

Early Detection and Prevention of Melanoma

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I have no significant relationships to disclose.

No off-label discussion.

Objectives

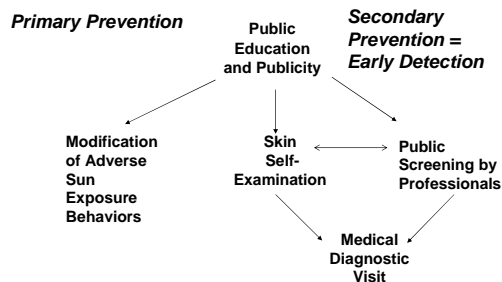
- To define current concepts in melanoma incidence and mortality
 - by gender, age, and socioeconomic status
- To describe secondary prevention in high-risk groups
 - including middle aged and older men
- To discuss controversies related to skin cancer screening
 - Focusing on role of physician skin exam
- To describe chemoprevention efforts

Melanoma Incidence

- Over 70,230 Americans will develop invasive melanoma in 2011 (40,010 men, 30,220 women)
 - estimated 53,360 additional cases of melanoma *in situ*
- Lifetime risk now >1 in 50 for invasive melanoma
 - 1 in 55 for women; 1 in 37 for men
- 5th most common cancer in men, 7th in women
- From 1973-2004: annual incidence increased by over 50% in women 15-39
 - Tanning bed use likely a factor

American Cancer Society. *Cancer Facts and Figures*, 2011.
Purdue MP et al. *J Invest Dermatol*. 2008;128:2905-8

Melanoma / Skin Cancer Control



Public Health Approach to Melanoma Control (education/awareness)

For the Public

- Prompt medical care for changing moles
- Perform careful (monthly) skin self-exams
- Avoid tanning beds
- Cover all parts of the skin exposed to the sun

For Health Care Professionals

- Integrate patient skin exam into routine care
- Increase melanoma awareness
- Teach patients how to perform skin self-exam

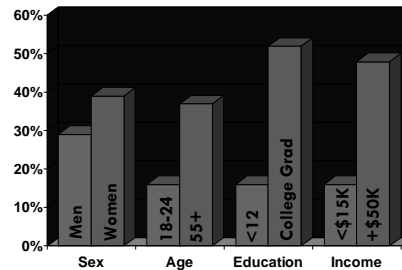
**“MELANOMA WRITES ITS
MESSAGE IN THE SKIN WITH ITS
OWN INK
AND FOR ALL OF US TO SEE”**

-Neville Davis, Queensland, Australia

...so why is early detection so hard?

1995 Melanoma Awareness Survey

Can you tell me what melanoma is?

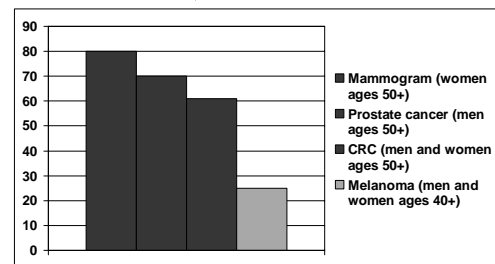


Miller DR et al. J Am Acad Dermatol. 1996;34:962-70.

Professional Education: Rationale for Primary Care Provider's Role in Early Detection

- Most Americans do not have a dermatologist
- Middle-aged and older men make at least 3-4 visits per year to a physician or medical care facility
- Nearly 2/3 of patients report seeing PCP in year prior to melanoma diagnosis
- MD detection compared with self or family detection = thinner melanoma
 - 0.5-1.00 mm thinner per multiple studies

Proportion of Americans Reporting a Cancer Screen Remains Low



Only 25% of those surveyed indicated that they had ever had a skin cancer examination [2005 National Health Interview Survey (n = 32,440)]

Melanoma Mortality 2011

- 8,790 individuals will die from disease in 2011
 - 5650 men, 3040 women
- Recent reductions in melanoma mortality (1969 to 1999)
 - nearly 40% in women and 30% in men aged 20 to 44 years
- Encouraging, but the role of prevention strategies on reduced mortality rates remains unclear

American Cancer Society. Cancer Facts and Figures, 2011.
Geller AC et al. JAMA. 2002;288:1719-20.

3 Key Points for Mortality Reduction

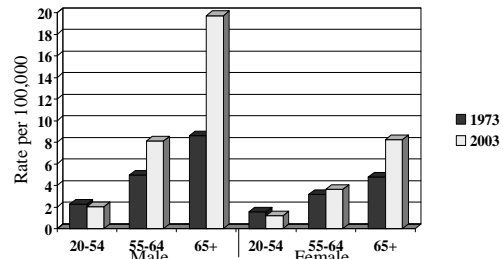
- Requires understanding of
 - biology (the tumor itself)
 - epidemiology (population demographics)
 - sociology (social structures & behavior of the population)
- MDs find thinner melanoma than patients or their partners
- Persons with lower SES and middle-aged and older men suffer disproportionate mortality

Socioeconomic Status (SES) and Melanoma

- Incidence rate uniformly higher among middle-high SES white populations
 - most studies show at least a 2:1 or 3:1 ratio
- Case-fatality rates (and mortality/incidence ratio) higher among lower SES populations
- Thinner melanomas continuing to grow at a higher rate for middle to high SES individuals
- BUT the rates of thicker melanomas growing faster for low SES individuals

Linos E et al. *J Invest Dermatol.* 2009;129:1666-74.

