Article:
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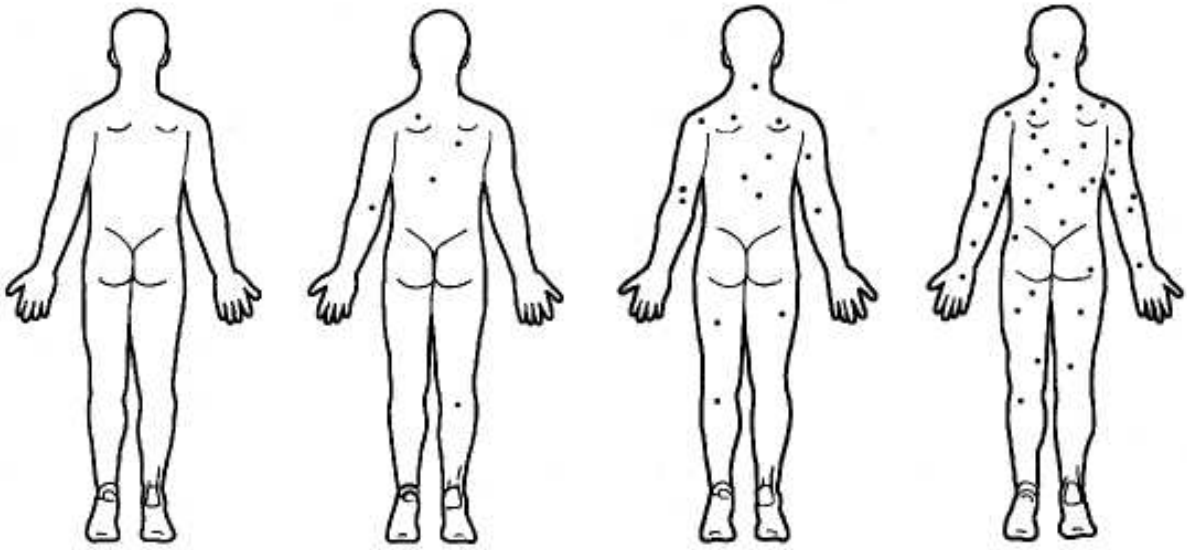
Supplementary Online Content

eFigure1. Nevus density pictograms used in the Australian Melanoma Family Study



None Few Some Many

eTable1. Australian melanoma incidence and competing mortality rates per 100,000 by age group and sex from 2007-2009

Men		
Age	Melanoma incidence rate (h_1*) [1]	Mortality rate without melanoma (h_2) [1,2]
0 to 4	0	117.17
5 to 9	0	10.57
10 to 14	1.00	11.91
15 to 19	3.00	49.08
20 to 24	6.90	70.56
25 to 29	11.85	83.16
30 to 34	20.25	98.61
35 to 39	29.48	121.53
40 to 44	37.87	159.55
45 to 49	52.03	233.14
50 to 54	79.01	350.80
55 to 59	106.80	520.83
60 to 64	140.09	824.74
65 to 69	180.62	1364.82
70 to 74	222.15	2256.97
75 to 79	269.59	4056.83
80 to 84	331.62	7169.49
Women		
Age	Melanoma incidence rate (h_1*) [1]	Mortality rate without melanoma (h_2) [1,2]
0 to 4	0	93.42
5 to 9	0.10	8.85
10 to 14	0.40	9.40
15 to 19	3.18	23.27
20 to 24	10.70	26.42
25 to 29	16.10	32.63
30 to 34	24.79	42.51
35 to 39	34.43	61.50
40 to 44	42.40	90.25
45 to 49	53.20	143.89
50 to 54	60.29	215.91
55 to 59	74.41	318.69
60 to 64	85.42	502.90
65 to 69	93.39	799.20
70 to 74	109.02	1366.44
75 to 79	123.96	2476.91
80 to 84	135.82	4793.44

eTable2. Distributions of the risk factors in the melanoma risk prediction model in the development and independent validation studies

