the entire spectrum of ultraviolet radiation (UVA, UVB, and UVC) carcinogenic in 2009. Only UVA and UVB reach the Earth’s surface, and radiation at different wavelengths also has different carcinogenic mechanisms. As a result, melanoma and NMSC differ morphologically and in their risk factors. Based on epidemiological studies on the effect of UVA-emitting tanning and medical devices, there is a possible link between UVA exposure and cutaneous melanoma, including lentigo maligna, superficial spreading melanoma, nodular and acral lentiginous melanoma (IARC, 2012). Basal cell carcinoma and squamous cell carcinoma are the most common types of NMSC. UVB rays are the primary cause of sunburn and erythema, initiating tumour development (Gordon, 2013).

The ability of UVA (320-400 m) to penetrate deeper into the skin can explain the different mechanisms. It indirectly damages the DNA through the formation of reactive oxygen species. In contrast, UVB (280 – 320 nm) is absorbed in the epidermis (the outermost layer of the skin) and causes direct DNA damage. Specific phenotypic characteristics are linked with melanoma development. Skin-phototypes are measured on the Fitzpatrick scale (I-VI). The most vulnerable population (Fitzpatrick I-II) reside in the UK and Northern Europe and characterized by fair skin, blond/red hair, blue eyes, freckles (Raimondi, Suppa and Gandini, 2020; Serpone, 2021).

Malignant melanoma and, to some extent, SCC is associated with intermittent and childhood UVR exposure, whereas SCC is assumed to result from cumulative sun exposure (Gordon, 2013). Thus, skin cancer risk may be measured on the scale of sun exposure and a common risk factor for melanoma and NMSC is working outdoors and any type of recreational activity (Maguire and Spurr, 2016). There is a historical tendency to link outdoor work activities with increased skin cancer risk in men. It has been hypothesised that the underlying reason is that men are overrepresented in work performed open-air. Notable examples for such outdoor exposure include road and construction jobs, agricultural jobs (including gardening and farming), police officers, firefighters, postal workers, military and athletes and fitness coaches (Maguire and Spurr, 2016). Since the mid-1960s, higher standardised melanoma incidence in professional and technical workers and administrators have been detectable in the United States. Indoor administrative white-collar and blue-collar jobs (bartenders, plumbers, pipeline workers) exhibited the highest mortality ratios (Lee and Strickland, 1980). This laid ground for the concept that higher social classes are more at risk of melanoma than the lower classes of agricultural or construction workers who spend a significant time under the Sun (Lee and Strickland, 1980).

Being male may also predict a poorer prognosis. It is assumed that men are less likely to participate in screening, and therefore, their melanoma may be diagnosed at a later stage (Smalley, 2018). Sun-seeking behaviour, for example, sunbathing, is also a known risk factor for skin cancer. Appreciation of tanned appearance has undergone significant changes in the last century. Historically, white and pale skin meant a distinguishable symbol of higher social classes, while sun-tanned skin stigmatised lower-class people. This view was held until the development of the working class in the 1920s in the United States. Working-class people inhabited crowded and polluted parts of cities and suffered from TB, rickets, alcoholism and depression. Conversely, bronze skin became a symbol for consumerism and a conspicuous signifier for leisure. Not only sunbathing was endorsed, but fashion also loosened (Hunt, Augutson, Rutten and Moser, 2012 in Heckman and Manne, p. 10). By the 1940s, the average workweek was reduced to 42.5 hours from the previous 62 hours, and this allowed more outdoor leisure time for playing tennis, spending time on the beach and in parks. The "American social experience" came to life (Chang et al., 2014). If the same processes have shaped body image in Hungary is out of the scope of this article.

Physicians warned of the harmful effects of sunbathing without success. Fashion pushed these suspicious thoughts aside, and another risk factor was introduced to the market: indoor tanning (Chang et al., 2014). Despite IARC’s unambiguous opinion on the dangers of sunbed use, regulation is missing in many countries, including Hungary

(IARC, 2012). Traditionally, sunbed salons customers were primarily white adults of higher socioeconomic status. The higher-income and managerial and self-employed status were also more common among users as well as higher educational status. However, the latter was often challenged (Suppa et al., 2019). A study conducted among sunbed salon customers in Hungary observed that sunbed users were below 35 years old in Budapest, mostly women. 62.1% completed secondary school and 32% completed college education (Bakos et al., 2014).

In summary, firm assumptions can be made for risk factors of melanoma and NMSC in terms of susceptible skin type and inherited factors at the individual level, but other important risk factors such as socioeconomic factors (e.g. education and income) may experience changes over time at the national and district level that may also differ in men and women and according to age. Areas may prosper or may be left behind, resulting in a visible change in incidence and mortality rates. The most affected areas may shift, and the focus of primary and secondary prevention shall follow such a change. The first step in adjusting prevention programmes is the examination of temporal hanges at the national level and the visual analysis of spatial patterns of skin cancer incidence at the district level.

