



Published in final edited form as:

J Natl Cancer Inst. 2016 January ; 108(1): . doi:10.1093/jnci/djv381.

Stemming the Rising Incidence of Melanoma: Calling Prevention to Action

Jeffrey E. Gershenwald and **Gery P. Guy Jr**

Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX (JEG); Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA (GPG)

Melanoma is the most deadly form of skin cancer and an important public health concern. In 2012, 67 753 people were diagnosed with melanoma and 9251 individuals died from the disease (1). Melanoma is the fifth most common cancer among males and sixth among females in the United States (1). Although melanoma represents fewer than 5% of all skin cancers diagnosed annually in the United States, deaths from melanoma represent more than 75% of all skin cancer deaths (1). The majority of patients diagnosed with melanoma have early-stage disease, and the prognosis is generally favorable although heterogeneous (2). In contrast, outcomes for patients with stage IV (distant) disease have historically been poor, with a five-year survival rate of approximately 10% (3). Fortunately, achievements in understanding the molecular underpinnings and cancer immunology in melanoma have ushered in a new era of tremendous advances in molecularly driven targeted therapy and immunotherapy for advanced disease in the past five years (4–10).

Although the incidence of most solid tumors decreased or stabilized between 1975 and 2010, the incidence of melanoma continued to rise approximately 3% per year during this period (11). The average number of adults treated annually for melanoma in the United States increased from approximately 373 000 to 701 000 between 2002 to 2006 and 2007 to 2011 (12). Subgroup analyses indicated increases among adults age 65 years and older and among women age 18 to 64 years (12). Remarkably, during the same time, the average annual total cost for melanoma treatment increased by 288%, from \$0.86 billion to \$3.35 billion, while the average annual total cost for all other cancers increased by 25.1% (12). Of additional concern are recent analyses projecting that the burden of melanoma will continue to increase through 2030. By 2030, the number of newly diagnosed cases is expected to more than double, while the annual cost of treating newly diagnosed melanomas is estimated to triple (13). Melanoma treatment costs may increase even faster than expected given new targeted therapies and immunotherapies that have been approved in recent years (14).

Correspondence to: Jeffrey E. Gershenwald, MD, Department of Surgical Oncology, Department of Cancer Biology, Melanoma and Skin Center, MD Anderson Melanoma Moon Shot, The University of Texas MD Anderson Cancer Center, 1400 Pressler St, FCT17.6000, Houston, TX 77030 (jgershen@mdanderson.org).

Notes

The findings and conclusions in this editorial are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Dr. Gershenwald has participated on an advisory board for Merck since June 2014, and this advisory role is not related to the content of this editorial.

Previous research suggests that increases in melanoma incidence reflect increases in cumulative exposure to ultraviolet (UV) radiation as well as increases in skin cancer awareness and early detection (15). However, with increasing incidence and stable mortality, some have questioned whether the increase in melanoma incidence is real. In this issue of the Journal, Shaikh et al. observe increases in melanoma incidence across all thickness categories, as well as a growing divergence in thickness between thin and thick lesions, with thick lesions becoming thicker in recent years (16). Together, these findings suggest that melanoma incidence is truly increasing and that observed trends are not solely because of increased awareness and the detection of thin lesions. The growing burden of melanoma highlights the importance of skin cancer prevention efforts, which if successful can potentially reduce the health and economic burden of melanoma in the United States.

The majority of melanoma cases in the United States are attributed to UV radiation exposure (17). Nearly 40% of Americans report sunburns each year, indicating that many are not adequately protecting their skin from damaging UV exposure that can cause melanoma (18). Moreover, recent studies, including the melanoma initiative of The Cancer Genome Atlas (TCGA) program, have demonstrated that melanoma has the highest somatic mutation rate among all tumors thus far explored and that the vast majority of these mutations is associated with a UV signature (19,20). Taken together, it follows that effective prevention strategies to reduce UV exposure, encourage and facilitate sun protection, and prevent sunburn are key components in reducing melanoma incidence. To reduce melanoma risk, individuals can increase sun protection behaviors such as using sunscreen, wearing protective clothing, wide brim hats, and sunglasses, and seeking shade, especially during the midday hours.

