Screening for Skin Cancer

Prepared by:
Oregon Health Sciences University
Evidence-based Practice Center

Mark Helfand, MD, MPH
Susan Mahon, MPH,
Karen Eden, PhD

Preface

The Agency for Healthcare Research and Quality (AHRQ) sponsors the development of Systematic Evidence Reviews (SERs) through its Evidence-based Practice Program. With guidance from the third U.S. Preventive Services Task Force[*] (USPSTF) and input from Federal partners and primary care specialty societies, two Evidence-based Practice Centers—one at the Oregon Health Sciences University and the other at Research Triangle Institute-University of North Carolina—systematically review the evidence of the effectiveness of a wide range of clinical preventive services, including screening, counseling, immunizations, and chemoprevention, in the primary care setting. The SERs—comprehensive reviews of the scientific evidence on the effectiveness of particular clinical preventive services--serve as the foundation for the recommendations of the third USPSTF, which provide age- and risk-factor-specific recommendations for the delivery of these services in the primary care setting. Details of the process of identifying and evaluating relevant scientific evidence are described in the "Methods" section of each SER.

The SERs document the evidence regarding the benefits, limitations, and cost-effectiveness of a broad range of clinical preventive services and will help to further awareness, delivery, and coverage of preventive care as an integral part of quality primary health care.

AHRQ also disseminates the SERs on the AHRQ Web site (http://www.ahrq.gov/uspstfix.htm) and disseminates summaries of the evidence (summaries of the SERs) and recommendations of the third USPSTF in print and on the Web. These are available through the AHRQ Web site (http://www.ahrgq.gov/uspstfix.htm), through the National Guideline Clearinghouse (http://www.ncg.gov), and in print through the AHRQ Publications Clearinghouse (1-800-358-9295).

We welcome written comments on this SER. Comments may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

	Douglas B. Kamerow, M.D.
John M. Eisenberg, M.D.	Director, Center for Practice and
Director	Technology Assessment
Agency for Healthcare Research and	Agency for Healthcare Research and
Quality	Quality

---

[*] The USPSTF is an independent panel of experts in primary care and prevention first convened by the U.S. Public Health Service in 1984. The USPSTF systematically reviews the evidence on the effectiveness of providing clinical preventive services--including screening, counseling, immunization, and chemoprevention--in the primary care setting. AHRQ convened the third USPSTF in November 1998 to update existing Task Force recommendations and to address new topics.

**U. S. Department of
Health and Human Services**

Structured Abstract

Context. Malignant melanoma is often lethal, and its incidence in the United States has increased rapidly over the past 2 decades. Nonmelanoma skin cancer is seldom lethal, but, if advanced, can cause severe disfigurement and morbidity. Early detection and treatment of melanoma might reduce mortality, whereas early detection and treatment of nonmelanoma skin cancer might prevent major disfigurement and, to a lesser extent, prevent mortality. Current recommendations from professional societies regarding screening for skin cancer vary.

Objective. To examine published data on the effectiveness of screening for skin cancer by a primary care provider.

Data Sources. We searched the MEDLINE database for papers published from January 1994 to June 1999, using search terms for screening, physical examination, morbidity, and skin neoplasms. For information on accuracy of screening tests, we used the search terms sensitivity and specificity. We identified the most important studies from before 1994 from the *Guide to Clinical Preventive Services,* second edition, and from high-quality reviews. We used reference lists and expert recommendations to locate additional articles.

Study Selection. Two reviewers independently reviewed a subset of 500 abstracts. After consistency was established, 1 reviewer reviewed the remaining abstracts. We included studies if they contained data on yield of screening, screening tests, risk factors, risk assessment, effectiveness of early detection, or cost effectiveness.

Data Extraction. We abstracted the following descriptive information from full-text published studies of screening and recorded it in an electronic database: type of screening study, study design, setting, population, patient recruitment, screening test description, examiner, advertising targeted at high-risk groups or not targeted, reported risk factors of participants, and procedure for referrals. We also abstracted the yield-of-screening data, including probabilities and numbers of referrals, types of suspected skin cancers, biopsies, confirmed skin cancers, stages, and thickness of skin cancers. For studies that reported test performance, we recorded the definition of a suspicious lesion; the gold standard determination of disease; and the number of true-positive, false-positive, true-negative, and false-negative test results. When possible, we recorded positive predictive values, likelihood ratios, sensitivity, and specificity.

Data Synthesis. No randomized or case-control studies demonstrate that screening for melanoma reduces morbidity or mortality. Basal cell carcinoma and squamous cell carcinoma are common, but detection and treatment in the absence of formal screening is almost always curative. No controlled studies have shown that formal screening programs improve this already high cure rate.

Although the efficacy of screening has not been established, the screening procedures themselves are noninvasive, and the follow-up test—skin biopsy—has low morbidity. Estimates of accuracy of screening are based on cross-sectional studies that suffer from workup bias. One prospective study tracked patients who had negative results to determine the number of patients who had false-negative results. In this study, the sensitivity of screening for skin cancer was 0.94 and specificity was 0.975.

Several recent case-control studies confirm earlier evidence that patients who have atypical moles, many (>50) common moles, or both are at increased risk for melanoma. One well-done

prospective study demonstrated that risk assessment by limited physical examination identified a relatively small (<10%) group of primary care patients for more thorough evaluation.

Conclusions. The quality of the evidence for routine screening by primary care providers for early detection of melanoma or nonmelanoma skin cancer ranged from poor to fair. Despite the lack of evidence, skin cancer screening, perhaps by means of a risk-assessment technique to identify high-risk patients who are seeing a physician for other reasons, is the most promising strategy for addressing the excess burden of disease in older adults.

Keywords: *Skin Cancer, skin neoplasms, mass screening, physical examination*

Contents

  Table 1. Skin cancer screening accuracy
  Table 2. Studies of screening for skin cancer
  Table 3. Thickness of malignant melanoma lesions found in screening studies
  Table 4. Summary of evidence for screening for skin cancer

  Figure 1. Melanoma age-specific incidence and mortality
  Figure 2. Ratio of incidence to mortality by age
  Figure 3. Analytic framework
  Figure 4. Key questions in analytic framework

  Appendix 1. Strategy for Skin Cancer Search
  Appendix 2. Inclusion Criteria for Evidence Tables

Evidence Review

.

Chapter 1. Introduction

 In the United States in 1999, approximately 1 million new cases of basal cell and squamous cell carcinoma, and approximately 44,000 new cases of malignant melanoma, were expected to be diagnosed.[1] Malignant melanoma is often lethal, and its incidence in the United States has increased rapidly over the past 2 decades. Nonmelanoma skin cancer is seldom lethal, but, if advanced, can cause severe disfigurement and morbidity.

Advanced melanoma and invasive squamous cell carcinoma of the skin occur most often in the elderly, especially elderly men. Early detection and treatment of melanoma might reduce mortality, whereas early detection and treatment of squamous cell carcinoma and basal cell carcinoma might prevent major disfigurement and reduce the need for expensive reconstructive surgery and, to a lesser extent, prevent mortality.

In this paper, we examine published data on the effectiveness of screening for skin cancer by primary care physicians. Specifically, we examine the accuracy of the tests used for screening, the diagnostic yield of screening in the general population, and the evidence that treatment of cancers found by screening improves outcomes.

We use the term screening to denote a systematic effort to detect unsuspected disease by either performing a total-body skin examination or assessing the risk for skin cancer in all patients seen in the primary care setting. We did not examine the effect of skin surveillance in children or in patients who had familial syndromes or who have a history of medical treatments such as UV-A radiation or immunosuppressive therapy that confer a high risk of melanoma. Monitoring in these very high-risk patients was judged to be beyond the scope of this report.

We also did not examine the value of routine diagnosis and treatment of skin cancer in clinical practice. In everyday primary care, the clinician sees the skin of every patient's face; in many cases, the clinicians also see the skin of their patients' extremities, chest, and back. Clinicians almost universally agree that incidental discovery of a suspicious skin lesion should prompt an evaluation, including a skin biopsy and a thorough inspection of the skin. The data we reviewed about screening do not address the value of attention to the skin as part of conscientious clinical care.

Other strategies to prevent skin cancer, such as promotion and counseling to reduce risky health behaviors and skin self-examination, are not addressed in this review. Many studies combine screening with health-promotion programs, and screening may itself contribute to primary prevention, because it provides the primary care provider with an opportunity to increase awareness of skin cancer and to demonstrate examination techniques that patients can apply themselves.

Epidemiology and Burden of Suffering

Melanoma

In the United States, the lifetime risk of being diagnosed with melanoma is 1.74% in white men and 1.28% in white women. The lifetime risk of dying of melanoma is 0.36%

in white men and 0.21% in white women. According to data from the California Cancer Registry, from 1988 to 1993, average, annual, age-adjusted incidence rates per 100,000 population were 17.2 for men and 11.3 for women for non-Hispanic whites; 2.8 for men and 3.0 for women for Hispanics; 0.9 for men and 0.8 for women for Asians; and 1.0 for men and 0.7 for women for non-Hispanic blacks.[2]

Between 1973 and 1995, the incidence of melanoma in the United States increased approximately 4% per year, from 5.7 per 100,000 in 1973 to 13.3 in 1995, according to data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute[3]; by comparison, the overall rate in Queensland, Australia is 55 per 100,000.

The elderly and, in particular, elderly men, bear a disproportionate burden of morbidity and mortality from melanoma. As shown in Figure 1, older men have the highest incidence of invasive melanoma. In 1995, the age-adjusted incidence rate was 68.7 per 100,000 in white men older than 65 years of age and 30.6 in white women older than 65 years of age. Men older than 65 years of age, who constitute 5.2% of the U.S. population, have 22% of newly diagnosed malignant melanomas each year; women older than 65 years of age, who constitute 7.4% of the population, have 14%.

Melanoma in the elderly is not only more common but also more lethal than in younger populations. In Australia, where for many years public education about melanoma has been intense, 75% of thick (>3 mm) melanoma lesions and 75% of deaths occur in people older than 50 years of age, and 50% of deaths occur in men older than 50 years of age.[4] Similarly, in the United States, approximately 50% of deaths from melanoma are in men older than 50 years of age.[3] Figure 2 shows that melanoma in the elderly, particularly in elderly men, is more likely to be detected in advanced stages. For men in their 40s, for example, there were 6 times as many cancers diagnosed as there were deaths; for men in their 70s, there were approximately 4 times as many cancers diagnosed per death. Some experts argue that the elderly, particularly elderly men, may have lower skin awareness and lower rates of skin self-examination, resulting in higher rates of advanced melanoma.[5]

Overall mortality from melanoma has increased. Between 1973 and 1995, overall mortality rates for melanoma increased by 1.3% per year, from 1.6 per 100,000 in 1973 to 2.2 in 1995. Nearly all of the increase was in white men (2.2%–3.6%), especially older white men. Currently, 5-year survival for melanoma has improved to 88% from the 80% it was 20 years ago. During this time, the rate of diagnosis of early or thin melanoma increased sharply, but so did the incidence of thicker (>3 mm) melanomas.[6] According to data from the California Cancer Registry, among men, melanoma is diagnosed after it has metastasized to a remote site for 15% of Hispanics, 13% of Asians, and 12% of blacks, compared with 6% of non-Hispanic whites. Among women, diagnosis is late stage in 7% of Hispanics, 21% of Asians, and 19% of blacks, compared with 4% of non-Hispanic whites.[2]

Several experts have commented that changes over time in ascertainment, diagnostic criteria, self-examination, and registry procedures make it difficult to draw reliable inferences about the effectiveness of early detection from epidemiologic data.[6-8] In an analysis of trends in Australia and New Zealand, Burton and Armstrong[9] noted that, although there has been a huge increase in the incidence of very thin melanomas, the incidence of thick melanomas has increased as well. Some experts interpret this to mean

that increased surveillance in the population may detect a relatively unaggressive, unimportant type of thin melanoma.[8-11] According to this view, increased detection of these very thin, nonmetastasizing melanomas would increase the incidence and 5-year survival rates of melanoma but would have little effect on mortality. However, in contrast to prostate and thyroid cancers, in which a large reservoir of unaggressive cancers are known to exist, longitudinal studies of melanoma have not established the frequency or existence of histologically malignant, but behaviorally benign, melanoma in the general population.

Nonmelanoma Skin Cancer

Rates of nonmelanoma skin cancer (NMSC) in the United States are difficult to determine because these cancers are not typically tracked by cancer registries. Cancer registries in Denmark and Canada do include NMSC. In British Columbia, Canada, the age-standardized incidence rate for basal cell cancer in men was 70.7 per 100,000 in 1973, increasing to 120.4 per 100,000 in 1987.[12] In women, basal cell cancer incidence rose from 61.5 to 92.2 per 100,000 over the same period. Squamous cell cancer incidence rose from 16.6 to 31.2 per 100,000 in men and from 9.4 to 16.9 per 100,000 in women.

A survey of 1 large health plan in Albuquerque, NM, which was not population-based, found age-standardized basal cell cancer rates of 1,073 per 100,000 in non-Hispanic white men and 415 per 100,000 in non-Hispanic white women. Squamous cell cancer rates were 214 and 50 per 100,000 for non-Hispanic white men and women, respectively.

