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Sun exposure prior to diagnosis is associated with improved survival in melanoma patients: Results from a long-term follow-up study of Italian patients

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ABSTRACT

We followed up 260 melanoma patients included in a population-based case–control study in Turin, Italy. We collected information on host factors and sun exposure history, and analysed their relative survival.

Intermittent sun exposure was inversely associated with the risk of death (hazard ratios, HR = 0.41 95% confidence interval, CI = 0.17–0.98). Outdoor work was not associated with an increased risk of death. Multivariate models including anatomic site, melanoma thickness and histology, showed that intermittent sun exposure had a tendency to be inversely associated with the risk of death from melanoma with a HR of 0.60 (95%CI = 0.24–1.5) in the patients with 1 to 59 weeks and a HR of 0.54 (95%CI = 0.23–1.2) in patients with more than 60 weeks spent on the beach during their lifetime.

This study, with similar methods and a longer follow-up, confirms the finding that sun exposure prior to diagnosis of melanoma is associated with improved survival.

1. Introduction

Melanoma, amongst Caucasian populations, has shown to be one of the fastest growing increase in incidence in the last 50 years. Since the seventies, melanoma incidence in USA (in whites) increased from 8.7 per 100,000 inhabitants in 1975 to 22.3 in 2003[1] with an annual percentage change (APC) of about 5.8%. In Europe, an annual increment of 4–15% was observed,[2] with a different pattern of increase amongst Northern countries,[3] where the increase was more dramatic, and amongst Southern countries, where the increase was more modest.[4,5] In Australia, the country that has suffered the highest toll, the annual percent increase was about 4% from the eighties to the end of 2000, despite the prior incidence rate was already the highest in the world.[6,7] Fortunately, some recent data show a stabilisation of the increasing trend or even a small decrease in North America and in Australia in the youngest cohorts of birth.[1,6,7]

On the contrary, mortality did not parallel the increase in incidence: in USA, there were 2.3 melanoma deaths per 100,000 in 1975 and 3.0 in 2003. In Australia, mortality rates peaked in 1985 and then stopped rising.[8,9] This discrepancy was generally ascribed to the increase of thinner melanoma, easier to remove at an early stage and therefore with a more favourable prognosis, whilst thicker melanoma increased at a lower rate and was probably responsible for the constant mortality. It has also been suggested that the improved survival associated with increased incidence, and observed across several countries, was due to a different and more benign type of melanoma.[10] Traditionally, increased melanoma incidence

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was thought to be associated with the more widespread habit of exposing the skin to the sun during leisure activities without an adequate protection or to a permanent tan, the so-called 'intermittent' sun exposure.[11]

Recently, another hypothesis was put forward[12]: the increased number of, mainly thin, melanoma, and the improved survival were both related to sun exposure because of a possible metabolic pathway linking sun exposure to vitamin D induction, which is supposed to have an intra-cellular anti-oxidative and pro-apoptosis effect. This hypothesis arose from the results of the follow-up of melanoma patients in Connecticut previously interviewed in a case–control study.[13] The authors found a positive association between intermittent sun exposure indicators and longer survival. An indirect confirmation of these findings was recently seen analysing the fatality of melanoma in New South Wales, where the measurement of sun exposure was indirectly assumed by the season of diagnosis.[14] The authors found that melanomas diagnosed in summer had a decreased fatality, independently from the lesion thickness. Alternative hypotheses included the increased surveillance, particularly in people who practice sun exposure; but also a possibly different genetic pathways amongst some patients leading to a different type of melanoma, as in the case of B-raf.[15] It was therefore relevant to evaluate these results from an independent source in a study with a different population. We studied the survival of a cohort of melanoma patients previously recruited in a case–control study in a Mediterranean population in the middle of the eighties,[16–18] where detailed information on sun exposure and other risk factors was collected.

