

## INVESTIGATIVE REPORT

**Melanoma Incidence Increases in the Elderly of Catalonia But Not in the Younger Population: Effect of Prevention or Consequence of Immigration?**

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**All cases of malignant melanoma diagnosed in 23 hospitals in Catalonia, from 2000 to 2007 were recorded and melanoma incidence calculated and adjusted for the European standard population via the direct method. The age standardised rate/100,000 inhabitants varied from 6.74 in 2000 to 8.64 in 2007 for all melanomas and from 4.79 to 5.80 for invasive melanomas; the Breslow thickness was stable during the period. The increase in invasive melanoma incidence in the elderly was remarkable, the crude rate/100,000 inhabitants increasing from 11.04 (2000) to 15.49 (2007) in the 60–64 year population, while remaining more stable in the 30–34 year range, from 3.97 in 2000 to 4.55 in 2007, and with a tendency to decrease from 5.1 in 2000 to 2.5 in 2007 for the age range of 25–29 years. These lower age ranges are much more affected by immigration. Despite the large immigrant population (nearly one million immigrants arrived in Catalonia during the study period from countries with a low melanoma incidence), melanoma incidence in our region has risen considerably and this trend is likely to persist in the near future. Key words: malignant melanoma; hospital based registry; incidence; epidemiology; skin cancer.**

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The incidence of cutaneous malignant melanoma (CMM) has increased in recent decades more than any other malignant neoplasm (1, 2). In the United States, the number of melanomas diagnosed has increased by 619% and the mortality has increased 165% between 1950 and 2000

(2). The highest incidence rates of CMM are observed in Australia and New Zealand followed by North America and Northern Europe (1, 3–5).

The incidence and mortality of melanoma in people living in Europe vary considerably between countries (6), the highest incidence rates being in northern and western countries and the lowest in southern countries (1). These variations are likely to be linked to specific behaviour (winter holidays, sun-seeking behaviour) as well as prevalent skin phototype and other clinical characteristics of the population such as the number of naevi or the prevalence of red hair (7). Some regions have reported a declining trend in melanoma incidence, whilst for others the rise in incidence persists (8, 9).

Spain has one of Europe's lowest incidence and mortality rates. Although there are only a few studies on the epidemiology of melanoma in Spain, an increase in incidence over the past decades has also been reported (10).

Our region of study is Catalonia, located in the North-eastern part of Spain. In Catalonia only 2 cancer population registries exist, which together covered a population of 1,174,977 in 2001, representing only 19% of the total Catalan population living in an area far away from the city of Barcelona and most populated cities of the region. According to these registries, over the past 20 years, CMM incidence has increased substantially at a faster rate than any other neoplasm in Catalonia (11). Marcos-Gragera et al. (11), suggested that this trend will probably continue for the next few years. Nevertheless, CMM mortality trends have already been published, the crude rate between 2000–2004 being 2.52 for men and 2.11 for women and for 2005–2009 being 2.72 for men and 2.28 for women (crude rates per 100,000 person-years). On the contrary, epidemiological data from other regions of Spain suggest that melanoma mortality rates have been decreasing over the past 10 years, at least in males (12).

A study performed in one hospital from our region reported an increase in the incidence of both *in situ* and invasive melanomas. Among the invasive melanomas not only thin melanomas increased, but also thick ones with a resulting stable mean Breslow thickness of 1.9 mm (13).

Knowledge of the overall incidence of melanoma in our region is crucial for public health care organisation. Furthermore, the knowledge of the distribution according to Breslow thickness, age, gender, subtype of melanoma or localisation would help to establish adequate preventive or early detection policies for targeted populations.

### Rationale

To perform a hospital-based registry of melanoma encompassing all Catalonia in order to describe the incidence of *in situ* and invasive melanomas diagnosed over an 8-year period (2000–2007) and their clinico-pathological characteristics.

## METHODS

Twenty-three hospitals covering most of the population of Catalonia, 7 million inhabitants, reported the melanoma cases diagnosed from 2000 to 2007. Five of the hospitals were tertiary-care hospitals located in Barcelona and its suburbs. The remaining hospitals were community-based hospitals and one private hospital.

Data collected included date of birth, gender, date of diagnosis, location of the melanoma, histopathological subtype, Clark Index, Breslow thickness and presence of ulceration.

Data was collected from the melanoma-unit's databases when available (Hospital Clinic de Barcelona, Hospital de Bellvitge and Hospital Germans Trias I Pujol). For the remaining hospitals, data was retrospectively collected for the first 5-year period (2000–2004), and prospectively for the period 2005–2007.