	Australian Melanoma Family Study[a]		Western Australia Melanoma Study[b]		Leeds Melanoma Case-Cotnrol Study		Epigene-QSkin Study[c]		Swedish Women's Lifestyle and Health Cohort Study[d]	
Predictor variable	Cases n (%)	Control n(%)	Cases n(%)	Control n (%)	Cases n(%)	Control n (%)	Cases n (%)	Control n (%)	Cases n (%)	Control n (%)
Age										
10-14	0	0	6 (1.2)	6 (1.2)	0	0	0	0	0	0
15-19	0	0	15 (2.9)	9 (1.8)	7 (0.7)	0	2 (0.3)	0	0	0
20-24	18 (2.9)	3 (0.7)	27 (5.3)	33 (6.5)	21 (2.2)	4 (0.8)	12 (1.6)	0	0	0
25-29	60 (9.6)	31 (7.5)	45 (8.8)	50 (9.8)	35 (3.6)	4 (0.8)	21 (2.7)	0	0	0
30-34	123 (19.6)	64 (15.5)	54 (10.6)	49 (9.6)	68 (7.1)	17 (3.3)	28 (3.7)	0	53 (19.4)	10108 (20.7)
35-39	191 (30.4)	143 (34.5)	46 (9.0)	42 (8.2)	80 (8.3)	39 (7.6)	31 (4.0)	0	66 (24.2)	12252 (25.1)
40-44	236 (37.6)	173 (41.8)	53 (10.4)	54 (10.6)	97 (10.1)	45 (8.8)	44 (5.7)	5102 (11.7)	65 (23.8)	12173 (24.9)
45-49	0	0	31 (6.1)	31 (6.1)	104 (10.8)	43 (8.4)	57 (7.4)	6570 (15.0)	82 (30.0)	12728 (26.0)
50-54	0	0	38 (7.4)	39 (7.6)	115 (12.0)	68 (13.3)	65 (8.5)	8005 (18.3)	7 (2.6)	1654 (3.4)
55-59	0	0	52 (10.2)	57 (11.2)	117 (12.2)	70 (13.6)	108 (14.1)	8584 (19.6)	0	0
60-64	0	0	54 (10.6)	46 (9.0)	109 (11.4)	61 (11.9)	123 (16.1)	7942 (18.1)	0	0
65-69	0	0	36 (7.0)	43 (8.4)	113 (11.8)	66 (12.9)	106 (13.8)	7157 (16.3)	0	0
70-74	0	0	42 (8.2)	36 (7.0)	87 (9.1)	73 (14.2)	81 (10.6)	413 (0.9)	0	0
75-79	0	0	12 (2.3)	16 (3.1)	6 (0.6)	22 (4.3)	88 (11.5)	5 (0.01)	0	0
Missing	0	0	0	0	1 (0.1)	1 (0.2)	0	0	0	0
Sex										
Female	386 (61.5)	249 (60.1)	278 (54.4)	278 (54.4)	575 (59.9)	302 (58.9)	244 (31.9)	23878 (54.5)	273 (100)	48915 (100)
Male	242 (38.5)	165 (39.9)	233 (45.6)	233 (45.6)	384 (40.0)	211 (41.1)	522 (68.1)	19900 (45.5)	0	0
Missing	0	0	0	0	1 (0.1)	0	0	0	0	0
Hair colour										
Black/ dark brown	163 (26.0)	163 (39.4)	165 (32.3)	216 (42.3)	169 (17.6)	149 (29.0)	247 (32.2)	18863 (43.1)	37 (13.6)	13776 (28.2)
Light brown	245 (39.0)	175 (42.3)	223 (43.6)	204 (39.9)	454 (47.3)	258 (50.3)	245 (32.0)	16090 (36.8)	122 (44.7)	20816 (42.6)
Blonde	140 (22.3)	53 (12.8)	85 (16.6)	65 (12.7)	182 (19.0)	68 (13.3)	159 (20.8)	6089 (13.9)	91 (33.3)	12096 (24.7)
Red	72 (11.5)	19 (4.6)	33 (6.5)	20 (3.9)	121 (12.6)	29 (5.7)	104 (13.6)	2475 (5.7)	16 (5.9)	1491 (3.0)
Missing	8 (1.3)	4 (1.0)	5 (1.0)	6 (1.2)	34 (3.5)	9 (1.8)	11 (1.4)	261 (0.6)	7 (2.6)	736 (1.5)