2. Methods

2.1. Patients

Between May 1984 and October 1987, we conducted a population-based case–control study of melanoma in Turin, Italy; the details of this study are described above.[16] All new cases with a histological diagnosis of CM and resident in the province of Turin were identified through the Piedmont Cancer Registry. Subjects whose age averaged to 56 years, with range 12–92, with a participation rate of 85% were interviewed out of 305 eligible patients. The original study had a total of 260 cases and 416 controls. Amongst these cases, 186 were women and 74 men: such an imbalanced sex ratio was due to the fact that the recruitment of women was prolonged in order to get statistical power for studying the role of oral contraceptives in melanoma.[18]

2.2. Data collection and study variables

All interviews were carried out by trained interviewers using a questionnaire, which included socio-demographic variables (age at melanoma diagnosis, sex, level of education and occupation), host factors (pigmentation and skin reaction to sun exposure) and sun exposure history. The level of education was used as a proxy of SES. In the previous studies on the effect of social deprivation and survival from cancer, the level of education in Italy proved to be the best indictor of SES.[19] Pigmentation was measured by assessing hair and eye colour. We graded hair colours using a visual scale on 11 levels. Eye colours were assessed on a three-level scale (black or brown, green, blue or grey). Reaction to sun exposure was measured with the usual four-level scale ranging from subjects who always tan and never burn to subjects who always burn when exposed to sun. Past experiences of sunburns were assessed by asking questions about the frequency and severity of sunburns during childhood and the number of lifelong severe sunburns (which caused pain for at least 2 days). The use of sunscreen was also investigated, with questions on the type of sunscreen, period and frequency of use. However, from a qualitative analysis of answers provided it emerged that for the vast majority of people in Italy at that time, effective sunscreens were not yet available: most of the product were homemade (mainly water in a suspension of olive or bergamot oil), and there was no awareness or recollection of using sun screen with an adequate protection factor.

Questions on sun exposure were arranged by life periods (childhood, adolescence, adulthood, after retirement) with separate sections relative to place of residence, work, type of holiday resort (beach, mountain, country, cruises, town), sports and other outdoor recreational activities. Every time a subject reported an outdoor exposure, we asked him or her to report number of years and weeks over the years during which this activity took place, seasons and number of hours of exposure. For each type of activity, we estimated cumulative sun exposure summing up the number of weeks spent during lifetime, and incident exposure (weeks/year) as the ratio of cumulative exposure to years of activity. For the analyses, we then grouped the original values in percentiles of the cumulative distributions in exposed cases. Outdoor sports were classified as low, medium and high risk and subject assigned to one of these categories. Pathology reports and clinical records of all the 260 patients provided the needed information on lesion thickness, Clark's staging, histology type and site of melanoma (head and neck, trunk, upper limb and lower limb). Although present in the original pathology reports, information on ulceration, on solar elastosis and on other characteristics of the lesion and the surrounding tissue was not recorded. In the analyses, we used information on lesions' thickness since it was more complete (18% missing) than Clark's staging (20% missing); and grouped its first two categories (0.75 mm and 0.75–1.50 mm) since we had not many thin lesions (14%) to justify their use as the reference category.

We used the facilities of the Piedmont Cancer Registry to perform an active follow-up of all the cases up to 31st December 2005, to ensure a standardised assessment of the survival time. For deceased patients, the actual date and place of death was recorded, as well as the initial cause of death and other associated pathological conditions. Surviving patients were censored at the date of the last contact or, if still alive, on 31st December 2005.

2.3. Statistical methods

Our aim was to investigate the determinants of net survival, that is, the determinants of mortality due to melanoma. To avoid inaccuracy, due to the misreporting of death certificates, we used relative survival as a means of estimating net survival in our population. Relative survival is the ratio between the patients' observed survival and the expected sur-

vival of a group in the general population comparable by age and sex, and assumed to be practically free from cancer. To calculate the expected number of deaths, we used 1-year age class life tables stratified by sex. The life tables of the Turin province were provided by the Italian National Institute of Statistics (ISTAT) for the periods 1986–1990, 1991–1995, 1996–2000 and 2001–2005. For the years 1984–1985 when the recruitment and follow-up of melanoma patients started, we used the life tables of the closest available period (1985–1990). To investigate the differential risk in relative survival amongst the factors studied, we used generalised linear models with a Poisson error, and a log offset of person–years at risk.[20] We included adjustment for age and sex in the models, because excess mortality was not constant by age and sex. The parameters estimated from these relative survival regression models can be interpreted analogously to Cox's proportional hazard regression models, where the exponential of the estimated parameters have an interpretation as excess hazard ratios (HR), discounted for mortality due to other causes. Presenting our results in tables, we also included the number of expected deaths for a better evaluation of the effect of this factor on melanoma fatality. The independent effect of risk factors was investigated in a multivariate model introducing all variables and terms for interactions, then keeping only those statistically significant or showing a confounding effect on the studied factors.

