

Screening for Skin Cancer

US Preventive Services Task Force

Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Basal and squamous cell carcinoma are the most common types of cancer in the United States and represent the vast majority of all cases of skin cancer; however, they rarely result in death or substantial morbidity, whereas melanoma skin cancer has notably higher mortality rates. In 2016, an estimated 76 400 US men and women will develop melanoma and 10 100 will die from the disease.

OBJECTIVE To update the 2009 US Preventive Services Task Force (USPSTF) recommendation on screening for skin cancer.

EVIDENCE REVIEW The USPSTF reviewed the evidence on the effectiveness of screening for skin cancer with a clinical visual skin examination in reducing skin cancer morbidity and mortality and death from any cause; its potential harms, including any harms resulting from associated diagnostic follow-up; its test characteristics when performed by a primary care clinician vs a dermatologist; and whether its use leads to earlier detection of skin cancer compared with usual care.

FINDINGS Evidence to assess the net benefit of screening for skin cancer with a clinical visual skin examination is limited. Direct evidence on the effectiveness of screening in reducing melanoma morbidity and mortality is limited to a single fair-quality ecologic study with important methodological limitations. Information on harms is similarly sparse. The potential for harm clearly exists, including a high rate of unnecessary biopsies, possibly resulting in cosmetic or, more rarely, functional adverse effects, and the risk of overdiagnosis and overtreatment.

CONCLUSIONS AND RECOMMENDATION The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in adults (I statement).

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- ◀ Editorial [page 398](#)
- + Author Audio Interview at [jama.com](#)
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The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendation and Evidence

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in adults (I statement) (Figure 1).

Rationale

Importance

Skin cancer includes melanoma and basal and squamous cell carcinoma. Basal and squamous cell carcinoma, known together as

Figure 1. US Preventive Services Task Force Grades and Levels of Certainty

What the USPSTF Grades Mean and Suggestions for Practice		
Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit	
Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as “likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.” The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

nonmelanoma skin cancer, are the most common types of cancer in the United States and represent the vast majority of all cases of skin cancer (>98%).¹ However, nonmelanoma skin cancer rarely results in death or substantial morbidity (<0.1% of patient deaths are caused by this type of cancer), whereas melanoma skin cancer has notably higher mortality rates.¹ For this reason, although a visual skin examination by a clinician will detect all 3 of these cancer types, in understanding the potential benefit of screening, the USPSTF prioritized outcomes related to melanoma in developing this recommendation statement. In 2016, an estimated 76 400 US men and women will develop melanoma and 10 100 will die from the disease.¹

Detection

Evidence is adequate that visual skin examination by a clinician has modest sensitivity and specificity for detecting melanoma. Evidence is more limited and inconsistent regarding the accuracy of the clinical visual skin examination for detecting nonmelanoma skin cancer.²

Benefits of Early Detection and Treatment

Evidence is inadequate to reliably conclude that early detection of skin cancer through visual skin examination by a clinician reduces morbidity or mortality.

Figure 2. Screening for Skin Cancer: Clinical Summary

Population	Asymptomatic adults
Recommendation	No recommendation. Grade: I (insufficient evidence)
Risk Assessment	Skin cancer occurs more commonly in men than in women and among persons with a fair complexion, persons who use indoor tanning beds, and persons with a history of sunburns or previous skin cancer. Specific risk factors for melanoma include having a dysplastic nevus (atypical mole), multiple (≥ 100) nevi, and a family history of melanoma. Risk of melanoma also increases with age.
Screening Tests	The clinical visual skin examination assesses skin lesions using the "ABCDE rule," which involves looking for the following characteristics: asymmetry, border irregularity, nonuniform color, diameter >6 mm, and evolving over time.
Treatment and Interventions	Treatment of screen-detected melanoma generally involves excision, with or without lymph node management, depending on the stage at diagnosis. There are a variety of treatments available for squamous and basal cell carcinoma, including surgical excision, Mohs micrographic surgery, radiation therapy, curettage and electrodesiccation, and cryosurgery.
Balance of Benefits and Harms	The USPSTF concludes that the current evidence is insufficient and that the balance of benefit and harms of visual skin examination by a clinician to screen for skin cancer in asymptomatic adults cannot be determined.
Other Relevant USPSTF Recommendations	The USPSTF recommends that children, adolescents, and young adults aged 10 to 24 years who have fair skin be counseled about minimizing their exposure to ultraviolet radiation to reduce their risk of developing skin cancer. This recommendation is available on the USPSTF website (http://www.uspreventiveservicestaskforce.org).

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to <http://www.uspreventiveservicestaskforce.org>.


