Continued Increase in Melanoma Incidence across all Socioeconomic Status Groups in California, 1998–2012

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Melanoma incidence has been increasing in light-skinned populations worldwide, but the reasons for the increase have been controversial. Our prior assessment in California non-Hispanic whites showed substantial increases in invasive melanoma incidence for tumors of all thicknesses in all neighborhoods categorized by socioeconomic status (SES) between 1988–1992 and 1998–2002. To understand whether these trends continued, we updated our assessment to include the diagnosis period 2008–2012 and more accurate pathologic stage at diagnosis. We used the California Cancer Registry to calculate age-adjusted incidence rates for over 58,000 newly diagnosed melanomas. Incidence rates not only continued to rise over the 10-year period from 1998–2002 and 2008–2012 but also showed significant increases in almost all groups defined jointly by tumor thickness or stage at diagnosis and a small area (census tract) SES measure. The largest relative rate increases were seen for regional, distant, and ulcerated disease, especially among males living in the lowest SES neighborhoods. Considering tumor thickness and stage as proxies for time to screening detection and neighborhood SES as a proxy for health care access, we interpret this pattern to indicate continued, true increases in melanoma occurrence as opposed to a thin tumor phenomenon simply driven by improved access to care.

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INTRODUCTION

Dramatic increases in the incidence of cutaneous melanoma have occurred among populations in the United States and other parts of the world in the last half of the 20th century, with rates increasing 3- to 5-fold over the span of only two to three decades (Dennis, 1999; Garbe and Leiter, 2009; Giblin and Thomas, 2007; Hall et al., 1999; Jemal et al., 2001; Levell et al.; 2009). Although these increases have raised public health concerns (US Department of Health and Human Services Office of the Surgeon General, 2014), they have also sparked controversy as to whether they represent a true melanoma epidemic or an artifact of expanded screening programs (De Giorgi et al., 2012; Dennis, 1999; Erickson and Driscoll, 2010; Levell et al., 2009; Swerlick and Chen, 1996; Swerlick and Chen, 1997).

To inform answers to this question, we previously published a study of invasive cutaneous melanoma occurrence during the period of 1988 through 2002 among non-Hispanic whites in California, in which we conducted the first examination of incidence trends across small-area (census tract) neighborhoods categorized by socioeconomic status (SES) (Linos et al., 2009). These analyses showed consistent 2-fold incidence increases for lesions of all thicknesses (including thick [>4-mm] melanomas) across all levels of neighborhood SES over the two study decades. The greatest increases were observed for thick melanomas (>4 mm) among the lowest SES groups, who were presumably less likely to have access to regular skin screening. These observations confirmed that the increases in melanoma incidence were not restricted to more indolent thin tumors discovered via intensive screening in populations with better access to medical care (Linos et al., 2009).

More recent data regarding melanoma incidence among US non-Hispanic whites suggest continued, increasing trends among males and females of all ages (Geller et al., 2013; Guy et al., 2015; Jemal et al., 2011; Shaikh et al., 2016; Watson et al., 2015; Whiteman et al., 2016). However, there is some indication that the rate of overall increase has slowed over the last decade (Erdmann et al., 2013; Geller et al., 2013; Guy et al., 2015; Whiteman et al., 2016), although projections based on data through 2011 predict 5 to 10 years of continued increase (Whiteman et al., 2016).

To further understand whether increasing melanoma incidence is occurring preferentially in groups with better access

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Abbreviations: CI, confidence interval; IRR, incidence rate ratio; SES, socioeconomic status

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to health care, including screening and other early detection efforts, we extended our prior analyses of melanoma incidence in California, covering two more recent periods (1998–2002 and 2008–2012). We focused on these periods to take advantage of decennial census data for neighborhood population estimation, as well as more consistent reporting of primary tumor thickness and pathologic staging of the regional lymph nodes via sentinel lymph node biopsy (SLNB). Capitalizing on the unique opportunity in California Cancer Registry data to assess incidence among the non-Hispanic white population jointly by tumor thickness, stage at diagnosis, and small-area neighborhood SES, we aimed to determine the extent to which recent melanoma incidence varies over time among population subgroups likely to have differential access to screening or early detection.

RESULTS

Characteristics of melanoma patients over the two time periods are summarized in Table 1. These data confirm observations from prior assessments of melanoma occurrence among white non-Hispanic persons in the United States showing substantially greater numbers in males than females. In both sexes, there was a shift in the age distribution of cases over time such that the proportion of cases diagnosed before age 40 years declined and the proportion among those age 65 years or older increased in the more recent time period, more dramatically among males than females. Most diagnoses (≥70%) occurred among persons living in neighborhoods in the top two quartiles of SES, and most patients (≥55%) were diagnosed with a melanoma ≤1 mm in thickness or with localized stage (≥81%). In 1998–2002, 78.7% of the group who had tumors ≤2 mm had tumors that were actually ≤1 mm. In 2008–2012, 81.8% of the group with tumors ≤2 mm had tumors ≤1 mm.

