

Supplementary Table 1: Anatomic distribution and adjusted odds ratios (ORs) for tumor development at specific anatomic site compared to trunk for men and women

	Non-carriers		CDKN2A carriers		CDK4 carriers		CDKN2A carriers vs. Non-carriers		CDK4 carriers vs. Non-carriers		CDK4 carriers vs. CDKN2A carriers		CDKN2A carriers vs. Non-carriers	CDK4 carriers vs. Non-carriers	CDK4 carriers vs. CDKN2A carriers
	N	%	N	%	N	%	OR ¹	95% CI	OR ¹	95% CI	OR ¹	95% CI	Global P-value	Global P-value	Global P-value
Female															
Total melanomas	73	100%	186	100%	34	100%									
Anatomic site													0.14 ²	0.004 ²	0.001 ²
Trunk	39	53%	56	30%	3	9%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	34	47%	130	70%	31	91%	3.54**	1.80-6.94	13.6**	3.62-50.9	3.84*	1.10-13.4	0.04 ³	0.0002 ³	0.0001 ³
Lower extremities	14	19%	56	30%	17	50%	3.94*	1.68-9.21	18.4**	4.34-78.1	4.68*	1.26-17.4			
Upper extremities	12	16%	52	28%	12	35%	3.06*	1.31-7.15	11.1*	2.48-49.9	3.63	0.90-14.7			
Head and neck	8	11%	22	12%	2	6%	4.01	0.96-16.8	9.73	0.74-128	2.43	0.22-26.3			
Male													Global P-value	Global P-value	Global P-value
Total melanomas	84	100%	162	100%	20	100%									
Anatomic site													0.14 ²	0.046 ²	0.006 ²
Trunk	48	57%	77	48%	4	20%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	36	43%	85	53%	16	80%	2.02	0.87-4.69	8.62*	1.80-41.2	4.27*	1.03-17.7	0.046 ³	0.10 ³	0.007 ³
Lower extremities	8	10%	21	13%	5	25%	1.95	0.66-5.81	9.38*	1.78-49.4	4.80*	1.17-19.8			
Upper extremities	16	19%	27	17%	5	25%	0.96	0.39-2.35	2.90	0.59-14.3	3.03	0.70-13.1			
Head and neck	12	14%	37	23%	6	30%	5.96*	1.56-22.7	25.6*	3.26-202	4.30	0.83-22.5			

* $P < .05$

** $P < .001$

¹ Multinomial random effects model adjusting for within individual and within family correlations, age at diagnosis, and superficial spreading melanoma subtype

² Global p-value comparing differences in melanoma distribution (trunk, lower extremities, upper extremities, or head and neck) between groups with adjustments for within individual and within family correlations, age at diagnosis, and superficial spreading melanoma subtype

³ Global p-value comparing differences in melanoma distribution (trunk or non-truncal) between groups with adjustments for within individual and within family correlations, age at diagnosis, and superficial spreading melanoma subtype

Supplementary Table 2: Anatomic distribution and adjusted odds ratios (ORs) for tumor development at specific anatomic site compared to trunk according to median age of diagnosis

	Non-carriers		CDKN2A carriers		CDK4 carriers		CDKN2A carriers vs. Non-carriers		CDK4 carriers vs. Non-carriers		CDK4 carriers vs. CDKN2A carriers		CDKN2A carriers vs. Non-carriers	CDK4 carriers vs. Non-carriers	CDK4 carriers vs. CDKN2A carriers
	N	%	N	%	N	%	OR ¹	95% CI	OR ¹	95% CI	OR ¹	95% CI	Global P-value	Global P-value	Global P-value
≤39 years old⁴															
Total melanomas	48	100%	203	100%	30	100%									
Anatomic site													0.046 ²	0.06 ²	0.003 ²
Trunk	30	63%	87	43%	6	20%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	18	38%	116	57%	24	80%	2.77*	1.32-5.85	8.11**	2.60-25.3	2.92*	1.10-7.77	0.03 ³	0.007 ³	0.0003 ³
Lower extremities	6	13%	35	17%	10	33%	2.18	0.78-6.11	11.9**	2.84-50.2	5.49*	1.68-18.0			
Upper extremities	8	17%	52	26%	10	33%	3.05*	1.16-8.01	6.95*	1.77-27.4	2.28	0.74-7.05			
Head and neck	4	8%	29	14%	4	13%	3.47	0.83-14.6	6.41	0.89-46.2	1.85	0.39-8.76			
>39 years old⁴															
Total melanomas	109	100%	145	100%	24	100%									
Anatomic site													0.15 ²	0.01 ²	0.006 ²
Trunk	57	52%	46	32%	1	4%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	52	48%	99	68%	23	96%	3.45*	1.01-11.8	58.0*	2.99-999	16.8*	1.08-263	0.04 ³	0.048 ³	0.007 ³
Lower extremities	16	15%	42	29%	12	50%	3.18*	1.21-8.36	43.8*	4.16-460	13.6*	1.41-133			
Upper extremities	20	18%	27	19%	7	29%	1.19	0.53-2.69	9.61	1.00-92.7	8.01	0.85-75.2			
Head and neck	16	15%	30	21%	4	17%	8.19*	1.67-40.2	97.5*	4.08-999	12.0	0.78-185			

