Screening for Skin Cancer: An Update of the Evidence for the U.S. Preventive Services Task Force

Tracy Wolff, MD, MPH; Eric Tai, MD, MS; and Therese Miller, DrPH

Background: Skin cancer is the most commonly diagnosed cancer in the United States. The majority of skin cancer is nonmelanoma cancer, either basal cell cancer or squamous cell cancer. The incidence of both melanoma and nonmelanoma skin cancer has been increasing over the past 3 decades. In 2001, the U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to recommend for or against routine screening for skin cancer by using whole-body skin examination for early detection of skin cancer.

Purpose: To update the evidence of benefits and harms of screening for skin cancer in the general population.

Data Sources: MEDLINE and Cochrane Library searches from 1 June 1999 to 9 August 2005 for English-language articles; recent systematic reviews; reference lists of retrieved articles; and expert suggestions.

Study Selection: English-language studies were selected to answer the following key question: Does screening in asymptomatic persons with whole-body examination by a primary care clinician or by self-examination reduce morbidity and mortality from skin cancer? Randomized, controlled trials and case–control studies of screening for skin cancer were selected. One author selected English-language studies to answer the following contextual questions: Can screening with whole-body examination by primary care clinicians or by self-examination accurately detect skin cancer? Does screening with whole-body examination or by self-examination detect melanomas at an earlier stage (thinner lesions)?

Data Extraction: All studies for the key question were reviewed, abstracted, and rated for quality by using predefined USPSTF criteria.

Data Synthesis: No new evidence from controlled studies was found that addressed the benefit of screening for skin cancer with a whole-body examination by a physician. One article of fair quality, which reanalyzed data from a 1996 study identified for the 2001 report for the USPSTF, provides limited but insufficient evidence on the benefit of skin self-examination in the reduction of morbidity and mortality from melanoma.

Limitations: Direct evidence linking skin cancer screening to improved health outcomes is lacking. Information is limited on the accuracy of screening by physicians or patients using real patients and lesions.

Conclusion: The limited evidence prevents accurate estimation of the benefits of screening for skin cancer in the general primary care population.

Ann Intern Med. 2009;150:194-198. www.annals.org
For author affiliations, see end of text.

Skin cancer is the most commonly diagnosed cancer in the United States (1). The majority of skin cancer is nonmelanoma cancer, either basal cell cancer or squamous cell cancer (2). In the United States, melanoma of the skin is the sixth most common type of cancer in white men and women (3). The incidence of both melanoma and nonmelanoma skin cancer has been increasing over the past 3 decades (4). Several preventive strategies, including routine screening, have been proposed by professional organizations.

The U.S. Preventive Services Task Force (USPSTF) last reviewed screening for skin cancer in 2001 and concluded that evidence was insufficient to recommend for or against routine screening for skin cancer by using whole-body skin examination for the early detection of cutaneous melanoma, basal cell cancer, or squamous cell cancer (5).

See also:

Print
Related articles 188, 199
Summary for Patients. I-40

Web-Only
Conversion of graphics into slides
Downloadable recommendation summary

The USPSTF made this statement after reviewing the available evidence and identifying 2 major gaps: the lack of quality evidence that links screening to improved health outcomes and limited information about the ability of primary care providers to perform adequate examinations in the context of usual care. To update its recommendation, the USPSTF determined that an update of the evidence would need to focus on these 2 issues.

On the basis of an analytic framework (**Figure**), the USPSTF determined that this evidence update would focus on a systematic review of the evidence of controlled trials on screening for skin cancer with morbidity and mortality outcomes to answer the following key question: Does screening in asymptomatic persons with whole-body examination by a primary care clinician or by self-examination reduce morbidity and mortality from skin cancer? In addition, the USPSTF asked for information concerning several contextual questions. The issues for this review that were identified as contextual questions that were nonsystematically reviewed are:

Contextual Question 1. Can screening with whole-body examination by primary care clinicians or by self-examination accurately detect skin cancer?

Contextual Question 2. Does screening with whole-body examination or by self-examination detect melanomas at an earlier stage (thinner lesions)?

This review does not include evidence on counseling for skin cancer. The USPSTF previously reviewed the evidence for counseling; the evidence review and recommendation can be found at www.preventiveservices.ahrq.gov.

METHODS

Data Sources and Searches

We searched the English-language literature in MEDLINE to identify randomized, controlled trials (RCTs) or case–control trials published from 1 June 1999 to 9 August 2005 to answer the following key question: Can screening reduce morbidity and mortality from skin cancer? We used the terms *skin neoplasms, squamous cell neoplasms, basal cell neoplasms, melanoma,* and *mass screening*. In addition to the MEDLINE search, we identified further literature by reviewing reference lists of review articles and editorials and by consulting with experts. For the contextual questions, we performed targeted literature searches, reviewed the searches performed for other questions, identified studies from reference lists, and consulted with experts.