JAMA

USPSTF indicates US Preventive Services Task Force.

Harms of Early Detection and Treatment

Evidence is adequate that visual skin examination by a clinician to screen for skin cancer leads to harms that are at least small, but current data are insufficient to precisely bound the upper magnitude of these harms. Potential harms of skin cancer screening include misdiagnosis, overdiagnosis, and the resulting cosmetic and—more rarely—functional adverse effects resulting from biopsy and overtreatment.

USPSTF Assessment

The USPSTF concludes that the current evidence is insufficient and that the balance of benefit and harms of visual skin examination by a clinician to screen for skin cancer in asymptomatic adults cannot be determined.

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic adults who do not have a history of premalignant or malignant skin lesions (Figure 2). Patients who present with a suspicious skin lesion or who are already under surveillance because of a high risk of skin cancer, such as those with a familial syndrome (eg, familial atypical mole and melanoma syndrome), are outside the scope of this recommendation statement.

Assessment of Risk

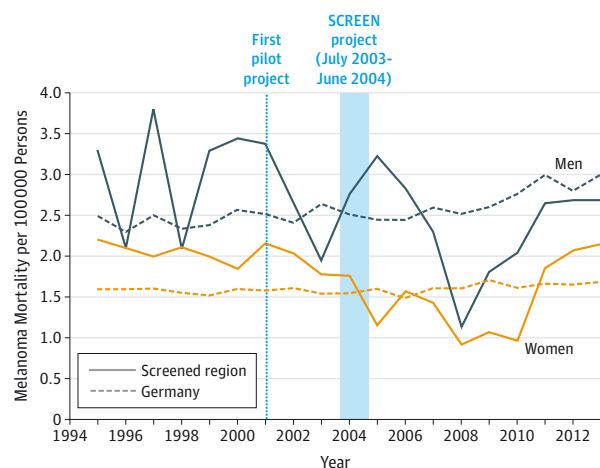
Skin cancer of any type occurs more commonly in men than in women and among persons with a fair complexion, persons who use indoor tanning beds, and persons with a history of sunburns or previous skin cancer. Specific risk factors for melanoma include having a dysplastic nevus (atypical mole), having multiple (ie, ≥ 100) nevi, and having a family history of melanoma.^{3,4} Like most types of cancer, the risk of melanoma increases with age; the median age at diagnosis is 63 years, and the median age at death is 69 years.¹

Suggestions for Practice Regarding the I Statement

Potential Benefit of Early Detection and Treatment

Direct evidence to assess the effect of screening with a clinical visual skin examination on the risk of death from skin cancer is limited.³ A single ecologic study (Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany [SCREEN]) with important methodological limitations suggests that a 1-time, general population-based screening program (with limited participation of 19%) combined with a disease awareness campaign may result in, at most, 1 fewer death due to melanoma per 100 000 persons over a decade.⁵ An independent analysis of the SCREEN population found that the observed melanoma mortality rate returned to preintervention levels after 5 years of follow-up (Figure 3).⁶

Figure 3. Cutaneous Melanoma Mortality Rates in the Schleswig-Holstein Region Participating in the SCREEN Study as Compared With the Whole of Germany, 1994-2013



Melanoma mortality rates for men and women in the Schleswig-Holstein region of Germany, which participated in the Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany (SCREEN) study,⁶ as compared with the whole of Germany. The original SCREEN study reported a relative 48% reduction in melanoma mortality (or 1 fewer death per 100 000 screened) resulting from a program of 1-time clinical visual skin cancer screening combined with a disease awareness campaign. The screening program occurred during 2003-2004, and the mortality results were calculated based on follow-up until 2008. An independent study provided an additional 5 years of follow-up (through 2013) and found that the observed declines in melanoma mortality rates for men and women in the region that had participated in the SCREEN study did not persist with time. (Image originally published in: Boniol M, Autier P, Gandini S. Melanoma mortality following skin cancer screening in Germany. *BMJ Open*. 2015;5:e008158.⁶)

Potential Harms of Early Detection and Treatment

Information on the harms of screening is also sparse.³ The majority of suspicious skin lesions excised during screening are not cancerous; for example, the SCREEN study found that between 20 and 55 excisions were performed to detect 1 case of melanoma, depending on patient age.⁷ The SCREEN study did not report the number of excisions required to prevent 1 death from melanoma, but it can be estimated at more than 4000. Overdiagnosis and overtreatment—the diagnosis and treatment of cancer that would never have harmed the patient in the absence of screening—are other important potential harms. Ecologic evidence suggests that screening with a visual skin examination results in the overdiagnosis of skin cancer^{8,9}; however, current evidence is insufficient to be reliably certain of the magnitude of this effect.