Rates are much lower in other U.S. studies. A population-based study in Rochester, Minn, covering the years 1976 to 1984, found that age-standardized incidence rates per year of basal cell cancer were 175 per 100,000 in men and 124 per 100,000 in women.[13,14] Rates of squamous cell cancer were 63.1 per 100,000 in men and 22.5 in women. Rates of both basal cell cancer and squamous cell cancer rose with advancing age. A population-based study of NMSC in New Hampshire suggests that incidence rates are increasing. This study looked at incidence rates for 2 time periods, 1979–1980 and 1993–1994.[15] In men, the age-adjusted incidence of basal cell cancer increased from 170 per 100,000 in 1979–1980 to 310 per 100,000 in 1993–1994, and in women, basal cell cancer incidence rose from 91 to 166 per 100,000. For squamous cell cancer, incidence rates in men rose from 29 to 97 per 100,000 over the 2 periods, and in women squamous cell cancer incidence rose from 7 to 32 per 100,000.

Natural History, Diagnosis, and Staging of Skin Cancer

Melanoma

There are 4 major subtypes of melanoma: superficial spreading, nodular, lentigo maligna, and acral lentiginous.[16] Superficial spreading melanoma, the most common subtype in whites, is usually diagnosed in an early (thin) stage, before there is a high risk

of metastasis. Nodular melanoma is the second most common subtype in whites. Nodular melanomas are difficult for patients to find and are usually diagnosed in a more advanced stage.[17] The natural history of nodular melanoma is controversial.[18] The prevailing view is that nodular melanoma is characterized by rapid, early vertical growth and lack of an identifiable radial growth phase.

To determine which skin lesions are suspicious for melanoma, some clinicians in the United States use the ABCD checklist for detecting melanoma.[19] In this system, pigmented lesions are classified as suspicious for melanoma if they have an asymmetric shape (A); an irregular border that is scalloped, uneven, or ragged (B); varied color (C); or a diameter larger than 6 mm (D). Some add a fifth criterion (E) for elevation or enlargement. Some clinicians in the United Kingdom use a 7-point checklist that consists of change in mole size, shape, and color; crusting or bleeding; sensory change; and a mole larger in diameter than 7 mm.[19]

Once a lesion suspected of being cancerous is identified, one of several biopsy techniques is employed to obtain tissue for analysis.   The pathologic diagnosis of suspicious pigmented lesions can be difficult, especially for borderline and in situ neoplasms. In 1 recent study, 4 histopathologists evaluated 140 slides and classified each lesion as melanoma or other pigmented lesion; they were in agreement on diagnoses for 74% (kappa = 0.61) of the slides.[20] Similarly, when 8 expert pathologists (recruited based on publications and reputations) classified 37 slides as benign, malignant, or indeterminate, they had almost complete agreement—only one discordant—on 62% (kappa = 0.50) of the cases.[21]

Stage is the most important prognostic factor in melanoma. The American Joint Commission on Cancer classification, which is based on the tumor, node, metastasis (TNM) system, describes the stages from I to IV. Stage I is a primary tumor less than 1.5 mm in thickness with no regional lymph-node metastases; Stage II is a primary tumor 1.5 to 4.0 mm in thickness with no regional lymph-node metastases; Stage III is any primary tumor with regional lymph-node metastases or in-transit metastases; and Stage IV is any primary tumor with distant metastases.[22] According to SEER data through 1995, 5-year relative survival rates for localized, regional, and distant disease were 96%, 59%, and 12%, respectively.[3]

The thickness of the primary tumor is the strongest predictor of prognosis. To measure thickness of a melanoma, the pathologist uses a device called a micrometer, which is similar to a small ruler under the microscope. This technique is called the Breslow measurement.[23] In general, melanomas less than 1 mm in depth have a very small chance of metastasizing. For those who have melanomas between 1.5 and 4 mm, 5-year survival is approximately 70%; for those who have melanomas thicker than 4 mm, 5-year survival is approximately 45%. Thickness of the melanoma also guides the choice of therapy.

Nonmelanoma Skin Cancer

Basal cell carcinoma and squamous cell carcinoma are the most common forms of skin cancer. Despite their very high incidence, they account for fewer than 0.1% of cancer deaths. There are several morphologic types of basal cell cancer, such as nodular,

ulcerative, and plaquelike; but regardless of type, metastasis is very rare. Basal cell carcinoma can be locally destructive and frequently recurs.

Squamous cell cancers usually occur in chronically sun-exposed areas of the skin, especially on the face, ears, or backs of the hands. Squamous cell cancer has the potential to metastasize and may account for as much as 20% of deaths from skin cancer. Nonmelanoma skin cancer accounts for the majority of skin cancer deaths in very elderly men and blacks.[24] A large primary tumor (>2 cm) is associated with an increased risk of metastasis.

There are few data on the natural history of squamous cell cancer in the general population. Most studies of the natural history of squamous cell cancer have been done in selected patients who have an elevated risk owing to environmental exposures, such as Psorolen plus UV–A radiation for psoriasis.[25,26] Although there is strong suspicion on clinical grounds that advanced locally invasive or metastatic squamous cell cancers result from medical neglect, careful studies of the rate of progress of squamous cell cancers in the elderly are lacking.

Previous Task Force Recommendations and Recommendations of Others

Current recommendations of professional societies regarding screening for skin cancer vary. The U.S. Preventive Services Task Force[27] (1996) and the American College of Preventive Medicine recommend total-body skin examination in high-risk individuals who see a physician for other reasons, but they do not recommend routine screening. The American Cancer Society recommends skin examination every 3 years for people between 20 and 40 years old and yearly for anyone older than 40 years of age. All of these organizations advise some form of public or patient education to change behaviors that may increase the risk of skin cancer and to increase the likelihood of early self-detection.

Analytic Framework and Key Questions

Before the consequences of screening can be estimated, a necessary first step is to formulate the screening problem by specifying the target population that will be reached by screening; the screening tests, follow-up tests, and treatments that will be used; and the types of outcomes that will be affected by screening.

The analytic framework in Figure 3 shows the interventions, intermediate outcome measures, and health outcome measures we examined. The accompanying key questions (Figure 4) correspond to the numbered arrows in the analytic framework and articulate the main questions that guided our literature review and that we address in Chapter 3, "Results," of this review.

We studied screening in the general adult population and in the elderly, the group with the highest prevalence and mortality from skin cancer. We have included studies of both mass screening and casefinding programs to detect and treat melanoma and NMSC

in the general population. We sought studies of the accuracy of 2 methods of screening for skin cancer (Figure 3, Arrow 2[a]): (1) performing a total-body skin examination in all patients seen in the primary care setting and (2) assessing the risk for skin cancer in all patients, followed by a total-body skin examination in those found to be high risk. The primary aim in using these strategies is earlier detection of melanoma; with examinations that are confined to areas not covered by clothing, a high proportion of potentially lethal cancers is likely to be missed.[28] To assess the accuracy of these methods, both for melanoma and for NMSC, we sought studies that used these initial tests to screen in the general population or in the elderly and then confirmed positive screening test results with skin biopsy results.

We examined the consequences of screening on detection of squamous cell carcinoma, basal cell carcinoma, and malignant melanoma (Figure 3, Arrow 2[b]). Specifically, we examined how often patients are found to have skin cancer, how often suspected skin cancer is confirmed by biopsy, and at what stage cancer is found.

In addition to early detection, screening itself might confer a potential benefit by improving patients' knowledge and self-examination skills. We therefore sought evidence about the effect of screening on patients' health beliefs and practices regarding skin cancer prevention (Figure 3, Arrow 1[c]). We also considered the adverse effects of screening, including the frequency and the consequences of false-positive examinations or biopsies and the diagnosis of noncancerous lesions that may not require treatment (Figure 3, Arrow 3).

In considering outcomes, we sought, but did not find, direct evidence from controlled studies of the effect of screening on health outcomes (Figure 3, Arrow 1) such as mortality and quality of life. In the absence of randomized trials of screening, these links may be made by studies of the association between a delay of diagnosis and the outcome of cancer or of screened versus nonscreened populations.

Note that we did not examine the effectiveness or the adverse consequences of various treatments for skin cancer. We investigated the evidence that detection of earlier cancers by screening in the general population is associated with reduced mortality and morbidity.

Chapter 2. Methods

Literature Search Strategy

   To find relevant articles on screening for skin cancer, we searched the MEDLINE database for papers published from January 1994 to June 1999, using search terms for screening, physical examination, morbidity, and skin neoplasms. For information on accuracy of screening tests, we used the search term "sensitivity and specificity." Additional search terms were added to locate articles for background on skin cancer morbidity and mortality and on epidemiology. The search was updated monthly during the course of the project. We also used reference lists and expert recommendations to locate additional articles published after 1994. (See Appendix 1: Strategy for Skin Cancer Search Terms.)

   Two reviewers independently reviewed a subset of 500 abstracts. Once consistency was established, 1 reviewer reviewed the remainder. We included studies if they contained data on yield of screening, screening tests, risk factors, risk assessment, effectiveness of early detection, or cost effectiveness (CE). Of 54 included studies, 5 contained data on accuracy of screening tests, 24 contained data on yield of screening, 7 contained data on stage or thickness of lesions found through screening, 11 addressed risk assessment, and 7 addressed the effectiveness of early detection (some studies addressed more than one topic). (See Appendix 2: Inclusion Criteria for Evidence Tables.) We retrieved the full text of these articles and abstracted the data as described below. In addition, we retrieved the full text of 47 studies of various risk factors for skin cancer. We read these articles but did not systematically abstract them.

   We identified the most important studies from before 1994 from the *Guide to Clinical Preventive Services,* second edition[27] and from high-quality reviews published in 1994 and in 1996; from reference lists of recent studies; and from experts.

Literature Synthesis and Preparation of Systematic Evidence Review

   We abstracted the following descriptive information from full-text, published studies of screening and recorded it in an electronic database: study type (mass screening, population based, casefinding, other), study design (prospective, case control, retrospective, observational, other), setting (hospital, community, specialty clinic, primary care, other), population (percent white, age), recruitment (volunteers, invitation, random sampling), screening test (total-body skin examination, partial skin examination, lesion-specific examination, other), examiner (dermatologist, primary care physician, other), advertising targeted at high-risk groups or not targeted, reported risk factors of participants, and procedure for referring patients found to have a positive screen.

   We also abstracted the number and the probability of the following events from each study: referrals for skin examination; compliance with referral; suspected basal cell cancers, squamous cell cancers, actinic keratoses, and melanoma; confirmed melanoma and melanoma in situ; negative screening examinations; biopsies performed; the persons

who had confirmed melanoma, suspected melanoma, or both; and the persons who had confirmed melanoma, the number of all suspicious lesions, or both. When available, the type, stage, or thickness of lesions found through screening was also recorded.

For studies that reported test performance, we also recorded the definition of a suspicious lesion, the gold standard determination of disease, and the number of true-positive, false-positive, true-negative, and false-negative test results. To analyze data from these studies, we defined sensitivity as the proportion of people who had a histologic diagnosis of skin cancer and who had a positive test result—that is, a suspicious lesion on examination. Specificity was defined as the proportion of people who did not have skin cancer and who had no suspicious lesions detected during the skin examination.

The positive predictive value (PV+) was computed in 2 ways to account for noncompliance in studies. We computed the lower bound PV+ (Low PV+) by dividing the number of patients who had confirmed skin cancer by the number of patients who were diagnosed with a suspicious lesion, and we computed the upper bound PV+ (High PV+) by dividing the number of patients who had confirmed skin cancer by the number of patients who had biopsies. If the study provided sufficient detail, we calculated the PV+ of examination for each type of skin cancer. Most studies, however, did not report results in sufficient detail; for these, we combined the results for different types of skin cancer.

We calculated likelihood ratios (LRs) for each study. The LR for a positive test was calculated with the formula

$$LR = [High\ PV/(1\text{-}High\ PV)]/\{p(cancer)/[1\text{-}p(cancer)]\},$$

where p(cancer) is the observed prevalence of disease, estimated as p(cancer) = (number of true positives + number of false negatives)/(number of patients screened).[29]

This formula was derived from the odds ratio (OR) form of Bayes' theorem.[30] The advantage of using the OR form is that LR can be computed in studies that reported findings only for patients who had positive tests. The computation is based on the following:

$$Posttest\ odds = pretest\ odds \times LR.$$

In computing the LRs, we used the High PV+, which included only those patients who went on for biopsy. We assumed that the High PV+ was more representative of screening in a primary care setting. These patients would be more likely to follow through with a biopsy than those attending a mass screening.

In studies that did not measure the false-negative rate, we assumed that there were no false-negative results. We calculated the observed prevalence by dividing the number of patients who had true-positive results by the number of screened patients. If there were, in fact, patients in these studies with false-negative results, the observed prevalence was underreported. Since the computation of the LR depends on an accurate measure of prevalence, LRs computed with an underreported prevalence are inflated. We performed a sensitivity analysis to record the effect on the estimate of LR when the number of false negatives and the prevalence were varied over a reasonable range of values.

Chapter 3. Results

Accuracy of Screening Tests

Before considering the consequences of screening, we raised and attempted to answer the following questions about the accuracy of the screening tests most commonly used in detecting skin cancers.

How Accurate Is Total-Body Skin Examination in the Detection of Skin Cancer?

Table 1 summarizes 5 recent prospective studies[31-34,37] of the accuracy of skin examination in screening programs. In all the studies the participants were self-selected individuals who responded to an advertisement that may have emphasized skin cancer risk factors. In some studies, total-body skin examinations were performed on all participants; in others, the examination focused on specific lesions identified by the patient. [32,33] Few data from screening studies exist on the accuracy of skin cancer screening by primary care physicians; in all but 1 study,[31] the skin examinations were conducted by dermatologists.