Table 2 shows age-adjusted incidence rates and rate changes, expressed as incidence rate ratios (IRRs), over time. Incidence rates were higher among males than females and among those living in high SES neighborhoods compared with those living in lower SES neighborhoods. Incidence rates increased significantly between the two time periods for both males and females, overall and across each SES level ($P < 0.01$). The incidence rate for males rose by 25% from 34.7 per 100,000 in 1998–2002 to 43.5 per 100,000 in 2008–2012. For females, the incidence rate increased by 21%, from 21.7 to 26.2. IRRs indicated significant rate increases among all quartiles of SES but generally suggested greater proportional increases among the top strata of SES over time. For example, in the more recent time period compared with the earlier period, rates increased 27% in the highest SES neighborhoods and 12% in the lowest SES neighborhoods among males and 28% in the highest SES neighborhoods and 13% in the lowest SES neighborhoods among females. For females, the increase was strongest in the highest quartile of SES, but for males, increases were comparable in the highest three quartiles compared with the lowest.

Tables 3 through 5 show incidence rate increases over time according to neighborhood SES and measures of extent of disease. Rates for males and females increased significantly between 1998–2002 and 2008–2012 for most categories of stage at diagnosis and neighborhood SES (Table 3). The most substantial relative rises were observed for regional or distant stage tumors among males and females in the poorest neighborhoods. In these neighborhoods, rates of regional and distant disease nearly doubled among males (IRR for distant disease = 1.87, 95% confidence interval [CI] = 1.39–2.53; IRR for regional disease = 1.93, 95% CI = 1.51–2.47). Among women, an increase in regional disease was significant in the poorest neighborhoods (IRR = 1.44, 95% CI = 1.00–2.08); however, for distant disease, increases were statistically significant only in the two highest neighborhood SES quartiles. In general, these patterns did not vary by patient age at diagnosis (<50, 50–64, 65+ years; data not shown).

Patterns of incidence increase by tumor thickness and neighborhood SES (Tables 4 and 5) were generally similar to those observed for stage at diagnosis. For the thickest tumors (>4 mm), incidence rate increases over time were statistically significant in most neighborhood SES quartiles. One important exception is the observation of lower-magnitude and borderline significance among males in the poorest neighborhood quartile. For thinner (≤1.00-mm) tumors, IRRs were comparatively larger among persons living in the highest versus lowest SES neighborhoods for both males (IRR = 1.38 vs. 1.16, Table 4) and females (IRR = 1.42 vs. IRR = 1.19, Table 5). When tumor thickness was dichotomized at 2 mm (e.g., ≤2 mm vs. >2 mm), the incidence rates for thicker tumors among males almost doubled (data not shown). Although IRRs for the group with tumors measuring ≤2 mm remained similar for the lower SES groups, the IRR increased from 1.20 (95% CI = 1.07–1.35) to 1.28 (95% CI = 1.17–1.40) for males living in the highest SES neighborhoods.

For melanomas of unknown thickness (6–7% of all tumors in 2008–2012), statistically significant declines in incidence between the study periods were observed for most levels of SES in both sexes (Tables 4 and 5). For melanomas with unknown stage (3% of all tumors in 2008–2012), incidence trends were stable over the time period (Table 3).

DISCUSSION

Using recent population-based data for more than 58,000 cases of melanoma newly diagnosed among non-Hispanic white persons in California, we show that melanoma incidence rates not only continued to rise between the periods 1998–2002 and 2008–2012 but also showed significant increases in almost all groups defined jointly by tumor thickness or stage at diagnosis and neighborhood SES. Considering tumor thickness and stage at diagnosis as proxies for time to screening detection considering and neighborhood SES as a proxy for health insurance or access, we interpret this overall pattern to indicate a true increase in melanoma occurrence as opposed to a phenomenon driven mainly by access to care, for which we would have expected rate increases to be limited to thin, early-stage tumors diagnosed among high SES groups. On the contrary, we observed the largest rate increases for regional, distant, and ulcerated disease, especially among lower SES males.

These findings from California and our interpretation are consistent with other recent assessments in the United States

Table 1. Case counts for non-Hispanic white patients diagnosed with malignant melanoma by patient sex and time period (1998–2002, 2008–2012) of diagnosis, California