Current Practice

Contemporary data on clinician practice patterns related to skin cancer screening are limited. A 2005 survey of US physicians found that 81% of dermatologists, 60% of primary care physicians, and 56% of internists reported performing a full-body visual skin cancer screening examination on their adult patients.¹⁰

Screening Tests

The clinical visual skin examination assesses skin lesions using the “ABCDE rule,” which involves looking for the following characteris-

tics: asymmetry, border irregularity, nonuniform color, diameter greater than 6 mm, and evolving over time.

Screening Interval

The optimal interval for visual skin examination by a clinician to screen for skin cancer, if it exists, is unknown.

Treatment

Treatment of screen-detected melanoma generally involves excision, with or without lymph node management, depending on the stage at diagnosis. There are a variety of treatments available for squamous and basal cell carcinoma (which have excellent cure rates), including surgical excision, Mohs micrographic surgery, radiation therapy, curettage and electrodesiccation, and cryosurgery, among other options.

Other Approaches to Prevention

The USPSTF recommends that children, adolescents, and young adults aged 10 to 24 years who have fair skin be counseled about minimizing their exposure to ultraviolet radiation to reduce their risk of developing skin cancer.¹¹

Useful Resources

The Community Preventive Services Task Force has made a number of recommendations related to preventing skin cancer through the use of interventions that target child care centers; outdoor occupational, recreational, and tourism settings; primary and middle schools; and communities (available at <http://www.thecommunityguide.org/cancer/index.html>).

Other Considerations

Research Needs and Gaps

The USPSTF recognizes the challenge of conducting a definitive randomized clinical trial (RCT) on primary screening, with cause-specific mortality as an end point, to provide clear evidence on the efficacy of the clinical visual skin examination in screening for skin cancer, given the comparatively low rate of death from melanoma in the population (even among persons at higher risk). If adequately powered RCTs are not possible, a high-quality case-control study could provide sufficient power without requiring a large sample size. However, this study design has limitations in the ability to create an appropriate comparison group, the ability to accurately measure the exposure of interest (because of recall bias and other sources of misclassification), healthy volunteer bias (persons receiving skin examinations likely have other good health habits), and other unmeasured sources of confounding. Studies would have to be carefully designed to avoid these threats to validity. Despite these challenges, the USPSTF concludes that further evidence is necessary to advance the field on this essential question. An optimized version of the SCREEN study (ie, a time-series study), in which the clinical visual skin examination alone, without the potential confounding of a second intervention, is evaluated, would also be useful. Additional research on the possible harms of screening for skin cancer—particularly the potential for overdiagnosis and overtreatment—is also needed to help fully understand the ultimate net benefit of the clinical visual skin examination.

Discussion

Scope of Review

The USPSTF commissioned a systematic evidence review^{3,4} to update its 2009 recommendation on screening for skin cancer. The review addressed several questions about screening for skin cancer with the clinical visual skin examination, including its effectiveness in reducing skin cancer morbidity and mortality and death from any cause; its potential harms, including any harms resulting from associated diagnostic follow-up; its test characteristics when performed by a primary care clinician vs a dermatologist; and whether its use leads to earlier detection of skin cancer compared with usual care.³ Unlike in the previous review, the evidence concerning patient self-examination for skin cancer was not included in this statement. The visual skin self-examination will be addressed in a separate recommendation statement on counseling to prevent skin cancer.

Accuracy of Screening Tests

A systematic review of 11 studies on the diagnostic accuracy of screening by primary care clinicians and dermatologists identified during the previous evidence review found that screening by primary care clinicians had a sensitivity of 42% to 100% and a specificity of 98% for the diagnosis of melanoma.¹² Since then, 2 additional studies on the test characteristics of the clinical visual skin examination have been published: 1 evaluating screening performed by primary care clinicians and 1 evaluating screening performed by dermatologists or plastic surgeons. These studies found that sensitivity ranged from 40% to 70%, which sharply decreased as the length of follow-up increased (from 12 to 24 or 36 months). Specificity ranged from 86% to 98%.^{3,13,14} None of the studies could draw reliable conclusions as to whether screening performed by any of the clinical specialties differed in diagnostic accuracy.^{3,12-14}