In addition, clear and compelling evidence has shown that artificial UV exposure from indoor tanning is an independent risk factor for melanoma (21,22). Nonetheless, the use of indoor tanning, classified as a known carcinogen by the World Health Organization (WHO) International Agency for Research on Cancer (23), remains common in the United States. An estimated 11.3 million individuals continue to engage in indoor tanning each year, including 1.6 million individuals younger than age 18 years (24,25). Reducing the use of indoor tanning can prevent future cases of melanoma. Indeed, in 2014, the US Food and Drug Administration issued an order requiring that sunlamp products carry a visible boxed warning that states “Attention: This sunlamp product should not be used on persons under the age of 18 years”(26). Additionally, 13 states currently restrict indoor tanning for minors under age 18 years and several other states are considering similar restrictions (27). Comprehensive community-level skin cancer prevention efforts focused on raising awareness and changing personal behaviors have been effective in preventing melanoma in Australia (28,29). The Guide to Community Preventive Services (Community Guide) recommends interventions that combine education and policy approaches to increase sun-protective behaviors in settings that include childcare centers, primary and middle schools, outdoor recreational and tourism settings, and outdoor occupational settings (30). The implementation of a comprehensive skin cancer prevention program in the United States has the potential to prevent 230 000 melanoma cases and \$2.7 billion in initial-year treatment costs from 2020 to 2030 (13).

In 2014, the US Surgeon General released a Call to Action to Prevent Skin Cancer (31). The Call to Action sets forth five main goals that can serve as a road map for skin cancer prevention efforts: 1) increase opportunities for sun protection in outdoor settings; 2) provide individuals with information to make informed, healthy choices about UV radiation exposure; 3) promote policies that advance the national goal of preventing skin cancer; 4) reduce the harms from indoor tanning; and 5) strengthen research, surveillance, monitoring, and evaluation related to skin cancer prevention.

Skin cancer prevention is a key opportunity for health care providers. The US Preventive Services Task Force (USPSTF) recommends behavioral counseling among individuals age 10 to 24 years with fair skin about minimizing their exposure to UV radiation and avoiding indoor tanning to reduce their risk of skin cancer (32). According to the USPSTF, which issued its most recent skin cancer screening recommendation in 2009, there is currently insufficient evidence to recommend for or against regular skin cancer screening for early detection of skin cancer in the adult general population (33). However, screening among individuals at increased risk for melanoma may be cost-effective (34,35). Future research on the effectiveness of skin cancer screening on reducing melanoma mortality is clearly warranted, and the development of an updated USPSTF recommendation is currently in progress.

Although we anticipate that an increasing proportion of patients diagnosed with potentially fatal melanoma will ultimately be successfully treated in this new era of targeted therapy and immunotherapy for melanoma, based on our understanding of melanoma etiology and the profound association with UV radiation—from the sun and from indoor tanning devices—there is an important opportunity to stem the rising incidence of melanoma with skin cancer prevention efforts. There is an unprecedented opportunity to raise the bar in terms of both prevention and treatment, necessitating an “all hands on deck” collaborative approach.

The US Surgeon General’s Call To Action to Prevent Skin Cancer provides a clear path for primary prevention initiatives. One such transdisciplinary effort is under way at The University of Texas MD Anderson Cancer Center, where as part of an initiative called the Moon Shots Program—a collaborative project to reduce cancer mortality by accelerating development of new treatments and prevention programs—the Melanoma Moon Shot (36) focuses on innovative prevention strategies (eg, public policy outreach and evidence-based early childhood education), as well as rapidly developing personalized management of the disease.