3. Data and methods

In the Global context, the IARC-maintained Global Cancer Observatory (Globocan) provides the backbone for comparison of country-specific cancer incidence (IARC, 2020). Estimated age-standardised incidence rates are always actualised and currently available 2020 for melanoma (ICD-10: C43) and non-melanoma type of skin cancer (ICD-10: C44). European standardised death rates were obtained from the European Center for Disease Control (ECDC) for 2015 (ECDC, 2015). ECDC relies on the Revised European Standard Population (2012) (EUROSTAT, 2013).

The area of international comparison comprises the United Nation's Central and Eastern European (CEE) region (Belarus, Bulgaria, Czechia, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia and Ukraine) (Ferlay et al., 2019). Additionally, neighbouring countries were also included in the comparison (Austria, Croatia, Slovakia). As these international databases synchronise rates using country-specific registries, these databases can only provide the means of comparisons through estimates.

The Hungarian input to these international cancer registry databases comes from the National Institute of Oncology, which maintains annual incidence data for the National Cancer Registry (National Institute of Oncology, 2020). In addition, Hungarian mortality data were obtained from the Hungarian Central Statistical Office (Hungarian Central Statistical Office, 2020). For long-term analysis, the age-standardised incidence rates (ASIR) and age-standardised death rates (ASDR) per 100 000 people for melanoma and non-melanoma skin cancer were recalculated with the Revised European Standard Population for the period 2001 and 2015 in Hungary. In addition, in situ incidence rates were also calculated for melanoma (ICD-10: D03) and NMSC (ICD-10: D04). The reason not to extend the examination period beyond 2015 is that morphological verification could occur years after the primary diagnoses, and the registry changes accordingly (National Institute of Oncology, 2020).

In the national context, the population was divided into a younger (15-64 years) and older cohort (over 65 years) and morbidity and death rates were analysed according to age and gender. The study period was between 2001 and 2015. Analysis of the spatial distribution of melanoma and non-melanoma skin cancer in Hungary was undertaken using empirical Bayesian smoothed indirectly standardised relative risk for the population aged 65 years old or older at the district level for the period 2001-2015 (Beale et al., 2010). This district division, comprising of 197 districts altogether, corresponds to local administrative unit 1 (LAU1) The older age group was chosen because development of skin cancer seems to be age-related as discussed by Urban et al. (2021). The relative risk values were extracted from the Rapid Inquiry Facility (RIF) maintained by SAHSU (Imperial College London) that is designed to help policymakers in disease mapping and risk analysis (Small Area Health Statistics Unit; London Imperial College, 2020). The source of cancer incidence data for RIF is the National Cancer Registry, while the population data comes from the Central Statistical Office (National Institute of Oncology, 2020). The Bayesian smoothing technique gives a weighted average applicable to areas with small populations and/or small case numbers, smoothing the effect of varying population sizes in different administration units (Piel et al., 2020).

4. Results

4.1. Epidemiology of melanoma

4.1.1. Incidence and mortality of melanoma – International outlook

The estimated number of melanoma cases for 2020 was 154 473 in the wider European Region (WHO EURO), extracted from the Globocan registry (IARC, 2020). Western and Northern Europe reported the highest number of melanoma cases and, accordingly, the highest ASIR. Central and Eastern Europe (CEE) saw the highest number of deaths due to melanoma and a relatively high age-standardised death rate (ASDR) despite the lowest age-standardised incidence rate (ASIR) in Europe (Table 1).

According to Globocan (2020), the highest estimated ASIR in the region was in Czechia (13.3 in men, 12.4 in women), followed by Hungary, Slovakia, Serbia (9.7) in men and by Hungary (10.1) in women (Table 2). Austria (not part of the standard definition of the CEE region) had the highest ASIR (15 in men, 18.8 in men). Melanoma incidence in Hungary was considered to be average in the European context for 2020.

Table 1. The estimated numbers and age-standardised incidence and death rates of melanoma in Europe (2020)

Region*	Mortality		Incidence	
	Number of deaths	Estimated age-standardised death rate per 100 000	Number of new cases	Estimated age-standardised incidence rates per 100 000
Western Europe	7,415	1.5	65,168	18.9
Northern Europe	4,747	1.9	33,551	17.8
Central and Eastern Europe (CEE)	9,272	1.7	27,993	5.6
Southern Europe	4,926	1.4	27,993	9.0

* Countries divided according to the United Nations (Ferlay *et al.*, 2015). *Central and Eastern Europe:* Belarus, Bulgaria, Czechia, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia and Ukraine.
Source: Globocan - IARC, 2020

Table 2. The estimated age-standardised incidence rates (2020) and death rates (2015) of melanoma in the CEE region and neighbouring countries

	Estimated age-standardised incidence rates* per 100 000		Age-standardised death rate** per 100 000	
	Men	Women	Men	Women
Austria	13.2	14.2	6.5	2.9
Belarus	5.9	5.5	-	-
Bulgaria	4.7	4.8	3.2	2.1
Croatia	10.6	7.9	7.2	3.6
Czechia	13.8	12.7	5.6	3.0
Hungary	*9.8*	*7.3*	*6.1*	*2.4*
Rep. of Moldova	4.0	2.0	-	-
Poland	5.5	4.6	5.8	3.6
Romania	5.2	4.4	2.8	1.9
Russian Federation	4.9	5.3	-	-
Slovakia	9.7	7.8	7.9	4
Slovenia	19.9	19.8	8.0	5.0
Serbia	8.7	7.2	6.3	2.8
Ukraine	5.0	5.9	-	-

*Database: Globocan – 2020, using the World Reference Population (1960).
**Revised European Standard Population (2012).
Source: Globocan - IARC, 2020, ECDC - 2015

ASDR of Hungary showed a different pattern in the international comparison. The highest estimated death rates in men were in Slovenia, Slovakia and Croatia. The third highest ASDR in women was predicted to occur in Poland. The ASDR of melanoma in the Hungarian male population occupied an upper-middle position in the ranking of the CEE and neighbouring countries. The ASDR in women was located in the lower half of the ranking.