Table continued

	Australian Melanoma Family Study[a]		Western Australia Melanoma Study[b]		Leeds Melanoma Case-Control Study		Epigene-QSkin Study[c]		Swedish Women's Lifestyle and Health Cohort Study[d]	
Predictor variable	Cases n (%)	Control n(%)	Cases n(%)	Control n (%)	Cases n(%)	Control n (%)	Cases n (%)	Control n (%)	Cases n (%)	Control n (%)
Naevi density (self-reported)										
None	21 (3.3)	33 (8.0)	203 (39.7)	302 (59.1)	67 (7.0)	100 (19.5)	152 (19.8)	12068 (27.6)	175 (64.1)	38825 (79.4)
Few	176 (28.0)	197 (47.6)	199 (38.9)	173 (33.9)	345 (35.9)	258 (50.3)	332 (43.3)	22621 (51.7)	69 (25.3)	7196 (14.7)
Some	268 (42.7)	133 (32.1)	61 (11.9)	28 (5.5)	346 (36.0)	121 (23.6)	193 (25.2)	6485 (14.8)	13 (4.8)	987 (2.0)
Many	152 (24.2)	45 (10.9)	48 (9.4)	8 (1.6)	134 (14.0)	34 (6.6)	89 (11.6)	1427 (3.3)	5 (1.8)	235 (0.5)
Missing	11 (1.8)	6 (1.4)	0	0	68 (7.1)	0	0	1177 (2.7)	11 (4.0)	1672 (3.4)
First-degree family history of melanoma										
No	570 (90.8)	395 (95.4)	459 (89.8)	488 (95.5)	899 (93.6)	503 (98.1)	554 (72.3)	27030 (61.7)	268 (98.2)	48046 (98.2)
Yes	58 (9.2)	19 (4.6)	52 (10.2)	23 (4.5)	51 (5.3)	10 (1.9)	212 (27.7)	10065 (23.0)	4 (1.5)	323 (0.7)
Missing	0	0	0	0	10 (1.0)	0	0	6683 (15.3)	1 (0.4)	546 (1.1)
Personal history of non-melanoma skin cancer										
No	575 (91.6)	400 (96.6)	440 (86.1)	487 (95.3)	924 (96.3)	502 (97.9)	308 (40.2)	16879 (38.6)	273 (100)	48906 (100)
Yes	50 (8.0)	12 (2.9)	71 (13.9)	24 (4.7)	22 (2.3)	10 (1.9)	458 (59.8)	26392 (60.3)	0	9
Missing	3 (0.5)	2 (0.5)	0	0	14 (1.5)	1 (0.2)	0	507 (1.2)	0	0
Number of sunbed sessions										
None	485 (77.2)	340 (82.1)	468 (91.6)	466 (91.2)	454 (47.3)	271 (52.8)	766 (100)	38925 (88.9)	65 (23.8)	15435 (31.6)
1 to 10	74 (11.8)	46 (11.1)	43 (8.4)	45 (8.8)	165 (17.2)	91 (17.7)	0	3531 (8.1)	0	0
>10	69 (11.0)	28 (6.8)	0	0	284 (29.6)	137 (26.7)	0	1013 (2.3)	208 (76.2)	33480 (68.4)
Missing	0	0	0	0	57 (5.9)	14 (2.7)	0	309 (0.7)	0	0
Total participants included in the analyses	628 (100)	414 (100)	485 (94.9)	490 (95.9)	835 (87.0)	496 (96.7)	753 (98.3)	35453 (81.0)	255 (93.4)	46267 (94.6)

[a] In the Australian Melanoma Family Study, the ages were at the time of questionnaire completion.
[b] In the Western Australian Melanoma Study, the number of raised nevi on the arms were matched to the approximate nevus counts shown on the Australian Melanoma Family Study nevus density pictograms and sunlamp was used to infer sunbed use.
[c] In the Epigene Study, sunbed variable was not collected , thus for this analysis, we assumed none of its participants used sunbeds.
[d] In the Swedish Women's Lifestyle and Health Cohort Study, the number of large asymmetric nevi on lower limbs were matched to the approximate nevus counts shown on the Australian Melanoma Family Study nevus density pictograms.

eMethods1. Area under the receiver operating curve (AUC) after reweighting the age and sex distribution of the case-control study controls to the general population

In the Western Australia Melanoma Study[3] and the Leeds Melanoma Case-Control Study[4,5] the case-control study controls were frequency-matched to the study cases by age (within 5 years) and sex. Therefore the distribution of risk among the study controls may be more similar to the study cases than to the general population. To correct for potential biases in the estimates of area under the receiver operating curve (AUC), we used methods proposed by Pepe and colleagues[6] to reweight the age and sex distribution of the Western Australia Melanoma and Leeds Melanoma Case-Control studies' controls to the Western Australian and Leeds population respectively.