	Male				Female			
	1998–2002		2008–2012		1998–2002		2008–2012	
	n = 14,886		n = 20,446		n = 10,185		n = 12,809	
Characteristics	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Neighborhood SES								
Quartile 1 (lowest)	1,324	9	1,618	8	866	9	1,015	8
Quartile 2	3,069	21	3,969	19	2,148	21	2,516	20
Quartile 3	4,442	30	5,958	29	3,234	32	3,779	30
Quartile 4 (highest)	6,049	41	8,901	44	3,937	39	5,499	43
Age at diagnosis, years								
<40 years	1,489	10	1,093	5	1,991	20	1,533	12
40–64 years	6,680	45	8,183	40	4,662	46	5,921	46
65+ years	6,717	45	11,170	55	3,532	35	5,355	42
Tumor thickness								
≤1 mm	8,117	55	11,931	58	6,236	61	8,299	65
1.01–2.00 mm	2,371	16	3,033	15	1,509	15	1,781	14
2.01–4.00 mm	1,403	9	1,955	10	763	8	956	8
>4.00 mm	855	6	1,294	6	376	4	640	5
Distant or ulcerated[1]	496	3	753	4	228	2	303	3
other	1,644	11	1,480	7	1,073	11	830	7
Stage at presentation								
Localized	12,465	84	16,746	82	8,870	87	11,023	86
Regional	1,090	7.	1,956	10	612	6	980	8
Distant	645	4	1,029	5	286	3	417	3
Unstaged/not applicable	686	5	715	4	417	4	389	3
Histopathological subtype								
Superficial spreading Melanoma	4,245	29	4,747	23	3,321	33	3,364	26
Nodular melanoma	1,103	7	1,374	7	683	7	719	6
Lentigo malignant melanoma	968	6	983	5	446	4	418	3
Acral-lentiginuous melanoma	84	1	94	1	90	1	125	1
Not otherwise specified	7,490	50	12,089	59	5,086	50	7,655	60
Other[2]	996	7	1,159	6	559	6	522	4

[1]Tumor thickness unknown, but stage known to be distant or site-specific code known to be ulcerated.
[2]Histology codes: 8723, 8730, 8740, 8745, 8761, 8770–8773, and 8790.

as a whole (Erdmann et al., 2013; Geller et al., 2013; Jemal et al., 2011; Little and Eide, 2012; Shaikh et al., 2016; Whiteman et al., 2016). Analyses of Surveillance, Epidemiology, and End Results (SEER) incidence statistics through the year 2009 also showed continued increases in melanoma incidence in the United States across all tumor thicknesses (Jiang et al., 2015; Shaikh et al., 2016). The most recent of these, by Shaikh et al., showed an overall reduction in median thickness of melanoma tumors since 1990 but an increase in the median thickness of T4 melanoma through 2009, further supporting the notion that increasing rates of melanoma are not solely an artifact of early detection of thinner tumors related to more aggressive screening efforts. These same data for the period 2000–2009 showed the largest increase in incidence, representing a nearly 30% expansion for the thickest (>4-mm) tumors, which are the most deadly (Shaikh et al., 2016).

Compounding the continued increase in incidence for most thickness and stage strata are recent projections of substantial increases in the absolute number of melanoma diagnoses because of the aging population of non-Hispanic US whites, continuing until at least 2030 (Guy et al., 2015; Whiteman et al., 2016). Together, these trends portend a substantial increase in the burden of melanoma in this population. Similar rising trends in melanoma incidence have been estimated for other high melanoma–incidence regions such as the United Kingdom, Sweden, and Norway (Whiteman et al., 2016). However, trends of overall melanoma incidence in Australia and New Zealand are different, with some evidence of a recent stabilization and perhaps even a decline in rates, at least in Australia (Erdmann et al., 2013; Whiteman et al., 2016). These patterns have been attributed to the implementation of effective skin cancer prevention programs, although it should be noted that the trend assessments did not evaluate disease stage. The more detailed analysis by Baade et al. (2012) of Australian cancer incidence data through 2006 suggests that the rate stabilization may be limited to thin tumors, with continued increases in the incidence of thick melanomas likely. Analyses of more recent cancer incidence data from New Zealand and Australia, taking into consideration metastasis or stage at diagnosis, will be required to fully understand the degree to

Table 2. Average annual age-adjusted incidence rates per 100,000 person-years for non-Hispanic white patients diagnosed with malignant melanoma by patient sex, quartile of neighborhood socioeconomic status, and time period (1998–2002, 2008–2012) of diagnosis, California

	1998–2002		2008–2012			
Neighborhood SES	Count	Rate (95% CI)	Count	Rate (95% CI)	IRR[1] (95% CI)	*P*-Value
Males						
Q1 (lowest)	1,324	29.5 (27.9–31.1)	1,618	33.0 (31.4–34.7)	**1.12 (1.04–1.21)**	**< 0.01**
Q2	3,070	29.8 (28.8–30.9)	3,969	37.1 (35.9–38.3)	**1.24 (1.19–1.30)**	**< 0.01**
Q3	4,442	34.0 (33.0–35.0)	5,958	42.7 (41.6–43.9)	**1.26 (1.21–1.31)**	**< 0.01**
Q4 (highest)	6,050	40.4 (39.4–41.4)	8,901	51.2 (50.1–52.3)	**1.27 (1.23–1.31)**	**< 0.01**
Overall	14,886	34.7 (34.1–35.3)	20,446	43.5 (42.9–44.1)	**1.25 (1.23–1.28)**	**< 0.01**
Females						
Q1 (lowest)	866	17.3 (16.1–18.6)	1,015	19.6 (18.3–20.9)	**1.13 (1.03–1.25)**	**0.01**
Q2	2,148	19.0 (18.2–19.8)	2,516	22.0 (21.0–22.9)	**1.16 (1.09–1.23)**	**< 0.01**
Q3	3,234	22.3 (21.6–23.1)	3,779	25.5 (24.7–26.4)	**1.14 (1.09–1.20)**	**< 0.01**
Q4 (highest)	3,937	24.5 (23.7–25.3)	5,499	31.5 (30.6–32.4)	**1.28 (1.23–1.34)**	**< 0.01**
Overall	10,185	21.7 (21.3–22.2)	12,809	26.2 (25.7–26.7)	**1.21 (1.17–1.24)**	**< 0.01**

Bold values indicate statistically different from 1.0.