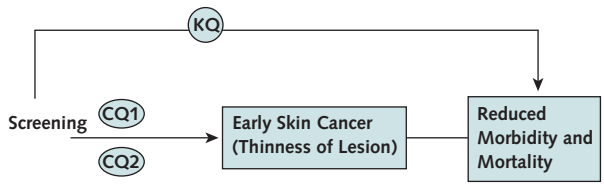
Study Selection

Two reviewers independently reviewed the title lists, abstracts, and full articles for the key question. We excluded studies if they did not address skin cancer, did not report morbidity or mortality outcomes, were editorials or review articles, had no control group, or had a study population that included only persons with rare skin cancer syndromes. We also excluded studies if the intervention was not screening with whole-body visual examination by a physician or by the patient, was not performed in a primary care setting, or was designed to improve diagnostic ability (and not screening). We discussed studies selected by fewer than 2 reviewers and based selection on consensus. A third reviewer was consulted if necessary. For contextual question 1, 1 author selected studies published since June 1999 that provided information on accuracy of screening examinations by primary care clinicians or by patient self-examination. For contextual question 2, 1 author selected studies published since June 1999 that provided information on thinness of lesions detected by screening examinations.

Data Extraction and Quality Assessment

For all citations that met the eligibility criteria for the key question, 2 reviewers independently reviewed, abstracted, and quality-rated the full articles. The 2 reviewers achieved consensus about article inclusion, content, and quality through discussion; a third reviewer resolved disagreements. We extracted data on the following items from the studies included for the key question: identification of case patients, case definition, selection of control participants, comorbid conditions, sun exposures, demographic characteristics of case patients and control participants, definition of screening examination, exposure to screening, rates of follow-up, and results. We performed quality evaluations of articles for the key question by using standard USPSTF methodology on internal and external validity (6). We evaluated the quality of RCTs and cohort studies on the following items: initial assembly of comparable groups, maintenance of comparable groups, important differential loss to follow-up or overall high loss to follow-up, measurements (equality, reliability, and validity of outcome measurements), clear definition of the interventions, and appropriateness of outcomes. We evaluated the quality of case–control studies on the following items: accurate ascertainment of cases, nonbiased selection of case patients and control participants with exclusion criteria applied equally to both, response rate, diagnostic testing procedures applied equally to each group, accurate measurement of exposure applied equally to each group, measurement of exposure accurate and applied equally to each group, and appropriate attention to potential confounding variables.

Figure. **Analytic framework for screening for skin cancer.**



KQ: Does screening in asymptomatic persons with whole-body examination by a primary care clinician or by self-examination reduce morbidity and mortality from skin cancer?
CQ1: Can screening with whole-body examination by primary care clinicians or by self-examination accurately detect skin cancer?
CQ2: Does screening with whole-body examination or by self-examination detect melanomas at an earlier stage (thinner lesions)?

CQ = contextual question; KQ = key question.

Data Synthesis and Analysis

Data from the included studies was synthesized qualitatively in a narrative format.

Role of the Funding Source

The general work of the USPSTF is supported by the Agency for Healthcare Research and Quality. This specific review did not receive separate funding.

RESULTS

Key Question

Does screening in asymptomatic persons with whole-body examination by a primary care clinician or by self-examination reduce morbidity and mortality from skin cancer?

We found no new evidence on the effectiveness of skin examination by a physician in reducing the morbidity or mortality of skin cancer. One article of fair quality by Berwick and colleagues (7), which reanalyzed data from a 1996 study identified for the 2001 report for the USPSTF

(8), provides limited but insufficient evidence on the benefit of skin self-examination in the reduction of morbidity and mortality from melanoma.

Data on case patients ($n = 650$) in Berwick and colleagues' study (7) were obtained from the Connecticut Tumor Registry, a National Cancer Institute Surveillance Epidemiology and End-Results (SEER) site. Control participants ($n = 549$) were identified from the general public through random-digit dialing and were frequency-matched on age and sex. Nurses performed a limited skin examination to count nevi on the back and arms. Participants were followed biannually for a mean of 5.4 years.

Identification of case patients was probably fairly complete because of a state reporting mandate and the research team's active monitoring of dermatopathology laboratories. The response rate for case patients and control participants was 75% and 70%, respectively. The mortality tally was probably complete because the research team used several sources to identify deaths of the participants. Limitations of the research design include potential selection bias of case patients and control participants, lack of information on the initial comparability of the case patients and control participants, potential recall bias because information on many variables (including the history of any clinical screening) relied on patient report, and lack of information on masking of the nurse or dermatologist to the case status.