In these studies, a positive screening test result was defined as the clinical diagnosis of a suspicious skin lesion. Histologic diagnosis on skin biopsy was the gold standard determination of disease. In 4 of the studies, skin examination was considered positive if the lesion was suspected of being any type of skin cancer.[32-36] In these studies, from 4.2% to 28.4% of subjects had suspicious lesions, and from 1% to 6% proved to have skin cancer. Basal cell cancer accounted for 74% to 93% of the confirmed skin cancer cases; melanoma, 7% to 27%; and squamous cell cancer, 0% to 4%.   This suggests that basal cell cancers contributed heavily to the summary estimates of the accuracy of skin examination reported in these studies.

Workup bias was present in all of these studies—that is, only suspicious lesions were biopsied. This design permits measurement of the PV+ of screening, but not of the false-negative rate. In Table 1, High PV+ estimates (as defined in Chapter 2, "Methods") for all types of skin cancer values ranged from 0.30 to 0.58, indicating that between 30% and 58% of patients found to have a suspicious lesion were eventually diagnosed to have skin cancer on biopsy.[31-35] The variation in High PV+ may be related to variation in the prevalence of disease, which, in turn, could be related to the type of patients recruited (high risk or not targeted).

The Low PV+ (also defined in Chapter 2, "Methods") takes into account the effect of noncompliance with the recommendation to have a biopsy done. The 2 smallest studies[31,34] had great differences between the lower and the upper estimates of PV. In both of these small studies the percentage of patients who had suspicious lesions was high (21%[31] and 28%[34]), but the percentage of those patients who went on for biopsy was low (36%[34] and 65%[31]).   The clinicians in these studies[31,34] appeared to have less rigid criteria for diagnosing skin cancer from skin examinations than was used in the other, larger studies,[32,33,37] since they were 4 times as likely to find a suspicious lesion. Low PV+ results may better represent the actual effect of mass screening in which the patient

must comply with referral to a physician for biopsy for screening to affect follow-up and treatment.

The last study shown in Table 1 focuses on detection of melanoma in self-selected individuals.[36] The study demonstrated that dermatologists found lesions suspected of being melanoma in a very small proportion of individuals (0.03%). In this study, 282,555 members of the general public were recruited for free examinations without regard to risk factors for skin cancer. Clinical suspicion was classified as suspected melanoma or rule-out melanoma. Only 0.3% ($n = 763$) of the participants had a clinical diagnosis of suspected melanoma at the skin examination. Of the 679 patients who went on for biopsies, 130 patients had melanoma (PV+ of 0.191). Although the use of a lower cutoff, rule-out melanoma, identified an additional 234 patients who had melanoma, an additional 2,316 patients who do not have melanoma were biopsied, and the PV was 0.09. Interestingly, compliance with biopsy was significantly lower for participants given a diagnosis of rule-out melanoma—0.69, compared with 0.89 for patients who had a diagnosis of suspected melanoma.

Although data are sparse, the sensitivity of a complete skin examination performed by a dermatologist is thought to be high.[37] One of the studies in Table 1 provided an indirect measure of sensitivity and specificity through registry data.[37] In this study, performed in the Netherlands, 1,551 of 1,763 participants who had negative screening examinations consented to be followed through 2 population-based cancer registries for 42 months. Similarly, 87 of 93 patients who had positive tests were also followed. Fifteen patients who had negative screening results (approximately 1%) appeared in at least 1 of the cancer registries to have skin cancer. Review of medical records revealed that 12 of the patients had new lesions, whereas 3 patients had documented lesions that had been misdiagnosed: 1 patient had a basal cell carcinoma, diagnosed as a common nevus, on his back; 1 patient had a squamous cell carcinoma, recorded as a seborrheic keratosis, on his wrist; and 1 patient had a basal cell carcinoma, originally diagnosed as an actinic keratosis, on the forehead. Overall sensitivity of the initial examination was 0.940, and specificity was 0.975. For a patient who had a negative initial skin examination, the probability of having no skin cancer on follow-up was 0.998.

Although this follow-up study[37] provides the best available data on sensitivity and specificity in a screening setting, caution should be raised about generalizing this study to screening in a primary care setting because the examiners were dermatologists rather than general practitioners (GPs). Additionally, it unclear how many lesions diagnosed as precursor lesions were, in fact, skin cancer. Patients who had precursor lesions ($n = 111$) were excluded from the study.

Since PV+s highly depend on the probability of skin cancer in each study, positive LRs were computed. The positive LRs in Table 1 ranged from 12 to 38 for patients screened for all types of skin cancer.[31-34,37] Thus, according to the conditional probability definition of LR,

p(positive test| skin cancer)/p(positive test| no skin cancer),

patients who had suspicious lesions for any type of skin cancer were 12 to 38 times more likely to have skin cancer than not to have skin cancer. When screened specifically for melanoma, patients who had a suspected melanoma diagnosis were 184 times more likely

to have melanoma than not to have melanoma.[36] Patients who had a rule-out melanoma diagnosis were 78 times more likely to have melanoma than not to have melanoma.

Most LR results shown in Table 1 must be considered with caution. With the exception of 1 study,[37] the computation of LRs assumed there were no false-negative results. In this study, 3 of 50 skin cancer patients had false-negative results, suggesting that skin examinations have a false-negative rate of 6%.[37] When the LR was recomputed in this study with the assumption that the false-negative rate was 0%, the LR increased from 37.32 (using false-negative rate of 6%) to 39.78 (assuming 0% false-negative rate). Similarly, if the false-negative rate had actually been 10%, the LR for this study would be 35.84. If it had been assumed to be 0%, the computed LR would be 39.78. Taken to an extreme, if the examiner missed 1 of every 5 patients who had skin cancer (a false-negative rate of 20%), the computed LR would be overestimated by 27%. However, if the false-negative rate found in the follow-up study[37] can be generalized to the studies that did not identify false negatives,[31,32,34,36] the inflation may be approximately 6%.

In summary, estimates of accuracy are based on a handful of mass-screening, cross-sectional studies. All studies suffer from workup bias. However, 1 study[37] attempted to reduce this bias by following all patients who had negative tests to determine how many patients who had skin cancer were missed. Also, all studies except 1 (Ref. 31) provided accuracy measures for dermatologists in mass-screening settings but not for primary care physicians. Accuracy for dermatologists screening patients is thought to be high, with a sensitivity of 0.94 and a specificity of 0.975.[37]

Nonscreening studies. Several studies have examined the accuracy of nondermatologists' assessments of photographs of skin lesions or of preselected patients who have lesions, with the histologic diagnosis used as the reference standard. One recent review summarized studies that used color slides (rather than actual patients) to test physicians' accuracy in predicting the histologic diagnosis (mostly NMSC).[39] When these studies were combined, dermatologists performed better (93% correct) than family medicine attending physicians (70% correct) and internal medicine attending physicians (52% correct). Another recent review found that, in studies in which photographs or in which selected patients who had known lesions were used, use of the ABCD(E) or the 7-point checklist had a sensitivity of 50% to 97% and a specificity of 96% to 99% for the histologic diagnosis of skin cancer.[19] Nondermatologists' examinations were less sensitive than examinations performed by dermatologists. Many of these studies were small and used convenience samples of attending physicians at academic medical centers. More important, these studies did not examine the accuracy of a total-body skin examination or the ability of physicians to identify suspicious lesions efficiently in the setting of a screening program.[19]

One well-designed prospective study of the accuracy of total-body skin examination found that skin cancer specialists' decisions about biopsy were more sensitive and much more specific than those of GPs.[40] In Australia, 4 skin cancer specialists and 63 randomly selected GPs performed total-body skin examinations on 109 selected patients, 43 of whom had suspicious pigmented lesions diagnosed previously by a skin specialist. The sensitivity of total-body skin examination for detecting suspicious lesions was 0.72 for the GPs, versus 0.97 for 4 skin specialists. The PV+ for the GPs was 0.39. Of the 43 patients, 12 (28%) who had suspicious lesions had melanomas. Although the GPs'

diagnoses were highly sensitive for melanomas (0.97), they classified approximately 11 benign lesions as suspicious for each melanoma. For the 4 dermatologists, the ratio was 2.1 benign lesions to 1 melanoma. Because the proportion of patients who had suspicious lesions (and melanoma) was much higher in this study than would occur in unselected patients, the PV+ of primary care physicians' examinations would be lower in an actual screening study.

How Accurate Are Risk-Assessment Tools as a Screening Test for Skin Cancer?

Another screening strategy is to use a questionnaire or interview to identify a group of high-risk patients. In this strategy, only high-risk patients would have total-body skin examinations. Potentially, such a strategy could reduce the cost of screening because fewer total-body skin examinations and biopsies would be needed to diagnose patients who have skin cancer. The association of demographic, behavioral, and clinical factors with the risk of skin cancer has been well studied, and studies have established that physicians and patients can reliably measure some of these factors. As discussed below, however, the validity of formal risk-assessment tools to screen unselected patients in primary care has not been established.

Risk factors for nonmelanoma skin cancer. A history of skin cancer or of actinic keratoses (AK) and white race are the strongest risk factors for NMSC. Among whites who have no history of skin cancer or AK, sun exposure is the most important risk factor for NMSC. Cumulative sun exposure and possibly intermittent intense sun exposure,[41] total time spent outdoors,[42] geographic area of residence,[43] and lifetime number of severe sunburns[43] have all been shown to be associated with higher risk of NMSC. Other risk factors include history of NMSC,[44] light-colored or red hair,[42,43] propensity to sunburn,[43,44] and family history of skin cancer.

Risk factors for melanoma. A high count of common moles larger than 2 mm and the presence of atypical moles are risk factors for melanoma.[45-48] The risk of malignant melanoma rises with the number of common moles, with relative risks of 1.7 to 1.9 for 11 to 50 moles, 3.2 to 3.7 for 51 to 100 moles, and 7.6 to 7.7 for more than 100 moles, compared with the risk to people with less than 10 common moles.[45,47] Similarly, the likelihood of melanoma increases several times (OR range, 1.6-7.3) for patients who have 1 to 4 atypical moles compared with patients who have no atypical moles. [45,47]

Other risk factors for melanoma are red or light-colored hair (OR ranged from 1.4 to 3.5); a few (OR 1.9) or many actinic lentigines (OR 3.5); heavy sun exposure (OR 2.63); reported growth of a mole (OR 2.3); skin that does not tan easily (OR 1.98); a family history of melanoma (OR 1.81); light-colored eyes (OR ranged from 1.55 to 1.60); and light-colored skin, (OR ranged from 1.40 to 1.42).[45-47,49,50] The validity of some risk factors, such as hair color and sun exposure, is lower in the elderly.[45,51]

The relation of sun exposure to melanoma is complex. Since the second edition of the U.S. Preventive Services Task Force's *Guide to Clinical Preventive Services* was published in 1996, a meta-analysis of case-control studies found intermittent sun exposure was associated with increased risk of melanoma, whereas heavy occupational

exposure was found to be slightly protective.[52] This meta-analysis included 23 case-control studies on intermittent sun exposure; 20 case-control studies on occupational sun-exposure; and 21 case-control studies on sunburn, all completed by 1992. Intermittent exposure was defined as recreational and vacation sun exposure. Patients who had the highest level of intermittent exposure had nearly twice the risk of melanoma as those who had the lowest intermittent exposure (OR 1.71; 95% confidence interval [CI], 1.54–1.90). Patients who had heavy occupational exposure were at slightly decreased risk compared with those who had low occupational exposure (OR 0.86, 95% CI, 0.77–0.96). Patients who had histories of sunburn (usually a result of intermittent sun exposure) were at increased risk for melanoma (OR was 1.91) compared with those who did not have a history of sunburn. Since the meta-analysis[52] was published, an analysis of body site distribution among incident melanoma cases in British Columbia found that intermittent sun exposure was a risk factor for melanoma in individuals younger than 50 years of age.[53] A recent case-control study also supported the hypothesis that intermittent ultraviolet exposure is a risk factor for melanoma in younger (<50 years of age) individuals who are susceptible to burning.[54]

Reliability of risk-assessment tools. To be useful as practical tools for classifying patients into risk groups, risk factors must be reliably assessed by patients or physicians. As noted above, the 2 strongest risk factors for melanoma are presence of atypical moles and a large number of common moles.

Several studies have examined the reliability of mole counts by patients, interviewers, and dermatologists. In these studies, having a trained interviewer or the patient count the moles on the arm was not useful as an indicator of total-body mole count,[55-57] but patients' counts of moles on the trunk or total body were more reliable.[56-58] In a large, population-based prospective study, 670 Swedish women completed a melanoma risk-assessment questionnaire twice (1–3 years apart). The test-retest reliability of a mole count by the patient was high (kappa = 0.52–0.83).[56] In a worksite screening study, 104 of 125 employees correctly placed themselves in high- or low-risk melanoma categories based on a count of total-body moles larger than 5 mm.[58] Of 104 lower-risk patients (had fewer than 6 large moles), 92 correctly assessed themselves when compared with a dermatology fellow's assessment. However, only 12 of 21 high-risk patients (more than 6 large moles) correctly assessed themselves. This suggests that patients can screen themselves for large-mole-count risk with specificity of 0.88 and sensitivity of 0.57. Women tended to overcount moles and men tended to undercount moles. Untrained patients cannot accurately distinguish atypical moles from others.[59]

There is less information on the reliability of self-report of other risk factors. In the Swedish study[56] described above, response agreement was good for questions related to hair color (kappa = 0.77) and freckles (kappa = 0.83), but only fair for the number of raised nevi on the left arm (none, 1–3, or >3) (kappa = 0.40) and for sunburn history (kappa = 0.54). In another study, the agreement between patients' self-appraisal of skin characteristics and clinical skin examinations by a physician was reflected in kappa values of 0.67 for freckles and 0.43 for atypical nevi.[60]

Use of risk-assessment tools in practice. The ideal study to measure the accuracy of risk-assessment tools would assign risk levels for patients in a primary care

setting, perform total-body skin examinations on patients classified as high and low risk, and then monitor the patients regularly to determine what proportion of incident melanomas occurred in the high-risk group. In fact, no longitudinal studies of the use of a risk-assessment tool in primary care practice have been reported.