### Statistical analysis

Incidence rates were age-standardised via the direct method using the European standard population. Categorical variables compared by means of the  $\chi^2$ -test, or the Fisher's exact test, when the expected observations were  $<5$ . For continuous variables, mean and standard deviation (SD) were reported. The Student *t*-test was used to compare means between males and females. Two-way ANOVA tests were conducted in order to detect differences in means of age and Breslow thickness over time. Statistical analyses were performed with SPSS 10.0 and STATA 10.

## RESULTS

A total of 5,407 cases were reported in the 8-year study period (2000–2007); 408 cases were reported by more than one centre and thus duplicated. In all these cases one of the entries was eliminated. Ultimately, 4,999 melanoma patients were included in the study of which 4,850 patients were included in the calculation of incidence rates because the age at diagnosis and the year of diagnosis was known. One third (33%) of cases were reported by one referral centre in Barcelona (Hospital Clinic Barcelona) and 26% were reported by the other 2 referral hospitals in

Barcelona's suburbs (Hospital de Bellvitge and Hospital Germans Trias I Pujol) together. In 3,884 cases the melanoma was invasive and the remaining 1,125 were *in situ*. Females had 2,748 cases of melanoma (55%), whereas men had 2,216 cases (44.3%). In 35 cases, gender data was not available. An increasing trend in the number of incident cases of melanoma was observed throughout the study period (481 cases in 2000; 610 in 2001; 581 in 2002; 541 in 2003; 551 in 2004; 692 in 2005; 668 in 2006 and 726 in 2007) (Table I). The total crude rate for melanoma (including *in situ*) per 100,000 inhabitants increased from 7.74 in 2000 to 10.13 in 2007 and the age standardised rate/100,000 inhabitants for the European population increased from 6.74 in 2000 to 8.64 in 2007 (Table I). For invasive melanomas the total crude rate/100,000 inhabitants increased from 5.42 in 2000 to 6.77 in 2007 and the age standardised invasive melanoma rate/100,000 inhabitants for the European population increased from 4.79 in 2000 to 5.8 in 2007 (Table I). Crude rates and age adjusted for European population rates increased in both sexes (Table II). Detail of rates according to age and years (2000 to 2007) are detailed in Table S1<sup>1</sup> and Fig. S1<sup>1</sup>.

The majority of melanomas were located on the trunk (37.5%) followed by lower extremities (20.1%), upper extremities (11.7%), face (11.4%), palms and soles (7.8%), head and neck (5.1%) and mucosa (1%). The location was not properly reported in 5.4% of tumours.

### Histopathological characteristics

The most frequent histopathological subtype was superficial spreading melanoma (SSM) which represented 59.5%

Table I. Incidence of melanoma (including *in situ* melanoma) and invasive melanoma

Year	Cases <i>n</i>	Population in Catalonia	Crude rate <sup>a</sup>	Age standar- dised <sup>a,b</sup>	Truncated <sup>a</sup> (35–64 years)	Cumulative (0–74 years)
Melanoma (including <i>in situ</i> melanoma)						
2000	481	6,213,904	7.74	6.74	9.94	0.517%
2001	610	6,305,080	9.67	8.39	12.79	0.694%
2002	581	6,442,797	9.02	7.87	12.70	0.631%
2003	541	6,590,233	8.21	7.02	10.34	0.564%
2004	551	6,727,680	8.19	7.03	10.87	0.555%
2005	692	6,873,649	10.07	8.66	12.93	0.723%
2006	668	7,020,207	9.52	8.17	11.44	0.684%
2007	726	7,168,354	10.13	8.64	13.41	0.709%
Invasive melanoma						
2000	337	6,213,904	5.42	4.79	7.29	0.369%
2001	421	6,305,080	6.68	5.85	9.08	0.488%
2002	391	6,442,797	6.07	5.33	8.85	0.426%
2003	341	6,590,233	5.17	4.43	6.57	0.353%
2004	371	6,726,395	5.52	4.77	7.32	0.382%
2005	461	6,873,649	6.71	5.80	8.63	0.487%
2006	443	7,020,207	6.31	5.40	7.82	0.445%
2007	485	7,168,354	6.77	5.80	9.06	0.473%

<sup>a</sup>Rates reported per 100,000 subjects.