US Melanoma Mortality among Whites, 1973 and 2003, (by age/gender)



Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) Public-Use Data (1973-2003), National Cancer Institute, released April 2006, based on the November 2005 submission.

Rationale for Targeting Older Men

- Nearly 50% of all melanoma deaths are in white men aged 50 yrs and older
- Less likely to:
 - have a regular health care provider
 - receive routine preventive health care
 - participate in cancer prevention programs
- AAD screening analysis: greatest utility in men 50+ with changing mole or skin type I/II
 - Only 25% screenees but 44% confirmed melanoma cases

Centers for Disease Control and Prevention, National Center for Health Statistics, US Dept. of Health and Human Services, Public Health Service, 1997.
Geller AC et al. *Cancer.* 2002;95:1554-61.

Melanoma Discovery and Thickness (n=227 men, ages 40+)

- Of physician-detected melanomas, nearly 70% were ≤ 1 mm (T1), compared with 33% detected by the patient ($p < 0.001$)
- Back lesions comprised 46% of all physician-detected melanoma but only 16% of self-detected lesions
- Over 90% percent of physician-detected back-of-the-body melanomas were < 2 mm compared with 63% of self-detected ($p = 0.004$) lesions

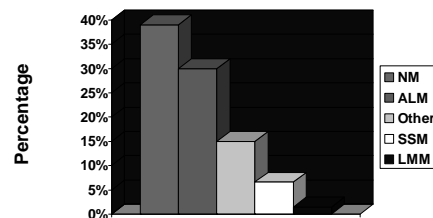
Swetter SM et al. *Arch Dermatol.* 2009;145:397-404.
Geller AC et al. *Arch Dermatol.* 2009;145:409-414.

Novel Melanoma Educational Campaign



Geller AC et al. *Arch Dermatol.* 2009;145:409-414.

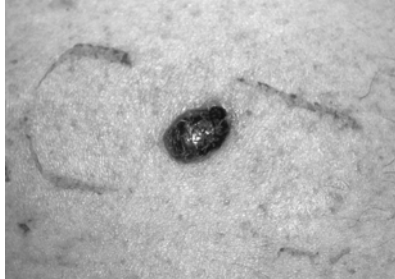
Proportion of Late-stage Melanoma by Histology, SEER, 1973-2006



Nodular melanoma accounts for 10% of all melanoma but 50% of all melanoma > 2 mm

Demierre MF et al. *Arch Dermatol.* 2005;141:745-50.

How Can We Detect Nodular Melanoma Earlier?



Ways to Improve Secondary Prevention

- Emphasize the ABCDEs of melanoma with aim of reducing late detection of thick melanomas
- Teach the “ugly duckling” for melanoma recognition
- Focus screening efforts on older men and enlist the help of women/spouses for early detection
- Does screening make a difference?

Skin Cancer Screening

- NO NEW EVIDENCE from controlled studies to address benefit of skin cancer screening
- USPSTF 2009 Statement:
 - *“Current evidence is insufficient to assess benefits and harms of whole-body skin exam by primary care clinicians or patient skin self-examination for early detection of melanoma in the adult general population.”*
- Bottom line: targeted screening of subsets at high risk is more effective than mass screening

United States Preventive Services Task Force. *Ann Int Med.* 2009;150:188-93.

Most Definitive Proof of Value of Physician Screening

- Australian population based case-control study, 2000-2003:
 - 35% of Queensland melanoma cases had physician skin exam
- Screening was associated with a 38% greater likelihood of being diagnosed with thin invasive melanoma (≤ 0.75 mm)
- Estimated mortality reduction of over 20% for screened cases

Aitken JF et al. *Int J Cancer.* 2010;126:450-458.

Additional Data to Support Physician Skin Examination

- Surveyed 566 newly-diagnosed adults with invasive melanoma:
 - Only 19% reported physician detection
- Physician skin exam in year prior to diagnosis:
 - associated with 2.5 times greater likelihood of being diagnosed with thin (≤ 1 mm) melanoma
 - (OR 2.51, 95% CI, 1.62-3.87)
- Greatest reduction in men >age 60
 - (OR 4.09, 95% CI 1.88-8.89)

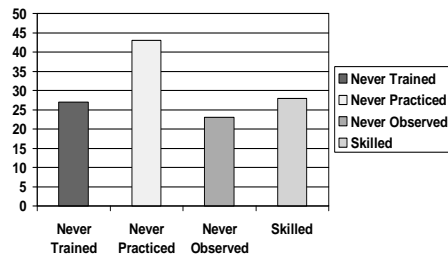
Swetter SM et al. Unpublished data.

