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Melanoma Survival by Age Group: Population-Based Disparities for Adolescent and Young Adult Patients by Stage, Tumor Thickness, and Insurance Type

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Abstract

Background: Melanoma survival literature predominantly represents patients >65 years of age. Study of younger patients may reveal potential age-group-specific differences in survival outcome.

Objective: Identify factors associated with differences in melanoma survival in two age groups, adolescents and young adults (AYAs; ages 15–39) and older adults (ages 40–64).

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Methods: This population-based registry study included all cases (n=81,597) of cutaneous melanoma diagnosed at ages 15–64 from 2004–2015 in California. Age-group-specific multivariable Cox hazard regressions were used.

Results: In the adjusted, age-group-specific models, AYA patients with Stage IV melanoma had worse survival (HR: 20.39, 95%CI: 13.30–31.20) than was observed among older adults (HR: 10.79, 95%CI: 9.33–12.48). Thicker tumors and public insurance were also associated with worse survival for AYAs than observed in models for older adults. AYAs experienced better survival when detected at earlier stages.

Limitations: Registry data does not routinely collect behavioral information or family history of melanoma.

Conclusions: Survival was much worse for AYAs with stage IV melanoma than observed among older adults. To improve AYA survival, early melanoma detection is critical. Greater awareness, suspicion, and screening for AYA melanoma may disrupt delays in diagnosis and reduce the excess burden of mortality from Stage IV melanoma in young patients.

Keywords

melanoma; adolescent and young adult; AYA; survival; disparities; health services; skin cancer

INTRODUCTION

Melanoma remains one of the most common cancers among adolescents and young adults (AYAs; defined as 15–39 years of age at cancer diagnosis by the National Cancer Institute (NCI)).[1,2 3] Advanced melanoma has poor survival, particularly in AYAs (<20% for advanced stage),[4] yet information on the contributing factors remains scarce, lacking the level of detail readily available for older adult patients. While melanoma in children ages 0–14 occurs far less frequently, a body of literature exists detailing risk factors, subtypes, and clinical features that distinguish it from melanomas at older ages; childhood melanoma survival is also higher (<60% for advanced stage).[5,6] This limits our understanding of AYA melanoma survival to the experience of persons >65 years of age. Sample size can be a challenge to studying AYA melanoma. In the large, diverse population of California, where some of the highest rates of melanoma in the world occur,[7] population-based registry data supports a larger sample. It also contains the level of detail needed to identify subgroups or tumor characteristics most relevant to survival in young melanoma patients.

We performed a survival analysis of melanoma among AYAs and older adults to identify potential age-group-specific disparities in survival outcomes and describe key sociodemographic and tumor-specific factors associated with survival outcomes within the population of California.

MATERIALS & METHODS

Population & Data Sources.

Cases of cutaneous melanoma (herein “melanoma,” ICD-O-3 sites C440–449 and histology 8720–8780; total n=81,597) diagnosed at 15–64 years of age from January 1, 2004 through

December 31, 2015 were identified from the California Cancer Registry (CCR; release date January 2018), which is the State of California's population-based cancer registry. CCR data are ≥95% complete per the standards set jointly by the Centers for Disease Control's (CDC) National Program of Cancer Registries (NPCR) and the NCI's Surveillance, Epidemiology, and End Results (SEER) program. This records based-study was conducted as part of ongoing efforts to monitor melanoma survival trends by registry staff of the Cancer Surveillance Program, which is the population-based cancer registry of Los Angeles County.

All study variables were obtained from routinely collected registry data. Demographic information included age at diagnosis, race, ethnicity, sex, socioeconomic status (SES),[8,9] and insurance at diagnosis. Clinical characteristics included histological subtype, year of diagnosis, clinical stage at diagnosis,[10] tumor thickness (Breslow's depth), ulceration status, and mitotic activity present (yes/no), along with anatomic location, sentinel lymph node biopsy performed (yes/no), and chemotherapy or immunotherapy treatment.

Survival Time & Vital Status.

Observed survival was the primary outcome, reflecting survival from all causes of death after a melanoma diagnosis, to address the paucity of AYA survival information in the literature. All survival time available over the study period was used. Survival time in months was obtained from the registry variables (diagnosis date and follow-up date), which had a cut-off of December 31, 2017 for calculation of survival time. Cases were presumed alive if not known to be deceased at the last registry death clearance.

Statistical Analysis.

Multivariable Cox proportional hazard regressions were used to control for confounding and estimate adjusted hazard ratios (HR) with 95% confidence intervals (CI) for overall risk of death by age group. The assumption of proportional hazards was satisfied for each covariate when examining the correlation between time and scaled Schoenfeld residuals. No evidence of collinearity between the variables was observed. Melanoma-specific survival and analyses restricted to non-Hispanic white (NHW) cases were conducted for sensitivity analysis. Kaplan-Meier plots with log-rank tests were used to compare observed survival by age group and clinical stage for males and females. Analyses were conducted with SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Population characteristics.