<sup>b</sup>Standardised using the European standard population, Source: 1991 World Health Annual of Statistics – based on J Waterhouse et al, Cancer Incidence in Five Continents, Lyon, IARC, 1976 (Vol, 3, page 456).

Table II. Melanoma incidence by sex

Year	Cases <i>n</i>	Population in Catalonia	Crude rate <sup>a</sup>	Age standar- dised <sup>a,b</sup>	Truncated <sup>a</sup> (35–64 years)	Cumulative (0–74 years)
<b>Males</b>						
2000	195	3,037,429	6.42	5.69	8.09	0.440%
2001	245	3,088,541	7.93	7.04	10.20	0.596%
2002	253	3,164,113	8.00	7.17	10.44	0.561%
2003	263	3,242,996	8.11	7.12	9.63	0.570%
2004	241	3,316,066	7.27	6.40	9.56	0.506%
2005	324	3,396,257	9.54	8.52	11.34	0.744%
2006	307	3,473,240	8.84	7.71	9.57	0.662%
2007	331	3,550,658	9.32	8.33	12.08	0.699%
<b>Females</b>						
2000	286	3,176,475	9.00	7.86	11.75	0.599%
2001	363	3,216,539	11.29	9.77	15.35	0.787%
2002	327	3,278,684	9.97	8.68	14.93	0.698%
2003	278	3,347,237	8.31	7.10	11.05	0.566%
2004	309	3,411,315	9.06	7.74	12.18	0.606%
2005	366	3,477,392	10.53	8.90	14.47	0.713%
2006	359	3,546,967	10.12	8.70	13.13	0.710%
2007	391	3,617,696	10.81	9.04	14.56	0.723%

<sup>a</sup>Rates reported per 100,000 subjects.

<sup>b</sup>Standardised using the European standard population. Source: 1991 World Health Annual of Statistics - based on J Waterhouse et al. Cancer Incidence in Five Continents, Lyon, IARC, 1976 (Vol. 3, page 456).

of tumours, followed by nodular melanoma (NM) (11.7%), lentigo maligna melanoma (LMM) (8.4%) and acral lentiginous melanoma (ALM) (4.4%). In 11.4% of melanomas, the histopathological subtype was not reported and in 2.6% it was unclassifiable. The rare melanoma subtypes found were lentiginous melanoma of the mucosa (0.5%), desmoplastic (0.3%) and Spitzoid melanoma (0.2%).

The Clark level was not reported in 11.3% of the cases. *In situ* melanomas represented 25.5% of the tumours, Clark II 15.6%, Clark III 30.0%, Clark IV 17.3% and Clark V 3.6%. During the 8 years of the registry, the incidence of *in situ* melanomas remained stable ( $p=0.12$ ) (Fig. 1).

The distribution of melanomas according to Breslow thickness also remained stable during the study (data not shown). Mean Breslow thickness remained stable throughout the study period ( $p=0.222$ ) (Fig. S2a<sup>1</sup>) while mean age at diagnosis increased during the period ( $p<0.001$ ) (Fig. S2b<sup>1</sup>). Only 13% of cases were reported as ulcerated, but the presence/absence of ulceration was not reported in 24% of cases.

The mean age at diagnosis varied according to the histopathological subtype and was lower in SSM (mean 52.6 years) and Spitzoid melanomas (mean 50.6 years) compared to NM (mean 59.3 years), ALM (mean 63.01 years), mucosal MM (62.4 mean years) and LMM (70.3 mean years) ( $p<0.01$ ).

#### Trends by sex

As previously described in other populations, location of the melanoma differed significantly between Catalan

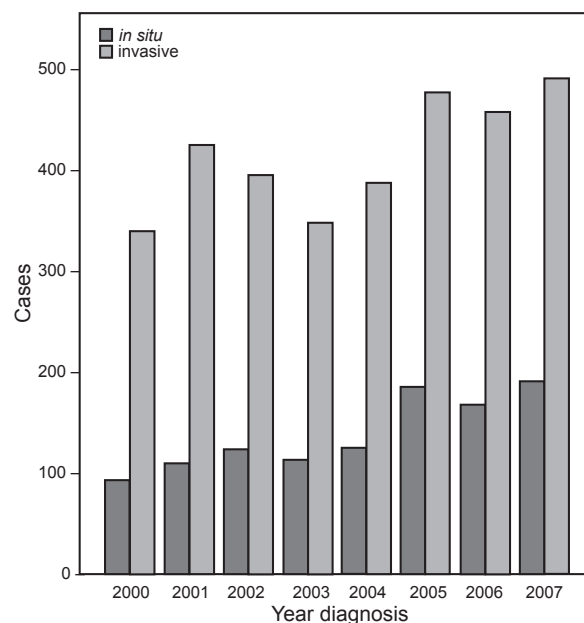


Fig. 1. Distribution of *in situ* melanoma (dark grey) and invasive melanoma (light grey) during the 8-year period of the study. The proportion of *in situ* melanomas remained stable ( $p=0.12$ ).

