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SUPPLEMENT ARTICLE

Association of sunbed use with skin cancer risk factors in Europe: an investigation within the Euromelanoma skin cancer prevention campaign

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Abstract

Introduction Sunbed use has been significantly associated with increased risk of melanoma and non-melanoma skin cancer (NMSC), but its relationship with melanoma's risk factors such as high nevus count, atypical nevi and lentigines is poorly studied. Euromelanoma is a skin cancer prevention campaign conducted all over Europe. It offers a once-a-year screening during which participants' data, including sunbed use and phenotype, are collected via questionnaires.

Objectives To investigate the association of sunbed use with nevus count, atypical nevi, lentigines and suspicion of skin cancer.

Methods To ensure reliability of the data, we defined inclusion and exclusion criteria for countries' eligibility for the risk analysis. Multivariate logistic regression models (including age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use) were used to calculate summary odds ratios (SORs) of each clinical endpoint for ever sunbed use.

Results Overall, 227 888 individuals from 30 countries completed the Euromelanoma questionnaire. After the data quality check, 16 countries were eligible for the multivariate analysis, for a total of 145 980 participants (64.8% females; median age 43 years; 62.3% highly educated; 28.5% skin type I–II; 11.0% ever sunbed use). Ever sunbed use was independently associated with nevus count >50 [SOR = 1.05 (1.01–1.10)], atypical nevi [SOR = 1.04 (1.00–1.09)], lentigines [SOR = 1.16 (1.04–1.29)] and suspicion of melanoma [SOR = 1.13 (1.00–1.27)]. Conversely, no significant association was found between ever sunbed use and suspicion of NMSC [SOR = 1.00 (0.91–1.10)].

Conclusions Indoor tanning is significantly associated with well-recognized risk factors for melanoma (including high nevus count, presence of atypical nevi and lentigines) as well as suspicion of melanoma within the Euromelanoma screenees. In order to reduce the prevalence of melanoma risk factors, avoidance/discontinuation of sunbed use should always be encouraged, especially but not exclusively for individuals with high-risk phenotypes.

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[a]Euromelanoma Working Group members' details are listed in Appendix 1.

Conflict of interest
None.

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Introduction
The use of artificial tanning lamps for cosmetic purposes is extremely common in developed areas of the world including Europe.[1] This raises concern among health providers and legislators, as sunbed use has been associated with an increased risk of melanoma and non-melanoma skin cancer (NMSC) by several studies, summarized in meta-analyses.[2–8] Indeed, the International Agency for Research on Cancer (IARC) currently regards the whole spectrum of ultraviolet (UV) radiation as well as UV-emitting tanning devices as first-group carcinogens alongside tobacco smoking and asbestos.[9,10] Associations between indoor tanning exposure and melanoma's risk factors such as high nevus count, atypical nevi and lentigines have also been suggested, though not extensively studied up to date.[11–19]

Euromelanoma is a skin cancer prevention campaign that is conducted all over Europe since almost two decades.[20–22] Its main goal is to promote awareness of skin cancer among the general public. Euromelanoma aims therefore to inform and educate the population as to how to prevent skin cancer by avoiding modifiable risk factors, and to recognize suspicious skin lesions by skin self-examination. Moreover, Euromelanoma offers once-a-year free screenings to the general public, during which screenees and physicians are requested to complete a questionnaire enquiring about participants' socio-demographics, phenotype, risk factors (including sunbed use) and several clinical findings.

The objective of this study was to investigate the association of sunbed use with established melanoma's risk factors such as high nevus count, presence of atypical nevi and lentigines as well as with suspected skin cancers detected by dermatologists during the Euromelanoma screening.

Materials and methods

Euromelanoma campaign and questionnaire
The Euromelanoma campaign was organized annually by the Euromelanoma Networking Group, under the auspices of the European Academy of Dermatology and Venereology (EADV) and the European Association of Dermato-Oncology (EADO). Every year, a media campaign focusing on particular aspects of skin cancer prevention was conducted on TV, radio, newspapers/magazines and Internet (www.euromelanoma.org) during the month of April. The campaign then culminated each year with the Euromelanoma day (usually in May), during which free-of-charge skin examinations were offered by both public and private dermatology clinics in several European countries. As previously described,[20,21] participants were evaluated by means of the Euromelanoma questionnaire, which was standardized for all participating countries since 2009. The questionnaire was divided in two sections: the first was to be completed by the screenees and enquired about their demographics and risk factors; the second was then filled in by the screening dermatologist and focused on clinical findings that emerged during the visit. Questionnaires were sent to the coordinator centre of each country and data were then entered in a unique database (developed with Limesurvey version 1.82+), located at the Department of Dermatology, Université Libre de Bruxelles, Brussels, Belgium.

Statistical analysis
The variable 'any sunscreen use' (no/yes) was created by pooling together sunscreen use when outdoors for >1 h and sunscreen use when sunbathing. The variable 'any sun exposure' (no/yes) was created by pooling together outdoor occupation, history of sunburn and sunny holidays.

Sunbed use was investigated by two questions: 'Do you use solarium?' (possible answers 'No', 'Yes, ≤20 sessions/year', 'Yes, >20 sessions/year') enquired about current sunbed use; and 'Number of years using solarium (including in the past only)' enquired about duration of ever sunbed use. Participants not reporting current sunbed use but reporting duration of sunbed use were considered ever users along with those reporting current use.

The following clinical variables were used as endpoints: presence of suspected melanoma, presence of suspected basal cell carcinoma (BCC), presence of suspected squamous cell carcinoma (SCC), presence of actinic keratoses (AKs), nevus count, presence of atypical nevi (defined as nevi with asymmetric, ill-defined borders, irregular pigmentation and diameter >6 mm) and presence of lentigines on the back/chest, all categorized as no/yes variables.