There were 12,505 AYA and 69,092 older adult melanomas in 2004–2015 in California (Table I). AYA melanomas were majority female (63%); older adult melanomas were majority male (56%) (p<.0001). Melanoma was frequently detected at early clinical stages for both age groups (*in situ*/Stage 0 and Stage I; Table II), but melanoma *in situ* was detected less frequently among AYAs (30%) than in older adults (40%) (p <0.001). Distribution of Stage II-IV was similar for both age groups (all p<.0001). Ulceration was rare but observed for both age groups (5% AYA, 6% older adults; p=0.03). Mitotic activity (≥1 mitosis/mm^2) was present in 22% of AYA and 18% of older adult patients (p<.0001), but upwards of

40% these data were missing. Greater prevalence of performing sentinel lymph node biopsy was observed for AYAs (19%) than older patients (15%) (p<.0001). Mean time to surgery appeared to differ by type of insurance for AYAs and older adults, particularly by public insurance or uninsured status, but sample size was limited (data not shown). For Medicare recipients, mean time to surgery was 18 days for AYAs (n=129) and 14 days for older adults (n=849). For Medicare recipients with Stage IV melanoma, mean time to surgery was 22 days for AYAs (n<20) and 16 days for older adults (n=51). For uninsured Stage IV patients, mean time to surgery was 59 days for AYAs (n<20) and 21 days for older adults (n=34).

Adjusted Estimates for All-Cause Mortality (relative survival).

Males had worse survival than females in both age groups (Table IIIa; AYA HR: 1.43, 95%CI: 1.21–1.70; older adult HR: 1.39, 95%CI: 1.31–1.47). Medicaid, Medicare, or military insurance (vs. private insurance) was associated with higher risk of death in both age groups. Hazard ratios were larger among young patients with either Medicaid (AYA HR: 2.47; 95%CI: 1.96–3.12; older adult HR: 2.07; 95%CI: 1.89–2.27) or Medicare (AYA HR: 2.99; 95%CI: 2.01–4.45; older adult HR: 2.15; 95%CI: 1.96–2.35).

The most striking differences between AYAs and older adults were observed with clinical stage and tumor thickness (Table IIIa). In the adjusted age-group-specific models, the AYA HR for Stage IV melanoma was 20.39 (95%CI: 13.30–31.20), much larger than the older adult HR for Stage IV melanoma which was 10.79 (95%CI: 9.33–12.48) versus in situ/Stage1 melanoma. The AYA HR for thick tumors ≥4.00mm was 5.58 (95%CI: 3.56–8.73), again larger than the older adult HR of 2.87 (95%CI: 2.49–3.31). Melanoma-specific survival estimates (Mendeley Supplementary Table IIIb) and analyses restricted to NHW cases (Mendeley Supplementary Tables Va and Vb) were conducted for sensitivity analysis. NHW-restricted all-cause estimates generally supported the primary analyses; melanoma-specific estimates may be biased by inconsistent cancer-site-specific death coding procedures, warranting caution.

Kaplan Meier Plots (absolute survival).

Age-group and stage-specific survival curves by sex are shown (Figure 1, all-cause; see Mendeley Supplementary Figure 2, melanoma-specific). AYAs had better survival than older adults when detected at Stage I (p <.0001 for AYA males or females vs. older adult counterparts), Stage II (AYA males, p=0.007; AYA females p=0.129 vs older adult counterparts), and Stage III (p <.0001 for AYA males or females vs. older adult counterparts). The exception was for Stage IV disease. In Figure 1 (males, left panel), the survival curve for Stage IV AYA males crosses the curve for older adult males. At five years post-diagnosis, survival is low (<20%) and there is no longer an observable difference between younger and older adult males. A stronger survival disparity for males versus females occurred within AYA patients at every stage of disease. Up to an 11% difference in 5-year survival occurred with Stage III disease (73 vs. 84% for AYA males and females, respectively). AYA males remained at a 5% survival disadvantage with Stage IV disease (20 vs. 25% for males and females, respectively).

DISCUSSION

Our knowledge about factors impacting AYA melanoma survival has been limited by studies primarily focusing on older adults, limiting the visibility of age-group-specific differences. In this large study of melanoma from the population-based records of the California Cancer Registry, we examined survival among 12,505 AYA patients (diagnosed at ages 15–39) and 69,092 older adults (diagnosed at ages 40–64). We observed worse survival outcomes among AYA patients with Stage IV melanoma, thick tumors (≥4mm), and public insurance than observed among older adults. These disparities persisted after adjustment for sociodemographic and tumor characteristics.

Clinical Stage and Tumor Thickness.