3. Results

Out of the 260 patients with CM enrolled in the original case–control study, 9 cases (3.5%) were lost to follow-up soon after the interview. No significant differences were found by age, sex and melanoma thickness between patients with complete follow-up and patients with lost to follow-up. During the follow-up period (range 1 month to 21 years; median 17 years), 128 deaths occurred. The number of death exceeded the expected mainly in the first four years, but some excess deaths were still observed up to 18 years of follow up. Cumulative relative survival was 83%, 78%, 74% at 5, 10 and 15 years, respectively. The main cause of death reported in the death certificates was melanoma of the skin (74 deaths), whilst 32 patients died for other causes. It was not possible to identify the cause of death of other 22 subjects from the available documents.

Superficial spreading melanoma (SSM) accounted for 52% of all the cases, without any significant difference between sexes. Lentigo malignant melanoma (LM) accounted for 9% in men and 11% in women. The most frequent site in men was the trunk (35% versus 27% in women), whilst lower limbs were the predominant site in women (48% versus 19% in men). Table 1 shows hazard rates by age group, sex, level of education and melanoma site and microscopic characteristics for the 251 CM cases with follow-up information. Women showed a lower risk than man did (HR = 0.44 95%CI = 0.25–0.78), and the

Table 1 – Demographic and clinical predictors of risk of death from Melanoma in a population-based study of Turin residents, Italy

	Number of cases alive at the beginning of follow-up	Observed deaths (%)	Expected deaths (%)[a]	Hazard ratio[b]	95%CI
Age at diagnosis (years)					
Less than 65	175	61 (45)	16 (17)	Reference	
65 and over	76	67 (95)	34 (60)	2.7	(1.4; 5.1)
Sex					
Men	73	45 (62)	16 (22)	Reference	
Women	178	83 (47)	34 (19)	0.44	(0.25; 0.78)
Education					
Up to high school	225	118 (52)	46 (20)	Reference	
Further than high school	26	10 (38)	3 (13)	0.59	(0.20; 1.78)
Anatomic site of melanoma					
Head and neck	60	40 (67)	20 (34)	Reference	
Upper limbs	36	17 (47)	10 (26)	0.75	(0.27; 2.1)
Lower limbs	100	43 (43)	14 (14)	0.55	(0.19; 1.6)
Trunk	53	26 (49)	6 (12)	1.5	(0.59; 3.7)
Melanoma thickness					
<1.50 mm	92	30 (33)	19 (21)	Reference	
[1.50; 3.00) mm	51	24 (47)	9 (18)	4.5	(0.82; 22.2)
>3.00 mm	59	45 (76)	11 (19)	12.8	(2.5; 64.6)
Not available	49	29 (59)	10 (21)	6.5	(1.1; 38.0)
Histologic type of melanoma					
Superficial spreading	131	52 (40)	24 (18)	Reference	
Nodular	24	16 (67)	2.1 (8.8)	2.0	(0.82; 4.7)
Acral	13	10 (77)	2.2 (17)	2.3	(0.62; 8.4)
Lentigo	26	16 (62)	13 (50)	0.42	(0.04; 4.4)
Not available	57	34 (60)	7.9 (14)	1.3	(0.52; 3.1)

a Number of deaths expected in the same group of cases if they had experienced the same mortality as the general population only.
b Hazard ratios estimated from log-linear models adjusted for age, sex, education and follow-up period.

greatest excess risk was observed amongst 65-year-old and above at diagnosis (HR = 2.7 95%CI = 1.4–5.1). More educated patients showed a lower, although not significant, risk (HR = 0.59 95%CI = 0.20–1.8). Melanoma thickness was confirmed as the best predictor of risk of death with a statistically significant hazard ratio of 12.8 (95%CI = 2.5–64.6) for the thickness of 3 mm or more, in comparison to lesions less than 1.5 mm thick. The 49 cases without lesion thickness showed some risk excess (HR = 6.5 95%CI = 1.1–38.0), suggesting that the lack of information was more prevalent on more advanced melanoma. The patients with melanoma of the limbs were at lower risk of death than those with head and neck melanomas (HR = 0.75 for upper limb and HR = 0.55 for lower limb), whilst in our population melanoma of the trunk showed an excess risk of death, although not significant (HR = 1.5 95%CI = 0.59–3.7). When we combined lower and upper limbs and compared this group with head/neck and trunk, the lower risk of death remained statistically not significant. An excess risk was observed for nodular (HR = 2.0 95%CI = 0.82–4.7) and acral melanomas (HR = 2.3 95%CI = 0.62–8.4).