Abbreviations: CI, confidence interval; IRR, incidence risk ratio; Q, quartile; SES, socioeconomic status.

[1]IRR comparing 2008–2012 to 1998–2002 average annual incidence rates.

which aggressive skin cancer prevention programs in these countries are changing stage-specific incidence patterns.

Our study has a number of strengths, most importantly the evaluation of a large, consistently monitored population of California. Unlike some prior assessments of US whites that grouped together whites regardless of Hispanic ethnicity and thus differential melanoma risk, (Geller et al., 2013; Hall et al., 1999) we specifically addressed trends only among those whites at highest risk (i.e., non-Hispanic whites). Moreover, our approach of examining incidence trends jointly by thickness or regional/metastatic spread and neighborhood SES allowed us to assess incidence among populations across a range of presumed access to skin cancer screening.

Our assessment also had several important limitations. Although small-area SES data were available for all California census tracts during the study time periods, this measure represented the relative SES of the patient's neighborhood at diagnosis and thus does not necessarily capture individual-level socioeconomic characteristics. We were not able to assess trends in melanoma mortality by neighborhood SES because death records are not routinely geocoded to census tracts. Our time-based comparisons by stage (especially stage III) may be confounded by the increased prevalence of sentinel lymph node biopsy for pathologic staging of primary melanoma since the mid-1990s. This has resulted in stage migration for regional nodal disease, the vast majority of which presents with micrometastases identified by sentinel lymph node biopsy. However, this issue is mitigated somewhat by excluding data from 1988–1992 (as in our prior analysis). In addition, because thicker primary tumors are more likely to have positive sentinel lymph nodes, our observed increases in stage III melanoma among lower SES groups remain valid. We could not address trends in other histologic factors that may contribute to higher risk of recurrence or death, like tumor ulceration or mitotic rate, because these factors were collected by the cancer registry only from the year 2004 forward and therefore were not available through both time periods assessed. A further limitation involves the high proportion of patients reported to the cancer registry whose tumors had *not otherwise specified* histology, obfuscating efforts to understand histology-specific trends. Additionally, the well-documented underreporting (Cockburn et al., 2008; Koh et al., 1992; Zippin et al., 1995) and delayed reporting (Clegg et al., 2002) of melanoma to cancer registries suggest that most assessments of melanoma occurrence are based on underestimated case counts. Altogether, these limitations emphasize the importance of accurate melanoma surveillance and timely, complete reporting of all melanomas and their characteristics to cancer registries by the diagnosing hospitals or community-based physicians (Hall et al., 2003).

Our identification of a continued increase in the melanoma burden in California underscores the importance of public health efforts toward primary prevention of skin cancer in the United States. In 2014, the US Surgeon General released a "Call to Action to Prevent Skin Cancer" (US Department of Health and Human Services Office of the Surgeon General, 2014), proposing a number of important public health and policy goals, including improvements in sun protection in outdoor settings; providing individuals with the information needed to make informed, healthy choices about UVR exposure; promoting legislation and policies that advance the national goal of preventing skin cancer; reducing access to indoor tanning; and strengthening the research, surveillance, monitoring, and evaluation needed to better quantify our efforts in skin cancer prevention. Although progress is occurring in the implementation of some of these recommendations, and there is clear evidence of prevention success in Australia, our findings of a continued, marked increase in melanoma occurrence across thickness, stage, and SES strata should provide further impetus for prioritizing primary prevention activities in the United States.

Table 3. Average annual age-adjusted incidence rates per 100,000 person-years for non-Hispanic white patients diagnosed with malignant melanoma by patient sex, stage at diagnosis, quartile of neighborhood socioeconomic status, and time period (1998–2002, 2008–2012) of diagnosis, California