Although a clear path regarding screening is not currently present, there is a significant opportunity to expand on existing research to further develop a scientific evidence base for screening recommendations by the USPSTF. Some initial lessons learned from a pilot observational study in the German state of Schleswig-Holstein demonstrate a proof of concept that comprehensive, multidimensional screening initiatives may indeed reduce the burden of melanoma (37). Never before has there been so much opportunity to reduce the burden of melanoma as a public health problem in the United States; the time is now to leverage our knowledge and collaborate and coordinate across multiple disciplines—

thinking both inside and outside the box—to reverse the increase of melanoma in the United States.

References

1. United States Cancer Statistics Working Group. [Accessed November 4, 2015] United States Cancer Statistics: 1999–2012 Incidence and Mortality Web-Based Report <https://ncccd.cdc.gov/uscs/>
2. Gershenwald JE, Ross MI. Sentinel-lymph-node biopsy for cutaneous melanoma. *N Engl J Med*. 2011; 364(18):1738–1745. [PubMed: 21542744]
3. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol*. 2009; 27(36):6199–6206. [PubMed: 19917835]
4. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med*. 2010; 363(8):711–723. [PubMed: 20525992]
5. Flaherty KT, Infante JR, Daud A, et al. Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations. *N Engl J Med*. 2012; 367(18):1694–1703. [PubMed: 23020132]
6. Long GV, Stroyakovskiy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. *N Engl J Med*. 2014; 371(20):1877–1888. [PubMed: 25265492]
7. Larkin J, Ascierto PA, Dreno B, et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med*. 2014; 371(20):1867–1876. [PubMed: 25265494]
8. Robert C, Karaszewska B, Schachter J, et al. Improved overall survival in melanoma with combined dabrafenib and trametinib. *N Engl J Med*. 2015; 372(1):30–39. [PubMed: 25399551]
9. Robert C, Thomas L, Bondarenko I, et al. Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. *N Engl J Med*. 2011; 364(26):2517–2526. [PubMed: 21639810]
10. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. *N Engl J Med*. 2015; 373(1):23–34. [PubMed: 26027431]
11. Siegel R, Ma J, Zou Z, et al. Cancer statistics, 2014. *CA Cancer J Clin*. 2014; 64(1):9–29. [PubMed: 24399786]
12. Guy GP Jr, Machlin SR, Ekwueme DU, et al. Prevalence and costs of skin cancer treatment in the U.S., 2002–2006 and 2007–2011. *Am J Prev Med*. 2015; 48(2):183–187. [PubMed: 25442229]
13. Guy GP Jr, Thomas CC, Thompson T, et al. Vital signs: melanoma incidence and mortality trends and projections - United States, 1982–2030. *MMWR Morb Mortal Wkly Rep*. 2015; 64(21):591–596. [PubMed: 26042651]
14. DePeralta DK, Boland GM. Melanoma: Advances in targeted therapy and molecular markers. *Ann Surg Oncol*. 2015; 22(11):3451–3458. [PubMed: 26224403]
15. Jemal A, Saraiya M, Patel P, et al. Recent trends in cutaneous melanoma incidence and death rates in the United States, 1992–2006. *J Am Acad Dermatol*. 2011; 65(5 Suppl 1):S17–S25. e1–e3. [PubMed: 22018063]
16. Shaikh WR, Dusza SW, Weinstock MA, et al. Melanoma thickness and survival trends in the United States, 1989 to 2009. *J Natl Cancer Inst*. 2015; :djv294.doi: 10.1093/jnci/djv294 [PubMed: 26563354]
17. Armstrong BK, Krickler A. How much melanoma is caused by sun exposure? *Melanoma Res*. 1993; 3(6):395–401. [PubMed: 8161879]
18. Holman DM, Berkowitz Z, Guy GP Jr, et al. The association between demographic and behavioral characteristics and sunburn among U.S. adults - National Health Interview Survey, 2010. *Prev Med*. 2014; 63:6–12. [PubMed: 24589442]
19. Genomic Classification of Cutaneous Melanoma. *Cell*. 2015; 161(7):1681–1696. [PubMed: 26091043]
20. Lawrence MS, Stojanov P, Polak P, et al. Mutational heterogeneity in cancer and the search for new cancer-associated genes. *Nature*. 2013; 499(7457):214–218. [PubMed: 23770567]
21. Wehner MR, Chren MM, Nameth D, et al. International prevalence of indoor tanning: a systematic review and meta-analysis. *JAMA Dermatol*. 2014; 150(4):390–400. [PubMed: 24477278]
22. Boniol M, Autier P, Boyle P, et al. Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. *BMJ*. 2012; 345:e4757. [PubMed: 22833605]