women and men ( $p<0.000$ ) (Table III). The trunk was the most frequent location in males (48.9%) followed by the face (11.4%). In females the trunk represented 28.5% of cases followed by, almost in equal proportion, the lower extremities 28.3%, then upper extremities (13.4%) and face (10.9%).

The mean Breslow also differed, being thicker in men (mean 2.3, SD 3.21) than women (mean 1.8, SD 3.1) ( $p<0.001$ ).

Men were diagnosed at an older age (mean 57.7 years, SD 16.9) than women (mean 54.3 years, SD 17.9) ( $p<0.01$ ) (see Fig. S3<sup>1</sup>). An increase in incidence was observed in both sexes.

#### Trends by subtype and age

The most frequent subtype of melanoma observed throughout the study period was SSM in patients aged between 50–55 years. However, an increase in LMM was also detected among the elderly, usually in their seventies.

## DISCUSSION

The incidence of melanoma has been increasing worldwide (1) but with differences according to the characteristics of the population living in a given country (skin type, red hair, etc), sunlight incidence during the year and sun-exposure behaviour (9, 14). Other factors such as the Mediterranean diet were also reported as a modifying factor of melanoma incidence (15).

Ribes et al. (16) performed a melanoma incidence projection in Catalonia for the period 2005–2019. Bayesian

<sup>1</sup><http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1997>



age-period-cohort models were fitted to age-specific rates for 1985–2004 to obtain the expected number of cases for the 5-year periods 2005–2009, 2010–2014 and 2015–2019. They estimated 307 new melanoma cases per year in men and 478 in women in the period 2005–2009 with a crude rate/100,000 inhabitants of 10.43 in men and 15.57 in women and a world age standardised rate of 8.31 in men and 13.21 in women.

Our results confirm that melanoma has been rising considerably among men and women in Catalonia over the past decade and that this trend is likely to persist in the near future, as suggested by Ribes et al. (16). The incident cases that we reported are similar to those estimated by Ribes et al., while the crude and age standardised rates were lower than expected according to their study. The immigrant population settling in Catalonia has grown significantly in the past decade (Table SI<sup>1</sup>). From representing only 2.9% of the total population in Catalonia in 2000, growing to 13.1% in 2006 and reaching 16.4% in 2010. They originate mainly from countries with a pigmented skin population and/or low melanoma incidence (Table SII<sup>1</sup>). Among the different nationalities, the most frequent are: Moroccans (19.6%), Rumanians (8%), Ecuadorians (6%) and Bolivians (4.7%) (<http://www10.gencat.cat/gencat/AppJava/es/actualitat2/2010/dadesimmigraciacatalunya.jsp>).

One may hypothesise that the increasing number of new melanoma cases that we have observed has been diluted by the million immigrants that arrived in Catalonia during this period. In favour of this hypothesis is the fact that crude rates per 100,000 inhabitants for invasive melanoma incidence increased from 11.04 in 2000 to 15.49 in 2007 for the 60–64 year population, an age range less affected by immigration, while the crude rate/100,000 inhabitants remained more stable from 3.97 in 2000 to 4.55 in 2007 for the 30–34 year old group or with a tendency to decrease from 5.1 in 2000 to 2.5 in 2007 for the 25–29-year-olds (Table SI<sup>1</sup> and Fig. S1<sup>1</sup>), much more affected by immigration (as usually it is young people that migrate for work reasons as reflected in Table SI<sup>1</sup>).