Firstly participants in each study were divided by their matching variables into 5 year age and sex specific groups. Secondly each age and sex specific stratum was reweighted based on its proportion of the general population to the proportion of the study controls. For example, in the Western Australian Melanoma Study, we divided the proportion of Western Australian population from 1983-1984, 13.56%, with the proportion of Western Australian Melanoma Study controls, 7.12%, to get the AUC weight of 1.91 for stratum 1, and repeated the calculations for each stratum (eTable 3). Similarly in the Leeds Melanoma Case-Control Study, we divided the proportion of Leeds population from 2005-2005, 9.10%, with the proportion of Leeds Melanoma Case-Control Study controls, 1.37%, to get the AUC weight of 6.64 for stratum 1, and repeated the calculations for each stratum (eTable 4).

The AUC was estimated by fitting the logistic regression model to melanoma outcome with controls reweighted by the proportion of general population to proportion of matched case-control study controls. This reweighting procedure did not change the AUC in the Western Australia Study and reduced the AUC in the Leeds Melanoma Case-Control Study. This may be due to the very small number of controls (and hence large weights) among the youngest age strata in the Leeds Melanoma Case-Control Study(eTable 5).

eTable3. Area under the receiver operating curve (AUC) weights in the Western Australia Melanoma Study

Strata	Age group (years)	Sex	Western Australian population 1983-1984[7] (n)	Western Australian population in 1983-1984 (%)	Western Australian Melanoma Study controls (n)	Western Australian Melanoma Study controls (%)	AUC weight
1	20-24	Female	120028	13.56	19	7.12	1.91
2	25-29	Female	118043	13.34	35	13.11	1.02
3	30-34	Female	115248	13.02	31	11.61	1.12
4	35-39	Female	102282	11.56	23	8.61	1.34
5	40-44	Female	79805	9.02	32	11.99	0.75
6	45-49	Female	67167	7.59	15	5.62	1.35
7	50-54	Female	61046	6.90	21	7.87	0.88
8	55-59	Female	58030	6.56	28	10.49	0.63
9	60-64	Female	53169	6.01	18	6.74	0.89
10	65-69	Female	43978	4.97	23	8.61	0.58
11	70-74	Female	38814	4.39	15	5.62	0.78
12	75-79	Female	27502	3.11	7	2.62	1.19
13	20-24	Male	123852	13.73	14	6.28	2.19
14	25-29	Male	122299	13.56	15	6.73	2.02
15	30-34	Male	119061	13.20	17	7.62	1.73
16	35-39	Male	110799	12.28	18	8.07	1.52
17	40-44	Male	86049	9.54	22	9.87	0.97
18	45-49	Male	71886	7.97	15	6.73	1.18
19	50-54	Male	65685	7.28	18	8.07	0.90
20	55-59	Male	61498	6.82	29	13.00	0.52
21	60-64	Male	51145	5.67	28	12.56	0.45
22	65-69	Male	37928	4.20	19	8.52	0.49
23	70-74	Male	31535	3.50	19	8.52	0.41
24	75-79	Male	20500	2.27	9	4.04	0.56

eTable4. Area under the receiver operating curve (AUC) weights in the Leeds Melanoma Case-Control Study

Strata	Age group (years)	Sex	Yorkshire population 2000-2005 (n)	Yorkshire population in 2000-2005 (%)	Leeds Melanoma Case-Control Study controls (n)	Leeds Melanoma Case-Control Study controls (%)	AUC weight
1	20-24	Female	988833	9.10	4	1.37	6.64
2	25-29	Female	912911	8.40	1	0.34	24.54
3	30-34	Female	1093420	10.06	15	5.14	1.96
4	35-39	Female	1157162	10.65	22	7.53	1.41
5	40-44	Female	1092773	10.06	33	11.30	0.89
6	45-49	Female	977603	9.00	31	10.62	0.85
7	50-54	Female	981023	9.03	43	14.73	0.61
8	55-59	Female	935492	8.61	44	15.07	0.57
9	60-64	Female	770520	7.09	33	11.30	0.63
10	65-69	Female	718552	6.61	24	8.22	0.80
11	70-74	Female	655924	6.04	32	10.96	0.55
12	75-79	Female	579585	5.34	10	3.42	1.56
13	20-29	Male	1884685	18.15	1	0.49	37.03
14	30-34	Male	1058589	10.20	2	0.98	10.40
15	35-39	Male	1131577	10.90	16	7.84	1.39
16	40-44	Male	1078801	10.39	11	5.39	1.93
17	45-49	Male	972114	9.36	11	5.39	1.74
18	50-54	Male	973834	9.38	24	11.76	0.80
19	55-59	Male	923894	8.90	24	11.76	0.76
20	60-64	Male	740763	7.13	28	13.73	0.52
21	65-69	Male	654917	6.31	40	19.61	0.32
22	70-74	Male	541474	5.21	37	18.14	0.29
23	75-79	Male	422556	4.07	10	4.90	0.83

eTable5. Reweighted area under the receiver operating curve (AUC) in the Western Australia Melanoma Study and Leeds Melanoma Case-Control Study