Descriptive statistics, with frequencies, median values and interquartile ranges, are presented to report the socio-demographic characteristics of the surveyed population. Percentages and 95% confidence intervals (CIs) are presented to define the

Table 1 Frequency of the main clinical variables for each participating country

Country	N	Suspected melanoma			Suspected BCC			Suspected SCC			Suspected AKs			Nevus count			Atypical nevi (≥1)			Lentigines		
			n	%		n	%		n	%		n	%		n	%		n	%		n	%
Belgium	10 179	Missing	341	3.4	Missing	325	3.2	Missing	361	3.6	Missing	739	7.3	Missing	362	3.6	Missing	435	4.3	Missing	439	4.3
		No	9589	94.2	No	9577	94.1	No	9787	96.2	No	8722	85.7	≤50	8447	83.0	No	8054	79.1	No	5443	53.5
		Yes	249	2.5	Yes	277	2.7	Yes	31	0.3	Yes	718	7.1	>50	1370	13.5	Yes (≥1)	1690	16.6	Yes	4297	42.2
Bosnia-Herzegovina	7187	Missing	156	2.2	Missing	225	3.1	Missing	243	3.4	Missing	290	4.0	Missing	166	2.3	Missing	227	3.2	Missing	257	3.6
		No	6874	95.6	No	6620	92.1	No	6896	96.0	No	6048	84.2	≤50	6584	91.6	No	5234	72.8	No	4082	56.8
		Yes	157	2.2	Yes	342	4.8	Yes	48	0.7	Yes	849	11.8	>50	437	6.1	Yes	1726	24.0	Yes	2848	39.6
Croatia	4800	Missing	145	3.0	Missing	210	4.4	Missing	222	4.6	Missing	228	4.8	Missing	97	2.0	Missing	194	4.0	Missing	200	4.2
		No	3931	81.9	No	4455	92.8	No	4554	94.9	No	4011	83.6	≤50	4154	86.5	No	3275	68.2	No	2735	57.0
		Yes	724	15.1	Yes	135	2.8	Yes	24	0.5	Yes	561	11.7	>50	549	11.4	Yes	1331	27.7	Yes	1865	38.9
Cyprus	35	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0
		No	31	88.6	No	35	100.0	No	35	100.0	No	27	77.1	≤50	31	88.6	No	26	74.3	No	18	51.4
		Yes	4	11.4	Yes	0	0.0	Yes	0	0.0	Yes	8	22.9	>50	4	11.4	Yes	9	25.7	Yes	17	48.6
Czech Republic	16 992	Missing	124	0.7	Missing	166	1.0	Missing	176	1.0	Missing	211	1.2	Missing	584	3.4	Missing	193	1.1	Missing	204	1.2
		No	16234	95.5	No	16505	97.1	No	16780	98.8	No	15519	91.3	≤50	15514	91.3	No	14061	82.8	No	14030	82.6
		Yes	634	3.7	Yes	321	1.9	Yes	36	0.2	Yes	1262	7.4	>50	894	5.3	Yes	2738	16.1	Yes	2758	16.2
Denmark	2487	Missing	246	9.9	Missing	239	9.6	Missing	256	10.3	Missing	439	17.7	Missing	249	10.0	Missing	372	15.0	Missing	402	16.2
		No	2152	86.5	No	2094	84.2	No	2183	87.8	No	1825	73.4	≤50	2058	82.8	No	1882	75.7	No	1649	66.3
		Yes	89	3.6	Yes	154	6.2	Yes	48	1.9	Yes	223	9.0	>50	180	7.2	Yes	233	9.4	Yes	436	17.5
Estonia	1318	Missing	5	0.4	Missing	3	0.2	Missing	5	0.4	Missing	3	0.2	Missing	53	4.0	Missing	13	1.0	Missing	246	18.7
		No	1270	96.4	No	1279	97.0	No	1310	99.4	No	1260	95.6	≤50	1165	88.4	No	1033	78.4	No	677	51.4
		Yes	43	3.3	Yes	36	2.7	Yes	3	0.2	Yes	55	4.2	>50	100	7.6	Yes	272	20.6	Yes	395	30.0
Georgia	2689	Missing	3	0.1	Missing	7	0.3	Missing	3	0.1	Missing	5	0.2	Missing	15	0.6	Missing	4	0.2	Missing	10	0.4
		No	2632	97.9	No	2592	96.4	No	2675	99.5	No	2487	92.5	≤50	2526	93.9	No	2215	82.4	No	2353	87.5
		Yes	54	2.0	Yes	90	3.4	Yes	11	0.4	Yes	197	7.3	>50	148	5.5	Yes	470	17.5	Yes	326	12.1
Germany	9347	Missing	2110	22.6	Missing	2325	24.9	Missing	2446	26.2	Missing	832	8.9	Missing	487	5.2	Missing	1171	12.5	Missing	1458	15.6
		No	6668	71.3	No	6584	70.4	No	6754	72.3	No	7495	80.2	≤50	6912	74.0	No	6101	65.3	No	4332	46.4
		Yes	569	6.1	Yes	438	4.7	Yes	147	1.6	Yes	1020	10.9	>50	1948	20.8	Yes	2075	22.2	Yes	3557	38.1
Greece	33252	Missing	3167	9.5	Missing	3259	9.8	Missing	3355	10.1	Missing	2335	7.0	Missing	1616	4.9	Missing	1704	5.1	Missing	1541	4.6
		No	29499	88.7	No	29524	88.8	No	29787	89.6	No	29065	87.4	≤50	27915	84.0	No	23302	70.1	No	21410	64.4
		Yes	586	1.8	Yes	469	1.4	Yes	110	0.3	Yes	1852	5.6	>50	3721	11.2	Yes	8246	24.8	Yes	10301	31.0
Hungary	13256	Missing	1011	7.6	Missing	1033	7.8	Missing	1085	8.2	Missing	455	3.4	Missing	396	3.0	Missing	642	4.8	Missing	497	3.8
		No	11885	89.7	No	11844	89.4	No	12125	91.5	No	11336	85.5	≤50	11719	88.4	No	9606	72.5	No	8003	60.4
		Yes	360	2.7	Yes	379	2.9	Yes	46	0.4	Yes	1465	11.1	>50	1141	8.6	Yes	3008	22.7	Yes	4756	35.9
Ireland	380	Missing	53	14.0	Missing	54	14.2	Missing	57	15.0	Missing	63	16.6	Missing	39	10.3	Missing	66	17.4	Missing	66	17.4
		No	316	83.2	No	316	83.2	No	322	84.7	No	270	71.1	≤50	338	89.0	No	297	78.2	No	246	64.7
		Yes	11	2.9	Yes	10	2.6	Yes	1	0.3	Yes	47	12.4	>50	3	0.8	Yes	17	4.5	Yes	68	17.9
Italy	3529	Missing	300	8.5	Missing	326	9.2	Missing	347	9.8	Missing	681	19.3	Missing	253	7.2	Missing	497	14.1	Missing	605	17.1
		No	3161	89.6	No	3113	88.2	No	3173	89.9	No	2631	74.6	≤50	3018	85.5	No	2485	70.4	No	1506	42.7
		Yes	68	1.9	Yes	90	2.6	Yes	9	0.3	Yes	217	6.2	>50	258	7.3	Yes	547	15.5	Yes	1418	40.2