4.1.2. Melanoma in Hungary between 2001-2015

In 2001, melanoma cases constituted only 1.5% of total cancer cases in men, and in 2015 they accounted for 2.8%. By 2015, melanoma jumped from the 15th most common to the 10th most common cancer site in males in Hungary. A similar tendency can be seen in women. The percentage of newly diagnosed cases of melanoma increased from 1.6% to 2.8% of total cancer cases in the examined period, and it became the 8th most frequently diagnosed cancer in 2015.

Diagnosed cases showed a 2.5-fold increase by 2015 (Table 3). There is an apparent increase in ASIR in both men and women. The ASIR increased from 10.3 per 100 000 to 19.4 in 15-64 years old men and women melanoma incidence overtook men's incidence since it increased from 10.9 to 25.2 per 100 000 in women between 2001 and 2015. In the older population, the ASIR increased by more than 2-fold. In both men and women, most cases were identified before 65 years of age in 2001. In 2015, the proportions shifted to the older cohort; 53% of cases belonged to men aged 65 years or older, and 40% were older than 65 years in women. This shift is also reflected when the standardised incidence rates are analysed according to age groups. The highest ASIR in 2001 was in the 70-74 years old men (2.48 per 100 000) and 50-54 years old women (1.59 per 100 000). In 2015, in both men and women, the highest ASIR was in older generations 70-74 years old in men (7.36 per 100 000), 65-69 years old in women (3.44 per 100 000) (National Institute of Oncology, 2020; data not shown).

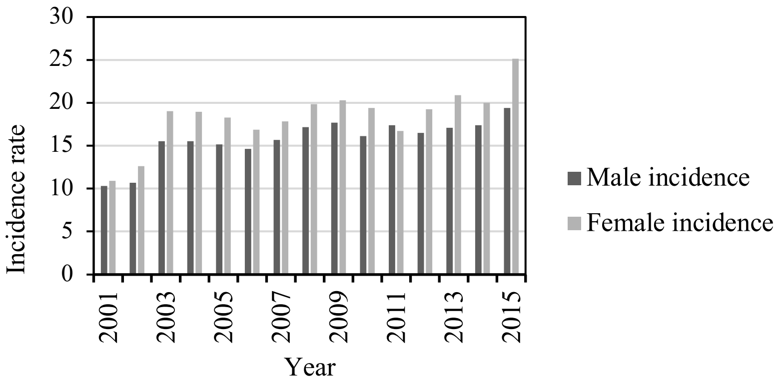
Melanoma in situ was diagnosed under 65 years in most men and women in 2001. In 2015, only 46% and 61% of cases occurred under 65 years, suggesting an age shift. The number of diagnoses was 3.5-4 times higher in 2015 than in 2001. ASIR of melanoma in situ shows a different temporal pattern than melanoma because in women over 65 years, the ASIR was less than in men in 2001. Men produced a nearly 8-fold increase in the ASIR in the examined period The ASIR in women increased by 4.5-fold because it increased 14.1 per 100 000. Melanoma in situ increased from 1.9 to 3.9 in men and from 2.0 to 6.9 per 100 000 in women in the younger population.

Table 3. Melanoma mortality and incidence in Hungary (2001-2015)

	2001		2015	
Melanoma	Men	Women	Men	Women
sex ratio	46	54	48	52
% of all cancer cases	1.5	2.8	1.6	2.8
total number of cases	542	626	1350	1465
% of melanoma cases < 65 years old	58	59	47	60
ASIR in 15-64 years old	10.3	10.9	19.4	25.2
ASIR in ≥ 65 years old	44.3	25.1	113.4	53.3
ASDR in ≥ 65 years old	20.6	9.1	22.8	7.9
	2001		2015	
Melanoma *in situ*	Men	Women	Men	Women
sex ratio	47	53	44	56
total number of cases	89	99	314	400
% of melanoma cases < 65 years old	65	70	46	61
ASIR in 15-64 years old	1.9	4.89	7.2	7.2
ASDR in the ≥65 years old	3.4	3.1	26.9	14.1