Host factors (skin type, eye and hair colour) did not show any significant association with fatality for melanoma; neither sunscreen use (HR = 0.75 95%CI = 0.41–1.4), sunburns in childhood (HR = 0.96 95%CI = 0.51–1.8), or lifelong exposure (HR = 1.4 95%CI = 0.79–2.5) was associated with the risk of death from melanoma (Table 2). Some protective effect was observed for variables related to recreational outdoor activities such as sports (HR = 0.64 95%CI = 0.32–1.3) and hobbies (HR = 0.60 95%CI = 0.27–1.3), whilst a variable like outdoor work, activity related to chronic sun exposure, was associated with an

Table 2 – Skin type, eye and hair colour, sunscreen use, sunburns, sun exposure and risk of death from melanoma in a population-based study of Turin residents, Italy

	Number of cases alive at the beginning of follow-up	Observed deaths (%)	Expected deaths (%)[a]	Hazard ratio[b]	95%CI
Skin type					
IV	83	49 (59)	18 (22)	Reference	
III	67	30 (45)	11 (17)	0.75	(0.36; 1.5)
II	75	34 (45)	16 (22)	0.57	(0.28; 1.2)
I	19	11 (58)	2.3 (12)	1.4	(0.56; 3.6)
Eye colour					
Black/brown	136	56 (41)	21 (15)	Reference	
Blue	52	31 (60)	12 (24)	1.7	(0.80; 3.5)
Green	33	19 (58)	6.4 (19)	1.8	(0.77; 4.4)
Grey	29	22 (76)	9.8 (34)	1.9	(0.76; 4.9)
Hair colour					
Black/brown	178	88 (49)	38 (22)	Reference	
Blond/red	68	40 (59)	11 (16)	1.5	(0.83; 2.6)
Sunscreen use					
No	134	83 (62)	31 (23)	Reference	
Yes	117	45 (38)	18 (16)	0.75	(0.41; 1.4)
Sunburns in childhood					
Never	180	93 (52)	38 (21)	Reference	
Sometimes/often	67	33 (49)	12 (17)	0.96	(0.51; 1.8)
Severe sunburns lifelong					
Never	175	91 (52)	39 (22)	Reference	
Sometimes/often	72	36 (50)	10 (14)	1.4	(0.79; 2.5)
Outdoor sports					
No	176	94 (53)	37 (21)	Reference	
Yes	74	33 (45)	11 (15)	0.64	(0.32; 1.3)
Outdoor hobbies					
Never	199	104 (52)	38 (19)	Reference	
Sometimes/often	52	24 (46)	12 (22)	0.60	(0.27; 1.3)
Outdoor work					
No	194	89 (46)	33 (17)	Reference	
Yes	57	39 (68)	16 (28)	1.3	(0.65; 2.5)
Number of weeks on the beach in a lifetime					
0	70	52 (74)	18. (26)	Reference	.
1–59	67	27 (40)	9.5 (14)	0.41	(0.18; 0.90)
>60	114	49 (43)	22 (19)	0.39	(0.19; 0.79)

a Number of deaths expected in the same group of cases if they had experienced the same mortality as the general population only.
b Hazard ratios estimated from log-linear models adjusted for age, sex, education and follow-up period.

increased, although not statistically significant, risk of death from melanoma (HR = 1.3 95%CI = 0.65–2.5).

Intermittent sun exposure, measured by number of weeks spent over a lifetime on the beach (Table 2), was inversely associated with the risk of death: patients with 1 to 59 weeks spent on the beach during their lifetime had a significantly decreased risk of dying from melanoma (HR = 0.41 95%CI = 0.18–0.90) compared to those who did not visit the beach for holidays. A similar, but stronger effect was observed for the patients with more than 60 weeks spent on the beach in their lifetime (HR = 0.39 95%CI = 0.19–0.79), with a significant linear trend (p-value = 0.015). The cut-off at 60 weeks was derived from the quartile of the distribution of time spent at beach, grouping together the two highest quartiles for increasing the number of observed events.