	1998–2002		2008–2012			
Stage at Diagnosis	**Count**	**Rate (95% CI)**	**Count**	**Rate (95% CI)**	**IRR[1] (95% CI)**	***P*-Value**
Males						
Localized						
Q1 (lowest)	1,057	23.5 (22.1–25.0)	1,190	24.2 (22.8–25.7)	1.03 (0.95–1.12)	0.51
Q2	2,481	24.1 (23.1–25.0)	3,097	28.9 (27.8–29.9)	**1.20 (1.14–1.26)**	**<0.01**
Q3	3,717	28.4 (27.5–29.3)	4,867	34.8 (33.8–35.9)	**1.23 (1.17–1.28)**	**<0.01**
Q4 (highest)	5,210	34.7 (33.7–35.6)	7,592	43.6 (42.6–44.7)	**1.26 (1.21–1.3)**	**<0.01**
Regional						
Q1 (lowest)	103	2.3 (1.9–2.8)	209	4.4 (3.8–5.1)	**1.93 (1.51–2.47)**	**<0.01**
Q2	260	2.6 (2.3–2.9)	459	4.4 (4.0–4.8)	**1.70 (1.45–1.99)**	**<0.01**
Q3	330	2.5 (2.3–2.8)	575	4.2 (3.9–4.6)	**1.66 (1.44–1.91)**	**<0.01**
Q4 (highest)	397	2.7 (2.4–3.0)	713	4.1 (3.8–4.4)	**1.53 (1.35–1.74)**	**<0.01**
Distant						
Q1 (lowest)	72	1.6 (1.3–2.1)	146	2.99 (2.5–3.5)	**1.87 (1.39–2.53)**	**<0.01**
Q2	170	1.6 (1.4–1.9)	235	2.2 (1.9–2.5)	**1.34 (1.10–1.65)**	**<0.01**
Q3	191	1.5 (1.3–1.7)	310	2.23 (2.0–2.5)	**1.53 (1.27–1.84)**	**<0.01**
Q4 (highest)	212	1.4 (1.3–1.7)	338	1.95 (1.7–2.2)	**1.35 (1.13–1.62)**	**<0.01**
Unknown						
Q1 (lowest)	92	2.1 (1.7–2.5)	73	1.4 (1.1–1.8)	**0.70 (0.50–0.96)**	**0.03**
Q2	159	1.5 (1.3–1.8)	178	1.7 (1.4–1.9)	1.08 (0.86–1.35)	0.54
Q3	204	1.6 (1.4–1.8)	206	1.5 (1.3–1.7)	0.92 (0.75–1.12)	0.42
Q4 (highest)	231	1.6 (1.4–1.8)	258	1.5 (1.3–1.7)	0.94 (0.78–1.13)	0.55
Females						
Localized						
Q1 (lowest)	721	14.5 (13.4–15.6)	836	16.3 (15.1–17.5)	**1.12 (1.01–1.25)**	**0.03**
Q2	1,843	16.4 (15.6–17.2)	2,083	18.3 (17.5–19.2)	**1.12 (1.05–1.19)**	**<0.01**
Q3	2,828	19.6 (18.9–20.4)	3,225	22.1 (21.3–22.9)	**1.12 (1.07–1.18)**	**<0.01**
Q4 (highest)	3,478	21.7 (21.0–22.5)	4,879	28.1 (27.3–29.0)	**1.29 (1.24–1.35)**	**<0.01**
Regional						
Q1 (lowest)	59	1.2 (0.9–1.5)	89	1.7 (1.4–2.1)	**1.44 (1.00–2.08)**	**0.04**
Q2	128	1.1 (0.9–1.3)	231	2.0 (1.7–2.3)	**1.80 (1.43–2.28)**	**<0.01**
Q3	209	1.4 (1.2–1.6)	312	2.0 (1.8–2.26)	**1.41 (1.17–1.70)**	**<0.01**
Q4 (highest)	216	1.3 (1.2–1.5)	348	1.9 (1.7–2.1)	**1.40 (1.17–1.68)**	**<0.01**
Distant						
Q1 (lowest)	36	0.7 (0.5, –1.0)	39	0.7 (0.5–1.0)	1.01 (0.61–1.68)	1.00
Q2	85	0.7 (0.6–0.9)	109	0.9 (0.7–1.1)	1.23 (0.91–1.68)	0.18
Q3	76	0.5 (0.4–0.6)	136	0.8 (0.7–1.0)	**1.67 (1.24–2.26)**	**<0.01**
Q4 (highest)	89	0.5 (0.4–0.6)	133	0.7 (0.6–0.8)	**1.34 (1.00–1.79)**	**0.04**
Unknown						
Q1 (lowest)	50	0.9 (0.7–1.3)	51	0.9 (0.6–1.2)	0.94 (0.60–1.47)	0.88
Q2	92	0.8 (0.6–1.0)	93	0.8 (0.6–0.9)	0.97 (0.71–1.34)	0.93
Q3	121	0.8 (0.7–1.0)	106	0.7 (0.5–0.8)	0.83 (0.62–1.10)	0.21
Q4 (highest)	154	0.9 (0.8–1.1)	139	0.8 (0.7–1.0)	0.85 (0.66–1.09)	0.20

Bold values indicate statistically different from 1.0.

Abbreviations: CI, confidence interval; Q, quartile; SES, socioeconomic status.

[1]Incidence rate ratio comparing 2008–2012 to 1998–2002 average annual incidence rates.