Another interesting observation from our study is the already known fact that Catalan women develop melanoma at an earlier age and that they are affected at different sites of the body compared with men. Melanoma appears mostly on the trunk in men, but in women it affects trunk and lower limbs in almost equal proportions. The reason why legs are commonly affected in women, but not in men, is unknown but is similar in different populations. Other epidemiological studies of melanoma performed in central and northern Italy, where the climate and skin phototypes are similar to Catalonia, reveals that women are much more prone to develop melanoma on legs compared to men. The possible effect of intermittent sun exposure according to different dress in women (i.e. use of skirts or shorts) has been suggested as responsible for this increase in melanoma incidence on women's legs but this is probably not the main reason and other causes

Table III. Breslow thickness, age at diagnosis and distribution of body site according to sex

	Total	Men	Women	<i>p</i>
Breslow, mean (SD)	2.02 (3.18)	2.28 (3.29)	1.80 (3.09)	0.000
Age at diagnosis, mean (SD)	55.84 (17.51)	57.70 (16.90)	54.29 (17.84)	0.000
Body site, <i>n</i> (%)				
Acral	388 (7.8)	140 (6.3)	248 (9)	<0.000
Lower extr.	1,004 (20.1)	216 (9.7)	779 (28.3)	
Upper extr.	584 (11.7)	210 (9.5)	369 (13.4)	
Head and neck	253 (5.1)	158 (7.1)	91 (3.3)	
Face	571 (11.4)	269 (12.1)	300 (10.9)	
Trunk	1,876 (37.5)	1,083 (48.9)	783 (28.5)	
Mucosal	49 (1)	14 (0.6)	34 (1.2)	
Other	200 (4)	89 (4)	108 (3.9)	

may be argued such as the genetic background of different subtypes of melanoma influenced by gender.

It is noteworthy that, although the number of cases of melanoma in Catalonia was higher in women, the incidence increased in similar proportion in both sexes. A reason why melanoma is diagnosed at an earlier age in women than men may be that women seek medical attention for skin conditions sooner than men but also may be related to the location of the tumour, more visible on lower limbs than on the trunk or especially on the back. This may also explain why the Breslow index was lower in women than men, as melanomas were detected at earlier stages. Unfortunately, mean Breslow thickness does not decrease during the follow-up period and we have not observed an increase in the proportion of *in situ* melanoma even though physicians are now more aware and prepared to detect melanoma at earlier stages, suggesting that population based strategies for secondary prevention should be improved or implemented in our region.

Our mean age standardised incidence rate/100,000 inhabitants of 5.27 for invasive melanoma is lower than the finding by Crocetti et al. (17) who reported that the standardised incidence rate/100,000 inhabitants for invasive melanoma rose from 6.4 in 1985–1989 to 13.6 in 2000–2004 in central Italy. Pellacani et al. (18) in northern Italy showed a standardised incidence rate/100,000 inhabitants of 9.7 for invasive melanomas and 11.9 when also considering *in situ* ones. However, when including *in situ* melanomas, our standardised incidence rate/100,000 inhabitants rose to 7.8. As nearly 20% of Catalan people have private insurance ([http://www.csbcn.org/area\\_prov/doblecob\\_CSB.pdf](http://www.csbcn.org/area_prov/doblecob_CSB.pdf)) and this study was neither focused on private dermatologists nor private pathologists, any thin melanomas diagnosed in private practice and not sent to the referral hospital for treatment may have been lost. Taken together, these findings suggest that melanoma is rising in Catalonia, as in other Mediterranean countries, with a trend of increased mean age at diagnosis, an increase in *in situ* melanoma, but stable mean Breslow thickness with a possible dilution effect of new melanoma cases by immigration from low incidence melanoma countries – as it has been

recently reported in Australia (19) – suggesting that we should also register the origin of the patient as well as racial and cultural characteristics.

One limitation and possible bias of our study is that information was partially gathered retrospectively before 2005 and prospectively thereafter. However, it is the largest epidemiological melanoma study performed in Catalonia to date.

Melanoma incidence has risen significantly in the Mediterranean countries over the past decade and should be considered a public health care problem. Our findings may help to establish primary and secondary preventive measures aimed at a targeted risk-population. Further efforts are required to increase melanoma awareness in the general population and the importance of early detection among the medical community if we want this increasing trend in incidence to stop.

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#### REFERENCES

1. Arnold M1, Holterhues C, Hollestein LM, Coebergh JW, Nijsten T, Pukkala E, et al. Trends in incidence and predictions of cutaneous melanoma across Europe up to 2015. *Eur Acad Dermatol Venereol* 2014; 28: 1170–1178.
2. Howlader N, Noone A, Krapcho M, Neyman N, Aminou R, Waldron W, et al. SEER Cancer Statistics Review 1975–2008 National Cancer Institute SEER Cancer Statistics Review 1975–2008 National Cancer Institute. Miller Ba Ries La Hankey Bf Kosary Ci Kosary ADSAEB, editor. Cancer [Internet]. 2011; 2006: 1992–2008. Available from: <http://www.mendeley.com/research/cancer-breast-seer-stat-fact-sheets/>.
3. Cancer Series Number. Cancer incidence projections Australia 2002 to 2011. *Cancer* [Internet]. 2011; 66:150. Available from: <http://www.aihw.gov.au/publications/can/cipa02-11/cipa02-11.pdf>.
4. Hollestein LM, van den Akker SAW, Nijsten T, Karim-Kos HE, Coebergh JW, De Vries E. Trends of cutaneous mel-