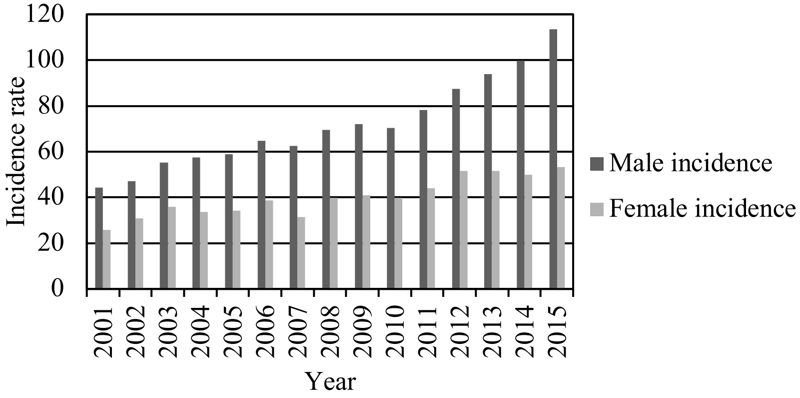
Source: raw data from National Institute of Oncology, 2020, data analysed by the author

Figure 1: Age-standardised incidence rate of melanoma (per 100 000) in 15-64 years old population in Hungary, 2001-2015



Source: raw data from National Institute of Oncology, 2020, data analysed by the authors

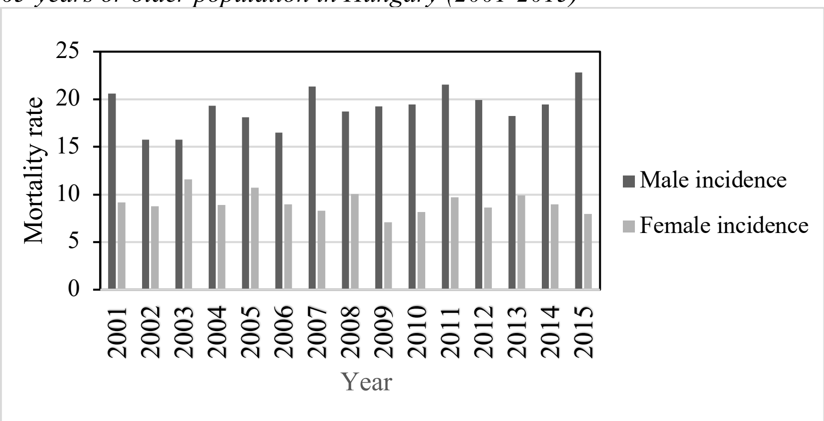
Figure 2. Age-standardised incidence of melanoma per 100 000 in > 65-years old population in Hungary (2001-2015)



Source: raw data from National Institute of Oncology, 2020, data analysed by the authors

As expected, melanoma mortality was higher in the 65 years old or older generations. The total number of deaths due to melanoma was 188 in men and 137 in women in 2001. In 2015, the reported number of deaths due to melanoma increased to 216 in men and remained constant in women. Men had two times higher ASDR than women in this age group. While men still show a slightly increasing trend in mortality, the ASDR in women began to (Figure 3).

Figure 3. The age-standardised death rate of melanoma per 100 000 in the 65-years or older population in Hungary (2001-2015)



Source: raw data from National Institute of Oncology, 2020, data analysed by the authors

Figure 4. Spatial distribution of melanoma incidence in the 65 years or older population in Hungary, 2001 – 2015

Source: National Cancer Registry and RIF

The spatial distribution of melanoma cases in the older cohort shows somewhat different patterns in men and women (Figure 4) for the period between 2001-2015. Incidence in the upper quantiles is found in Budapest, mainly in the inner districts. A higher incidence was centred in some districts between the western-lying districts and Budapest, encompassing districts around the Lake Balaton. Additionally, some Southern districts showed higher rates. In women, districts of increased incidences were more widely distributed. One notable difference to men is that incidence was less clustered in Southern districts. However, several districts in the Great Plain were affected. Similar to men, districts of in the west and around Lake Balaton showed incidences in the highest quantiles. Moreover, there were some singular increased incidences without clustering across the country. In Budapest, not only inner but outer districts were impacted by high melanoma incidence.

4.2. Epidemiology of non-melanoma skin cancer

4.2.1 Incidence and mortality of non-melanoma skin cancer – International outlook

Non-melanoma skin cancer is one of the most commonly diagnosed cancers. Globocan's highest standardised incidence rate was seen in Western and Northern Europe. Hungary ranked high in estimated incidence rates within the CEE region with neighbouring countries, overtaking all the countries in the region. In terms of ASDR, the CEE region and neighbouring countries were the most affected in the wider European area, even though the population in these areas is considered less vulnerable (Table 4). The ASDR of NMSC was significantly lower than melanoma, but similarly, it affects the older cohort (65+ years old) (Table 5).