Although these data confirm prior observations of substantial variation in melanoma incidence by SES, they also show that incidence has been increasing in low SES neighborhoods, especially in older men of lower SES who are most likely to die of their disease. This confluence does not bode well for future trends in melanoma mortality and reinforces the need for clear strategies for secondary prevention programs to detect melanoma when it is at its thinnest, earliest stages. However, melanoma mortality rates remain stable in California and the United States (Howlader et al., 2016). In 2016, the US Preventive Services Task Force again cited insufficient evidence to recommend for or against clinician skin examination for skin cancer morbidity and mortality reduction (US Preventive Services Task Force, 2016). Uncertainty persists regarding the potential harms of screening, including physical and psychologic harms to the patient from overdiagnosis and

Table 4. Average annual age-adjusted incidence rates per 100,000 person-years for non-Hispanic white male patients diagnosed with malignant melanoma by tumor thickness at diagnosis, quartile of neighborhood socioeconomic status, and time period (1998–2002, 2008–2012) of diagnosis, California

	1998–2002		2008–2012			
Tumor Thickness	**Count**	**Rate (95% CI)**	**Count**	**Rate (95% CI)**	**IRR[1] (95% CI)**	***P*-Value**
≤1.00 mm						
Q1 (lowest)	622	13.8 (12.7–14.9)	790	16.0 (14.9–17.2)	**1.16 (1.04–1.29)**	**<0.01**
Q2	1,552	15.0 (14.3–15.8)	2,126	19.9 (19.0–20.7)	**1.32 (1.24–1.41)**	**<0.01**
Q3	2,446	18.6 (17.9–19.4)	3,446	24.8 (23.9–25.6)	**1.33 (1.26–1.40)**	**<0.01**
Q4 (highest)	3,497	23.1 (22.3–23.9)	5,569	31.9 (31.1–32.8)	**1.38 (1.32–1.44)**	**<0.01**
1.01–2.00 mm						
Q1 (lowest)	188	4.2 (3.6–4.9)	230	4.7 (4.1–5.4)	1.12 (0.92–1.37)	0.27
Q2	475	4.6 (4.2–5.1)	599	5.6 (5.2–6.1)	**1.22 (1.08–1.38)**	**<0.01**
Q3	708	5.4 (5.0–5.9)	877	6.3 (5.9–6.7)	**1.15 (1.04–1.28)**	**<0.01**
Q4 (highest)	1,000	6.6 (6.2–7.1)	1,327	7.7 (7.3–8.1)	**1.16 (1.07–1.26)**	**<0.01**
2.01–4.00 mm						
Q1 (lowest)	156	3.5 (3.0, –4.1)	186	3.8 (3.3–4.4)	1.09 (0.88–1.37)	0.45
Q2	317	3.1 (2.8–3.5)	420	4.0 (3.6–4.3)	**1.28 (1.10–1.49)**	**<0.01**
Q3	389	3.0 (2.7–3.3)	583	4.2 (3.9–4.6)	**1.40 (1.22–1.59)**	**<0.01**
Q4 (highest)	541	3.68 (3.4–4.0)	766	4.4 (4.1–4.8)	**1.20 (1.07–1.35)**	**<0.01**
>4.00 mm						
Q1 (lowest)	109	2.4 (2.0–2.89)	141	3.0 (2.5–3.6)	1.25 (0.97–1.63)	0.0919
Q2	219	2.2 (1.9–2.5)	293	2.7 (2.4–3.0)	**1.25 (1.04–1.50)**	**0.01**
Q3	254	2.0 (1.7–2.2)	391	2.8 (2.51–3.1)	**1.40 (1.19–1.65)**	**<0.01**
Q4 (highest)	273	1.9 (1.7–2.2)	469	2.7 (2.5–3.0)	**1.42 (1.22–1.67)**	**<0.01**
Distant/ulcerated[2]						
Q1 (lowest)	54	1.2 (0.9–1.6)	105	2.1 (1.7–2.6)	**1.79 (1.27–2.54)**	**<0.01**
Q2	141	1.4 (1.1–1.6)	160	1.5 (1.3–1.8)	1.12 (0.89–1.42)	0.36
Q3	147	1.1 (1.0–1.3)	234	1.7 (1.5–1.9)	**1.48 (1.20–1.84)**	**<0.01**
Q4 (highest)	154	1.1 (0.9–1.2)	254	1.5 (1.3–1.7)	**1.39 (1.13–1.72)**	**<0.01**
Otherwise unknown						
Q1 (lowest)	195	4.4 (3.8–5.0)	166	3.4 (2.9–4.0)	**0.77 (0.62–0.96)**	**0.02**
Q2	366	3.6 (3.2–4.0)	371	3.4 (3.1–3.8)	0.95 (0.82–1.11)	0.57
Q3	498	3.8 (3.5–4.2)	427	3.1 (2.8–3.4)	**0.80 (0.70–0.92)**	**<0.01**
Q4 (highest)	585	4.0 (3.7–4.4)	516	3.0 (2.7–3.2)	**0.74 (0.66–0.84)**	**<0.01**

Bold values indicate statistically different from 1.0.
Abbreviations: CI, confidence interval; IRR, incident rate ratio; Q, quartile; SES, socioeconomic status.
[1]IRR comparing 2008–2012 to 1998–2002 average annual incidence rates.
[2]Thickness unknown, but tumor was distant stage or ulcerated.

procedure-related adverse events. However, these adverse consequences were not reported from the recent population-based melanoma screening program by trained primary care providers in western Pennsylvania (Weinstock et al., 2016).