Table 1 *Continued*

Country	N	Suspected melanoma			Suspected BCC			Suspected SCC			Suspected AKs			Nevus count			Atypical nevi (≥1)			Lentigines		
			n	%		*n*	%		*n*	%		*n*	%		*n*	%		*n*	%		*n*	%
Latvia	2400	Missing	439	18.3	Missing	404	16.8	Missing	443	18.5	Missing	63	2.6	Missing	69	2.9	Missing	74	3.1	Missing	53	2.2
		No	1939	80.8	No	1921	80.0	No	1955	81.5	No	2104	87.7	≤50	2083	86.8	No	1945	81.0	No	1301	54.2
		Yes	22	0.9	Yes	75	3.1	Yes	2	0.1	Yes	233	9.7	>50	248	10.3	Yes	381	15.9	Yes	1046	43.6
Lithuania	5902	Missing	426	7.2	Missing	446	7.6	Missing	464	7.9	Missing	485	8.2	Missing	402	6.8	Missing	493	8.4	Missing	487	8.3
		No	5235	88.7	No	5283	89.5	No	5416	91.8	No	4484	76.0	≤50	4861	82.4	No	4328	73.3	No	3150	53.4
		Yes	241	4.1	Yes	173	2.9	Yes	22	0.4	Yes	933	15.8	>50	639	10.8	Yes	1081	18.3	Yes	2265	38.4
Macedonia (FYROM)	1292	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	3	0.2	Missing	0	0.0	Missing	0	0.0
		No	1238	95.8	No	1180	91.3	No	1271	98.4	No	997	77.2	≤50	1175	90.9	No	962	74.5	No	717	55.5
		Yes	54	4.2	Yes	112	8.7	Yes	21	1.6	Yes	295	22.8	>50	114	8.8	Yes	330	25.5	Yes	575	44.5
Malta	432	Missing	4	0.9	Missing	5	1.2	Missing	5	1.2	Missing	14	3.2	Missing	8	1.9	Missing	15	3.5	Missing	14	3.2
		No	414	95.8	No	419	97.0	No	427	98.8	No	376	87.0	≤50	392	90.7	No	366	84.7	No	237	54.9
		Yes	14	3.2	Yes	8	1.9	Yes	0	0.0	Yes	42	9.7	>50	32	7.4	Yes	51	11.8	Yes	181	41.9
Moldova	56	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	0	0.0	Missing	6	10.7	Missing	0	0.0	Missing	0	0.0
		No	48	85.7	No	50	89.3	No	55	98.2	No	42	75.0	≤50	49	87.5	No	32	57.1	No	36	64.3
		Yes	8	14.3	Yes	6	10.7	Yes	1	1.8	Yes	14	25.0	>50	1	1.8	Yes	24	42.9	Yes	20	35.7
Norway	1323	Missing	85	6.4	Missing	98	7.4	Missing	106	8.0	Missing	76	5.7	Missing	28	2.1	Missing	70	5.3	Missing	60	4.5
		No	1178	89.0	No	1174	88.7	No	1215	91.8	No	1161	87.8	≤50	1068	80.7	No	1017	76.9	No	848	64.1
		Yes	60	4.5	Yes	51	3.9	Yes	2	0.2	Yes	86	6.5	>50	227	17.2	Yes	236	17.8	Yes	415	31.4
Poland	8391	Missing	1163	13.9	Missing	1195	14.2	Missing	1254	14.9	Missing	1341	16.0	Missing	379	4.5	Missing	989	11.8	Missing	1129	13.5
		No	7100	84.6	No	6968	83.0	No	7111	84.8	No	6320	75.3	≤50	7069	84.3	No	5423	64.6	No	5913	70.5
		Yes	128	1.5	Yes	228	2.7	Yes	26	0.3	Yes	730	8.7	>50	943	11.2	Yes	1979	23.6	Yes	1349	16.1
Portugal	7655	Missing	250	3.3	Missing	255	3.3	Missing	287	3.8	Missing	212	2.8	Missing	220	2.9	Missing	275	3.6	Missing	259	3.4
		No	7314	95.6	No	7187	93.9	No	7342	95.9	No	7068	92.3	≤50	6858	89.6	No	5977	78.1	No	4869	63.6
		Yes	91	1.2	Yes	213	2.8	Yes	26	0.3	Yes	375	4.9	>50	577	7.5	Yes	1403	18.3	Yes	2527	33.0
Romania	2875	Missing	160	5.6	Missing	179	6.2	Missing	183	6.4	Missing	188	6.5	Missing	92	3.2	Missing	83	2.9	Missing	208	7.2
		No	2694	93.7	No	2639	91.8	No	2686	93.4	No	2359	82.1	≤50	2675	93.0	No	2224	77.4	No	1748	60.8
		Yes	21	0.7	Yes	57	2.0	Yes	6	0.2	Yes	328	11.4	>50	108	3.8	Yes	568	19.8	Yes	919	32.0
Russia	19 400	Missing	7292	37.6	Missing	7531	38.8	Missing	7717	39.8	Missing	3811	19.6	Missing	2364	12.2	Missing	6915	35.6	Missing	6968	35.9
		No	11652	60.1	No	11391	58.7	No	11533	59.5	No	8991	46.4	≤50	15775	81.3	No	9677	49.9	No	8333	43.0
		Yes	456	2.4	Yes	478	2.5	Yes	150	0.8	Yes	6598	34.0	>50	1261	6.5	Yes	2808	14.5	Yes	4099	21.1
Serbia	9080	Missing	670	7.4	Missing	826	9.1	Missing	900	9.9	Missing	707	7.8	Missing	398	4.4	Missing	640	7.1	Missing	666	7.3
		No	7460	82.2	No	7922	87.3	No	8129	89.5	No	6445	71.0	≤50	7964	87.7	No	6393	70.4	No	5447	60.0
		Yes	950	10.5	Yes	332	3.7	Yes	51	0.6	Yes	1928	21.2	>50	718	7.9	Yes	2047	22.5	Yes	2967	32.7
Slovenia	808	Missing	5	0.6	Missing	7	0.9	Missing	5	0.6	Missing	5	0.6	Missing	10	1.2	Missing	1	0.1	Missing	2	0.3
		No	747	92.5	No	783	96.9	No	798	98.8	No	767	94.9	≤50	664	82.2	No	562	69.6	No	406	50.3
		Yes	56	6.9	Yes	18	2.2	Yes	5	0.6	Yes	36	4.5	>50	134	16.6	Yes	245	30.3	Yes	400	49.5
Spain	5191	Missing	1239	23.9	Missing	1252	24.1	Missing	1247	24.0	Missing	1220	23.5	Missing	1191	22.9	Missing	1220	23.5	Missing	1219	23.5
		No	3895	75.0	No	3828	73.7	No	3929	75.7	No	3660	70.5	≤50	3825	73.7	No	3269	63.0	No	2937	56.6
		Yes	57	1.1	Yes	111	2.1	Yes	15	0.3	Yes	311	6.0	>50	175	3.4	Yes	702	13.5	Yes	1035	19.9