Stage IV melanoma is understood to have poor outcomes. However, the corresponding adjusted HR of 20.39 for AYA patients is far worse than the HR of 10.79 observed in older adults. Increased levels of tumor thickness were associated with larger HRs for AYAs than older adults, yet the largest difference was for the thickest vs. thin tumors (AYA HR=5.58 and older adult HR=2.87). These differences may suggest tumor thickness is of particular prognostic value for AYA patients. It is unclear why the disparities for stage and tumor thickness by age group exist, as they were not explained by any sociodemographic or clinical factors included in our models. The sensitivity analysis for melanoma-specific mortality produced more similar stage IV HRs for AYAs and older adults, but caution is warranted due to substantial potential for outcome misclassification. Melanoma-specific cause of death is collected under a variety of circumstances at the population-level, namely, variation in access to medical examiners. Melanomas occurring at younger ages are thought to be more aggressive and, consistent with the literature,[11] we observed more mitotically active tumors among AYA patients, but their data was more complete, and numbers were small.

Socioeconomic Disparities.

Higher SES is associated with higher melanoma incidence,[12–15] and lower SES is associated with higher mortality,[16,17] presumably via challenges in access to care and delayed diagnosis/treatment. As with most of the melanoma literature, this information comes from studies of older adults. In the present study, the relationship between SES and survival was less clear for AYA patients; HRs did not consistently increase with lower SES level. One explanation may be that SES is not as reliable of a measure among AYA patients, possibly owing to the fluctuations in financial stability, insurance coverage, educational attainment, marital status, residential transience, etc., that may be more common for young patients. Further, AYAs have had less time than older adults to develop the life experience that contributes to health literacy and ability to navigate health care and insurance systems. Receipt of a cancer diagnosis without this experience may further reduce an AYA patient's ability to obtain the care they need.[18–22] Still, insurance at diagnosis provides some insights. No differences in time to treatment were observed, except for AYAs with public insurance (i.e., Medicare) or uninsured. Among Stage IV patients, mean time from diagnosis to surgery was longer for AYAs than older adults, notably with public insurance/uninsured status, suggesting potential delays that warrant further investigation. The impact of Medicaid

(due to income-qualified circumstances) or Medicare (due to disability) on AYA survival was nearly threefold the hazard observed among older adults, when compared to private insurance. This is consistent with other studies evaluating SES and AYA survival,[23–25] but those studies did not investigate melanoma, nor did they separate the impact by insurance type on survival.

Sex Differences.

A survival disparity by sex among melanoma patients has been described in older, non-Hispanic white adults,[26–29] and to a lesser degree among AYAs.[30,31] Our results are consistent, adding the disadvantage for AYA males persists after adjustment. In a European study of adults in a clinical trial with metastatic melanoma, males were at greater risk of experiencing relapse/progression than females,[32] despite having presumably higher engagement in healthcare and oversight that might otherwise partially explain sex differences in terms of outcome. The authors suggested a biological underpinning to the male survival disadvantage. A review of the role of biology in older adult melanomas noted the disparity occurred across time periods and countries,[33] perhaps reflecting inherently higher immune function and tumor suppression mechanisms among women, which may interact with sun exposure and dietary behaviors to influence vitamin D levels and oxidative response. Since melanoma incidence among AYA females is known to be higher than males,[34] related in part to tanning behaviors,[35] and women have higher health care utilization for preventive care than men,[36] it is also possible that screening and suspicion of melanoma for young males is lower relative to their female counterparts, but this remains to be examined. However, because melanoma incidence has historically been higher in older adults, there may be greater risk of late AYA melanoma detection, when prognosis is worse.

AYA-specific Complexities Accessing Healthcare.

Other issues impacting AYA survival after a melanoma diagnosis include: (1) limited availability of trials for AYAs stemming from policy and regulatory issues,[37] (2) challenges to trial participation by AYA patients,[38] and (3) age-specific developmental/behavioral barriers,[39,40] including adherence-related factors, which remain understudied, but may have large impact on outcomes. Although immunotherapy treatments have resulted in tremendous improvements for late-stage melanomas,[41] access for AYAs, combined with relatively low participation in trials and other research, remains a concern.[42,43] As more data becomes available, future studies could examine whether modern therapies close the gap in survival outcomes for late-stage melanoma in AYA and older adults.

After a melanoma is diagnosed, there is also heightened risk of subsequent melanoma, particularly when the first melanoma occurs before age 30,[44] making monthly skin self-exams and annual clinician skin exams critical for early detection. In our prior work, AYA melanoma survivors faced many barriers to receiving clinical skin exams, emphasizing the important role that skin self-exams may play as part of a cost-sensitive, guideline-recommended measure to enhance early detection among AYA patients after a primary melanoma has occurred.[45]

Study limitations included no information on prior/family skin cancer/other cancers, genetic susceptibility, comorbidities, or behaviors (i.e., ultraviolet radiation exposure via solar/artificial sources, skin protection, exercise/dietary habits, or adherence to treatment/follow-up, etc.); mitotic rate data was limited (missing in 43% AYAs, 49% older adults). Mortality for the most recent 5-years should be interpreted cautiously due to limited sample size. Modern therapies were not widely used during the study period and their impact will take time to observe. Since much of the literature focuses on overall survival (all-cause mortality), and melanoma-specified mortality has substantial potential for misclassification in population-level data, overall survival was the primary outcome. While other common causes of death may contribute to survival differences by age group, the mortality among AYAs with Stage IV disease is very likely from their melanoma. Limitations are mitigated by the large, population-based, records-based design; all cases were included, and no patient contact was necessary, reducing or eliminating selection bias; Cox hazard regressions controlled for sociodemographic and tumor characteristics. Information on excess deaths from overall estimates in each age group are not yet well-described but may be useful context for future studies evaluating the impact of modern treatments on survival.