Study	AUC (95% CI)	Reweighted AUC (95% CI)
Western Australian Melanoma Study	0.66 (0.63-0.69)	0.65 (0.65-0.72)
Leeds Melanoma Case-Control Study	0.67 (0.65-0.70)	0.60 (0.57-0.62)

eMethods2. Model recalibration using Swedish melanoma incidence and mortality rates to estimate 20 year absolute risk

Model calibration is sensitive to trends in incidence rates. In breast cancer risk prediction, the Gail model, which combined relative risk for breast cancer risk factors with U.S. breast cancer incidence and competing mortality rates from 1983 to 1987, significantly under-predicted breast cancer risk when it was externally validated on independent datasets collected from 1993 to 2006.[8] Recognizing that breast cancer incidence rates have increased in the 1990s, the Gail model was updated with U.S. breast cancer incidence and competing mortality rates from 1995 to 2003, and subsequently model calibration improved. [8]

Melanoma incidence rates in Sweden have been increasing since the 1990s but are lower compared with Australian rates.[9] We recalibrated the model firstly using Swedish melanoma incidence and competing mortality rates from 2009-2011 (eTable 6) and then using rates from 1991-2011 (eTable 7).[10,11] When Swedish melanoma incidence and competing mortality rates from 2009-2011 were used to estimate the 20 year absolute risk, calibration was very good with close agreement between predicted and observed numbers of incident melanomas over 20 years of follow up across all deciles of predicted risk(eFigure 2). In the lowest decile of risk, for example, the model predicted an average of 8.17 melanoma diagnoses, while 7 melanoma diagnoses were observed over 20 years of follow up. The calibration-in-the-large was 0.21 (95% CI 0.21 to 0.22), and calibration slope was 0.82 (95% CI 0.66 to 0.98), indicating that the recalibrated model could provide an over-prediction of risk.

As in breast cancer risk prediction, when appreciably lower Swedish melanoma incidence rates from 1991-2011 were used to estimate the 20 year absolute risk, calibration was poorer, with poorer agreement between predicted and observed numbers of incident melanomas over 20 years of follow up across all deciles of predicted risk (eFigure 3). In the lowest decile of risk, for example, the model predicted an average of 5.93 melanoma diagnoses, while 11 melanoma diagnoses were observed over 20 years of follow up. The calibration-in-the-large was 0.55 (95%CI 0.54 to 0.55), and calibration slope

was 0.82 (95% CI 0.66 to 0.97), indicating that the recalibrated model could provide an under-prediction of risk.

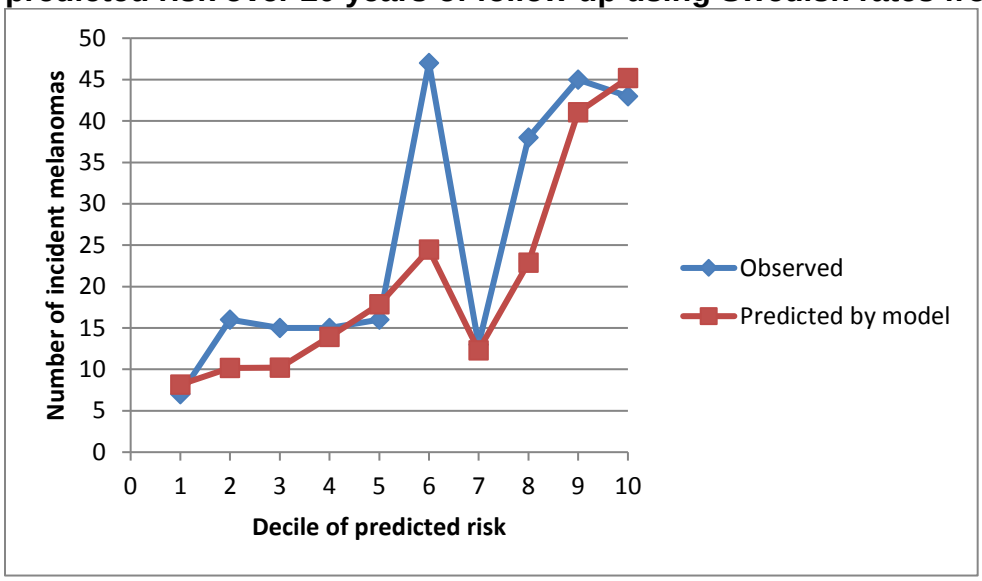
eTable6. Melanoma incidence and mortality without melanoma per 100,000 by age group for Swedish women 2009-2011