Table 1 *Continued*

Country	N	Suspected melanoma			Suspected BCC			Suspected SCC			Suspected AKs			Nevus count			Atypical nevi (≥1)			Lentigines		
			n	%		n	%		n	%		n	%		n	%		n	%		n	%
Sweden	17 978	Missing	1315	7.3	Missing	1238	6.9	Missing	1403	7.8	Missing	1651	9.2	Missing	1225	6.8	Missing	1419	7.9	Missing	1437	8.0
		No	16061	89.3	No	15656	87.1	No	16463	91.6	No	14479	80.5	≤50	15043	83.7	No	14288	79.5	No	10330	57.5
		Yes	602	3.4	Yes	1084	6.0	Yes	112	0.6	Yes	1848	10.3	>50	1710	9.5	Yes	2271	12.6	Yes	6211	34.6
Switzerland	19 751	Missing	1445	7.3	Missing	1405	7.1	Missing	1498	7.6	Missing	1720	8.7	Missing	4948	25.1	Missing	1807	9.2	Missing	1938	9.8
		No	17673	89.5	No	17532	88.8	No	18081	91.5	No	15719	79.6	≤50	12659	64.1	No	15056	76.2	No	11617	58.8
		Yes	633	3.2	Yes	814	4.1	Yes	172	0.9	Yes	2312	11.7	>50	2144	10.9	Yes	2888	14.6	Yes	6196	31.4
Turkey	1854	Missing	420	22.7	Missing	425	22.9	Missing	440	23.7	Missing	275	14.8	Missing	207	11.2	Missing	225	12.1	Missing	211	11.4
		No	1392	75.1	No	1391	75.0	No	1407	75.9	No	1493	80.5	≤50	1530	82.5	No	1227	66.2	No	1053	56.8
		Yes	42	2.3	Yes	38	2.1	Yes	7	0.4	Yes	86	4.6	>50	117	6.3	Yes	402	21.7	Yes	590	31.8
Ukraine	18 049	Missing	5013	27.8	Missing	5212	28.9	Missing	5344	29.6	Missing	5000	27.7	Missing	1847	10.2	Missing	4394	24.3	Missing	5105	28.3
		No	12734	70.6	No	12368	68.5	No	12624	69.9	No	11776	65.2	≤50	14409	79.8	No	10913	60.5	No	9743	54.0
		Yes	302	1.7	Yes	469	2.6	Yes	81	0.5	Yes	1273	7.1	>50	1793	9.9	Yes	2742	15.2	Yes	3201	17.7

N, number of participants for each country; *n*, frequencies; AK, actinic keratosis; BCC, basal cell carcinoma; FYROM, Former Yugoslav Republic of Macedonia; SCC, squamous cell carcinoma.

frequency of the clinical endpoints in each country. Chi-square and Fisher's exact tests were used to determine associations with clinical endpoints in univariate analysis to select variables to be included in multivariate analysis.

Multivariate logistic regression models (including age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use) were used to calculate the odds ratio (OR) of each clinical endpoint for ever sunbed use in each country. Summary ORs (SORs) of estimates from each country were then calculated for each clinical endpoint, with 95% CI, and forest plots were presented with estimates for each country. Between-country heterogeneities were assessed by Higgins and Thompson's I^2 statistics,[23] which can range from zero to 100% – zero indicating a lack of heterogeneity, that is, that the ORs are consistent with each other. All statistical tests were considered significant for *P*-values ≤0.05. Statistical analyses were carried out using SAS 9.2.

Data quality control: inclusion and exclusion criteria for countries' eligibility

Important clinical endpoints of this study were represented by suspected skin cancers; indeed, if a suspicious lesion was found during the screening, patients were advised for further diagnostics and treatment, but follow-up data on diagnosis were not collected in all countries due to privacy and legislative issues. Taking into consideration the lack of histopathological confirmation of suspected lesions, we performed a strict data quality check by which we formulated two inclusion criteria and two exclusion criteria for countries' participation in the multivariate analysis. Inclusion/exclusion criteria and related explanations are listed below.

Inclusion criterion 1: <15% of missing values for suspected melanoma and/or suspected BCC and/or suspected SCC. Missingness can significantly distort the validity of the conclusions, by reducing the representativeness of the sample.[24]

Inclusion criterion 2: <20% adolescents among participants. Adolescents are likely not to have had enough time to develop health consequences due to sunbed use, such as melanoma; indeed, a previous investigation showed an increased risk of melanoma associated with sunbed use ranging from 19% (non-significant) among adolescents to 49% and 61% (both significant) among 30–39 and 40–49 year olds.[25]

Exclusion criterion 1: >10% of adolescents diagnosed with AKs. Estimates from these countries were judged unreliable, as AKs are extremely rare among adolescents.[26]

Exclusion criterion 2: >20% of subjects with atypical nevi considered to have also a suspected melanoma. Probably, in these countries, atypical nevi were erroneously considered as suspected melanomas and therefore excised, although nevi and atypical nevi only rarely transform into melanomas.[27–30]

Table 2 Prevalence of suspected melanoma according to atypical nevi status for each participating country

	Prevalence of suspected melanoma in the absence of atypical nevi	Prevalence of suspected melanoma in the presence of atypical nevi
Belgium	70 (0.9)	167 (10.3)
Bosnia-Herzegovina	60 (1.2)	91 (5.3)
Croatia	107 (3.3)	**603 (46.0)**
Cyprus	2 (7.7)	**2 (22.2)**
Czech Republic	120 (0.9)	507 (18.6)
Denmark	28 (1.5)	**54 (23.9)**
Estonia	25 (2.4)	18 (6.6)
Georgia	25 (1.1)	29 (6.2)
Germany	151 (3.4)	**367 (20.1)**
Greece	172 (0.8)	399 (5.3)
Hungary	71 (0.8)	268 (9.5)
Ireland	6 (2.1)	3 (18.8)
Italy	10 (0.4)	52 (10.0)
Latvia	11 (0.7)	11 (3.2)
Lithuania	28 (0.7)	**209 (21.3)**
Macedonia (FYROM)	28 (2.9)	26 (7.9)
Malta	3 (0.8)	**11 (22.9)**
Moldova	5 (15.6)	3 (12.5)
Norway	18 (1.8)	40 (18.7)
Poland	25 (0.5)	94 (6.0)
Portugal	35 (0.6)	53 (3.9)
Romania	7 (0.3)	11 (2.1)
Russia	122 (1.6)	212 (11.8)
Serbia	96 (1.6)	**806 (41.6)**
Slovenia	11 (2.0)	45 (18.5)
Spain	15 (0.5)	42 (6.0)
Sweden	234 (1.7)	335 (15.8)
Switzerland	248 (1.7)	343 (12.7)
Turkey	7 (0.7)	34 (9.7)
Ukraine	122 (1.2)	126 (5.9)

N (%) shown in each box. Countries in which>20% of subjects with atypical nevi were considered to have also a suspected melanoma are highlighted in bold.