Other Ways to Reduce the Socioeconomic Burden of Melanoma

- ~90% of total annual direct cost of treating melanoma attributable to advanced disease
- Seek legislation and behavior change strategies to reduce tanning bed use
- Improve screening with emphasis on high-risk groups
- Train PCPs in skin screening and triage
- Integrate teaching of skin cancer examination into medical, nursing, PA school curriculums

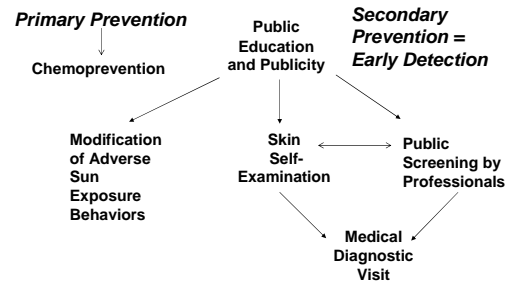
Tsao H, et al. *J Am Acad Dermatol.* 1998;38:669-80.
Moore MM, et al. *Arch Dermatol.* 2006;142:439-44.

Skin Cancer Exam Survey of US 3rd year Medical Students (n=659)



Moore MM, et al. Arch Dermatol. 2006;142:439-44.

Melanoma / Skin Cancer Control



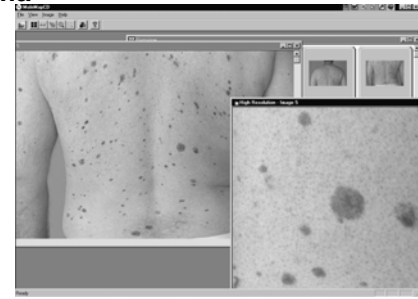
Melanoma - An Ideal Target for Chemoprevention

- Epidemic proportions:
 - -Incidence rising more rapidly than other solid tumors
 - -Includes thick tumors in low SES groups, not just a screening artifact
- Toll among young represents second largest loss in productive life-years of all solid tumors
- Association with clinical atypical nevi:
 - -Potential biologic intermediate in melanoma tumorigenesis
 - -May manifest progression/ predictive response markers
 - -Appropriate for evaluation of early phase candidate chemoprevention agents

Cutaneous Malignancies
May 23, 2011

Patients with Clinical Atypical Nevi are at Significant Risk of Developing Melanoma

Reported frequency of CAN among patients with a history of melanoma ranges from 34-59%



Melanoma Chemoprevention

- Prevent initial cancer in high-risk individuals, prevent cancers in those with premalignant conditions, prevent second primary cancers
- Potential topical/systemic agents for melanoma prevention:
 - Lipid-lowering agents (statins/fibrates)
 - Retinoids (systemic/topical)
 - NSAIDs/ASA - sulindac
 - Green Tea (polyphenols)
 - Vitamin D
 - Selenium (anti-oxidant effects)
 - Soy isoflavones (Genistein)
 - Resiquimod/Imiquimod
 - N-acetylcysteine
 - Sulforaphane
 - Pterostilbene

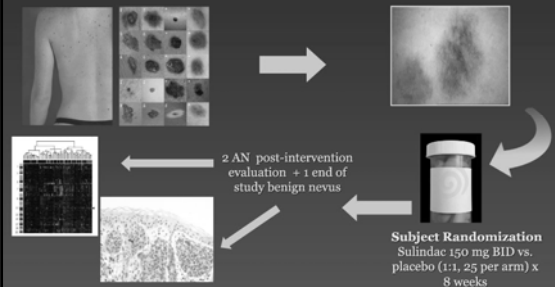
Demierre MF, Nathanson L. J Clin Oncol. 2003;21:158-165.

Phase IIa Clinical Trial on the Role of Sulindac in Atypical Nevi Patients

NCI/DCP Consortium protocol ongoing at the UA/AZCC and Stanford University

50 Healthy individuals with ≥ 4 clinical atypical nevi and ≥ 1 benign nevus

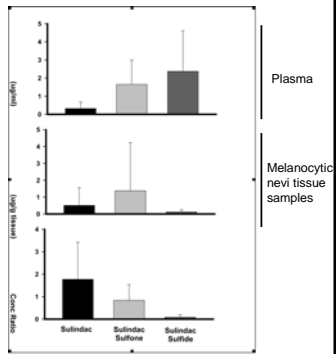
2 ANs randomized to baseline evaluation and 2 to post-intervention evaluation



Skin and plasma concentrations of sulindac and metabolites following sulindac intervention

❖ Sulindac and metabolites are bioavailable in nevi following sulindac treatment

❖ Nevus concentrations of sulindac and sulindac sulfone are comparable to the respective levels in plasma, while nevus distribution of sulindac sulfide is limited



Curiel-Lewandrowski C et al. Unpublished data.

Chemoprevention of Melanoma