CONCLUSIONS.

Among persons with melanoma, the risk of death was higher for AYAs for every stage of diagnosis than for older adults, notably for Stage IV melanoma, where the hazard ratio was much larger for AYAs. Although more aggressive tumors were present in AYA patients, there was no overall delay in time to treatment, suggesting potentially delayed diagnosis. A public health campaign to improve awareness of AYA melanoma, including in young persons of color, may disrupt potential delays in diagnosis and reduce the excess burden of mortality in young people. Efforts should be inclusive of adult and pediatric primary care settings, where young people are most often seen.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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IRB status:

This records based-study was conducted as part of ongoing efforts to monitor melanoma survival by registry staff of the Cancer Surveillance Program (CSP), which is the population-based cancer registry of Los Angeles County.

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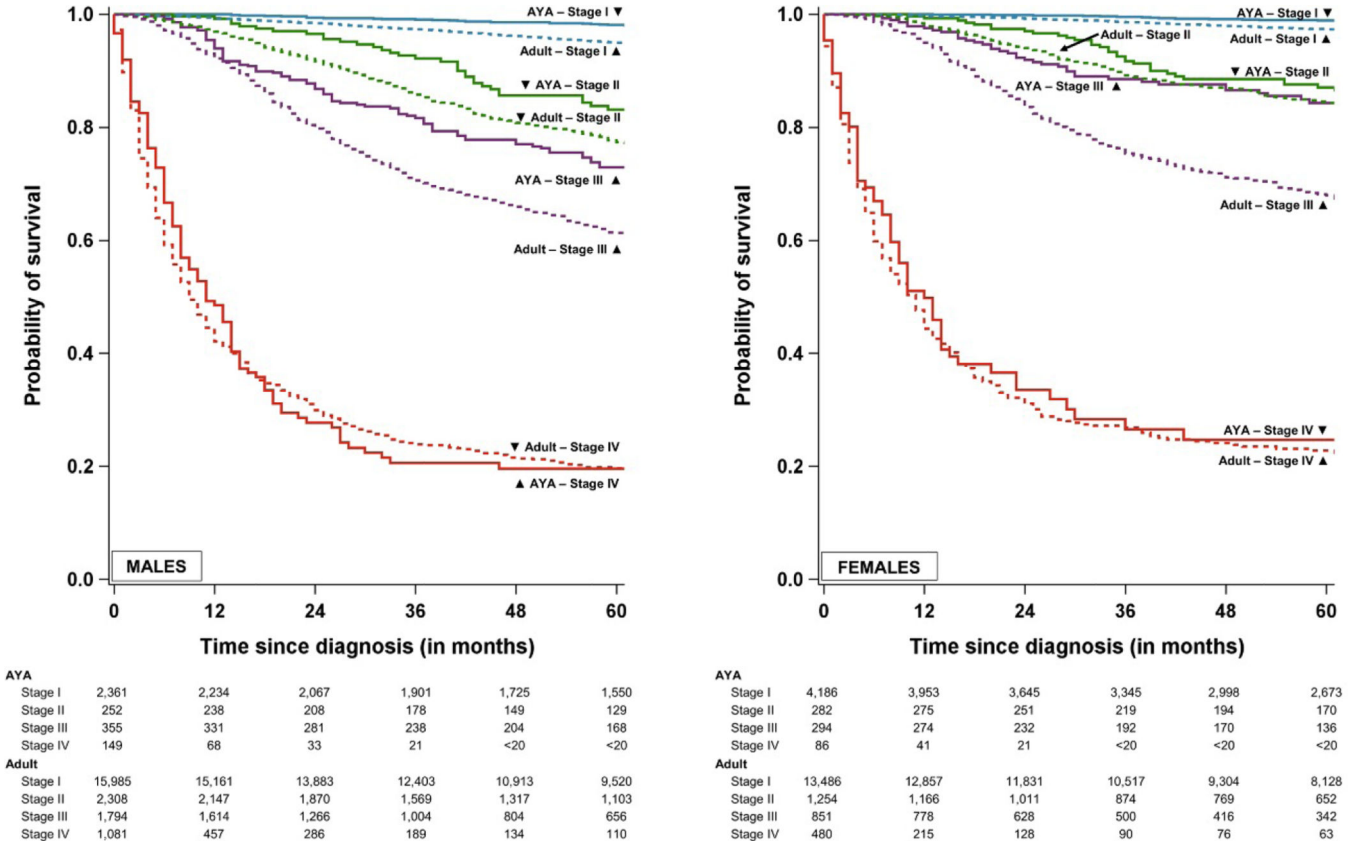
CAPSULE SUMMARY

- Melanoma literature often reflects older adults; age-group-specific differences may be underappreciated. We observed worse survival among adolescents and young adults with Stage IV and thick tumors, than among older adults.
- Earlier melanoma detection could improve adolescent and young adult survival, but requires greater melanoma awareness, suspicion, and screening for achievement.