Results

Thirty countries took part in the Euromelanoma campaigns 2009–2014, for a total of 227 888 participants. Details of countries' participation over time are provided in Table S1.

Fourteen countries were not eligible for the multivariate statistical analysis, as they failed the data quality check. In particular, seven countries could not be considered as they did not satisfy inclusion criteria: Germany, Latvia, Russia, Spain, Turkey and Ukraine did not meet inclusion criterion 1 (they all had >15% of missing values for suspected melanoma and/or suspected BCC and/or suspected SCC; Table 1); Romania did not meet inclusion criterion 2 (30.2% of participants were adolescents; Table S2). Moreover, seven other countries had to be subsequently removed as they fulfilled exclusion criteria: Moldova met exclusion criterion 1, as Russia would have done too had it been included (12.5% and 13.1% of adolescents diagnosed with AKs, respectively; Table S3); Croatia, Cyprus, Denmark, Lithuania, Malta and Serbia met exclusion criterion 2 (>20% of subjects with atypical nevi considered to have also a suspected melanoma), as Germany would have done too had it been included (Table 2).

Consequently, 16 countries were included in the main analysis, for a total of 145 980 participants. Details about the demographic, phenotypic and sunbed variables for each eligible country are presented in Table S4. Overall, 64.8% were females and 35.2% males; median age was 43 years (interquartile range 31–59, 6.9% adolescents); 62.3% attained high education and 37.7% low education; 28.5% reported skin type I–II and 71.5% skin type III–VI. Ever use of sunbed was reported by 11.0% of those who responded to the sunbed questions (15 650/142 204).

Melanoma suspicion rate varied from 1.2% (Portugal) to 7.0% (Slovenia) and was higher than BCC suspicion rate in 6 of 16 (37.5%) countries and than SCC suspicion rate in 16 of 16 (100%) countries (Table 3).

The summary estimate suggested a significant, independent association between suspected melanoma and ever sunbed exposure, with between-country heterogeneity [SOR = 1.13 (1.00–1.27), I2 = 11%] (Fig. 1a).

The SOR of suspected NMSC (pooling together suspected BCC, suspected SCC and AKs) for ever sunbed use was 1.00 (0.91–1.10), without between-country heterogeneity (I^2 = 0%; Fig. 1b). Models assessing the association of ever sunbed use with suspected NMSC combined in different ways (including suspected BCC and suspected SCC but excluding AKs or including suspected BCC alone, suspected SCC alone or AKs alone) produced similar results (data not shown).

Furthermore, the summary estimates suggested significant, independent associations between ever sunbed use and: naevus count >50 [SOR = 1.05 (1.01–1.10), I^2 = 0%] (Fig. 2); presence of atypical nevi [SOR = 1.04 (1.00–1.09), I^2 = 0%] (Fig. 3); and lentigines, [SOR = 1.16 (1.05–1.29), I^2 = 68%] (Fig. 4).

Estimates for dose–response effect were not available due to low numbers of intermediate and high sunbed users (data not shown).

Discussion

The use of sunbeds is currently permitted in Europe, but restrictions related to age and skin type of users have been put in place in several European countries. The European legislation for sunbeds, which falls within the Low Voltage Directive (2014/35/EU) for electrical equipment, sets the limits for UV radiation emission to 300 mW/m^2 of total effective irradiance (harmonized European standard EN 60335-2-27:2013). Recently, though, artificial tanning has been declared unsafe by the European

Table 3 Prevalence of the main clinical variables for the 16 countries eligible for the multivariate risk analysis.

	Suspected melanoma		Suspected BCC		Suspected SCC		Suspected AKs		Nevus count >50		Atypical nevi ≥1		Solar lentigos	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Belgium	**2.5**	2.2–2.9	**2.8**	2.5–3.2	**0.3**	0.2–0.5	**7.6**	7.1–8.2	**14.0**	13.3–14.7	**17.3**	16.6–18.1	**44.1**	43.1–45.1
Bosnia-Herzegovina	**2.2**	1.9–2.6	**4.9**	4.4–5.5	**0.7**	0.5–0.9	**12.3**	11.5–13.1	**6.2**	5.7–6.8	**24.8**	23.8–25.8	**41.1**	39.9–42.3
Czech Republic	**3.8**	3.5–4.1	**1.9**	1.7–2.1	**0.2**	0.2–0.3	**7.5**	7.1–7.9	**5.4**	5.1–5.8	**16.3**	15.7–16.9	**16.4**	15.9–17.0
Estonia	**3.3**	2.4–4.4	**2.7**	1.9–3.8	**0.2**	0.1–0.7	**4.2**	3.2–5.4	**7.9**	6.5–9.5	**20.8**	18.7–23.2	**36.8**	34.0–39.8
Georgia	**2.0**	1.5–2.6	**3.4**	2.7–4.1	**0.4**	0.2–0.7	**7.3**	6.4–8.4	**5.5**	4.7–6.5	**17.5**	16.1–19.0	**12.2**	11.0–13.5
Greece	**1.9**	1.8–2.1	**1.6**	1.4–1.7	**0.4**	0.3–0.4	**6.0**	5.7–6.3	**11.8**	11.4–12.1	**26.1**	25.7–26.6	**32.5**	32.0–33.0
Hungary	**2.9**	2.7–3.3	**3.1**	2.8–3.4	**0.4**	0.3–0.5	**11.4**	10.9–12.0	**8.9**	8.4–9.4	**23.8**	23.1–24.6	**37.3**	36.4–38.1
Ireland	**3.4**	1.7–5.9	**3.1**	1.5–5.6	**0.3**	0.0–1.7	**14.8**	11.1–19.2	**0.9**	0.2–2.6	**5.4**	3.2–8.5	**21.7**	17.2–26.6
Italy	**2.1**	1.6–2.7	**2.8**	2.3–3.4	**0.3**	0.1–0.5	**7.6**	6.7–8.7	**7.9**	7.0–8.9	**18.0**	16.7–19.5	**48.5**	46.7–50.3
Macedonia (FYROM)	**4.2**	3.2–5.4	**8.7**	7.2–10.3	**1.6**	1.0–2.5	**22.8**	20.6–25.2	**8.8**	7.4–10.5	**25.5**	23.2–28.0	**44.5**	41.8–47.3
Norway	**4.8**	3.7–6.2	**4.2**	3.1–5.4	**0.2**	0.0–0.6	**6.9**	5.6–8.5	**17.5**	15.5–19.7	**18.8**	16.7–21.1	**32.9**	30.3–35.5
Poland	**1.8**	1.5–2.1	**3.2**	2.8–3.6	**0.4**	0.2–0.5	**10.4**	9.7–11.1	**11.8**	11.1–12.5	**26.7**	25.7–27.8	**18.6**	17.7–19.5
Portugal	**1.2**	1.0–1.5	**2.9**	2.5–3.3	**0.4**	0.2–0.5	**5.0**	4.6–5.6	**7.8**	7.2–8.4	**19.0**	18.1–19.9	**34.2**	33.1–35.3
Slovenia	**7.0**	5.3–9.0	**2.2**	1.3–3.5	**0.6**	0.2–1.5	**4.5**	3.2–6.2	**16.8**	14.3–19.6	**30.4**	27.2–33.7	**49.6**	46.1–53.1
Sweden	**3.6**	3.3–3.9	**6.5**	6.1–6.9	**0.7**	0.6–0.8	**11.3**	10.8–11.8	**10.2**	9.8–10.7	**13.7**	13.2–14.3	**37.5**	36.8–38.3
Switzerland	**3.5**	3.2–3.7	**4.4**	4.1–4.7	**0.9**	0.8–1.1	**12.8**	12.3–13.3	**14.5**	13.9–15.1	**16.1**	15.6–16.6	**34.8**	34.1–35.5