Of the original 650 case patients, 112 were excluded: 26 because of diagnosis from node or organ metastases, 95 with a diagnosis of lentigo maligno melanoma, and 1 without follow-up. This analysis showed no significant association between screening examination (by self-examination or by a physician) and death from melanoma in those with melanoma. On univariate analysis, the hazard ratio for skin self-examination was 0.6 (95% CI, 0.2 to 1.5) and for physician screening examination was 0.7 (CI, 0.4 to 1.3); this does not differ greatly from the 1996 analysis that had more participants and a slightly broader definition of the outcome. The authors report a significant association between "skin awareness" and death from melanoma (hazard ratio, 0.5 [CI, 0.3 to 0.9)) after controlling for other confounders. The authors defined skin awareness as a positive response to the question, "Did you ever think about your skin, how it looked, whether there were any changes, or whether there were any abnormal marks?"

Contextual Question 1

Can screening with whole-body examination by primary care clinicians or by self-examination accurately detect skin cancers?

Accuracy of screening is an important link in the chain of evidence connecting screening in asymptomatic persons with improved health outcomes. Evidence for the accuracy of screening with whole-body examination by physicians or by patients is limited and inconsistent. A recent systematic review (9) using pictures of lesions reported a sensitivity that ranged from 42% to 100% and a specificity of 98%. The same systematic review reported a sensitivity of 70% to 91% and a specificity of 51% to 87% for appropriateness of referral or biopsy, using histopathology or expert consensus as the gold standard. Studies on the accuracy of skin self-examination reported sensitivity and specificity from 58% to 75% and 62% to 98%, respectively. The studies in physicians evaluated the accuracy of diagnosing pigmented lesions, not a screening examination, and many of the studies on self-examination were performed in selected patient populations. Therefore, these results may not be generalizable to a screening examination in the general population. In addition to the accuracy of a physician or patient examination, there is the uncertainty of the pathologist's reading of the biopsy specimen. There is some evidence of moderate disagreement among pathologists in reading skin biopsies (10, 11).

Several studies on diagnostic and referral accuracy of family physicians and general practitioners have been published since 2001 (12–14); these studies evaluated accuracy before and after educational interventions and generally concluded that educational interventions improve the diagnostic accuracy of skin cancer examinations. Most of these studies were performed outside the United States, and all used nonliving representations of lesions, including photographs and slides of lesions, limiting the applicability to screening accuracy in primary care.

A more recent, community-based RCT of screening in Australia (15) involving 16 383 whole-body skin examinations reported the specificity and positive predictive value of screening by a primary care physician for melanoma as 86% and 2.5%, respectively. The overall positive predictive value for all types of skin cancer was 29%. However, the researchers did not follow the participants with negative results, and therefore could not report the number of true-negative results or the true specificity.

Three published studies have evaluated the accuracy of skin self-examination (16–18). They generally showed variable specificity and sensitivity that was higher with greater size increases in lesions and higher with the use of photographs. Two of these studies assessed the accuracy, after artificial change of lesions, in the study participants' reports of the number or appearance of moles, and 1 study evaluated the accuracy of skin self-examination before and after education about the asymmetry, border, color, diameter (ABCD) criteria. Again, the applicability to primary care of studies of artificial change in lesions is questionable.

Contextual Question 2

Does screening with whole-body examination or by self-examination detect melanomas at an earlier stage (thinner lesions)?

We found no RCTs that compared screened and unscreened participants with respect to thickness of melanoma lesions. We identified 1 study that looked at a screened population to evaluate lesion thickness at detection (19). This study of 639 835 participants who were

screened during the American Academy of Dermatology Skin Cancer Screening Program from 1985 to 1999 compared the results of the American Academy of Dermatology screening efforts with the SEER registry. In the American Academy of Dermatology program, dermatologists performed screening examinations that were free and open to the public. Participants who had received screening through the American Academy of Dermatology program had a higher percentage of lesions smaller than 1.50 mm than cases documented in the SEER registry: 10% and 2%, respectively ($P < 0.001$). Conclusions are limited because of self-selection in the American Academy of Dermatology program, the ecological nature of the study, and problems with generalizing screening by a dermatologist to screening by a primary care clinician. A study in Queensland, Australia, reviewed the characteristics of all histologically confirmed first melanomas in residents age 20 to 75 years (20). They found that the rate of thin lesions (<0.75 mm) detected by a physician (81%) was higher than the rate detected by nonphysicians (62%).