5. De Vries E, Bray FI, Coebergh JWW, Parkin DM. Changing epidemiology of malignant cutaneous melanoma in Europe 1953–1997: rising trends in incidence and mortality but recent stabilizations in western Europe and decreases in Scandinavia. *Int J Cancer* 2003; 107: 119–126.
6. Severi G, Giles GG, Robertson C, Boyle P, Autier P. Mortality from cutaneous melanoma: evidence for contrasting trends between populations. *Br J Cancer* 2000; 82: 1887–1891.
7. De Snoo FA, Kroon MW, Bergman W, Ter Huurne JAC, Houwing-Duistermaat JJ, Van Mourik L, et al. From sporadic atypical nevi to familial melanoma: risk analysis for melanoma in sporadic atypical nevus patients. *J Am Acad Dermatol* 2007; 56: 748–752.
8. Waldmann A, Nolte S, Weinstock MA, Breitbart EW, Eisemann N, Geller AC, et al. Skin cancer screening participation and impact on melanoma incidence in Germany – an observational study on incidence trends in regions with and without population-based screening. *Br J Cancer* 2012; 106: 970–974.
9. Moan J, Baturaite Z, Porojnicu AC, Dahlback A, Juzeniene A. UVA, UVB and incidence of cutaneous malignant melanoma in Norway and Sweden. *Photochem Photobiol Sci* 2012; 11: 191–198.
10. Cayuela A, Rodríguez-Domínguez S, Lapetra-Peralta J, Conejo-Mir JS. Has mortality from malignant melanoma stopped rising in Spain? Analysis of trends between 1975 and 2001. *Br J Dermatol* 2005; 152: 997–1000.
11. Marcos-Gragera R, Vilar-Coromina N, Galceran J, Borràs J, Clèries R, Ribes J, et al. Rising trends in incidence of cutaneous malignant melanoma and their future projections in Catalonia, Spain: increasing impact or future epidemic? *J Eur Acad Dermatol Venereol* 2010; 24: 1083–1088.
12. Nieto A, Ruiz-Ramos M, Abdel-Kader L, Conde M, Camacho F. Gender differences in rising trends in cutaneous malignant melanoma in Spain, 1975–98. *Br J Dermatol* 2003; 148: 110–106.
13. Marcoval J, Moreno A, Torras A, Baumann E, Graells J, Gallego MI. Changes in incidence of malignant melanoma in the last 19 years in a tertiary hospital on the Mediterranean coast. *Actas Dermosifiliogr* 2008; 99: 464–468.
14. Bataille V, Winnett A, Sasieni P, Newton Bishop JA, Cuzick J. Exposure to the sun and sunbeds and the risk of cutaneous melanoma in the UK: a case-control study. *Eur J Cancer* 2004; 40: 429–435.
15. Fortes C, Mastroeni S, Melchi F, Pilla MA, Antonelli G, Camaioni D, et al. A protective effect of the Mediterranean diet for cutaneous melanoma. *Int J Epidemiol* 2008; 37: 1018–1029.
16. Ribes J, Clèries R, Buxó M, Ameijide A, Valls J, Gispert R. Predictions of cancer incidence and mortality in Catalonia to 2015 by means of Bayesian models. *Med Clin* 2008; Suppl 131: 32–41.
17. Crocetti E, Caldarella A, Chiarugi A, Nardini P, Zappa M. The thickness of melanomas has decreased in central Italy, but only for thin melanomas, while thick melanomas are as thick as in the past. *Melanoma Res* 2010; 20: 422–426.
18. Pellacani G, Lo Scocco G, Vinceti M, Albertini G, Raccagni AA, Baldassari L, et al. Melanoma epidemic across the millennium: time trends of cutaneous melanoma in Emilia-Romagna (Italy) from 1997 to 2004. *J Eur Acad Dermatol Venereol* 2008; 22: 213–218.
19. Czarnecki D. The incidence of melanoma is increasing in the susceptible young Australian population. *Acta Derm Venereol* 2014; 94: 539–541.