Although it was not done in a primary care setting, a large, prospective study validated the use of an initial count of atypical moles in predicting the incidence of melanoma over 5 years.[61] In that study, 3,889 employees at the Lawrence Livermore National Laboratory had total-body skin examinations performed by a dermatology fellow specializing in melanoma. Atypical moles were diagnosed clinically by use of previously defined criteria[62]: ill-defined border; irregular border; irregularly distributed pigmentation; a diameter more than 5 mm; erythema (blanchable in lesion or at edge); and accentuated skin markings. Seven percent of the subjects were in the highest-risk category—that is, had few to many moles that met 5 or more of these criteria. This highest-risk group accounted for 56% (5/9) of the subjects who developed melanoma over 5 years. By contrast, 64% of the patients were in the lowest-risk category—had no atypical moles. This lowest-risk group accounted for 11% (1/9) of the patients who developed melanoma.[61]

Two recent cross-sectional studies have examined the reliability and practicality of classifying primary care patients into risk groups by use of a standardized, self-administered instrument.[57,60] Jackson et al[60,63] applied a melanoma risk-assessment questionnaire[64] in 16 randomly selected group practices in Cheshire, United Kingdom. Patients were asked about freckling propensity, number of moles, existence of large moles with irregular borders or colors, and history of sunburn. Their responses were compared with the results of a physical examination by a physician.

Although this study did not track the incidence of melanoma over time, it did provide data on the proportion of primary care patients who would be classified as high risk. A total of 3,105 patients completed the questionnaire. According to their responses, patients were then placed into the following risk groups: marginally increased risk (49.2%); increased risk (26.6%); very increased risk (4.4%); worrying high risk (4.3%). Most patients in the 2 highest-risk groups were unaware of their high-risk status.

In summary, several recent case-control studies confirm earlier evidence that patients who have atypical moles, many (>50) common moles, or both are at increased risk for melanoma. Evidence suggests that patients can count the number of moles 5 mm or larger with reasonable agreement with physicians, but that they cannot accurately distinguish atypical moles from others. No prospective evidence is available linking risk assessment by limited physical examination with incidence of melanoma, but 1 well-done prospective study demonstrated that this strategy could identify a relatively small (<10%) group of primary care patients for more thorough evaluation.

Consequences of Screening

We examined the consequences of screening reported in 24 recent studies of screening programs (Table 2).[31-34,36,37,61,65-83] In these studies, we examined (1) how often skin cancer is suspected in individuals who are screened, (2) how often melanoma and NMSCs are diagnosed, (3) how often referrals for follow up and biopsies are performed,

and (4) how the type of skin examination, examiner, and compliance affect the yield of screening. This information is summarized in Table 2. We also examined the distribution of thickness and stage of lesions found through screening versus usual care (Table 3) and the adverse effects of screening.

There are limitations in using data from these studies to draw conclusions about screening in a casefinding setting. The majority of recently published studies were in a mass-screening setting. To be effective in reducing morbidity and mortality, it is necessary to screen those who are at high risk both for developing skin cancer and for presenting with thicker lesions in the absence of screening. People who attend mass screening are a self-selected group, tend to be more skin-aware, and may come because they are worried about a lesion that they have already discovered and for which they would have sought medical attention anyway.[66] Although some mass-screening programs tend to attract a relatively high risk group,[66,67] others do not, and very high risk individuals, particularly ill elderly individuals, may be underrepresented.[84,85]

How Often Does Screening Detect Suspicious Lesions?

Rates of suspected melanoma in mass screening, casefinding, and population-based screening ranged from 0 to 9 per 100 people screened, with the most common findings between 1 and 3 per 100. Most studies found from 2 to 10 suspected NMSCs per 100 screened. In some populations, the rate of suspected basal or squamous cell carcinoma was much lower (4 per 10,000 in a Japanese study[74]) or higher (21 per 100 screened in surfers).[71] Studies did not report the prevalence of NMSC by age, and we found no clear difference in prevalence between studies of mostly older individuals and studies of younger individuals.

Suspected AK was generally the most frequent finding in these studies, but rates were variable. The highest rates were 41 per 100 screened in the surfers,[71] 23 per 100 in a population sample of people older than 59 years of age,[71-73] and 15 per 100 in a small mass-screening study.[71]

How Often Does Screening Result in a Diagnosis of Cancer?

Rates of confirmed melanoma and melanoma in situ were consistently in the range of 1 to 4 per 1,000 people screened, with 2 exceptions. An Australian study that targeted high-risk people[68] had a rate of 8 confirmed melanomas per 100 people screened. The other, a population-based study in Sweden,[75] had no confirmed melanomas of 152 suspected melanomas in 1,654 people screened. In the largest screening study, 213 confirmed melanomas were diagnosed in 282,555 people screened, from 4,458 people with lesions suspected of being melanoma.

Eight studies reported the number of histologically confirmed NMSCs.[31,33,34,37,68,74,77,79] The prevalence varied widely, from 0.05 (of people screened) to 0.0004, with most reporting between 0.01 and 0.05.

How Often Does Screening Lead to Referral for Follow Up and Biopsy?

Among all the studies that we reviewed, rates of referral for follow-up care of suspicious lesions ranged from 2 to 34 per 100 people screened. Two studies reported rates of compliance with a recommendation to see a physician for follow-up. In 1 mass-screening study,[32] 95% of people complied with recommended follow-up, and in a worksite program,[79] 45% complied.

As for biopsies, 5 studies reported the number of biopsies performed as a result of screening.[31,32,34,75,78] In these studies, from 4 to 31 biopsies per 100 people screened were performed. Among patients who had suspected melanoma, from 0% to 17% had a final diagnosis of melanoma. Among all patients who underwent a biopsy, about 3% proved to have a melanoma.

How Do Characteristics of the Screening Program Affect the Yield of Screening?

Certain characteristics of a screening program could affect compliance with follow-up recommendations and, ultimately, with the yield of screening. We consider 3 such characteristics below: (1) the type of skin examination, (2) the recruitment strategy, and (3) the procedure for referring patients for follow up.

Type of skin examination. Examiners conducted either total-body skin examination,[31,34,68,69,71,80,81] partial skin examination (eg, only above the waist or on sun-exposed areas),[71-74,77,78] examination only of lesions the participant was worried about,[32,33] or some combination[32,33,37,70,71] (see Table 2). Overall, compared with partial skin examination or examination of lesions the patient was worried about, the use of total-body skin examination did not appear to increase the rate of confirmed melanomas. In 1 study,[84] the question, "In self-selected patients who have noticed a skin lesion, does total-body skin examination increase the likelihood of finding skin cancers?" was specifically addressed. In that study, 2,910 (70%) of 4,146 people screened complained of at least 1 skin lesion. When these lesions were examined, 13 melanomas and 44 NMSCs were diagnosed on biopsy. For these patients who originally came in with specific lesions, an additional total-body skin examination was offered. For the 1,356 patients who went on for a total-body skin examination, no malignant melanomas and 3 basal cell carcinomas were identified. This finding raises doubts about the benefits of conducting total-body skin examinations rather than lesion-specific examinations on everyone.

Recruitment strategy. In 12 studies,[31-34,36,37,66-71] screening involved a media campaign to encourage individuals to seek a skin examination (mass screening) (see Table 2); in 7 of these programs,[32,34,37,68-71] the media campaign targeted individuals who had suspicious lesions on self-examination or risk factors for melanoma, whereas 6 were not targeted.[31,33,36,66,67,71] We found no systematic relation between these characteristics and the proportion of individuals eventually diagnosed to have cancer. However, most studies did not report sufficient information to determine how well targeting succeeded in

recruiting a high-risk population, and the description of the study samples were not adequate to exclude differences in baseline risk factors between studies as the main cause of observed differences in results.

Procedure for referring patients for follow-up. In most studies the patient was instructed to see a primary care clinician or a dermatologist for follow up of suspicious lesions. In some studies, the patient's physician was contacted directly or the patient was sent to a study dermatologist. Some studies used reminders such as letters to the patient.

Although not depicted in the Table 2, we collected information on compliance rates for screening, follow up, and biopsy when possible. Three population-based studies invited a target group of people to be screened and reported response rates.[38,72,73,75,85] In these studies, between 60% and 70% of those invited attended screening. One worksite screening program that identified and invited high-risk people reported a lower response rate of 19%.[78] The mean age of this sample was somewhat lower than that in the population-based studies.

Compared with Usual Care, How Much Earlier Does Screening Detect Skin Cancers and Precancerous Lesions?

Eight studies[32,34,36,61,68,80-82] reported the thickness of melanoma lesions found through screening (Table 3). In 4 studies,[34,61,68,81] all detected melanoma lesions were 1.0 mm or thinner, and in a fifth study,[32] 92% were 1.0 mm or thinner. In 3 other studies that used 1.5 mm as the cutoff, the proportion of melanomas 1.5 mm or less was 67% to 87%.[36,80,82]

No study of screening directly followed an unscreened population to compare the distribution of thickness or the stage of melanomas detected. Nonetheless, the proportion of thin melanomas is clearly higher in screening programs than in usual care. SEER data from 1992 to 1994 were analyzed. (The SEER registry routinely reports the TNM stage, but not the thickness, of melanomas at the time of diagnosis. From 1989 to 1994, 81% of melanomas detected through usual care were localized, 9% regional, 4% distant, and 6% unstaged.[3]) The results of this analysis are as follows: 57% of melanomas were thinner than 0.76 mm, 23% were 0.76 to1.5 mm, 15% were 1.51 to 3.99 mm, and 5% were 4.0 mm or thicker.[36] Moreover, in population-based studies, the incidence of melanoma detected by screening is higher than base rates, and the increase is almost entirely attributable to thin melanomas.

What Is the Effect of Screening on Patients' Skin Knowledge and Self-Care Behavior?

Advocates of screening note that having a total-body skin examination could improve morbidity and mortality indirectly by promoting skin-awareness and sun-protection measures. In a follow-up study to the American Academy of Dermatology's Melanoma/Skin Cancer Screening Programs (see the first reference to Koh et al., 1996 in Table 1), 1,049 self-selected participants who had skin lesions were surveyed 2 months after undergoing a total-body skin examination. Among the 643 respondents, the

proportion of individuals who regularly checked their skin increased from 60% to 84% after screening.[86]

What Are the Adverse Effects of Screening?

Patient unease is a possible adverse effect of screening, despite total-body skin examination being noninvasive. In 1 study of self-selected participants found to have skin lesions by screening, patient satisfaction was high (81%), and only a small proportion of patients reported embarrassment or discomfort as a result of screening (4.8%).[86]

False-positive skin examination results might also be considered an adverse effect. In any screening program, most lesions referred for biopsy because of clinical suspicion of skin cancer are false positives. No studies exist by which to judge the extent of harm, if any, related to these tests.

Misdiagnosis is another potential adverse effect of screening. It is known to occur, but no studies have been done on its rate of occurrence. The diagnosis of melanoma has a serious emotional and financial effect for the patient, and even when the melanoma is very thin and has an excellent prognosis, obtaining insurance can be very difficult.[8] Critics worry that, if screening becomes widespread, pathologists may set the threshold low for diagnosing borderline lesions as melanoma, since the risk to the patient and the potential legal cost to the pathologists for missing melanoma are overwhelming.[11] However, there are no data about the frequency with which misdiagnosis occurs in community practice settings. The effects on diagnostic criteria of widespread screening are hard to predict, but uncertainty about these effects should be considered when one weighs a recommendation to screen.

Some experts consider diagnosis of common, nonmalignant skin lesions found incidentally in screening to be a costly adverse effect of screening. Screening detects large numbers of benign skin conditions, especially seborrheic keratoses, which are very common in the elderly. Detection of these lesions could be considered an adverse effect of screening if it leads to additional biopsies and unnecessary or expensive procedures. Although this has been shown to occur in usual care,[87] none of the screening studies examined the rate at which this occurred.

Is There Direct Evidence That Screening for Skin Cancers Leads to Reduced Morbidity and Mortality?

No data exists providing direct evidence that screening for skin cancer leads to reduced morbidity and mortality. No randomized trials or case-control studies of screening for skin cancer have been completed. Well-done, frequently cited observational studies of the relation between early detection and mortality have been done,[88] but in such studies the effect of promoting primary prevention and self-examination cannot be distinguished from that of routine screening in patients seeing the physician for unrelated reasons.[89] The lack of data reflects the lack of population-based programs that focus on routine total-body skin examination by a physician.