Table 4. Estimated numbers and age-standardised mortality and incidence of non-melanoma skin cancer in Europe (2020)

Region*	Mortality		Incidence	
	Number of deaths	Estimated age-standardised mortality rate per 100 000	Number of new cases	Estimated age-standardised incidence rates per 100 000
Western Europe	2,656	0.33	179,219	28.1
Northern Europe	2,523	0.71	67,614	21.2
Southern Europe	3,112	0.47	64 438	11.6
Central and Eastern Europe**	4,492	0.6	44,909	6.8

*Countries divided according to the United Nations (Ferlay *et al.*, 2015). **Central and Eastern Europe (CEE): Belarus, Bulgaria, Czechia, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia and Ukraine.
Source: Globocan - IARC, 2020

Table 5. Age-standardised mortality and incidence rates of non-melanoma skin cancer in CEE region and neighbouring countries in 2015, Globocan (2020, estimated)

	Estimated age-standardised death rates per 100 000		Estimated age-standardised incidence rates per 100 000	
	Men	Women	Men	Women
Austria	0.6	0.25	19.5	9.5
Belarus	0.73	0.32	7.1	5.0
Bulgaria	1.0	0.37	11.9	6.2
Croatia	0.79	0.54	9.9	5.0
Czechia	0.74	0.3	15.9	8.4
Hungary	*1.2*	*0.57*	*22.3*	*12.7*
Republic of Moldova	1.2	0.7	15.9	15.6
Poland	1.1	0.52	9.1	5.3
Romania	1.5	0.62	10.1	5.0
Russian Federation	0.77	0.33	5.6	4.9
Slovakia	0.9	0.4	8.7	4.8
Slovenia	0.61	0.33	11.3	6.9
Serbia	1.8	0.69	11.8	4.1
Ukraine	0.86	0.37	7	6.4

Source: Globocan - IARC, 2020

4.2.2. Non-melanoma skin cancer in Hungary between 2001-2015

NMSC in Hungary became the most commonly diagnosed cancer by 2015. In 2001, 12.1% of all cancer diagnoses were NMSC in men. This number increased to 14.7% by 2015. Similarly, in women, this ratio rose from 13.8% to 16.5% between 2001 and 2015. The total number of NMSC cases failed to show such spectacular growth as melanoma cases. The proportion of NMSC under 65 years was around 35% in men and 33% in women, suggesting that NMSC is a disease of the elderly. Similarly to melanoma, it occurs more frequently in women (Table 6).

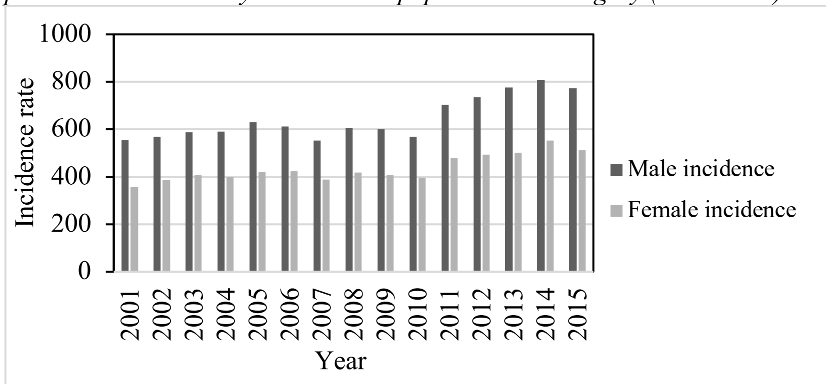
The ASIR fluctuated during the examined period. However, it can be established that men and women aged 15-64 years had smaller ASIR than in the older male and female populations. The ASIR increase was more profound in 15-64 years-old women than in men. High ASIR was recorded in the older cohort in 2001 (553.9 in men and 354.6 in women), further advancing by 39% and 44%, respectively, by 2015 (Table 6). When ASIR is further stratified to 5-year age groups, it was revealed that the highest ASIR were consistently recorded in the 70-74 and 75-79 years old populations (data not shown).

Table 6. Mortality and incidence of non-melanoma skin cancer in Hungary (2001-2015)

	2001		2015	
	men	women	men	women
Non-melanoma skin cancer				
sex ratio	39	61	38	62
% of all cancer cases	12.1	13.8	14.7	16.5
total number of cases	4351	5158	7124	8486
% of melanoma cases < 65 years old	36	35	33	33
ASIR in 15-64 years old	56	53	72	79
ASIR in ≥ 65 years old	554	355	772	511
Non-melanoma skin cancer in situ				
sex ratio	43	46	57	54
total number of cases	127	165	529	629
% of melanoma cases < 65 years old	38	20	36	23
ASIR in 15-64 years old	1.6	1.7	3.2	3.9
ASDR in the ≥ 65 years old	14.7	10.9	73.8	43.7

Source: raw data from National Institute of Oncology, 2020, data analysed by the authors

Figure 5. The age-standardised incidence rate of non-melanoma skin cancer per 100 000 in the 65 years or older population in Hungary (2001-2015)



Source: raw data from National Institute of Oncology, 2020, data analysed by the authors

Despite the relatively unremarkable increase in NMSC diagnoses between 2001 and 2015, in situ NMSC diagnoses showed a 4-fold increase. There were 127 cases in men and 165 cases in women in 2001, while 529 and 629 NMSC diagnoses were made in women in 2015. Most cases are diagnosed in the older population (>65 years). Ca. 80% of NSMC diagnoses were established in this age group. Accordingly, the ASIR increased, especially among older people between 2001 and 2015 (from 14.7 and 10.9 to 73.8 and 43.9 per 100 000 in men and women).