Effectiveness of Early Detection and Treatment

No RCT has directly evaluated the effectiveness of the clinical visual skin examination for reducing skin cancer morbidity or mortality (a pilot study by Aitken et al in Queensland, Australia, began in 2002, but a full trial was never completed).³ A single fair-quality ecologic study (SCREEN) compared trends in melanoma mortality rates in 1 region of Germany using a population-based skin cancer awareness campaign, clinician education and training, and clinical visual skin examination provided through a cancer screening program with several surrounding regions that did not have similar interventions available. After a 2-year public skin cancer awareness campaign, 360 288 adults 20 years and older (about 19% of the eligible population) received a single clinical visual skin examination. After 10 years, the study found a 48% relative reduction in the risk of dying from melanoma in the region that instituted the interventions compared with the control regions, which translates into an absolute reduction of 1 fewer death from melanoma per 100 000 persons screened.¹⁵

The SCREEN study has several important limitations. First, it does not provide individual patient-level data on the effect of the clinical visual skin examination, and as an ecologic observational study, it is subject to the potential effects of known and unknown biases and confounders. Second, the separate effects of the pub-

lic education component cannot be disentangled from those of the clinical visual skin examination component; therefore, it is likely that the effect of screening alone is smaller than estimated. In addition, the melanoma mortality rate in the region receiving the interventions was already declining prior to the introduction of the cancer screening program. This also suggests that the 48% relative reduction overestimates the true effect size of screening. Several other data points raise questions about the plausibility of the observed effect: (1) only 19% of the total eligible population was actually screened, and 37% of these individuals were lost to follow-up, yet the relative magnitude of the mortality reduction in the population is larger than in almost any other cancer screening intervention currently available; and (2) three-fourths of the population screened were women, yet equal reductions in melanoma mortality were observed among both men and women.¹⁵ Furthermore, an independent study evaluating an additional 5 years of follow-up in the SCREEN study population found that the observed reduction in melanoma mortality rates did not persist over time but essentially returned to the baseline rates observed before the screening program was initiated (Figure 3).⁶

When direct, overarching evidence concerning the benefit of a screening intervention on health outcomes is inconclusive, the USPSTF looks to a chain of indirect evidence to assess the effectiveness of the preventive service. In the case of the clinical visual skin examination, this includes linking together information about the ability of screening to detect melanoma earlier than in usual care and the link between earlier detection of skin cancer and resultant morbidity and mortality. The USPSTF identified only 1 fair-quality case-control study pertaining to the question of whether screening for skin cancer with a clinical visual skin examination leads to the earlier detection of melanoma compared with usual care.³ It found a modest association between the clinical visual skin examination and early detection (odds ratio, 0.84 [95% CI, 0.75-0.98]).¹⁶ However, because the study used patient self-report to identify exposure to clinician skin examination, recall bias is a potential concern.

Harms of Early Detection and Treatment

Evidence on the harms of the clinical visual skin examination is limited.³ In the SCREEN study, approximately 4.4% of screened individuals (1 of 23 participants) underwent a skin excision for a suspicious lesion. The majority of these biopsies did not result in a cancer diagnosis. Overall, for both men and women, 1 case of melanoma was detected per 28 excisions performed. However, this varied greatly by patient age. For example, among men aged 20 to 34 years vs 65 years and older, 1 case of melanoma was detected per 52 vs 20 skin excisions, respectively.⁷

Cosmetic or, more rarely, functional adverse effects may also result from an excisional biopsy prompted by clinical visual skin examination, although there are few data available on the frequency or specific details of these events. One fair-quality study of a single physician's performance of skin cancer screening and razor-blade shave biopsy among patients who were not ultimately diagnosed with skin cancer found that 7% of these patients expressed poor satisfaction with the cosmetic results (whereas the physician felt the results were poor in 16% of cases).^{3,17}

Overdiagnosis and overtreatment—the identification and treatment of cancer that would never have harmed the patient in

the absence of screening—is also a potential outcome of concern. It is not possible to directly determine for any individual patient whether a diagnosed cancer will progress or not; as such, measuring overdiagnosis is not a straightforward process and must be indirectly quantified. In the case of skin cancer, there is limited research to estimate the potential magnitude of the burden of overdiagnosis associated with screening. An ecologic study linking melanoma incidence and mortality data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program with Medicare claims for skin biopsy among patients 65 years and older found that from 1986 to 2001, the average incidence of melanoma increased 2.4 times (from 45 to 108 cases per 100 000 persons), while the average biopsy rate increased 2.5 times (from 2847 to 7222 biopsies performed per 100 000 persons). However, the increased cancer incidence was entirely due to extra cases of in situ and local disease, without the expected complementary decrease in the incidence of advanced melanoma or death from melanoma. The authors concluded that this pattern strongly suggested that screening efforts in the United States were generating overdiagnosis, rather than depicting a true increase in the occurrence of melanoma.⁸