The absence of randomized trials is also not surprising since melanoma is relatively rare in the general population. A recent review by Elwood[90] examined the options for

conducting a randomized trial of screening in detail. Elwood calculated that, to have a 90% chance of detecting a one-third reduction in mortality, a trial of screening with total-body skin examination in the general population 45 to 69 years of age would require 400,000 subjects in each group. Put differently, approximately 21,000 people would need to be screened to prevent 1 death.

An alternative would be to conduct a trial in patients classified as high risk by means of a risk-assessment questionnaire. Using this approach, Elwood[90] assumed that 7% of the population would be classified as high risk; 35% of all melanomas occur in this high-risk group; 60% of patients complete the questionnaire; and 80% of the high-risk patients would comply with total-body skin examination. He calculated that, to have a 90% chance of detecting a one-third reduction in mortality, 6 million questionnaires would need to be administered to enroll 100,000 high-risk subjects in each group.

In fact, a trial involving 600,000 subjects has begun in Australia.[90] It is expected that it will take 9 more years to complete.

Effectiveness of Screening in Early Detection and Early Treatment

Screening in a population is justified if there is evidence that early detection and treatment improve outcomes such as mortality and quality of life. Other considerations include consequences of false-negative and false-positive tests, acceptability of the test, and the risks of screening and of treatment.

Does Treatment of Nonmelanoma Skin Cancer Found by Screening Reduce Morbidity and Mortality?

Early treatment of basal and squamous cell carcinoma might reduce morbidity and disfigurement, but no studies have evaluated whether screening improves the outcomes of these cancers. Basic information, such as the proportion of Medicare patients who have NMSC who suffer disfigurement or death, is lacking. If we assume that 20% of squamous cell cancers in the elderly are either lethal or disfiguring (assumes a prevalence of 0.025 for men and women combined) and that screening would reduce this by 50%, approximately 400 patients would need to be screened to prevent 1 lethal or disfiguring case. These calculations, while theoretical, do suggest that screening is potentially beneficial and that a trial of early detection in the elderly should examine outcomes in NMSC rather than just in melanoma.

Does Early Detection and Treatment of Melanoma Found by Screening Reduce Morbidity and Mortality?

Well-designed observational studies can provide persuasive information about the effect of early detection on mortality. For some cancers, notably colon cancer, observational studies make a convincing case for the effectiveness of early detection,

even in the absence of randomized controlled trials. Such a conclusion must be based on data that link actions taken as a result of screening to health outcomes.

In the absence of randomized trials and case-control studies of screening or of early treatment, the inference that earlier treatment as a result of screening improves health outcomes must rely on 3 lines of indirect evidence: (1) a case-control study[46] in which skin self-examination reduces the incidence of lethal melanoma, (2) comparison of the stages of cancers and mortality found in screening[88,92] with those found in usual practice, and (3) evidence from studies of the consequences of delay in diagnosis. These are summarized below.

Case-control study of self-examination. Although there are no case-control studies of screening, 1 case-control study[46] has examined the effect of skin self-examination on mortality from melanoma. In this study, 650 incident cases of melanoma in 1987–1989 were identified through the Connecticut Tumor Registry and compared with randomly selected, age- and sex-matched controls. After 5 years of follow-up, cases were classified as lethal if the individual died or had distant metastases.

A structured questionnaire was used to assess skin self-examination attitudes and behavior. The question used to determine skin self-examination in this study was "…did you ever (in your life) carefully examine your own skin? By this I mean actually check surfaces of your skin deliberately and purposely?" Based on subjects' responses to this and related questions, 13% of the cases and 17.5% of the control subjects were classified as careful or rigorous examiners, and an additional 57.4% of the cases and 66.7% of control subjects were classified as casual examiners. The questionnaire also assessed potential confounding factors, such as risk factors for skin cancer, but did not assess general health behaviors, such as diet, exercise, and medical-care-seeking behavior that might affect the risk of cancer and the likelihood of early detection.

The investigators performed 2 multivariate analyses: 1 for primary prevention, and 1 for secondary prevention. In the first analysis, after adjustment for sun exposure, skin color, the number of nevi, and other risk factors, skin self-examination was negatively associated with incidence of melanoma (OR 0.66, CI, 0.44–0.99).

In the second analysis, after adjustment for confounding risk factors, skin self-examination was associated with a reduced risk of lethal melanoma (OR 0.37, CI, 0.16–0.84). Survival analysis comparing patients who practiced skin self-examination with those who did not suggested that, after an average of 5.4 years, self-examination was associated with a lower probability of lethal melanoma. The authors noted that the shape of the survival curves—the curve for the self-examination group plateaus after 3 years, whereas survival continues to decrease to 5 years in the patients who did not practice self-examination—offers some reassurance that the observed benefit is caused by actual improvement in survival rather than to lead-time bias.

As noted by the authors, this case-control study provides suggestive, rather than definitive, evidence for the effectiveness of skin self-examination. More direct evidence is needed to link self-examination behaviors to specific actions that could reduce the incidence or lethality of melanoma. To prevent melanoma, self-examination on the part of the patient must lead to actions—such as identification of a suspicious lesion, self-referral to the physician, earlier treatment of precancerous lesions, and health behavior changes—to prevent the development of new melanomas. Although the study

indicates that patients who practiced self-examination had undergone more biopsies than those who had not, it does not report the frequency of these intermediate steps or whether their frequency was different enough from that of other patients to explain the observed differences in outcome.

Apart from concerns about the strength of the study design, how relevant is a study of skin self-examination to screening by primary care providers? If skin self-examination prevents death from melanoma, it may be more likely that examination by a physician could also prevent deaths, especially if examination by a physician promotes more accurate self-examination. In fact, casefinding by a physician might be expected to be more effective because it reaches patients, especially elderly men, who are at high risk and are the least likely to practice self-examination effectively[91] or to respond to an invitation or health-promotion campaign. However, self-examination occurs much more frequently (monthly, on average, in the case-control study) than screening by a physician, and by means of self-examination, patients can note findings—in particular, changes in size, border, or color of lesions—that cannot be recognized easily by infrequent examinations by physicians. Nevertheless, this case-control study[46] provides the strongest available evidence that early detection of melanoma reduces mortality.

Comparing stages of cancers and mortality found in screening with those found in usual practice. Advocates cite the results of public information campaigns in Australia[92] and in the United Kingdom[88] as evidence of the potential benefits of screening. In Australia, public information campaigns have promoted sun-protection behaviors and early detection for more than 15 years. Melanoma mortality, which had increased for decades, reached a plateau in 1985 and, in recent years, has decreased slightly.[92] It is thought that this trend is related to skin health-promotion activities, including primary prevention and self-examination; however, because it is not a prominent feature of these campaigns, it is not possible to determine what role, if any, screening by physicians has played.

In the United Kingdom, registry data were used to compare rates of invasive melanoma before and after public information campaigns to promote early detection of skin cancers. In the west of Scotland, community-based, skin health-promotion campaigns compared melanoma thickness and mortality before and after implementing a public information campaign and rapid referral system in 1985.[88] The number and proportion of thin melanomas diagnosed yearly in the population increased immediately afterward. The response to the public information campaign was stronger in women than in men. In women, within 2 years the rate of diagnosis of thick melanomas (>3.5 mm) began to decrease, and within 5 years sustained decreases in thick melanomas and in melanoma mortality were observed. In men, the rate of diagnosis of thick melanomas did not change, and the melanoma mortality rate rose. As in Australia, the role of screening by physicians in these results is unclear.[93]

A subsequent implementation of a similar program in 7 British districts failed to replicate these results.[80,93,94] The incidence rates of both thin and thick melanomas increased during the public information campaign (1987–1989) and have remained higher than before the program began.

In contrast to these health-promotion efforts, mass-screening programs cannot be evaluated with population-based registries. Mass screening increases the proportion of

melanomas detected in an early stage (see Table 3), but the significance of this finding is unclear. Survival is strongly related to lesion thickness at the time of resection, but it is difficult to know the extent to which comparison of the distribution of the stage of cancers found by screening with those found in usual care is affected by lead-time bias or length bias. The natural history of melanoma, and in particular the significance of the many additional thin melanomas found in screened populations, is another source of uncertainty.

Retrospective studies of the consequences of delay in diagnosis. The argument for screening would be strengthened if evidence pointed to a consistent relation between a delay of diagnosis and the thickness of melanoma. Nine case series examined the causes and consequences of apparent delay in the diagnosis of melanoma. The validity of these studies is questionable because all of them assessed delay retrospectively. The 2 largest studies, 1 from Scotland and 1 from Australia, found no relation between delay in diagnosis and tumor thickness.[17,80] The Australian study found that male sex, nodular melanoma, and location on the head and the neck (but not delay) were associated with thick melanoma.

Five studies, which were performed in specialty clinics, observed patients who had melanoma of the hand, foot, eye, penis, or nailbeds.[95-99] In these studies, misdiagnosis was a common cause of delay in treatment. Effects of delay on tumor thickness or survival were reported in 3 of the studies, and the results were inconsistent. In a study of 83 patients who had acral melanomas, 17 of 33 subungual melanomas and 10 of 50 palmoplantar melanomas were clinically misdiagnosed by physicians.[95] Misdiagnosis caused a median delay of 12 months in the diagnosis of palmoplantar melanomas and of 18 months in the diagnosis of subungual melanomas. Delay in diagnosis was associated with increased tumor thickness, more advanced stage at time of melanoma diagnosis, and a lower estimated 5-year survival rate (15.4% versus 68.9% for palmoplantar; 68.5% versus 90.9% for subungual). In another series of 140 patients who had melanoma of the foot, delay in diagnosis had no effect on clinical outcome.[99] Another series of 102 consecutive melanoma patients found no relation between delay in diagnosis and tumor thickness.[100]

Two recent case series from specialized clinics in major referral centers reported that lesions detected by physicians were thinner than those detected by patients.[101,102] In 1 of these cases,[101] 24 of 102 consecutive patients had physician-detected melanomas; the median thickness was 0.23 versus 0.9 mm in self-detected melanomas. Of the 24 physician-detected melanomas, 11 were in situ. In the other study,[102] 172 of 590 consecutive patients had physician-detected melanomas; these were significantly thinner, but the difference was not as striking (0.9 versus 1.3 mm).

The latter study[102] also carefully examined the relation between melanoma thickness and delay either in seeking medical advice or after seeking medical care, and concluded that poor prognosis was due to rapidly growing tumors rather than to delays. They examined 4 time intervals:

1. From the time the patient first noticed a lesion to the time they considered it to be suspicious;

2. From the time that the patient considered the lesion suspicious to the time that the patient saw a physician;
3. From the time that the patient saw a physician to the time that the physician proposed removal; and
4. From the time that the physician proposed removal of the lesion to the time of surgical resection.

In the 418 patients who had self-detected cancers, the first, the third, and the fourth intervals were not associated with tumor thickness. Not surprisingly, once a lesion was recognized as being dangerous, patients who had thicker lesions sought medical attention more quickly (ie, for the second interval, thinner lesions had the longest delay). In a subgroup of 247 patients who reported a delay of less than 5 years between the time they noticed the lesion and the time they believed it to be dangerous, the time between noticing a lesion and considering it dangerous was longest for lesions 1.5 to 2.99 mm thick, but the time was shorter for lesions thicker and thinner than that.

Costs and Cost Effectiveness

A CE analysis[103] of screening for malignant melanoma found that the average projected discounted life expectancy without screening was 15.0963, versus 15.0975 with screening. This difference is equivalent to an increase of approximately 9 hours per person screened or 337 days for each person who had melanoma.

Assuming that a screening examination by a dermatologist costs $30, the incremental CE ratio was $29,170 per year of life saved. The CE ratio was unexpectedly low because, in the model, savings from prevention of late-stage melanomas offset most of the costs of screening. Thus the key assumptions in the model, affecting the calculation of both effectiveness and cost, were that the proportion of late-stage melanomas would decrease from 6.1% without screening to 1.1% with screening. Similarly, the model assumed that invasive cancers would decrease from 70.3% to 58.1% and that melanomas thicker than 1.5 mm would decrease from 20.1% to 12.6% of invasive melanomas. These assumptions are based on comparison of cross-sectional data on the stages of melanoma in individuals who attended the American Academy of Dermatology's mass-screening programs with data on usual care from the SEER registry.[3]

Chapter 4. Discussion

Table 4 summarizes the literature review by describing the evidence for each link in the analytic framework (see Figures 3 and 4). The quality of the evidence at each link ranged from poor to fair and is explained in Table 4.

The case for screening is based on the assumption that melanoma and other skin cancers have a long latency period during which they can be treated with a high rate of success. Another assumption is that early detection prevents progression of early-stage cancers to advanced, lethal stages. These assumptions are reasonable, but studies of early detection have not focused on screening and have not adequately linked it with reduced incidence of invasive disease.

Despite these information gaps, skin cancer screening, perhaps by means of a risk-assessment technique to identify high-risk patients who are seeing the physician for other reasons, is the most promising strategy for addressing the excess burden of disease in older individuals. This group has substantial morbidity and mortality from skin cancer. By themselves, primary prevention efforts and promotion of self-examination seem unlikely to change these rates substantially. Although the efficacy of screening has not been established, the screening procedures themselves are noninvasive, and the follow-up test, skin biopsy, has low morbidity.

Future Research Needs

The agenda for future research for skin cancer screening is a rich one, but one complicated by the low incidence of melanoma and the enormous study sample sizes required for vigorous demonstration of screening efficacy. We have identified numerous potentially promising research directions.