AK, actinic keratosis; BCC, basal cell carcinoma; CI, confidence interval; FYROM, Former Yugoslav Republic of Macedonia; SCC, squamous cell carcinoma.

Commission, whose Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) stated that there is no safe limit for exposure to UV radiation from sunbeds.[31] To corroborate the official opinion of the SCHEER, we decided to exploit the Euromelanoma database, which included information about a large number of participants from 30 countries. Our goal was to investigate the association of sunbed use with well-established risk factors, namely suspected skin cancer, nevus count, presence of atypical nevi and lentigines.

Our multivariate analysis found a significant association between ever exposure to sunbeds and suspected melanoma, after adjustment for potential confounders. Although it was impossible in this study to ascertain whether suspected melanomas were confirmed as such by histopathology, this result appears to confirm the current evidence that sunbed use increases melanoma risk. In particular, our estimate was consistent with those found in previous meta-analyses assessing melanoma risk associated with ever using sunbeds: 15% by the IARC,[2] 16% (10% for Europe alone) by Colantonio *et al.*,[6] 19% by Burgard *et al.*,[7] 20% by Boniol *et al.*,[4] 22% by Hirst *et al.*,[3] and 25% by Gallagher *et al.*[8] Like others before,[6,32] Burgard and co-workers recently raised criticisms about the association between sunbed use and melanoma risk, including limitations of individual studies (selection and recall biases, typical of case-control studies; non-adjustment for certain confounders) and lack of large randomized or prospective studies (which in the case of sunbeds would be unethical or too costly, respectively). Yet, they found similar results in their meta-analysis, even using a different statistical method.[7] In spite of their scepticism then, we believe their recent meta-analysis actually adds to the body of evidence suggesting that sunbed use should be strongly discouraged in order to reduce melanoma risk.

Although the relationship between sunbed use and increased risk of NMSC has been established by previous meta-analyses,[2–5] unfortunately, we were not able to confirm this association. Possible explanations include the lack of histopathological confirmation of the suspected NMSC and the relatively young age of the screenees (median 43 years), which could suggest that participants did not have sufficient time to develop NMSC – which usually occurs later in life than melanoma.[33] This is corroborated by the fact that in the present study, NMSC was suspected less than melanoma in multiple countries, in spite of NMSC being much more common than melanoma in epidemiological investigations.[34–37]

We found a significant association between ever sunbed use and lentigines after adjustment for potential confounders, including sun exposure and sunscreen use. This confirms previous case reports of lentigines occurring after sunbed exposure.[14–19] Interestingly, these observations reported that the lentigines induced by artificial tanning (so-called 'sunbed lentigines') have more worrisome pathologic and ultra-structural features than common solar lentigines, such as the presence of melanocytic nuclear atypia and abnormally clumped, pleomorphic melanosomes. Moreover, excised 'sunbed lentigines' lacked solar elastosis, which is instead typical of common solar