The spatial distribution of NMSC in men resembled the distribution of melanoma in some ways. High incidence areas were found between Budapest and the country's Western borders. Some districts showed high incidence in the Southern Great Plain. In Budapest, male residents in the Buda side (western part of the city) and outer skirt of Pest (eastern part of the city) showed elevated incidence. Some parts of north-eastern Hungary were affected. A band was visible below the capital in women, , and another in northeastern Hungary . In addition, high quantile incidences extended to the eastern parts of the country. In Budapest, mainly Buda districts belonged to higher quantile areas (Figure 6).

5. Discussion

The Globocan (2020) database is unquestionably a robust and valuable tool for comparing worldwide cancer incidence, however it has some limitations. For instance, Globocan employs the so-called Eastern-European model for the cancer incidence in Hungary, which estimates the incidence rates from mortality data (Global Cancer Observatory, 2020). Therefore, the results are not directly comparable with the validated results of the National Institute of Oncology. In respect of NMSC, many cancer registries excluded this type of cancer. Hence the quality of international comparison is debatable (Leiter and Garbe, 2008). The Revised European Standard Population provides the most accurate result for analysing the temporal trends of skin cancer in Hungary. The corrected higher rates reflect the most affected older population of melanoma patients.

In summary, the international comparison reiterates that wealthier countries show an increased incidence rate, but less affluent nations perform poorer in mortality statistics. De Vries et al. (2004) found that lower incidence rates but increased Breslow thickness, another factor of poor prognosis, were characteristic for Eastern Europe compared to Western Europe.

Melanoma has the most rapidly increasing incidence rate of all cancers worldwide. The estimated incidence of melanoma is predicted to double every 10-20 years worldwide (Leiter and Garbe, 2008). According to the National Cancer Registry, this is also valid for Hungary, where the case numbers doubled between 2001 and 2015. The ASIR of melanoma in the older and younger cohort increased by more than twofold. Melanoma death rates in men increased and in women decreased slightly. The highest increases were seen in the melanoma in situ incidence rates, which can be a sign of efficient screening programs and a starting point for improved survival. Therefore, the reason behind such increasing incidence needs further assessment to examine whether a change in the protocol for diagnosis of skin cancer, melanoma screening campaign or regulatory environment for tanning salons could be the reason for such increases in melanoma and non-melanoma incidence.

The estimated ASIR of NSMC in the CEE region is characterised by a low incidence and average death rate. Hungary has the highest predicted incidence rate in the region. However, it must be emphasised that NSMC national statistics has to be translated cautiously into international tables, as mentioned, due to the lack of rigorous data collection practices (Leiter and Eigentler, 2014). Most of the cases were diagnosed in people aged 65 or older between 2001 and 2015, and a very high incidence in this cohort is characteristic. ASIR of NMSC in situ was at a comparable rate between 2001 and 2015 in men and women alike. Similarly, to melanoma, this could indicate effective screening and earlier diagnosis.

The spatial distribution of skin cancer incidence was examined. The visual inspection of the spatial distribution reveals that men and women have a slightly different pattern of melanoma. In men, there is a visible clustering of melanoma cases in Budapest, which needs further research. There is no such effect in women. Indeed, one of the major differences between melanoma and NMSC distribution is that melanoma cases are more centred within or around Budapest.

The unequal distribution of skin cancer in Hungary partly complies with a disproportionate amount of incoming UV radiation which is the highest in the Southern districts in Csongrád-Csanád county and this increase is reflected in the accumulation of melanoma and NMSC cases. Since the incoming UV radiation show elevated levels mainly in the Csongrád-Csanád county and around Lake Balaton, there is no visible association between skin cancer and ultraviolet radiation in most areas of the country (Hungarian Meteorological Services, 2021). Such area is Budapest and its neighbourhood, which is not at risk when considering local ultraviolet radiation data. Because higher socioeconomic status has been linked to increase melanoma incidence, areas with an elevated risk of melanoma (e.g. the middle parts of the Great Plain) that seemingly do not belong to high exposure and high economic status, are of interest. . In addition, unlike melanoma, NMSC cases have a clear appearance in the Great Plain and north-eastern Hungary, and the underlying risk factors of this increased incidence (e.g. outdoor jobs) must be further investigated.

6. Conclusion and further research

The incidence of melanoma has increased worldwide, including in the CEE region. In this region, the incidence rates have been rising. However, it is the poor survival that makes it a subject for further analysis. Within this region, Hungary is middle ranking in melanoma incidence. The standardised incidence rate of melanoma doubled in 2001-2015. Mortality statistics stabilised, a slight increase in men and a decreasing tendency was observed in women. On the other hand, melanoma in situ showed an eight and 5-fold increase in men and women, respectively, promising prevention and survival.

International comparison is difficult to draw for NMSC because many countries do not publish separate statistics for this tumour type. However, it can be said that the NMSC incidence rate is the highest in Hungary in the CEE region. Diagnoses also continue to rise, mainly affecting the elderly.

Other aspects such as access to health care is a starting point for further research. In particular, financial and logistical access to private medical practices in more affluent districts (for example Budapest and its suburbs) could mean that people are diagnosed with a less advanced stage, and this could lead to a reduced death rate. Since high incidences were also observed in less affluent areas, other causes must be looked at such as proportion of outdoor workers or distribution of tanning salons. In addition, body image and perception of health and beauty must also be put into perspective because these greatly define risk behaviour of the population. Whether this could translate to a variation in the incidence rate or it is a national rather than a local trend also needs to be examined in the future.