Age	Melanoma incidence rate (h_1*) [10]	Mortality rate without melanoma (h_2)[10,11]
0 to 4	0	55.95
5 to 9	0	8.34
10 to 14	0.80	8.39
15 to 19	1.77	20.37
20 to 24	5.27	23.30
25 to 29	9.97	26.22
30 to 34	19.17	31.72
35 to 39	26.27	46.25
40 to 44	33.10	70.13
45 to 49	36.97	119.97
50 to 54	36.80	214.46
55 to 59	43.60	341.99
60 to 64	45.87	577.49
65 to 69	60.83	858.12
70 to 74	62.60	1489.53
75 to 79	67.07	2657.08
80 to 84	72.03	5164.23

eTable7. Melanoma incidence and mortality without melanoma per 100,000 by age group for Swedish women 1991-2011

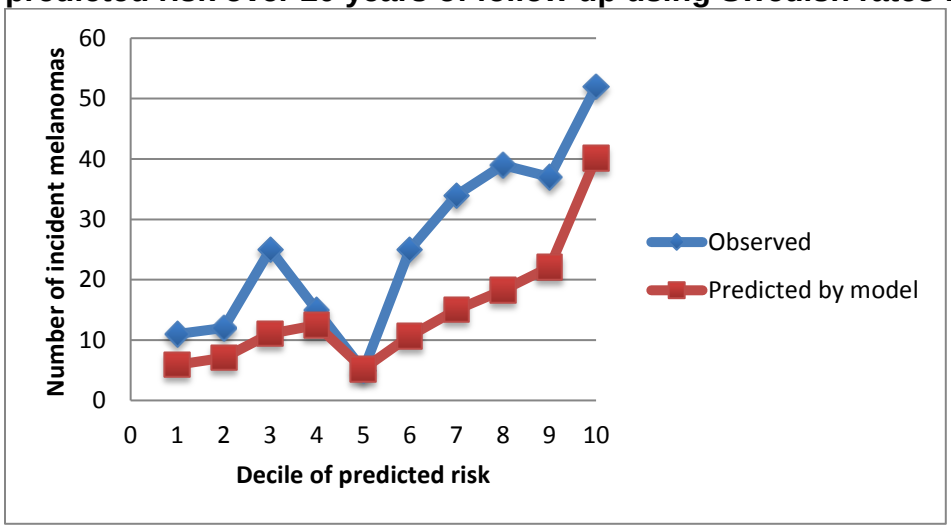
Age	Melanoma incidence rate(h_1*)[10]	Mortality rate without melanoma(h_2)[10,11]
0 to 4	0	75.29
5 to 9	0	8.86
10 to 14	0.22	10.42
15 to 19	1.92	22.11
20 to 24	5.59	25.86
25 to 29	10.07	29.02
30 to 34	14.17	38.10
35 to 39	18.01	57.27
40 to 44	23.16	92.06
45 to 49	24.73	159.33
50 to 54	28.93	256.19
55 to 59	31.69	402.30
60 to 64	35.65	637.59
65 to 69	39.54	1025.93
70 to 74	41.47	1752.19
75 to 79	46.35	3143.30
80 to 84	48.01	5966.29

eFigure2. Observed and predicted numbers of incident melanomas by deciles of predicted risk over 20 years of follow up using Swedish rates from 2009-2011[a]



[a]Estimated using Swedish melanoma incidence and competing mortality rates for women from 2009-2011[10,11]

eFigure3. Observed and predicted numbers of incident melanomas by deciles of predicted risk over 20 years of follow up using Swedish rates from 1991-2011[a]



[a]Estimated using Swedish melanoma incidence and competing mortality rates for women from 1991-2011[10,11]

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