* $P < .05$

** $P < .001$

¹ Multinomial random effects model adjusting for within individual and within family correlations, gender, and superficial spreading melanoma subtype

² Global p-value comparing differences in melanoma distribution (trunk, lower extremities, upper extremities, or head and neck) between groups with adjustments for within individual and within family correlations, gender, and superficial spreading melanoma subtype

³ Global p-value comparing differences in melanoma distribution (trunk or non-truncal) between groups with adjustments for within individual and within family correlations, gender, and superficial spreading melanoma subtype

⁴ Median age of diagnosis for all tumors (first and subsequent melanomas diagnosed) in the three groups (Non-carriers, *CDKN2A* carriers, *CDK4* carriers)

Supplementary Table 3: Anatomic distribution and adjusted odds ratios (ORs) for tumor development at specific anatomic site compared to trunk for first and subsequent melanomas

	Non-carriers		CDKN2A carriers		CDK4 carriers		CDKN2A carriers vs. Non-carriers		CDK4 carriers vs. Non-carriers		CDK4 carriers vs. CDKN2A carriers		CDKN2A carriers vs. Non-carriers	CDK4 carriers vs. Non-carriers	CDK4 carriers vs. CDKN2A carriers
	N	%	N	%	N	%	OR ¹	95% CI	OR ¹	95% CI	OR ¹	95% CI	Global P-value	Global P-value	Global P-value
First primary melanoma															
Total melanomas	117	100%	161	100%	24	100%									
Anatomic site													<.0001 ²	0.30 ²	0.01 ²
Trunk	65	56%	70	44%	5	21%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	52	44%	91	57%	19	79%	1.98*	1.07-3.67	6.17*	1.97-19.3	3.12*	1.07-9.11	0.04 ³	0.03 ³	0.002 ³
Lower extremities	16	14%	31	19%	6	25%	2.21	0.95-5.14	7.81*	1.79-34.0	2.99	0.81-11.1			
Upper extremities	22	19%	33	21%	9	38%	2.04	0.27-15.2	N.E.	N.E.	4.44*	1.12-17.6			
Head and neck	14	12%	27	17%	4	17%	N.E.	N.E.	N.E.	N.E.	8.41	0.02-999			
Melanomas diagnosed after first primary melanoma															
Total melanomas	40	100%	187	100%	30	100%									
Anatomic site													0.07 ²	0.01 ²	0.0008 ²
Trunk	22	55%	63	34%	2	7%	Reference	Reference	Reference	Reference	Reference	Reference			
Non-Truncal	18	45%	124	66%	28	93%	7.12*	1.78-28.6	63.8**	5.68-717	8.97*	1.26-64.1	0.03 ³	0.006 ³	0.0008 ³
Lower extremities	6	15%	46	25%	16	53%	5.95*	1.46-24.3	45.4**	6.06-340	7.61*	1.57-36.8			
Upper extremities	6	15%	46	25%	8	27%	3.80*	1.05-13.8	13.6*	1.81-102	3.58	0.66-19.3			
Head and neck	6	15%	32	17%	4	13%	20.9*	2.18-201	130*	5.89-999	6.19	0.69-55.8			

* $P < .05$

** $P < .001$

N.E. (no estimate)

¹ Multinomial random effects model adjusting for within individual and within family correlations, age at diagnosis, gender, and superficial spreading melanoma subtype

² Global p-value comparing differences in melanoma distribution (trunk, lower extremities, upper extremities, or head and neck) between groups with adjustments for within individual and within family correlations, age at diagnosis, gender, and superficial spreading melanoma subtype

³ Global p-value comparing differences in melanoma distribution (trunk or non-truncal) between groups with adjustments for within individual and within family correlations, age at diagnosis, gender, and superficial spreading melanoma subtype