- First, more research should focus on the elderly. Advanced melanoma and invasive squamous cell carcinoma occur most often in the elderly, especially older men, and older men are less likely than other groups to take part in mass-screening programs. Therefore, we especially need to learn more about primary-care-based strategies for identifying high-risk men older than 65 years of age and for referring them for screening and surveillance. As part of this effort, we need better information about the natural history of thick nodular melanoma typically found in the elderly, since currently, there is little evidence that lethal tumors in this group could be detected in a curable state. We also need to know more about reductions in disfigurement for NMSC in this group.
- Second, well-designed, prospective, population-based studies that compare incidence of lethal melanoma in screened and unscreened groups are needed to provide information about the consequences of delay and how much it can be reduced by screening. In theory, screening can find melanoma earlier than would occur without screening. But to date, studies have examined neither the average difference in time to diagnosis between screened and unscreened populations nor the rate of progression of undetected tumors during this interval.
- Third, in the absence of evidence for the accuracy, efficacy, or feasibility of total-body skin examination of unselected patients by primary care clinicians, more research attention should be given to identifying only patients at high risk for

melanoma for routine primary care screening and with the primary care provider either performing a total-body skin examination or referring the patient to a dermatologist for periodic skin examinations.

- Fourth, at least two types of research are needed: observational studies and validated risk-assessment program studies. Observational studies should assess the validity, reliability, and feasibility of standardized brief risk assessments to identify patients at high risk for melanoma. By use of a patient questionnaire and possibly limited examination, these studies would assess the risk levels of patients seen in primary care clinics and would monitor patients in the high- and the low-risk groups. No longitudinal studies of the use of a risk-assessment tool in primary care practice have been reported.

      Studies of validated risk-assessment programs in the primary care setting are needed to identify high-risk patients. However, as this review shows, prospective randomized trials of screening with risk-assessment instruments would need to include tens of thousands of patients in the treatment and in the control arms.

Future research also is needed to address whether screening increases the number of precancerous lesions removed and ultimately reduces the incidence of skin cancer. This will require population-based studies that carefully track removal of precancerous lesions and measure the effect on incidence of skin cancer in screened and unscreened groups. The case-control study of skin self-examination for melanoma conducted by Berwick et al.[46] provides some evidence that patients who self-examined their skin had more precancerous lesions removed than those who did not self-examine their skin. However, it was unclear how removal of these lesions related to the incidence of melanoma.

Finally, as with other screening protocols, patient behavior plays a critical role in determining the ultimate effect of screening on morbidity and mortality. Three important behavioral issues merit study:

Strategies for improving patient risk assessment. Given the unknown and uncertain yield of primary care skin examinations, it becomes particularly important to examine strategies for improving patient risk assessment. In fact, as noted above, the strongest available evidence that early detection of melanoma reduces mortality comes from a case-control study of skin self-examination. Although this study itself is problematic, it points out the need for a better understanding of the behavioral processes that could link self-examination to reduced incidence of lethality of melanoma. To prevent melanoma or to detect it earlier, patient self-examination must lead to activities such as the identification of suspicious lesions, self-referral to a physician, earlier treatment of precancerous lesions, and even health behavior changes to prevent the development of new melanomas. Therefore, clinicians must learn how best to teach or prompt this chain of behavior. There is also much for clinicians to learn about ways to improve the accuracy of patient self-examination (mole counts, identification of suspicious lesions) and ways to improve the effect of targeted media campaign for mass screening. These campaigns must do a better job of helping people to identify whether they are at high risk and to take part in mass screening, and, if necessary, in follow-up physician visits.

Explanation of the rates of compliance with referral. Clearly, whether primary care screening and early detection can reduce morbidity and mortality depends on whether it leads to referral for follow-up and biopsy—especially among high-risk groups. Rates of compliance with referral for follow-up skin examination or biopsy ranged from 45% to 95% in the studies reviewed; to explain these variations, we need to learn more about the characteristics of the screening programs and of the patients. What can providers do or say to promote follow-up? What systems supports must be in place to prompt and support patients and providers?

Emphasis on patient education and motivation. As noted in this review, little is known about the effect of screening on patients' skin knowledge and skin health behaviors. The yield of mass screening and casefinding could be improved by capitalization on primary care specialty screening as a teachable moment to communicate risk status, to motivate and educate patients about regular skin examination, and to promote sun-protection measures.

References

1. Landis SH, Murray T, Bolden S, Wingo PA. Cancer Statistics, 1999. *CA Cancer Jr Clin*. 1999;49:8.

2. Cress RD, Holly EA. Incidence of cutaneous melanoma among non-Hispanic whites, Hispanics, Asians, and blacks: an analysis of California cancer registry data, 1988-93. *Cancer Causes & Control*. 1997;8:246-252.

3. Ries LAG, Kosary CL, Hankey BF, Miller BA, Edwards BK. SEER Cancer Statistics Review, 1973-95. Bethesda (MD): National Cancer Institute; 1998.

4. Jelfs P, Coates M, Giles G. Cancer in Australia 1989-1990 (with projections to 1995). Canberra: Australian Institute of Health and Welfare; 1996.

5. Kelly J. Melanoma in the elderly—a neglected public health challenge. *Med J Aust*. 1998;169:403-404.

6. Dennis LK. Analysis of the melanoma epidemic, both apparent and real: data from the 1973 through 1994 surveillance, epidemiology, and end results program registry. *Arch Dermatol*. 1999;135:275-280.

7. Berwick M, Halpern A. Melanoma epidemiology. *Curr Opin Oncol*. 1997;9:178-182.

8. Swerlick RA, Chen S. The melanoma epidemic: more apparent than real? *Mayo Clin Proc*. 1997;72:559-564.

9. Burton R, Armstrong B. Recent incidence trends imply a nonmetastasizing form of invasive melanoma. *Melanoma Res*. 1994;4:107-113.

10. Burton R. An analysis of a melanoma epidemic. *Int J Cancer*. 1995;55:765-770.

11. Swerlick RA, Chen S. The melanoma epidemic. Is increased surveillance the solution or the problem? *Arch Dermatol*. 1996;132:881-4.

12. Gallagher RP, Hill GB, Bajdik CD, et al. Sunlight exposure, pigmentation factors, and risk of nonmelanocytic skin cancer. II. Squamous cell carcinoma. *Arch Dermatol*. 1995;131:164-169.

13. Chuang TY, Popescu NA, Su WP, Chute CG. Squamous cell carcinoma. A population-based incidence study in Rochester, Minnesota. *Arch Dermatol*. 1990;126:185-188.

14. Chuang TY, Popescu A, Su WP, Chute CG. Basal cell carcinoma. A population-based incidence study in Rochester, Minnesota. *J Am Acad Dermatol*. 1990;22:413-417.

15. Karagas MR, Greenberg ER, Spencer SK, Stukel TA, Mott LA. Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Group. *Int J Cancer*. 1999;81:555-559.

16. McGovern V, Cochran A, Van der Esch E. The classification of malignant melanoma, its histological reporting and registration: revision of the 1972 Syndey classification. *Pathology*. 1986;18:12-21.

17. Hersey P, Sillar RW, Howe CG, et al. Factors related to the presentation of patients with thick primary melanomas. *Med J Aust*. 1991;154:583-587.

18. Heenan PJ, Yu L, English DR. Melanoma in the elderly--a neglected public health challenge [letter]. *Med J Aust*. 1999;170:394-395.

19. Whited JD, Grichnik JM. Does this patient have a mole or a melanoma? *JAMA*. 1998;279:696-701.

20. Corona R, Mele A, Amini M, et al. Interobserver variability on the histopathologic diagnosis of cutaneous melanoma and other pigmented skin lesions. *J Clin Oncol*. 1996;14:1218-1223.

21. Farmer ER, Gonin R, Hanna MP. Discordance in the histopathologic diagnosis of melanoma and melanocytic nevi between expert pathologists. *Hum Pathol*. 1996;27:528-531.

22. Gershenwald JE, Buzaid AC, Ross MI. Classification and staging of melanoma. [Review] [114 refs]. *Hematol Oncol Clin North Am*. 1998;12:737-765.

23. Breslow A. Thickness, cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. *Ann of Surg*. 1970;172:902-908.

24. Weinstock MA. Death from skin cancer among the elderly: epidemiological patterns. *Arch Dermatol*. 1997;133:1207-1209.

25. Preston DS, Stern RS. Nonmelanoma cancers of the skin. *N Engl J Med*. 1992;327:1649-1662.

26. Stern RS, Liebman EJ, Vakeva L. Oral psoralen and ultraviolet-A light (PUVA) treatment of psoriasis and persistent risk of nonmelanoma skin cancer. PUVA Follow-up Study. *J Natl Cancer Inst*. 1998;90:1278-1284.

27. U.S. Preventive Services Task Force. Screening for Skin Cancer (Including Counseling to Prevent Skin Cancer). In: DiGuiseppi C, Atkins D, Woolf SH, Kamerow DB, eds. *Guide to Clinical Preventive Services, 2nd edition*. Washington, DC: Office of Disease Prevention and Health Promotion, U. S. Government Printing Office, 1996:141-152.

28. Rigel DS, Friedman RJ, Kopf AW, et al. Importance of complete cutaneous examination for the detection of malignant melanoma. *J Am Acad Dermatol*. 1986;14:857-860.

29. Sackett DL, Haynes RB, Guyatte GH, Tugwell P. Clinical Epidemiology, A Basic Science for Clinical Medicine, 2nd Edition. Boston: Little, Brown and Company; 1991.

30. Sox HC, Blatt MA, Higgins MC, Marton KI. Medical Decision Making. Boston: Butterworth-Heinemann; 1988.

31. Limpert GH. Skin-cancer screening: a three-year experience that paid for itself. *J Fam Pract*. 1995;40:471-475.

32. de Rooij MJ, Rampen FH, Schouten LJ, Neumann HA. Volunteer melanoma screenings. Follow-up, compliance, and outcome. *Dermatol Surg*. 1997;23:197-201.

33. de Rooij MJ, Rampen FH, Schouten LJ, Neumann HA. Skin cancer screening focusing on melanoma yields more selective attendance. *Arch Dermatol*. 1995;131:422-425.

34. Jonna BP, Delfino RJ, Newman WG, Tope WD. Positive predictive value for presumptive diagnoses of skin cancer and compliance with follow-up among patients attending a community screening program. *Prev Med*. 1998;27:611-616.

35. Rampen RH. Point-counterpoint. Mass population skin cancer screening is not worthwhile. *J Cutan Med Surg*. 1998;2:128-129.

36. Koh HK, Norton LA, Geller AC, et al. Evaluation of the American Academy of Dermatology's National Skin Cancer Early Detection and Screening Program. *J Am Acad Dermatol*. 1996;34:971-978.

37. Rampen FH, Casparie-van Velsen JI, van Huystee BE, Kiemeney LA, Schouten LJ. False-negative findings in skin cancer and melanoma screening. *J Am Acad Dermatol*. 1995;33:59-63.

38. de Rooij MJ, Rampen FH, Schouten LJ, Neumann HA. Factors influencing participation among melanoma screening attenders. *Acta Derm Venereol*. 1997;77:467-470.

39. Federman DG, Concato J, Kirsner RS. Comparison of dermatologic diagnoses by primary care practitioners and dermatologists. A review of the literature. *Arch Fam Med*. 1999;8:170-172.

40. Burton RC, Howe C, Adamson L, et al. General practitioner screening for melanoma: sensitivity, specificity, and effect of training. *J Med Screen*. 1998;5:156-161.

41. Gallagher RP, Ma B, McLean DI, et al. Trends in basal cell carcinoma, squamous cell carcinoma, and melanoma of the skin from 1973 through 1987. *J Am Acad Dermatol*. 1990;23:413-421.

42. Gamble JF, Lerman SE, Holder WR, Nicolich MJ, Yarborough CM. Physician-based case-control study of non-melanoma skin cancer in Baytown, Texas. *Occup Med*. 1996;46:186-196.

43. Grodstein F, Speizer FE, Hunter DJ. A prospective study of incident squamous cell carcinoma of the skin in the nurses' health study. *J Natl Cancer Inst*. 1995;87:1061-1066.

44. Kaldor J, Shugg D, Young B, Dwyer T, Wang YG. Non-melanoma skin cancer: ten years of cancer-registry-based surveillance. *Int J Cancer*. 1993;53:886-891.

45. Bataille V, Bishop JA, Sasieni P, et al. Risk of cutaneous melanoma in relation to the numbers, types and sites of naevi: a case-control study. *Br J Cancer*. 1996;73:1605-1611.

46. Berwick M, Begg CB, Fine JA, Roush GC, Barnhill RL. Screening for cutaneous melanoma by skin self-examination. *J Natl Cancer Inst*. 1996;88:17-23.

47. Garbe C, Buttner P, Weiss J, et al. Risk factors for developing cutaneous melanoma and criteria for identifying persons at risk: multicenter case-control study of the Central Malignant Melanoma Registry of the German Dermatological Society. *J Invest Derm*. 1994;102:695-699.

48. Tucker MA, Halpern A, Holly EA, et al. Clinically recognized dysplastic nevi. A central risk factor for cutaneous melanoma. *JAMA*. 1997;277:1439-1444.

49. English DR, Armstrong BK. Identifying people at high risk of cutaneous malignant melanoma: results from a case-control study in Western Australia. *BMJ (Clin Res Ed)*. 1988;296:1285-1288.