AYA						
Stage I	2,361	2,234	2,067	1,901	1,725	1,550
Stage II	252	238	208	178	149	129
Stage III	355	331	281	238	204	168
Stage IV	149	68	33	21	<20	<20
Adult						
Stage I	15,985	15,161	13,883	12,403	10,913	9,520
Stage II	2,308	2,147	1,870	1,569	1,317	1,103
Stage III	1,794	1,614	1,266	1,004	804	656
Stage IV	1,081	457	286	189	134	110

AYA						
Stage I	4,186	3,953	3,645	3,345	2,998	2,673
Stage II	282	275	251	219	194	170
Stage III	294	274	232	192	170	136
Stage IV	86	41	21	<20	<20	<20
Adult						
Stage I	13,486	12,857	11,831	10,517	9,304	8,128
Stage II	1,254	1,166	1,011	874	769	652
Stage III	851	778	628	500	416	342
Stage IV	480	215	128	90	76	63

Figure 1. Melanoma Patients and Age-Group-Specific Survival (All Cause).

Probability of survival since diagnosis in patients with cutaneous melanoma by age group and clinical stage, stratified by sex, from the California Cancer Registry (2004–2015 with follow-up through 2017).

Table I:

Demographic Characteristics by Age Group - Melanoma Incident Cases and Deaths, California Cancer Registry, 2004 – 2015* (with follow-up through 2017)

	Cases		All-Cause Deaths		Melanoma-Specific Deaths	
	AYA (15 – 39)	**Older Adults (40 – 64)**	**AYA (15 – 39)**	**Older Adults (40 – 64)**	**AYA (15 – 39)**	**Older Adults (40 – 64)**
Total Cases	***12,505***	***69,092***	***599***	***5,824***	***459***	***3,023***
	n *(%)*	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***
Sex						
Male	4,672 (37.4)	38,348 (55.5)	353 (58.9)	4,067 (69.8)	272 (59.3)	2,128 (70.4)
Female	7,833 (62.6)	30,744 (44.5)	246 (41.1)	1,757 (30.2)	187 (40.7)	895 (29.6)
Race/Ethnicity						
Non-Hispanic White	9,496 (75.9)	57,001 (82.5)	482 (80.5)	5,200 (89.3)	372 (81.0)	2,646 (87.5)
Hispanic	1,127 (9.0)	3,355 (4.9)	94 (15.7)	S 429 (7.4)	71 (15.5)	256 (8.5)
Black	35 (0.3)	124 (0.2)	*	37 (0.6)	*	20 (0.7)
Asian/Pacific Islander	149 (1.2)	462 (0.7)	*	88 (1.5)	*	65 (2.2)
Other	1,698 (13.6)	8,132 (11.8)	*	70 (1.2)	*	36 (1.2)
Socioeconomic Status						
Lowest	818 (6.5)	3,981 (5.8)	87 (14.5)	682 (11.7)	57 (12.4)	372 (12.3)
Lower-middle	1,478 (11.8)	8,028 (11.6)	114 (19.0)	1,041 (17.9)	87 (19.0)	554 (18.3)
Middle	2,504 (20.0)	13,130 (19.0)	142 (23.7)	1,255 (21.6)	110 (24.0)	651 (21.5)
Higher-middle	3,585 (28.7)	18,165 (26.3)	127 (21.2)	1,423 (24.4)	100 (21.8)	740 (24.5)
Highest	4,120 (33.0)	25,788 (37.3)	129 (21.5)	1,423 (24.4)	105 (22.9)	706 (23.4)
Insurance Status						
Private	8,389 (67.1)	45,086 (65.3)	337 (56.3)	3,299 (56.6)	259 (56.4)	1,741 (57.6)
Medicaid	509 (4.1)	2,067 (3.0)	131 (21.9)	665 (11.4)	100 (21.8)	432 (14.3)
Medicare	118 (0.9)	2,665 (3.9)	28 (4.7)	587 (10.1)	*	294 (9.7)
Military	226 (1.8)	1,345 (2.0)	21 (3.5)	210 (3.6)	*	76 (2.5)
Uninsured	316 (2.5)	1,308 (1.9)	26 (4.3)	235 (4.0)	*	136 (4.5)
Other/Unknown	2,947 (23.6)	16,621 (24.1)	56 (9.4)	828 (14.2)	44 (9.6)	344 (11.4)
Year of Diagnosis						
2004 – 2006	3,473 (27.8)	14,893 (21.6)	225 (37.6)	2,087 (35.8)	168 (36.6)	998 (33.0)