In summary, our study in California identifies unabated increases in melanoma incidence rates and evidence that these increases are not artefactual or due to more screening in higher SES populations. Based on the most recent trends in incidence rates, the annual cost of treating newly diagnosed melanoma in the United States is projected to grow from $457 million in 2011 to $1.6 billion by 2030 (Guy et al., 2015). It has been suggested that implementation of a comprehensive national skin cancer prevention program could prevent 230,000 cases of melanoma between 2020 and 2030 and save $2.7 billion in associated treatment costs (Guy et al., 2015). Stemming the substantial health and societal burdens of melanoma in the United States must include a stronger national commitment to both primary and secondary prevention.

MATERIALS AND METHODS

We obtained data regarding all new diagnoses of invasive cutaneous melanoma (*International Classification of Diseases for Oncology,* Third edition [World Health Organization, 2013], topography codes C44.0–C44.9, histology codes 8720-8790) from the California Cancer Registry occurring in January 1, 1998, through December 31, 2002, and in January 1, 2008, through December 31, 2012. These pericensal periods were selected based on the availability from the US decennial census of appropriate census tract-level denominators needed to calculate neighborhood SES rates, as will be described. All patient and tumor information for each newly diagnosed melanoma had previously been abstracted directly from medical records and reported to the California Cancer Registry. Population denominator estimates were based on US census data for census tracts of residence, as described herein. This analysis was overseen by the institutional review board of the Cancer Prevention Institute of California.

Table 5. Average annual age-adjusted incidence rates per 100,000 person-years for non-Hispanic white female patients diagnosed with malignant melanoma by tumor thickness at diagnosis, quartile of neighborhood socioeconomic status, and time period (1998–2002, 2008–2012) of diagnosis, California

	1998–2002		2008–2012			
Tumor Thickness	**Count**	**Rate (95% CI)**	**Count**	**Rate (95% CI)**	**IRR[1] (95% CI)**	***P*-Value**
≤1.00 mm						
Q1 (lowest)	452	9.4 (8.5–10.4)	568	11.2 (10.2–12.2)	**1.19 (1.04–1.35)**	0.01
Q2	1,262	11.5 (10.8–12.1)	1,465	13.1 (12.4–13.9)	**1.14 (1.06–1.24)**	**<0.01**
Q3	1,998	14.2 (13.6–14.8)	2,418	16.9 (16.2–17.6)	**1.19 (1.12–1.27)**	**<0.01**
Q4 (highest)	2,524	15.9 (15.3–16.6)	3,848	22.6 (21.9–23.4)	**1.42 (1.35–1.49)**	**<0.01**
1.01–2.00 mm						
Q1 (lowest)	142	2.8 (2.4–3.4)	153	3.1 (2.6–3.7)	1.09 (0.85–1.40)	0.54
Q2	299	2.6 (2.3–2.9)	392	3.6 (3.2–4.0)	**1.36 (1.16–1.60)**	**<0.01**
Q3	507	3.4 (3.1–3.7)	535	3.6 (3.3–4.0)	1.06 (0.93–1.21)	0.38
Q4 (highest)	561	3.4 (3.2–3.7)	701	3.9 (3.6–4.2)	**1.13 (1.01–1.28)**	0.03
2.01–4.00 mm						
Q1 (lowest)	81	1.5 (1.2–1.9)	91	1.7 (1.4–2.2)	1.16 (0.83–1.62)	0.41
Q2	177	1.5 (1.2–1.7)	224	1.8 (1.6–2.1)	**1.26 (1.02–1.56)**	0.03
Q3	229	1.5 (1.3–1.7)	280	1.7 (1.5–1.9)	1.18 (0.98–1.42)	0.08
Q4 (highest)	276	1.6 (1.5–1.9)	361	1.9 (1.7–2.1)	1.16 (0.98–1.37)	0.09
>4.00 mm						
Q1 (lowest)	42	0.74 (0.52–1.02)	65	1.11 (0.84–1.45)	1.51 (0.98–2.36)	0.06
Q2	105	0.83 (0.67–1.01)	173	1.35 (1.14–1.59)	**1.63 (1.25–2.14)**	**<0.01**
Q3	117	0.71 (0.58–0.85)	204	1.18 (1.01–1.36)	**1.67 (1.31–2.13)**	**<0.01**
Q4 (highest)	112	0.64 (0.53–0.78)	198	0.96 (0.83–1.12)	**1.50 (1.17–1.92)**	**<0.01**
Distant/ulcerated[2]						
Q1 (lowest)	30	0.6 (0.4–0.9)	30	0.5 (0.3–0.7)	0.83 (0.50–1.50)	0.59
Q2	65	0.5 (0.4–0.7)	75	0.6 (0.5–0.7)	1.08 (0.80–1.60)	0.75
Q3	63	0.4 (0.3–0.5)	104	0.6 (0.5–0.8)	**1.56 (1.12–2.20)**	**<0.01**
Q4 (highest)	70	0.4 (0.3–0.5)	94	0.5 (0.4–0.6)	1.22 (0.87–1.71)	0.26
Otherwise unknown						
Q1 (lowest)	119	2.3 (1.9–2.7)	108	2.0 (1.6–2.5)	0.89 (0.67–1.19)	0.48
Q2	240	2.1 (1.8–2.4)	187	1.5 (1.3–1.8)	**0.73 (0.59–0.90)**	**<0.01**
Q3	320	2.2 (1.9–2.4)	238	1.5 (1.3–1.7)	**0.69 (0.58–0.83)**	**<0.01**
Q4 (highest)	394	2.4 (2.2–2.7)	297	1.6 (1.4–1.8)	**0.66 (0.56–0.78)**	**<0.01**