There is evidence from retrospective studies of patients with diagnosed melanoma that, although most melanoma lesions are first noticed by someone other than a physician, lesions detected by a physician are thinner. A study of 471 patients with newly diagnosed melanoma (1995 to 1998) in New York found that 57% of patients first detected the melanoma lesion and another 15% were found by someone other than a physician (primarily a spouse) (21). There was a significant association between physician detection and thickness of 0.75 mm or less. In an Italian study of 816 consecutive patients with melanoma (22, 23), identification by a dermatologist was associated with significantly thinner melanoma lesions than those identified by others (0.68 mm vs. 0.90 mm). Of note, melanoma lesions in participants who performed skin self-examination were also significantly thinner than in those who did not perform skin self-examination (0.77 mm vs. 0.95 mm); however, the definition of skin self-examination was not reported. A study of 102 patients seen at the Johns Hopkins Melanoma Center between June 1995 and June 1997 reported that the majority of lesions were detected by the patient (24). The mean lesion thickness was 0.23 mm for physician-detected lesions and 0.9 mm for self-detected lesions. Compared with self- or other-detected lesions, physician-detected lesions were associated with a higher likelihood of thinner lesions (relative risk, 4.0 [CI, 1.08 to 14.3] for lesions ≤0.75 mm versus those >0.75 mm).

Discussion

The direct evidence to support the benefits of a screening examination by a physician or patient in reducing morbidity and mortality is limited. We reviewed 1 new fair-quality case–control study of skin self-examination that used data from a study identified in the 2001 report for the USPSTF. We found no new studies on the benefits of screening by a physician that met our inclusion and exclusion criteria and were of appropriate quality.

The evidence on accuracy of screening has limitations. Several different methods have been used to study the accuracy of screening for skin cancer by physicians and by patients. Many studies measure accuracy through the use of photographs of lesions of known histopathology. Other studies measure accuracy by following the referral patterns and ultimate histopathology of lesions from real patients. Both of these methods have obvious problems. Using photographs of known lesions may test the accuracy of the diagnostic ability of a physician but does not necessarily assess the accuracy of a full-body screening examination. The use of referral patterns and histopathology assumes that a dermatologist's assessment of the need for biopsy and the resultant histopathology constitute the gold standard. Without appropriate follow-up of patients, this method probably underestimates the number of false-negative results.

There is limited evidence on whether screening by physicians or by patients identifies lesions that are thinner than those identified in usual care. Older ecological studies reported conflicting results on the association of thickness of melanoma and screening. Newer limited evidence from 1 large study of a self-selected screened population and from retrospective studies indicates that physician examinations and self-examinations identify thinner melanoma lesions. However, the retrospective studies do not report whether the lesions were detected during a screening examination or coincidentally during an examination for other reasons. Therefore, there are problems with using this evidence to generalize about the ability of screening examinations to identify thinner lesions in the general public. In addition, the majority of melanoma lesions are identified by the patient, friend, or spouse, and the question remains whether encouraging skin self-examination would identify more lesions or lesions at an earlier stage than are currently being identified by nonphysicians.

Research Gaps

The literature on screening for skin cancer has several limitations. A major limitation is the lack of direct evidence linking skin cancer screening to improved health outcomes. An adequately powered, population-based RCT of screening demonstrating mortality outcomes would require approximately 800 000 participants because of the relatively low melanoma-related mortality rate in the United States. (7, 25) However, the incidence of melanoma and mortality are higher in Australia, requiring a smaller sample size. A 3-year RCT in 44 Australian communities ($n = 560\,000$ adults age ≥30 years) had been planned by Aitken and colleagues (26). The intervention included promotion of screening through skin self-examination and physician examination. Unfortunately, the study was performed only in 9 control and 9 intervention communities because of lack of funding. The preliminary

results may help inform future recommendations on skin cancer screening. Further analyses are needed to evaluate whether routine referral to dermatologic specialists might be effective. Given the lack of direct evidence, modeling studies using available indirect evidence, including cost-effectiveness studies, may provide some information on the usefulness of screening as a preventive strategy.

Other limitations of the literature include a lack of large studies on accuracy of screening in the general population and a lack of information on whether screening in the general population would result in the identification of lesions at an earlier stage than regular care.

From the Center for Primary Care, Prevention, and Clinical Partnerships, Agency for Healthcare Research and Quality, Rockville, Maryland.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Reprints are available from the Agency for Healthcare Research and Quality Web site (www.ahrq.gov/clinic/uspstfix.htm).

Current author addresses are available at www.annals.org.

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Current Author Addresses: Drs. Wolff and Miller: Center for Primary Care, Prevention, and Clinical Partnerships, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

Dr. Tai: Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, 4770 Buford Highway, Northeast, MS-K57, Atlanta, GA 30341-3717.