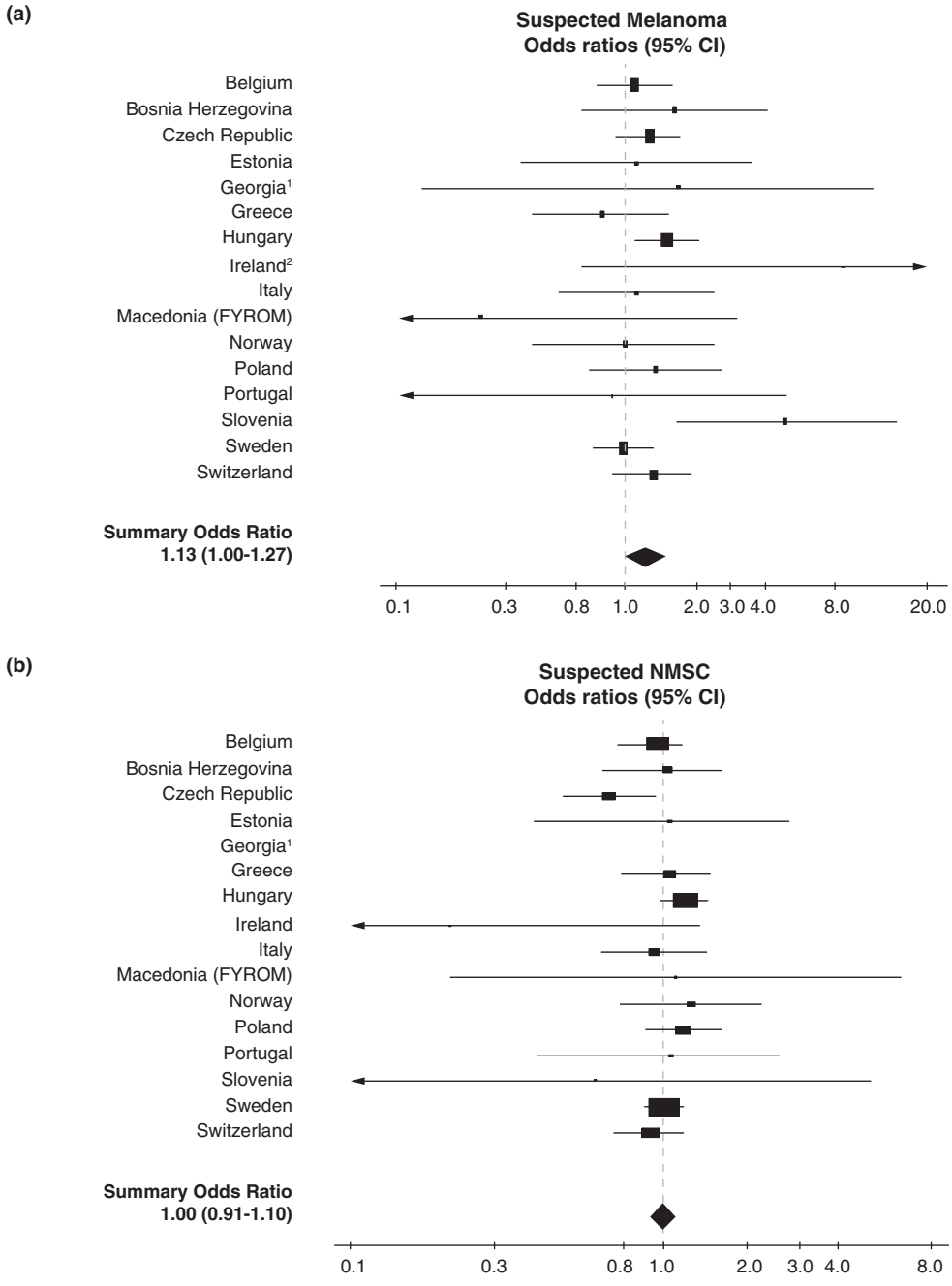

Figure 1 Forest plots of association of suspected skin cancer with ever use of sunbeds. All odds ratios are adjusted for age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use. FYROM, Former Yugoslav Republic of Macedonia. A. Suspected melanoma. Heterogeneity I^2 = 11% for all countries. [1]In order to calculate the odds ratio for Georgia, the model for this country was not adjusted for age, skin type and personal history of skin cancer, due to frequency of suspected melanoma being too low in exposed individuals. [2]A sensitivity analysis for Ireland, the only country with a considerable amount of missing data on sunbed use (20.3%, Table S2) found that the odds ratio of suspected melanoma associated with the missing values was similar to the odds ratio for exposed individuals [6.31 (0.74–53.71) and 6.27 (0.69–57.27), respectively]. B. Non-melanoma skin cancer (NMSC). Heterogeneity I^2 = 0% for all countries. [1]The odds ratio for Georgia was not available, due to frequency of suspected NMSC being too low in exposed individuals

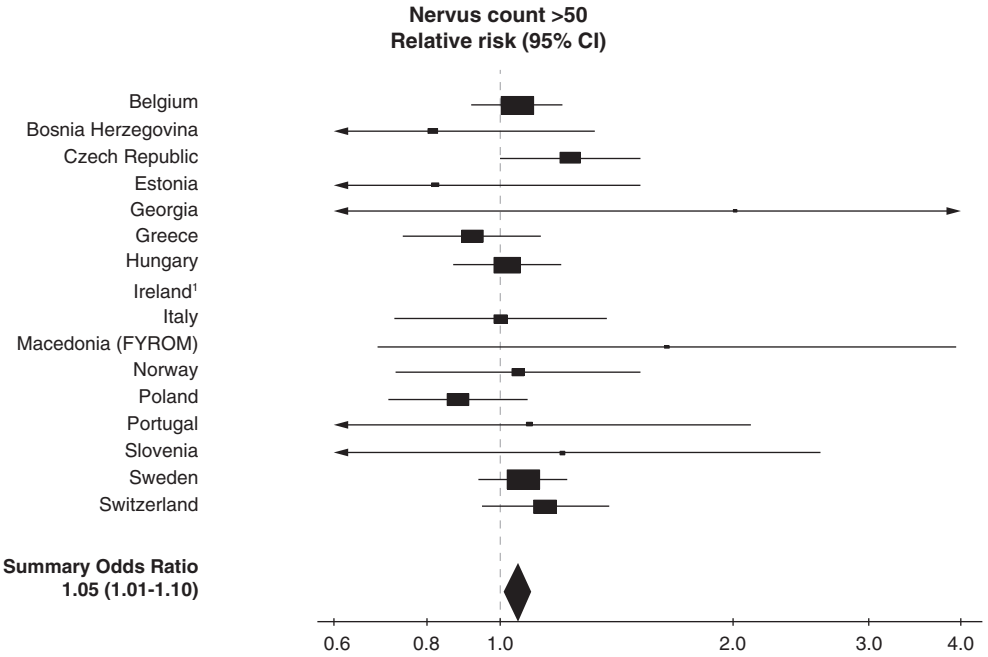

Figure 2 Forest plot of association of high nevus count (>50 nevi) with ever use of sunbeds. Heterogeneity $I^2 = 0\%$ for all countries. All odds ratios are adjusted for age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use. FYROM, Former Yugoslav Republic of Macedonia. [1]The odds ratio for Ireland was not available, due to frequency of high nevus count being too low in exposed individuals.

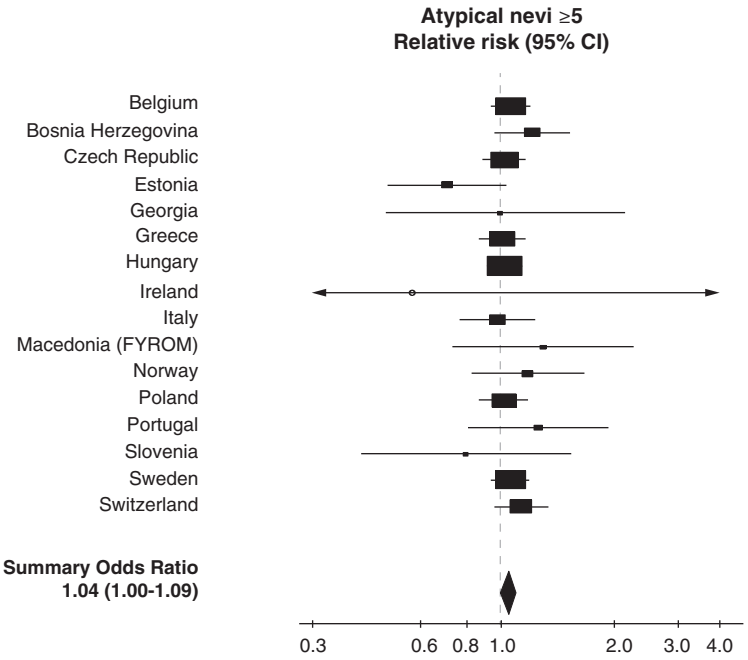

Figure 3 Forest plot of association of ≥1 atypical nevus with ever use of sunbeds. Heterogeneity $I^2 = 0\%$ for all countries. All odds ratios are adjusted for age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use. FYROM, Former Yugoslav Republic of Macedonia.