As a way forward, the author proposes a small-area spatial and temporal analysis to capture long-term changes in skin cancer incidence in Hungary. The proposed research aims to contest the hypothesis whether populations in more affluent areas are also more at risk of developing melanoma, whether less affluent areas are more likely to have poorer outcomes, and if NMSC development could be an occupational hazard in certain areas that needs attention in the future. This ecological study would be gap-filling since such detailed analysis at the district level has not been performed until now. The study could confirm and quantify the role of sun exposure in the development of melanoma and skin cancer by assigning local radiation measurement values to the districts. In addition, the role of socioeconomic factors such as income, education and occupation could be elucidated and could provide answer for the observed unequal distribution of melanoma and NMSC that was presented in this paper. The most vulnerable populations can be identified through spatial analysis, which opens up an opportunity to design targeted screening and prevention programmes. Educational programmes and awareness campaigns on sun protection have been successful and could significantly reduce sun exposure in affected groups, such as outdoor workers.

References

BAKOS, J. et al. (2014), Sunbed User's Motivations, Habits and Knowledge, CEJOEM, pp. 191–198.

BARBARIC, J. et al. (2016), Disparities in melanoma incidence and mortality in South-Eastern Europe: Increasing incidence and divergent mortality patterns. Is progress around the corner?, European journal of cancer, 55, pp. 47–55, Oxford, England. doi: 10.1016/j.ejca.2015.11.019.

BEALE, L. et al. (2010), Evaluation of Spatial Relationships between Health and the Environment: The Rapid Inquiry Facility, Environmental Health Perspectives, 118(9), pp. 1306–1312. doi: 10.1289/ehp.0901849.

CHANG, C. et al. (2014), More skin, more sun, more tan, more melanoma, American Journal of Public Health, 104(11), pp. e92–e99. doi: 10.2105/AJPH.2014.302185.

CIAZYNSKA, M. et al. (2021), The incidence and clinical analysis of non-melanoma skin cancer, Scientific Reports, 11(1), p. 4337. doi: 10.1038/s41598-021-83502-8.

DE VRIES, E. et al. (2004), Lower incidence rates but thicker melanomas in Eastern Europe before 1992: a comparison with Western Europe, European journal of cancer, 40(7), pp. 1045–1052, Oxford, England. doi: 10.1016/j.ejca.2003.12.021.

ECDC (2015), European Core Health Indicators (ECHI). Available at: https://ec.europa.eu/health/non_communicable_diseases/indicators_en (Accessed: 14 May 2020).

EUROPEAN COMMISSION (2017), State of Health in the EU, Hungary. Available at: http://www.euro.who.int/__data/assets/pdf_file/0006/355983/Health-Profile-Hungary-Eng.pdf?ua=1.

EUROPEAN COMMISSION (2019), State of Health in the EU. Hungary. Country Health Profile. Available at: https://www.euro.who.int/__data/assets/pdf_file/0007/419461/Country-Health-Profile-2019-Hungary.pdf.

EUROPEAN COMMISSION (2020), European Cancer Information System (ECIS), European estimates of cancer incidence and mortality in 2020. Available at: https://ecis.jrc.ec.europa.eu (Accessed: 14 September 2020).

EUROSTAT (2013), Revision of the European Standard Population, Report of Eurostat's task force.

EUROSTAT (2017), Statistics Explained, Health in the European Union – facts and figures.

FERLAY, J. et al. (2013), GLOBOCAN 2012 v1.0. cancer incidence and mortality worldwide, IARC CancerBase No. 11. (on line document).

FERLAY, J. et al. (2015), Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012, International Journal of Cancer, 136(5), pp. E359–E386. doi: 10.1002/ijc.29210.

FERLAY, J. et al. (2019), Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods, International Journal of Cancer, 144(8), pp. 1941–1953. doi: 10.1002/ijc.31937.

GLOBAL CANCER OBSERVATORY (2020), Data and Methods, IARC. Available at: https://gco.iarc.fr/today/data-sources-methods (Accessed: 17 May 2020).

GORDON, R. (2013), Skin Cancer: An Overview of Epidemiology and Risk Factors, Seminars in Oncology Nursing, 29(3), pp. 160–169. doi: https://doi.org/10.1016/j.soncn.2013.06.002.

HARRISON, R. A. et al. (1998), Socioeconomic characteristics and melanoma incidence, Annals of epidemiology, 8(5), pp. 327–333. doi: 10.1016/s1047-2797(97)00231-7.

HUNGARIAN CENTRAL STATISTICAL OFFICE (2020). Available at: http://www.ksh.hu/?lang=en.

HUNGARIAN METEOROLOGICAL SERVICES (2021), Solar radiation, sunshine duration and cloud cover of Hungary. OMSZ Informatics and Methodology Department. Available at: https://www.met.hu/en/eghajlat/magyarorszag_eghajlata/altalanos_eghajlati_jellemzes/sugarzas/ (Accessed: 25 October 2021).

HUNT Y, AUGUTSON E, RUTTEN L, MOSER R, Y. A. (2012), History and Culture of Tanning in the United States, in Heckman CJ, Manne SL, Shedding Light on Indoor Tanning. Springer Science + Business Media.