23. El Ghissassi F, Baan R, Straif K, et al. A review of human carcinogens—part D: radiation. *Lancet Oncol.* 2009; 10(8):751–752. [PubMed: 19655431]
24. Guy GP Jr, Berkowitz Z, Everett Jones S, et al. Trends in indoor tanning among US high school students, 2009–2013. *JAMA Dermatol.* 2015; 151(4):448–450. [PubMed: 25535810]
25. Guy GP Jr, Berkowitz Z, Holman DM, et al. Recent Changes in the Prevalence of and Factors Associated With Frequency of Indoor Tanning Among US Adults. *JAMA Dermatol.* 2015; 151(11):1256–1259. [PubMed: 26131768]
26. Federal Register. [Accessed November 4, 2015] General and Plastic Surgery Devices: Reclassification of Ultraviolet Lamps for Tanning, Henceforth To Be Known as Sunlamp Products and Ultraviolet Lamps Intended for Use in Sunlamp Products <https://www.federalregister.gov/articles/2014/06/02/2014-12546/general-and-plastic-surgery-devices-reclassification-of-ultraviolet-lamps-for-tanning-henceforth-to>
27. Aim at Melanoma. [Accessed November 4, 2015] Indoor Tanning Legislation website 2015 <http://www.aimatmelanoma.org/en/aim-for-a-cure/legislative-accomplishments-in-melanoma/2015-indoor-tanning.html>
28. Shih ST-F, Carter R, Sinclair C, et al. Economic evaluation of skin cancer prevention in Australia. *Prev Med.* 2009; 49(5):449–453. [PubMed: 19747936]
29. Carter R, Marks R, Hill D. Could a national skin cancer primary prevention campaign in Australia be worthwhile?: an economic perspective. *Health Promotion Int.* 1999; 14(1):73–82.
30. Task Force on Community Preventive Services. Recommendations to prevent skin cancer by reducing exposure to ultraviolet radiation. *Am J Prev Med.* 2004; 27(5):467–470. [PubMed: 15556745]
31. U.S. Department of Health and Human Services The Surgeon General's Call to Action to Prevent Skin Cancer Washington (DC): Office of the Surgeon General (US); 2014 Reports of the Surgeon General.
32. Moyer VA. U S. Preventive Services Task Force. Behavioral counseling to prevent skin cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2012; 157(1):59–65. [PubMed: 22751761]
33. Screening for skin cancer: U S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2009; 150(3):188–193. [PubMed: 19189908]
34. Gordon LG, Rowell D. Health system costs of skin cancer and cost-effectiveness of skin cancer prevention and screening: a systematic review. *Eur J Cancer Prev.* 2015; 24(2):141–149. [PubMed: 25089375]
35. Losina E, Walensky RP, Geller A, et al. Visual screening for malignant melanoma: a cost-effectiveness analysis. *Arch Dermatol.* 2007; 143(1):21–28. [PubMed: 17224538]
36. The University of Texas MD Anderson Center. [Accessed November 4, 2015] MD Anderson Melanoma Moon Shot <http://www.cancermoonshots.org/cancer-types/melanoma/>
37. Katalinic A, Waldmann A, Weinstock MA, et al. Does skin cancer screening save lives?: an observational study comparing trends in melanoma mortality in regions with and without screening. *Cancer.* 2012; 118(21):5395–5402. [PubMed: 22517033]