	Cases		All-Cause Deaths		Melanoma-Specific Deaths	
Total Cases	**AYA (15 – 39)** ***12,505*** **n (%)**	**Older Adults (40 – 64)** ***69,092*** **n (%)**	**AYA (15 – 39)** ***599*** **n (%)**	**Older Adults (40 – 64)** ***5,824*** **n (%)**	**AYA (15 – 39)** ***459*** **n (%)**	**Older Adults (40 – 64)** ***3,023*** **n (%)**
2007 – 2009	3,147 (25.2)	16,834 (24.4)	180 (30.1)	1,853 (31.8)	152 (33.1)	995 (32.9)
2010 – 2012	2,772 (22.2)	16,997 (24.6)	144 (24.0)	1,245 (21.4)	106 (23.1)	674 (22.3)
2013 – 2015	3,113 (24.9)	20,368 (29.5)	50 (8.3)	639 (11.0)	33 (7.2)	356 (11.8)

* =information suppressed for case counts less than 20

Table II:

Melanoma Tumor Characteristics by Age Group, California Cancer Registry, 2004 – 2015 (with follow-up through 2017)

	Cases		All-Cause Deaths		Melanoma-Specific Deaths	
	AYA	Older Adults	AYA	Older Adults	AYA	Older Adults
Total Cases	**12,505)**	**69,092**	**599**	**5,824**	**459**	**3,023**
	n *(%)*	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***
Clinical Stage						
In-Situ	3,741 (29.9)	28,213 (40.8)	23 (3.8)	879 (15.1)	*	99 (3.3)
Stage I	6,547 (52.4)	29,471(42.7)	120 (20.0)	1,520 (26.1)	76 (16.6)	475 (15.7)
Stage II	534 (4.3)	3,562 (5.2)	84 (14.0)	761 (13.1)	67 (14.6)	474 (15.7)
Stage III	649 (5.2)	2,645 (3.8)	135 (22.5)	942 (16.2)	114 (24.8)	722 (23.9)
Stage IV	235 (1.9)	1,561 (2.3)	171 (28.5)	1,182 (20.3)	146 (31.8)	934 (30.9)
Unknown	799 (6.4)	3,640 (5.3)	66 (11.0)	540 (9.3)	51 (11.1)	319 (10.6)
Location						
Head/Neck	1,784 (14.3)	14,169 (20.5)	88 (14.7)	1,241 (21.3)	70 (15.3)	575 (19.0)
Limbs	5,946 (47.5)	30,542 (44.2)	199 (33.2)	1,849 (31.7)	140 (30.5)	881 (29.1)
Trunk	4,512 (36.1)	22,753 (32.9)	180 (30.1)	1,800 (30.9)	139 (30.3)	875 (28.9)
Other	263 (2.1)	1,628 (2.4)	132 (22.0)	934 (16.0)	110 (24.0)	692 (22.9)
Histology [1]						
SSM	3,348 (26.8)	14,410 (20.9)	78 (13.0)	834 (14.3)	58 (12.6)	329 (10.9)
NM	389 (3.1)	2,175 (3.1)	74 (12.4)	646 (11.1)	61 (13.3)	464 (15.3)
ALM	84 (0.7)	442 (0.6)	*	74 (1.3)	*	52 (1.7)
LMM	219 (1.8)	5,626 (8.1)	*	280 (4.8)	*	40 (1.3)
NOS/Other	8,465 (67.7)	46,439 (67.2)	433 (72.3)	3,990 (68.5)	329 (71.7)	2,138 (70.7)
Tumor Thickness						
In-Situ	3,741 (29.9)	28,213 (40.4)	23 (3.8)	879 (15.1)	*	99 (3.3)
<1.00mm	5,950 (47.6)	26,316 (38.1)	90 (15.0)	1,246 (21.4)	49 (10.7)	380 (12.6)
1.00-<2.00mm	1,217 (9.7)	5,737 (8.3)	87 (14.5)	708 (12.2))	78 (17.0)	404 (13.4)
2.00-<4.00mm	518 (4.1)	2,761 (4.0)	87 (14.5)	656 (11.3)	70 (15.3)	453 (15.0)
≥4.00mm	336 (2.7)	2,110 (3.1)	112 (18.7)	849 (14.6)	92 (20.0)	630 (20.8)
Unknown	743 (5.9)	3,955 (5.7)	200 (33.4)	1,486 (25.5)	165 (35.9)	1,057 (35.0)
Ulceration						
No	10,922 (87.3)	59,949 (86.8)	300 (50.1)	3,389 (58.2)	206 (44.9)	1,344 (44.5)
Yes	638 (5.1)	3,927 (5.7)	154 (25.7)	1,231 (21.1)	135 (29.4)	882 (29.2)
Unknown	945 (7.6)	5,216 (7.5)	145 (24.2)	1,204 (20.7)	118 (25.7)	797 (26.4)
Immunotherapy						
No	12,070 (96.5)	67,451 (97.6)	472 (78.8)	5,217 (89.6)	348 (75.8)	2,534 (83.8)
Yes	390 (3.1)	1,402 (2.0)	126 (21.0)	555 (9.5)	111 (24.2)	452 (15.0)
Unknown	45 (0.4)	239 (0.3)	*	52 (0.9)	*	37 (1.2)
SLN Biopsy [2]						