50. Marrett LD, King WD, Walter SD, From L. Use of host factors to identify people at high risk for cutaneous malignant melanoma. *Can Med Assoc J*. 1992;147:445-453.

51. Bliss JM, Ford D, Swerdlow AJ, et al. Risk of cutaneous melanoma associated with pigmentation characteristics and freckling: systematic overview of 10 case-control studies. The International Melanoma Analysis Group (IMAGE). *Int J Cancer*. 1995;62:367-376.

52. Elwood JM, Jopson J. Melanoma and sun exposure: an overview of published studies. *Int J Cancer*. 1997;73:198-203.

53. Elwood JM, Gallagher RP. Body site distribution of cutaneous malignant melanoma in relationship to patterns of sun exposure. *Int J Cancer*. 1998;78:276-280.

54. Walter SD, King WD, Marrett LD. Association of cutaneous malignant melanoma with intermittent exposure to ultraviolet radiation: results of a case-control study in Ontario, Canada. *Int J Epidemiol*. 1999;28:418-427.

55. Byles JE, Hennrikus D, Sanson-Fisher R, Hersey P. Reliability of naevus counts in identifying individuals at high risk of malignant melanoma. *Br J Dermatol*. 1994;130:51-56.

56. Westerdahl J, Anderson H, Olsson H, Ingvar C. Reproducibility of a self-administered questionnaire for assessment of melanoma risk. *Int J Epidemiol*. 1996;25:245-251.

57. Little P, Keefe M, White J. Self screening for risk of melanoma: validity of self mole counting by patients in a single general practice. *BMJ*. 1995;310:912-916.

58. Lawson DD, Moore DH, 2nd, Schneider JS, Sagebiel RW. Nevus counting as a risk factor for melanoma: comparison of self-count with count by physician. *J Am Acad Dermatol*. 1994;31:438-444.

59. Titus-Ernstoff L, Thorn M, Tosteson TD, et al. The accuracy of skin self-examination

for atypical nevi. *Epidemiology*. 1996;7:619-623.

60. Jackson A, Wilkinson C, Ranger M, Pill R, August P. Can primary prevention or selective screening for melanoma be more precisely targeted through general practice? A prospective study to validate a self administered risk score. *BMJ*. 1998;316:34-38; discussion 38-39.

61. Schneider JS, Moore DH, 2nd, Sagebiel RW. Risk factors for melanoma incidence in prospective follow-up. The importance of atypical (dysplastic) nevi. *Arch Dermatol*. 1994;130:1002-1007.

62. Kelly JW, Crutcher WA, Sagebiel RW. Clinical diagnosis of dysplastic melanocytic nevi. A clinicopathologic correlation. *J Am Acad Dermatol*. 1986;14:1044-1052.

63. Jackson A, Wilkinson C, Pill R. Moles and melanomas--who's at risk, who knows, and who cares? A strategy to inform those at high risk. *Br J Gen Pract*. 1999;49:199-203.

64. MacKie RM, Freudenberger T, Aitchison TC. Personal risk-factor chart for cutaneous melanoma. *Lancet*. 1989;2:487-490.

65. Engelberg D, Gallagher RP, Rivers JK. Follow-up and evaluation of skin cancer screening in British Columbia. *J Am Acad Dermatol*. 1999;41:37-42.

66. McGee R, Elwood M, Williams S, Lowry F. Who comes to skin checks? *NZ Med J*. 1994;107:58-60.

67. Hourani LL, LaFleur B. Predictors of gender differences in sunscreen use and screening outcome among skin cancer screening participants. *J Behav Med*. 1995;18:461-477.

68. Katris P, Crock JG, Gray BN. Research note: the Lions Cancer Institute and the Western Australian Society of Plastic Surgeons skin cancer screening programme. *Aust NZ J Surg*. 1996;66:101-104.

69. Katris P, Donovan RJ, Gray BN. Nurses screening for skin cancer: an observation study. *Aust N Z J Public Health*. 1998;22:381-383.

70. Rivers JK, Gallagher RP. Public education projects in skin cancer. Experience of the Canadian Dermatology Association. *Cancer*. 1995;75:661-666.

71. Dozier S, Wagner RF, Jr., Black SA, Terracina J. Beachfront screening for skin cancer in Texas Gulf coast surfers. *South Med J*. 1997;90:55-58.

72. Harvey I, Frankel S, Marks R, Shalom D, Nolan-Farrell M. Non-melanoma skin cancer and solar keratoses. I. Methods and descriptive results of the South Wales Skin Cancer Study. *Br J Cancer*. 1996;74:1302-1307.

73. Harvey I, Frankel S, Marks R, Shalom D, Nolan-Farrell M. Non-melanoma skin cancer and solar keratoses II analytical results of the South Wales Skin Cancer Study. *Br J Cancer*. 1996;74:1308-1312.

74. Ichihashi M, Naruse K, Harada S, et al. Trends in nonmelanoma skin cancer in Japan. *Recent Results Cancer Res*. 1995;139:263-273.

75. Tornberg S, Mansson-Brahme E, Linden D, et al. Screening for cutaneous malignant melanoma: a feasibility study. *J Med Screen*. 1996;3:211-215.

76. Bergenmar M, Tornberg S, Brandberg Y. Factors related to non-attendance in a population based melanoma screening program. *Psychooncology*. 1997;6:218-226.

77. Ruskiewicz J. Skin cancer and actinic keratoses. *J Am Optom Assoc*. 1998;69:229-235.

78. Whited JD, Hall RP, Simel DL, Horner RD. Primary care clinicians' performance for detecting actinic keratoses and skin cancer. *Arch Int Med*. 1997;157:985-990.

79. Friedman LC, Webb JA, Bruce S, Weinberg AD, Cooper HP. Skin cancer prevention and early detection intentions and behavior. *Am J Prev Med*. 1995;11:59-65.

80. Herd RM, Cooper EJ, Hunter JA, et al. Cutaneous malignant melanoma. Publicity, screening clinics and survival--the Edinburgh experience 1982-90. *Br J Dermatol*. 1995;132:563-570.

81. Marghoob AA, Slade J, Salopek TG, Kopf AW, Bart RS, Rigel DS. Basal cell and squamous cell carcinomas are important risk factors for cutaneous malignant melanoma. Screening implications. *Cancer*. 1995;75:707-714.

82. van der Spek-Keijser LM, van der Rhee HJ, Toth G, Van Westering R, Bruijn JA, Coebergh JW. Site, histological type, and thickness of primary cutaneous malignant melanoma in western Netherlands since 1980. *Br J Dermatol*. 1997;136:565-571.

83. Veierod MB, Thelle DS, Laake P. Diet and risk of cutaneous malignant melanoma: a prospective study of 50,757 Norwegian men and women. *Int J Cancer*. 1997;71:600-604.

84. De Rooij MJ, Rampen FH, Schouten LJ, Neumann HA. Total skin examination during screening for malignant melanoma does not increase the detection rate. *Br J Dermatol*. 1996;135:42-45.

85. Dhir A, Orengo I, Bruce S, Kolbusz RV, Alford E, Goldberg L. Basal cell carcinoma on the scalp of an Indian patient. *Dermatol Surg*. 1995;21:247-250.

86. Geller AC, Halpern AC, Sun T, et al. Participant satisfaction and value in American Academy of Dermatology and American Cancer Society skin cancer screening programs in Massachusetts. *J Am Acad Dermatol*. 1999;40:563-566.

87. Stern RS, Boudreaux C, Arndt KA. Diagnostic accuracy and appropriateness of care for seborrheic keratoses. A pilot study of an approach to quality assurance for cutaneous surgery. *JAMA*. 1991;265:74-77.

88. MacKie RM, Hole D. Audit of public education campaign to encourage earlier detection of malignant melanoma. *BMJ*. 1992;304:1012-1015.

89. Koh HK, Geller AC. Public health interventions for melanoma. Prevention, early detection, and education. *Hematol Oncol Clin North Am*. 1998;12:903-298.

90. Elwood JM. Screening for melanoma and options for its evaluation. *J Med Screen*. 1994;1:22-38.

91. Hanrahan PF, Hersey P, D'Este CA. Factors involved in presentation of older people with thick melanoma. *Med J Aust*. 1998;169:410-414.

92. Giles GG, Armstrong BK, Burton RC, Staples MP, Thursfield VJ. Has mortality from melanoma stopped rising in Australia? Analysis of trends between 1931 and 1994. *BMJ*. 1996;312:1121-1125.

93. Melia J, Cooper EJ, Frost T, et al. Cancer Research Campaign health education programme to promote the early detection of cutaneous malignant melanoma. II. Characteristics and incidence of melanoma. *Br J Dermatol*. 1995;132:414-421.

94. Melia J. Early detection of cutaneous malignant melanoma in Britain. *Int J Epidemiol*. 1995;24:S39-S44.

95. Metzger S, Ellwanger U, Stroebel W, Schiebel U, Rassner G, Fierlbeck G. Extent and consequences of physician delay in the diagnosis of acral melanoma. *Melanoma Res*. 1998;8:181-186.

96. Warso M, Gray T, Gonzalez M. Melanoma of the hand. *J Hand Surg*. 1997;22:354-360.

97. Larsson K, Shaw H, Thompson J, Harman R, McCarthy W. Primary mucosal and glans penis melanomas: the Sydney Melanoma Unit experience. *Aust N Z J Surg*. 1999;69:121-126.

98. Holden R, Damato B. Preventable delays in the treatment of intraocular melanoma in the UK. *Eye*. 1996;10:127-129.

99. Bennett DR, Wasson D, MacArthur JD, McMillen MA. The effect of misdiagnosis and delay in diagnosis on clinical outcome in melanomas of the foot. *J Am Coll Surg*. 1994;179:279-284.

100. Baccard M, Chevret S, Chemaly P, Morel P. [Delay in diagnosing melanoma. A prospective study in 102 patients]. *Ann Dermatol Venereol*. 1997;124:601-606.

101. Epstein DS, Lange JR, Gruber SB, Mofid M, Koch SE. Is physician detection associated with thinner melanomas? *JAMA*. 1999;281:640-643.

102. Richard MA, Grob JJ, Avril MF, et al. Melanoma and tumor thickness: challenges of early diagnosis. *Arch Dermatol*. 1999;135:269-274.

103. Freedberg K. Screening for melanoma: A cost-effectiveness analysis. *J Am Acad Dermatol*. 1999;41:738-745.

Tables

Appendix 1. Strategy for Skin Cancer Search

1 skin neoplasms

2 exp mass screening
        genetic screening
        mass chest x-ray
        multiphasic screening
        vision screening
        mandatory screening

3 screen$.tw. (Text word taken from title and abstract of article)

4 exp physical examination
        self-examination
        skinfold thickness

5 exp neoplasms metastasis
        lymphatic metastasis
        neoplasm circulating cells
        neoplasm seeding
        neoplasms, unknown primary

6 neoplasm recurrence, local
7 recurrence
8 exp morbidity
        incidence
        prevalence

9 exp sensitivity and specificity
        predictive value of tests
        ROC curve

10 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

11 skin neoplasms/mo (*mortality*)
12 skin neoplasms/ep (*epidemiology*)

13 10 or 11 or 12

14 1 and 13
15 limit 14 to human
16 limit 15 to english language
17 looked at english abstracts for foreign language articles