Lifelong exposure reflects a composite pattern of exposure. We tried to investigate the joint effect of sun exposure in adulthood and childhood in our data. Time spent on the beach during adulthood (on average 3 weeks/year for 19 years) was inversely associated with the risk of death also amongst 177 cases that were not exposed during childhood and youth (Table 3). Seventy-four cases with some exposure during childhood continued exposure during adulthood, reaching a mean of 35 years of exposure with a mean of 4 weeks/year. Also amongst this group intermittent sun exposure seems to be protective (HR = 0.31 95%CI = 0.08–1.2). The protective effect of recreational sun exposure seems to be present also at a low level of exposure. On the contrary, a residual excess of risk was still detected amongst 70 patients who have never been on the beach during holidays. This group tends to be older, and with lower education.

In the multivariate analysis, the final model included the effects of lesion thickness, and number of weeks spent lifetime on the beach in addition to age, sex and education. The protective effect of intermittent sun exposure was maintained with only a slight drift towards unity, but still showing a statistically significant linear trend (Table 4). In addition, the protective effect for women remained also grouping the body site of lesion in limbs versus head/neck and trunk, whilst the effect of body site was not statistically significant (HR = 0.93; 95%CI: 0.41; 2.2). When observing the combined effect of melanoma thickness, education and sex on intermittent sun exposure we noted that the protective effect persisted amongst those with thin or thick lesions, and amongst highly and less educated people with substantially the same effect; however, the protective effect of sun exposure was more evident amongst men (Table 5).

We replicated the analyses for the patients who died for melanoma of the skin, considering the time of death for the patients who died of other causes as censored. Results were substantially in the same direction as those previously presented, but with larger confidence intervals.

Table 4 – Predictors of risk of death for melanoma in a population-based study of Turin residents, Italy

	Hazard ratio[a]	95%CI
Sex		
Men	Reference	
Women	0.37	(0.21; 0.67)
Age at diagnosis (years)		
Less than 65	Reference	
65 and over	1.9	(0.96; 3.7)
Education		
Up to high school	Reference	
Further than high school	0.89	(0.10; 10)
Melanoma thickness		
<3.00 mm	Reference	
> 3.00 mm	3.7	(2.0; 6.8)
Weeks on the beach in a lifetime		
0	Reference	
1–59	0.58	(0.27; 1.3)
>60	0.49	(0.24; 0.99)

a Hazard ratios estimated from log-linear models adjusted for follow-up period and all other factors in the table.

4. Discussion

We studied the survival of a cohort of melanoma patients recruited from a population-based case–control study. The

Table 3 – Joint effect of sun exposure on the beach during childhood and adulthood on risk of death for melanoma in a population-based study of Turin residents, Italy

Number of weeks on the beach during adulthood	Number of weeks on the beach during childhood		
	0	1–59	>60
0			
Observed/expected[a] deaths	52/18	3/0.1	2/0.8
Hazard ratio[b] and 95% CI	Reference	1.87 (0.49; 7.2)	0.75 (0.10; 5.7)
1–59			
Observed/expected[a] deaths	23/8.8	3/1.1	1/0.2
Hazard ratio[b] and 95% CI	0.40 (0.17; 0.94)	0.14 (0.02; 0.96)	0.13 (0.01; 5.1)
>60			
Observed/expected[a] deaths	25/13	8/3.4	11/3.8
Hazard ratio[b] and 95% CI	0.42 (0.18; 0.98)	0.36 (0.10; 1.3)	0.68 (0.25; 1.9)

a Number of deaths expected in the same group of cases if they had experienced the same mortality as the general population only
b Hazard ratios estimated from log-linear models adjusted for age, sex, education and follow-up period.

Table 5 – Joint effect of intermittent sun exposure, melanoma thickness, sex and education on risk of death for melanoma in a population-based study of Turin residents, Italy

	Intermittent sun exposure	
	Never	Sometimes/often
Melanoma thickness[a]		
<3.00 mm	Reference	0.46 (0.18; 1.2)
>3.00 mm	3.4 (1.4; 8.0)	1.8 (0.71; 4.7)
Sex[b]		
Men	Reference	0.32 (0.14; 0.76)
Women	0.23 (0.16; 0.53)	0.18 (0.08; 0.41)
Education[c]		
Up to high school	Reference	0.51 (0.27; 0.98)
Further than high school	0.96 (0.12; 7.8)	0.43 (0.11; 1.7)

a Hazard ratios estimated from log-linear models adjusted for age, sex, education and follow-up period.
b Hazard ratios estimated from log-linear models adjusted for age, education, melanoma thickness and follow-up period.
c Hazard ratios estimated from log-linear models adjusted for age, sex, melanoma thickness and follow-up period.