	Cases		All-Cause Deaths		Melanoma-Specific Deaths	
	AYA	**Older Adults**	**AYA**	**Older Adults**	**AYA**	**Older Adults**
Total Cases	**12,505)**	**69,092**	**599**	**5,824**	**459**	**3,023**
	n *(%)*	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***	**n *(%)***
No	10,022 (80.1)	58,047 (84.0)	428 (71.5)	4,397 (75.5)	319 (69.5)	2,119 (70.1)
Yes	2,413 (19.3)	10,699 (15.5)	155 (25.9)	1,303 (22.4)	126 (27.5)	825 (27.3)
Unknown	70 (0.6)	346 (0.5)	*	124 (2.1)	*	79 (2.6)
Chemotherapy						
No	12,202 (97.6)	67,854 (98.2)	450 (75.1)	5,097 (87.5)	326 (71.0)	2,429 (80.4)
Yes	248 (2.0)	998 (1.4)	139 (23.2)	667 (11.5)	124 (27.0)	550 (18.2)
Unknown	55 (0.4)	240 (0.3)	*	60 (1.0)	*	44 (1.5)
Mitotic Activity Present (2010–2015 only) [3]						
Total Cases	**5,885**	**37,365**	**194**	**1,884**	**139**	**1,030**
No	2,089 (35.5)	12,227 (32.7)	*	247 (13.1)	*	67 (6.5)
Yes	1,278 (21.7)	6,734 (18.0)	62 (32.0)	597 (31.7)	44 (31.7)	378 (36.7)
Unknown/Missing	2,518 (42.8)	18,404 (49.3)	113 (58.2)	1,040 (55.2)	83 (59.7)	585 (56.8)

*=information suppressed for case counts less than 20

[1]Histology definitions: SSM=Superficial Spreading Melanoma, NM=Nodular Melanoma, ALM=Acral Lentiginous Melanoma. LMM=Lentigo Maligna Melanoma, NOS/Other=Malignant Melanoma, NOS, and other rare subtypes.

[2]SLN=Sentinel Lymph Node; indicates biopsy was performed.

[3]Mitotic activity information was not routinely collected in this registry data until 2010; defined as present if ≥1 mitosis/mm^2

Table IIIa:

Hazard Ratio for Risk of All-Cause Death, by Age Group, in patients with cutaneous melanoma in California, 2004 – 2015 (with follow-up through 2017)