Bold values indicate statistically different from 1.0.
Abbreviations: CI, confidence interval; IRR, incidence rate ratio; Q, quartile; SES, socioeconomic status.
[1]IRR comparing 2008–2012 to 1998–2002 average annual incidence rates.
[2]Thickness unknown but tumor was distant stage or ulcerated.

We focused our analysis on the non-Hispanic white population because the highest rates of melanoma occur in persons with the lightest complexions (National Cancer Institute, 2015), and over 94% of all melanoma diagnoses in California were reported for non-Hispanic whites (data not shown). Within the California Cancer Registry, Hispanic ethnicity is assigned based on a Hispanic surname list (the National Hispanic Identification Algorithm).

Stage at Diagnosis and Tumor Thickness

Melanoma extent of disease was categorized according to tumor thickness and SEER Historic stage (local, regional, distant). Tumor thickness was classified according to 2002 (and later) American Joint Committee on Cancer tumor categories as ≤1 mm (T1), 1.01–2 mm (T2), 2.01–4 mm (T3), >4 mm (T4), or unknown. Tumor thickness was unknown for 8.6% of patients overall. Patients with missing melanoma thickness information did not differ significantly from patients with known melanoma thickness by age at diagnosis or sex, although missing thickness information was more common among higher SES groups. The proportion of melanomas with missing thickness information declined slightly over time. Stage of disease was unknown for 3.7% of patients. Compared with patients with documented stage of disease, those with unknown stage had similar distributions of age at diagnosis and race/ethnicity but were significantly more likely to live in lower- than higher SES neighborhoods.

Neighborhood SES Index

Each patient was assigned a neighborhood SES index quartile, determined from the patient's residential address at time of diagnosis, which is geocoded routinely by the California Cancer Registry to a US census tract and then can be linked to census information describing various aspects of neighborhood SES. We used an existing, multicomponent SES index based on this approach and showed meaningful variation in California melanoma incidence in prior studies (Clarke et al., 2005; Hausauer et al., 2011). This measure first applies principal component analysis to incorporate information from seven SES-defining census indicator variables (average

educational attainment, median annual household income, percentage living 200% below the federal poverty level, percentage of population classified as blue collar workers, percentage of workforce older than 16 years and unemployed, median monthly rent, and median house value) to assign a standardized score to each census tract. The scores are next categorized into quartiles, each representing 25% of the California distribution (1 = lowest SES and 4 = highest SES). We used this SES index incorporating data from the 2000 US census (for cases diagnosed 1998–2002) and the 2010 US Census (for cases diagnosed 2008–2012) (Yang et al., 2014; Yost et al., 2001).

Melanoma patients for whom census tract group was unknown (n = 5,692, 7.6%) were allocated to a randomly selected tract within the same county. These individuals did not differ significantly from patients with known tract group by distributions of neighborhood SES. Because census tract-level population denominators are available from the US Census Bureau for decennial census years only, we examined SES-specific trends across the 5-year pericensal periods 1998–2002 and 2008–2012.

Statistical Analysis

Our analyses included all 35,332 cases of invasive melanoma among non-Hispanic white men and 22,994 cases among non-Hispanic white women diagnosed during the two study time periods. We used SEER*Stat (version 8.2; National Cancer Institute) for all calculations, including case distributions and incidence rates per 100,000 person-years, and corresponding 95% CIs. All rates were age-adjusted to the 2000 US standard. IRRs and 95% CIs were calculated for comparison between the two time periods (2008–2012 vs. 1998–2002).

Sensitivity analyses to understand how improvements in the completeness of thickness and stage over time might affect the interpretation of the other thickness- and stage-specific trends generally indicated significant but slightly lower IRRs than those reported here. To carry these out, we repeated all analyses alternatively assigning all the missing/unknowns to each known stage (distant/regional/local) and thickness categories (0.01–1.0/1.01–2.0/>2.0) and assessed trends for material changes in direction or size.

CONFLICT OF INTEREST

The authors state no conflict of interest. Since completing this work, CAC has taken a position at GRAIL, Inc., a company working on cell free nucleic acid-based cancer detection.

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