IARC (2012), Review of Carcinogens, Part D: Radiation. IARC Working Group on the Evaluation Carcinogenic Risks to Humans. (2009: Lyon, France). ISBN: 978 92832 1321 5. ISSN: 1017-1606

IARC (2020), Global Cancer Observatory. Available at: 10.1007/s10549-004-1483-9 (Accessed: 20 November 2021).
LEE, J. A., STRICKLAND, D. (1980), Malignant melanoma: social status and outdoor work, British journal of cancer, 41(5), pp. 757–763. doi: 10.1038/bjc.1980.138.
LEITER U, EIGENTLER T, G. C. (2014), Epidemiology of skin cancer, Adv Exp Med Biol., 810, pp. 120–140. doi: 10.1007/978-1-4939-0437-2_7.
LEITER, U., GARBE, C. (2008), Epidemiology of Melanoma and Non melanoma Skin Cancer-The Role of Sunlight, in Sunlight, Vitamin D and Skin Cancer. Advances i. New York, NY: Springer, pp. 89–103.
LUCAS, R. et al. (2006), Solar Ultraviolet Radiation: Global burden of disease from solar ultraviolet radiation, Environmental Burden of Disease Series. Available at: http://who.int/uv/publications/solaradgbd/en/. ISBN: 9241594403, 9789241594400, ISSN: 1728-1652
MACKIE, R. M., HOLE, D. J. (1996), Incidence and thickness of primary tumours and survival of patients with cutaneous malignant melanoma in relation to socioeconomic status, BMJ (Clinical research ed.), 312(7039), pp. 1125–1128. doi: 10.1136/bmj.312.7039.1125.
MAGUIRE, E., SPURR, A. (2016), Implementation of Ultraviolet Radiation Safety Measures for Outdoor Workers: A Canadian Perspective, Journal of Cutaneous Medicine and Surgery, 21(2), pp. 117–124. doi: 10.1177/1203475416683389.
MATTHEWS, N., LI, W., QURESHI, A. (2014), Epidemiology of Melanoma, in Ward WH; Farma JM (ed.) Cutaneous Melanoma Etiology and Therapy. Brisbane: Codon Publications, Australia, pp. 676–688. doi: 10.1038/nrendo.2010.189.Glycogen.
NATIONAL INSTITUTE OF ONCOLOGY [Országos Onkológiai Intézet] (2020), National Cancer Registry. Available at: https://onkol.hu/?lang=en (Accessed: 1 March 2021).
ORTIZ, C. A. R., GOODWIN, J. S., FREEMAN, J. L. (2005), The effect of socioeconomic factors on incidence, stage at diagnosis and survival of cutaneous melanoma, Medical science monitor: international medical journal of experimental and clinical research, 11(5), pp. RA163-172.
PIEL, F. B. et al. (2020), Small-area methods for investigation of environment and health, International journal of epidemiology, 49(2), pp. 686–699. doi: 10.1093/ije/dyaa006.

RAIMONDI, S., SUPPA, M., GANDINI, S. (2020), Melanoma Epidemiology and Sun Exposure, Acta dermato-venereologica, 100(11), p. adv00136. doi: 10.2340/00015555-3491.
SERPONE, N. (2021), Sunscreens and their usefulness: have we made any progress in the last two decades?, Photochemical & photobiological sciences : Official journal of the European Photochemistry Association and the European Society for Photobiology, 20(2), pp. 189–244. doi: 10.1007/s43630-021-00013-1.
SMALL AREA HEALTH STATISTICS UNIT; LONDON IMPERIAL COLLEGE (2020), Rapid Inquiry Facility. Available at: https://www.imperial.ac.uk/school-public-health/epidemiology-and-biostatistics/small-area-health-statistics-unit/our-research/rapid-inquiry-facility/ (Accessed: 8 January 2021).
SMALLEY, K. S. (2018), Why do women with melanoma do better than men?, eLife, 7, p. e33511. doi: 10.7554/eLife.33511.
SUPPA, M. et al. (2019), Who, why, where: an overview of determinants of sunbed use in Europe, Journal of the European Academy of Dermatology and Venereology, JEADV, 33 Suppl 2, pp. 6–12. doi: 10.1111/jdv.15318.
TÓTH, Z., PÁLDY, A., ANTAL Z, L. (2019), Relationship of surface solar UV irradiation and atmospheric ozone with the climate system - physical background, as well as social and medical aspects, Magyar Tudomány, 180(9), pp. 1356–1375. doi: 10.1556/2065.180.2019.9.1.
UNEP OZONE SECRETARIAT (2020) THE MONTREAL PROTOCOL ON SUBSTANCES THAT DEPLETE THE OZONE LAYER. Available at: http://ozone.unep.org/en/treaties-and-decisions/montreal-protocol-substances-deplete-ozone-layer (Accessed: 7 February 2019).
URBAN, K. et al. (2021) 'The global burden of skin cancer: A longitudinal analysis from the Global Burden of Disease Study, 1990-2017.', JAAD international, 2, pp. 98–108. doi: 10.1016/j.jdin.