	AYA (15 – 39)		Older Adults (40 – 64)	
	HR (95% CI)	aHR[1] (95% CI)	HR (95% CI)	aHR[1] (95% CI)
Sex				
Female	1.00	1.00	1.00	1.00
Male	2.45 (2.08–2.88)	1.43 (1.21–1.70)	1.89 (1.79–2.00)	1.39 (1.31–1.47)
Race/Ethnicity				
NHW	1.00	1.00	1.00	1.00
Hispanic	1.82 (1.46–2.27)	1.06 (0.84–1.35)	1.57 (1.43–1.74)	0.91 (0.82–1.01)
Black	0.58 (0.08–4.09)	0.09 (0.01–0.64)	3.23 (2.34–4.46)	1.32 (0.95–1.83)
Asian/P.I.	2.08 (1.22–3.54)	1.55 (0.90–2.66)	2.37 (1.92–2.92)	1.11 (0.90–1.38)
Other	0.11 (0.05–0.21)	0.25 (0.13–0.53)	0.11 (0.09–0.14)	0.18 (0.14–0.23)
Socioeconomic Status				
Highest	1.00	1.00	1.00	1.00
High-Middle	1.15 (0.90–1.46)	1.01 (0.79–1.30)	1.45 (1.35–1.56)	1.29 (1.19–1.38)
Middle	1.86 (1.46–2.36)	1.50 (1.17–1.91)	1.79 (1.66–1.93)	1.39 (1.28–1.50)
Low-Middle	2.57 (2.00–3.31)	1.25 (0.95–1.64)	2.52 (2.33–2.73)	1.58 (1.46–1.72)
Lowest	3.67 (2.80–4.82)	1.45 (1.08–1.96)	3.46 (3.16–3.80)	1.85 (1.68–2.04)
Insurance Status				
Private	1.00	1.00	1.00	1.00
Medicaid	8.31 (6.78–10.17)	2.47 (1.96–3.12)	6.44 (5.92–7.00)	2.07 (1.89–2.27)
Medicare	6.97 (4.74–10.25)	2.99 (2.01–4.45)	3.44 (3.15–3.76)	2.15 (1.96–2.35)
Military	2.49 (1.60–3.86)	2.03 (1.30–3.18)	2.09 (1.82–2.40)	1.57 (1.37–1.81)
Uninsured	2.14 (1.43–3.18)	1.60 (1.07–2.41)	2.62 (2.30–2.99)	1.74 (1.52–1.99)
Other/Unknown	0.53 (0.40–0.71)	0.75 (0.56–1.01)	0.77 (0.72–0.83)	1.18 (1.09–1.28)
Clinical Stage				
In-Situ/Stage I	1.00	1.00	1.00	1.00
Stage II	11.90 (9.09–15.58)	2.08 (1.36–3.18)	5.67 (5.23–6.15)	1.53 (1.33–1.77)
Stage III	17.22 (13.61–21.79)	3.31 (2.27–4.83)	10.94 (10.14–11.80)	3.18 (2.80–3.62)
Stage IV	152.08 (121.20–190.82)	20.39 (13.30–31.20)	55.12 (51.32–59.20)	10.79 (9.33–12.48)
Unknown	6.52 (4.87–8.73)	2.08 (1.32–3.27)	3.90 (3.55–4.28)	1.50 (1.29–1.74)
Location				
Limbs	1.00	1.00	1.00	1.00
Head/Neck	1.53 (1.19–1.97)	.95 (0.73–1.24)	1.48 (1.38–1.59)	1.42 (1.32–1.53)
Trunk	1.20 (0.98–1.47)	1.12 (0.91–1.38)	1.33 (1.25–1.42)	1.19 (1.11–1.27)
Other	25.48 (20.42–31.78)	2.32 (1.64–3.29)	18.11 (16.73–19.60)	1.92 (1.68–2.18)
Histology [2]				
SSM	1.00	1.00	1.00	1.00
NM	8.92 (6.49–12.27)	0.86 (0.60–1.23)	6.12 (5.52–6.78)	1.30 (1.16–1.45)

	AYA (15 – 39)		Older Adults (40 – 64)	
	HR (95% CI)	aHR[1] (95% CI)	HR (95% CI)	aHR[1] (95% CI)
ALM	4.05 (1.96–8.39)	1.13 (0.53–2.41)	3.28 (2.59–4.16)	1.26 (0.99–1.61)
LMM	1.22 (0.53–2.81)	1.99 (0.86–4.61)	0.86 (0.75–0.98)	1.06 (0.92–1.22)
NOS/Other	2.25 (1.77–2.87)	1.08 (0.83–1.40)	1.57 (1.45–1.69)	1.08 (1.00–1.17)
Year oi Diagnosis				
2004 – 2006	1.00	1.00	1.00	1.00
2007 – 2009	0.98 (0.80–1.19)	0.99 (0.80–1.21)	0.92 (0.87–0.98)	0.98 (0.92–1.04)
2010 – 2012	1.09 (0.88–1.35)	1.04 (0.83–1.29)	0.80 (0.74–0.86)	0.81 (0.75–0.87)
2013 – 2015	0.59 (0.43–0.81)	0.57 (0.42–0.79)	0.61 (0.56–0.67)	0.62 (0.57–0.69)
Tumor Thickness				
In-Situ/<1.00mm	1.00	1.00	1.00	1.00
1.00-<2.00mm	6.22 (4.70–8.23)	3.27 (2.35–4.54)	3.12 (2.86–3.39)	1.87 (1.69–2.07)
2.00-<4.00mm	14.91 (11.27–19.71)	3.68 (2.37–5.71)	6.62 (6.07–7.23)	2.08 (1.80–2.40)
≥4.00mm	35.97 (27.69–46.73)	5.58 (3.56–8.73)	13.73 (12.68–14.87)	2.87 (2.49–3.31)
Unknown	28.61 (22.71–36.03)	3.51 (2.17–5.66)	12.92 (12.09–13.81)	2.40 (2.06–2.81)
Ulceration				
No	1.00	1.00	1.00	1.00
Yes	9.96 (8.20–12.10)	1.73 (1.34–2.23)	6.70 (6.28–7.15)	1.70 (1.56–1.85)
Unknown	6.16 (5.05–7.51)	1.15 (0.89–1.49)	4.72 (4.42–5.04)	1.30 (1.19–1.42)

[1]Fully adjusted models represent mutual adjustment for all the variables shown in the table

[2]Histology definitions: SSM=Superficial Spreading Melanoma, NM=Nodular Melanoma, ALM=Acral Lentiginous Melanoma. LMM=Lentigo Maligna Melanoma, NOS/Other=Malignant Melanoma, NOS, and other rare subtypes.