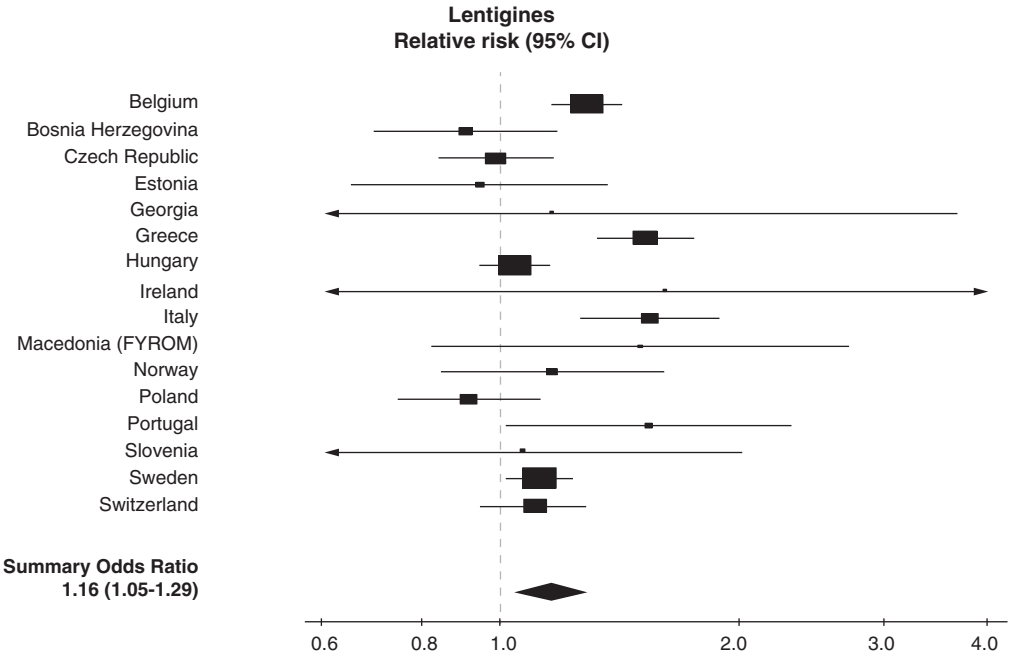

Figure 4 Forest plot of association of lentigines on back/chest with ever use of sunbeds. Heterogeneity I^2 = 68% for all countries. All odds ratios are adjusted for age, gender, education, skin type, family history of melanoma, personal history of skin cancer, any sun exposure and any sunscreen use. FYROM, Former Yugoslav Republic of Macedonia.

lentigines;[38] this suggests an acute phenomenon rather than a chronic one, consistent with excessive UV exposure resulting from indoor tanning.

The potential of sunbed exposure to cause melanocytic atypia might explain the significant, though small association of ever sunbed use with atypical nevi in our multivariate analysis. In 1989, Roth *et al.*[16] described the case of a woman developing several dysplastic junctional nevi after an extended period of UVA tanning booth use. To our knowledge, the present study provides the first significant association between ever use of sunbeds and presence of atypical nevi in a large multivariate analysis. Evidently, this result is of utmost importance as atypical nevi represent a significant risk factor for melanoma development.[39]

Exposure to solar UV radiation has been associated with high nevus count by a number of investigations.[40–58] The question arises as to whether exposure to UV radiation coming from sunbeds is also associated with high nevus count. Recently, Little and Lloyd observed that patients with a self-reported history of sunbed use displayed an increased frequency of multiple junctional nevi located on the buttocks, an area usually protected from sun exposure but not from tanning bed exposure.[13] Previously, Gellen *et al.*[11] reported in a large sample of Hungarian students that sunbed users were twice as likely to have >20 nevi as compared to non-users, after adjustment for skin colour, sunbathing and sunburn. Li *et al.*[12] found a significant, independent association between increasing number of annual sunbed sessions and higher nevus count in a large cohort of women. Our results corroborate these data by showing a significant association of sunbed ever use with high nevus count (>50 nevi), after controlling for any type of sun exposure and other confounders. Although this study was not designed to assess whether sunbed use increases the number of nevi and although we cannot exclude with absolute certainty that some solar lentigines were misdiagnosed as melanocytic nevi during the Euromelanoma screening, we believe this result is highly important because it suggests that sunbed use might possibly increase the number of nevi – and therefore the risk of melanoma[39,59,60] – independently from sun exposure. At any rate, individuals with high nevus count and/or atypical nevi should be particularly discouraged to use sunbeds because of a possible multiplicative effect of high nevus count, atypical nevi and indoor tanning on melanoma risk. Indeed, it was suggested that the negative impact of sunbed exposure on melanoma risk is generally greater in individuals with high-risk phenotypes.[25]

The obvious limitation of this study was that two important clinical endpoints (melanoma and NMSC) were represented by suspected rather than histopathologically confirmed lesions. However, we performed a strict data quality control (that forced us to exclude data of 14 countries from the main analysis) to ensure the reliability of our data; the fact that we obtained a SOR for suspected melanoma similar to the risk estimates obtained for histopathologically proven melanomas by previous

meta-analyses supports the validity of our results. Another limitation is that the study was not population based but instead included participants self-attending a skin cancer screening event: therefore, a selection bias (either towards a more responsible or irresponsible population as for indoor tanning practices; or towards more aware participants as for the presence of suspected lesions) as well as a desirability bias [under-reporting of a 'bad habit' (sunbed use) to please doctors] cannot be excluded. As a consequence, one might expect a high prevalence of risk factors among the study participants, who may be more likely to attend if they have noticed a suspicious lesion on their body or if they have used a sunbed in the past and are worried about skin cancer risk. However, if over-reporting of sunbed use by subjects aware of the risk may have rendered the association with the clinical endpoints stronger, on the other hand, under-reporting of sunbed use could have influenced the results towards a weaker association, thus producing a counterbalance of the above-mentioned limitations. A further limitation is that the study was retrospective, therefore, a recall bias cannot be ruled out.[61] The strengths of the study were the extremely large sample size, the use of a standardized questionnaire in all participating countries, the strict control of the quality of the data and the thorough multivariate analysis that included many potential confounders.

In conclusion, we presented a large, comprehensive European investigation about multiple skin cancer risk factors connected to sunbed use among participants in the Euromelanoma campaign. This study indicates that indoor tanning is associated with important risk factors for melanoma such as high nevus count, presence of atypical nevi and lentigines, as well as suspicion of melanoma. In order to reduce the prevalence of melanoma risk factors, avoidance or discontinuation of sunbed exposure should always be encouraged, especially but not exclusively in individuals with high-risk phenotypes such as high nevus count and atypical nevi.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Countries' participation in the Euromelanoma campaign over time (2009–2014).
Table S2. Age of participants for each country.
Table S3. Prevalence of actinic keratoses according to age group for each participating country.
Table S4. Descriptive features of the population from the 16 countries eligible for the multivariate risk analysis.