case–control study, conducted during the eighties in a Mediterranean population (Turin, Italy) found a strong association of skin sensitivity to sun (OR 5.0 in men and 2.2 in women) and sun exposure during recreational activities (OR 4.1 in men and 2.7 in women) with melanoma risk.[16] Furthermore, in the original case–control study, we found an increased risk of melanoma for the history of sunburns in childhood (OR 5.9), leaving an independent effect for recreational sun exposure during both adult and childhood.[17] The results of survival analysis confirmed the previous findings[13] of a protective effect of intermittent sun exposure prior to the development of melanoma against mortality. The association was also present with an indirect measure of intermittent sun exposure such as cumulative amount of time spent during leisure activities (holidays on the beach). In several studies across the world this sun exposure habit was also frequently associated with an increased risk of developing melanoma and a meta-analysis[21] estimated a risk of 1.6 (95%CI: 1.4; 2.0).

Although a reproducibility study[22] showed that sun exposure history could reliably be estimated through a questionnaire administered by properly trained interviewers, a certain amount of underreporting, probably due to public awareness about risk factors as shown in a case–control study on sunbed use and melanoma[23] may be still present. However, in Italy during the eighties, when the interviews were conducted and information on risk factors was collected, there were not yet educational campaigns on media about melanoma prevention, nor particular pressure for using UV effective skin protection or avoiding sun exposure. However, even if differential misclassification can be less important since here we are dealing only with melanoma cases, the timing of interviews limits our information at the time of diagnosis and before: sun exposure behaviours can have changed since then and influenced, in some way, patients survival.

The association between survival and intermittent sun exposure was not explained by confounding with social class, represented here by a high education level, which was also inversely associated with risk of dying of melanoma. In addition, the relative survival approach also took into account the differences in mortality for all causes by age and sex, considering the wide age range of incident cases included in this study. Even after adjustment for anatomic site, melanoma thickness and type of melanoma, intermittent sun exposure confirmed a tendency to be inversely associated with the risk of death.

The improved survival amongst subjects with an intermittent sun exposure can also be due to their increased skin surveillance, although the previous studies[13,14] showed that this was independently associated with survival. In the present study, there were no measure of skin surveillance and thus we were unable to directly evaluate its impact on survival. However, several studies have already showed that skin surveillance was substantially associated with high social class and/or high education.[24,25] As a matter of fact, in our study the protective effect of intermittent sun exposure was still present also amongst less educated people. In addition, the protective effect of sun exposure on risk of death from melanoma was similar whenever the patients had a thin or thick lesion.

Of course this study, and similar studies, cannot explain the biological plausibility of the effect of sun exposure on patient survival. However, it was important to find a confirmation of the study by Berwick and colleagues in a different population, with different, although similar, data collection methods, a longer follow-up (median time 17 years), and a low percentage of missed to follow-up cases (3.5%). And it was also quite interesting that our estimates of a protective effect, measured in terms of hazard ratios, were rather similar to those previously found: a HR of 0.6 (95%CI 0.3–1.0) for high versus low intermittent sun exposure. On the other hand, Berwick and colleagues found an improvement of survival also in the presence of solar elastosis, that can be viewed as a surrogate for chronic sun exposure, whilst in the present study, where solar elastosis was not recorded from the pathology reports, an indicator of chronic sun exposure such as exposure during occupation, did not show any effect. A possible explanation of the biological mechanism beyond the protective effect of sun exposure on melanoma mortality was proposed to lie in the anti-proliferative, pro-apoptotic and pro-differentiation effects of vitamin D,[26] which increases after sun exposure. Ecological studies put in relation sunlight and cancer survival[27] and mortality, but there is evidence also from other studies that personal habits of high sun exposure may improve outcome also for breast, colon and prostate cancer (for a review of the studies on sunlight and cancer see also Kricker and Armstrong).[28] However, the hypothesis of a positive role played by vitamin D is, in some way, in contradiction with our result of an increased risk of death, although not statistically significant, for chronic exposure, measured with cumulative time of sun exposure during outdoor work. Also in this case the amount of synthesis of 25-hydroxy vitamin D should be increased as well as during intermittent sun exposure.

In general, as Egan[12] remarked 'no one . . . is suggesting that sunbathing is the route to . . . a better cancer outcome. . .', however, it remains interesting to explore the hypothesis of a possible role of vitamin D in melanoma survival or the presence of

a genetic predisposition consistent with the two pathways for melanoma.[29]

Conflict of interest statement

None declared.

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