Estimate of Magnitude of Net Benefit

Evidence to assess the net benefit of screening for skin cancer with the clinical visual skin examination is limited. Direct evidence on the effectiveness of screening in reducing melanoma morbidity and mortality is limited to a single fair-quality ecologic study with important methodological limitations. This study suggests that, at best, a program of public education and disease awareness coupled with 1-time visual skin examination by a clinician may reduce the risk of dying from melanoma among average-risk adults by about 1 death per 100 000 persons screened after 10 years; however, there are reasons to believe that the effect size is likely smaller. The indirect pathway of evidence (ie, examining the accuracy of screening; the link between visual skin examination and earlier detection of melanoma, such as lesion thickness; and the link between earlier detection of melanoma and skin cancer–related morbidity and mortality) and the studies included as part of this pathway are subject to several important biases of screening, including lead-time bias and length-biased sampling. These biases preclude the USPSTF's ability to draw reliable conclusions about the efficacy of the clinical visual skin examination with reasonable certainty. Therefore, there is insufficient evidence to reliably conclude whether screening for skin cancer with a clinical visual skin examination reduces melanoma morbidity or mortality.

Information on harms is similarly sparse. The potential for harm clearly exists, including a high rate of unnecessary biopsies, possibly resulting in cosmetic or—more rarely—functional adverse effects, and the risk of overdiagnosis and overtreatment. It is difficult for the USPSTF to accurately bound the magnitude of these potential harms without better information about the frequency with which skin cancer is likely overdiagnosed and overtreated. Further, it is challenging for the USPSTF to correctly bound the magnitude of the net benefit without more accurate and precise information about the size of the potential mortality benefit, if one exists. As such, the USPSTF concludes that the evidence is insufficient to assess the balance of benefit and harms of screening for skin cancer in adults with a clinical visual skin examination.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from December 1 through December 28, 2015. In response to the comments received, the USPSTF added a reference to a study that examined longer-term melanoma mortality rates in the SCREEN study population.⁶ The USPSTF also clarified that the recommendation does encompass all forms of skin cancer (ie, squamous and basal cell carcinoma and melanoma). A clinical visual skin examination will detect all skin cancer types; however, in assessing the potential benefit of screening, the USPSTF focused on melanoma because the associated morbidity and mortality rates for this type of skin cancer are substantially greater than for the others. In addition, although the systematic evidence review searched for studies of all skin cancer types, the evidence that met the prespecified inclusion criteria for the review only described efficacy outcomes for melanoma.

Several comments stressed that the USPSTF should place greater emphasis on the benefits of detecting and treating nonmelanoma skin cancer, noting the risk for such cancer to become locally destructive and lead to disfigurement if left untreated. Although the USPSTF agrees that reduced morbidity from nonmelanoma skin cancer or its requisite treatment would be an important benefit of screening, there is currently no evidence available to address this outcome for the clinical visual skin examination. It is therefore unknown whether there is an incremental benefit to detecting nonmelanoma skin cancer through a program of regular visual clinical examination vs patient self-identification as part of general body awareness followed by reasonably prompt evaluation by a clinician.

Several comments suggested that the USPSTF should consider making a separate positive recommendation for persons who are at increased risk for skin cancer (eg, those with a family history of melanoma), as they may potentially benefit more from a screening intervention. At present, there is insufficient evidence for *any* population that regular visual skin examination by a clinician can reduce skin cancer–related morbidity and mortality; the USPSTF agrees that targeted research among populations with the highest burden of disease would be useful.

Update of Previous USPSTF Recommendation

This recommendation updates the 2009 USPSTF recommendation.¹⁸ The USPSTF has again concluded that the current evidence is insufficient to assess the balance of benefit and harms of screening for skin cancer in adults with a clinical visual skin examination. However, the USPSTF decided to no longer include a statement about patient skin self-examination in the current recommendation. This intervention will be addressed in the USPSTF's update of its recommendation statement on counseling to prevent skin cancer.

Recommendations of Others

Most professional organizations in the United States have no specific recommendations about screening for skin cancer with the clinical visual skin examination. The American College of Physicians has no current guidance on skin cancer screening performed by a

clinician, nor does the American College of Preventive Medicine (the latter has an archived statement from 1998¹⁹). The American Academy of Family Physicians concludes that the current evidence is insufficient to assess the balance of benefit and harms of visual skin cancer screening in adults.²⁰ The American Academy of Dermatology does not have formal guidelines on skin cancer

screening, although it does encourage and provide resources for its physician members to hold free skin cancer screening events for the public.²¹ The American Cancer Society recommends that adults 20 years and older who receive periodic health examinations should have their skin examined as part of a general cancer-related checkup.²²

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