Appendix 2. Inclusion Criteria for Evidence Tables

1,046 Abstracts

159 Reviews, Letters, Editorials

369 Addressed Link in AF

518 Excluded

17 From Reference Lists

24 Data on Screening
(Evidence Table 2)

47 Risk Factors
(No Evidence Table)

11 Risk Assessment
(No Evidence Table)

7 Early Detection
(No Evidence Table)

120 Counseling
(Pending)

5 Data on Accuracy
of Screening Tests
(Evidence Table 1)
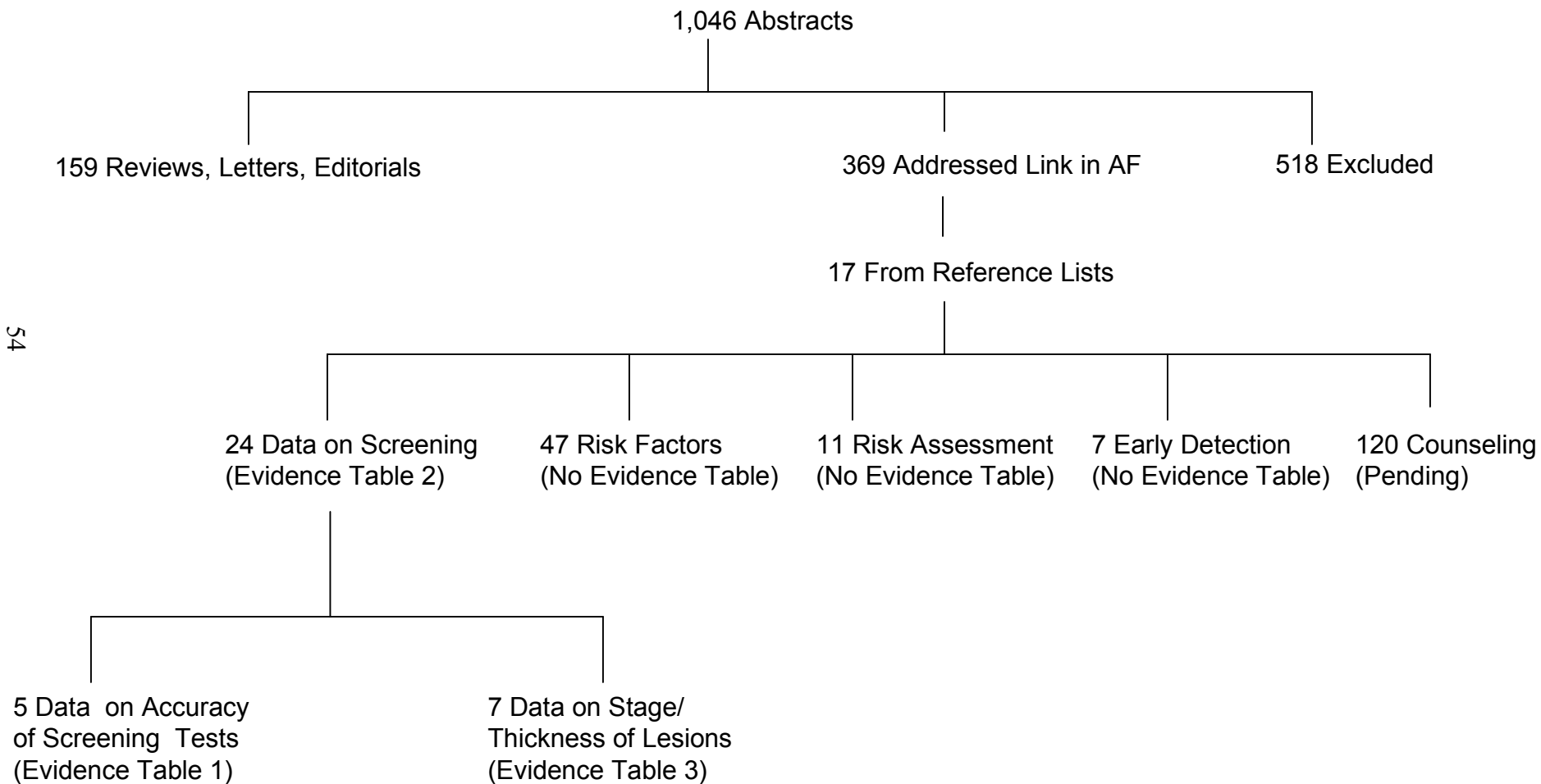
7 Data on Stage/
Thickness of Lesions
(Evidence Table 3)
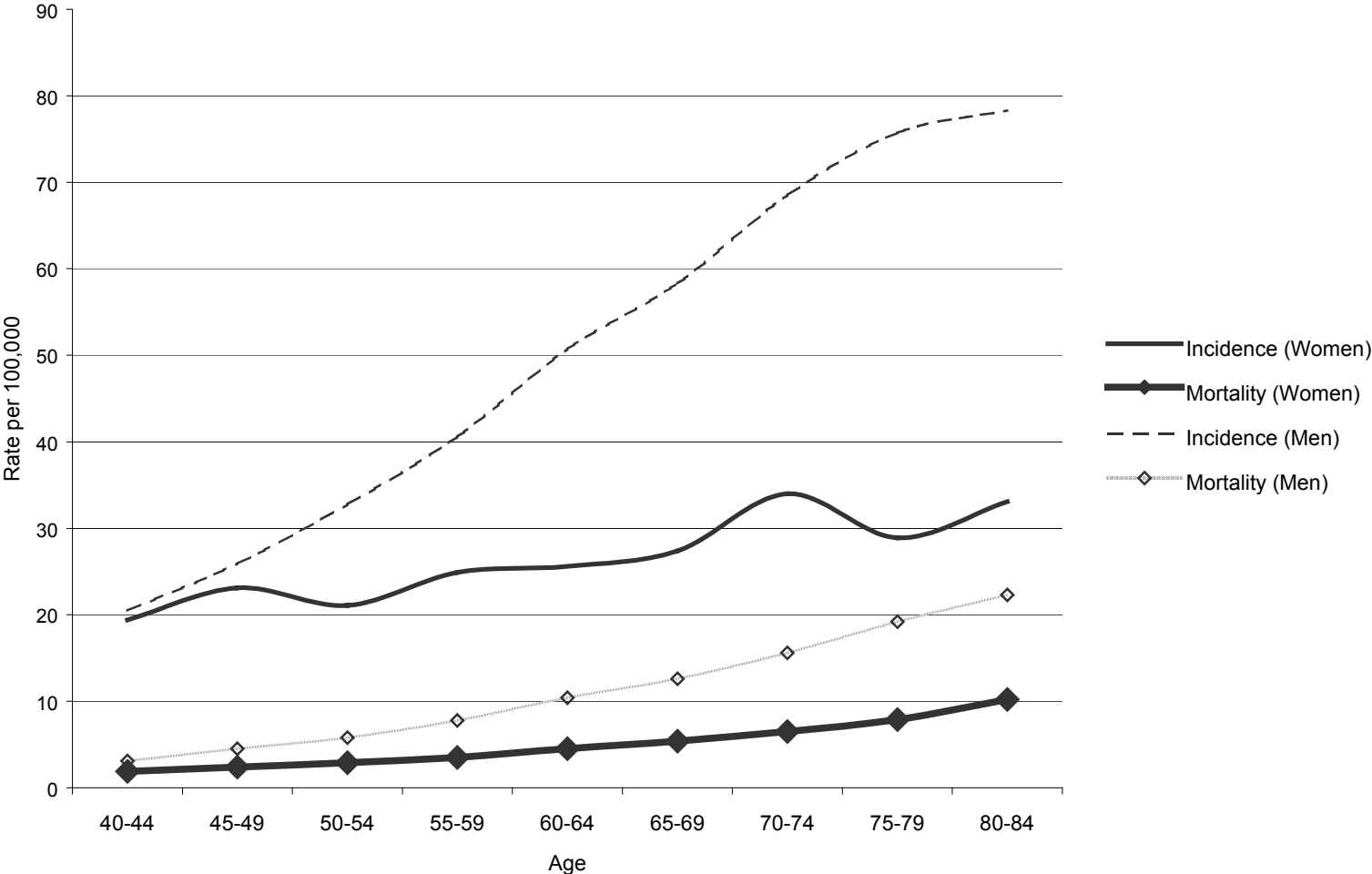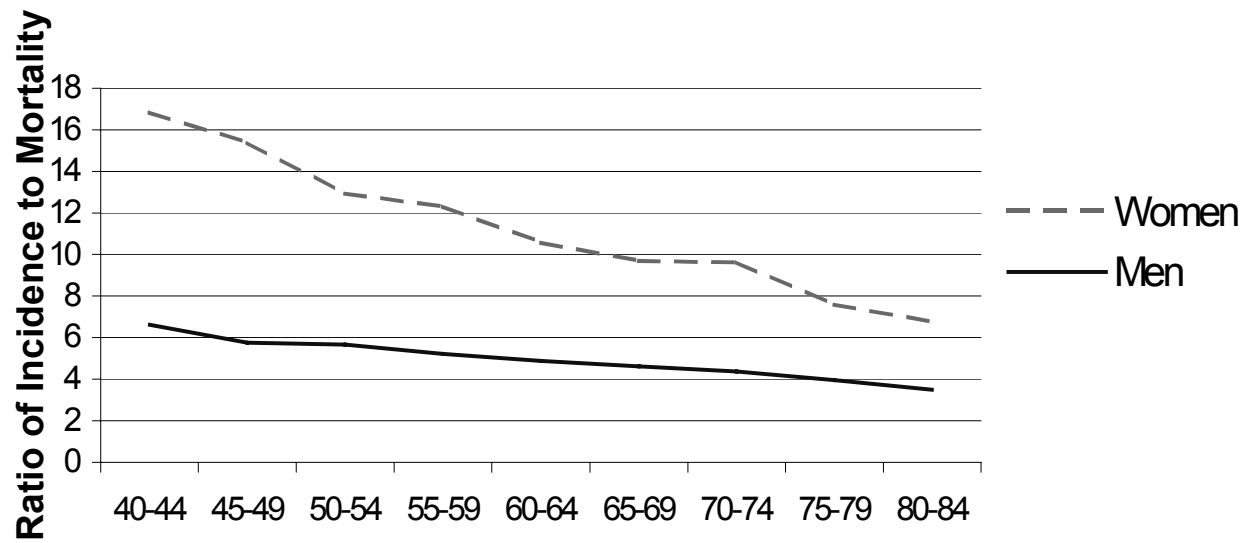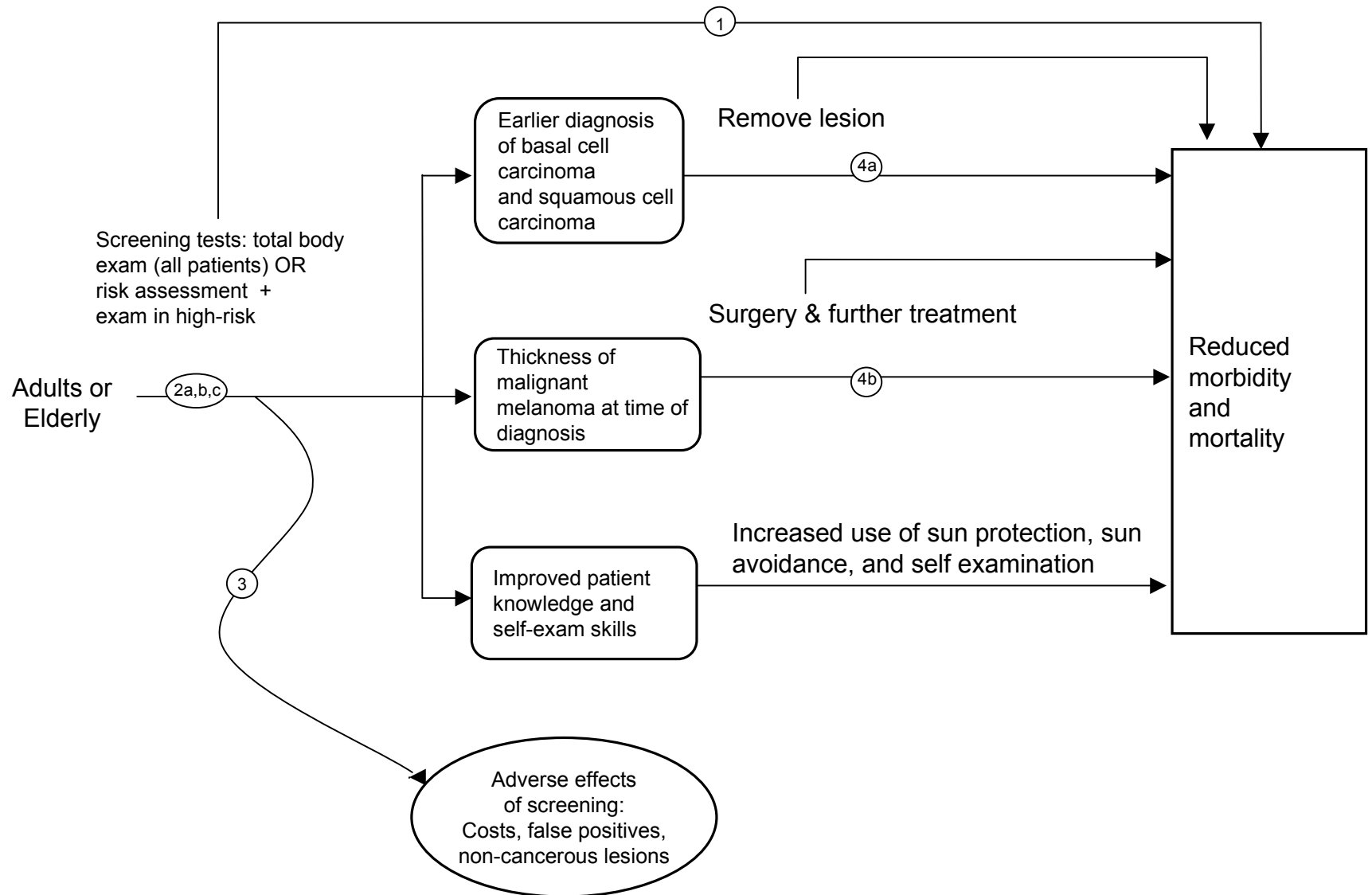
Figure 1. Melanoma age-specific incidence and mortality.

Figure 2. Ratio of incidence to mortality by age.

Figure 3

Figure 4. Key questions in analytic framework.

Accuracy of Screening

Arrow 1
Is there direct evidence that screening for skin cancers leads to reduced morbidity and mortality?

Arrow 2a
1. How accurate is total-body skin examination in the detection of cancer?
2. How accurate are risk-assessment tools as a screening test for skin cancer?

Consequences of Screening

Arrow 2b
1. How often does screening detect suspicious lesions?
2. How often does screening result in a diagnosis of melanoma?
3. How often does screening result in a diagnosis of nonmelanoma skin cancer?
4. How often does screening lead to referral for follow up and biopsy?
5. How do characteristics of the screening program affect the yield of screening?
6. Compared with usual care, how much earlier does screening detect skin cancers and precancerous lesions?

Arrow 2c
What is the effect of screening on patients' skin knowledge and self-care behavior?

Arrow 3
What are the adverse effects of screening?

Effectiveness of Early Treatment

Arrow 4a
Does treatment of nonmelanoma skin cancer found by screening reduce morbidity and mortality?

Arrow 4b
Does treatment of malignant melanoma found by screening reduce morbidity and mortality?

Table 1.   Skin Cancer Screening Accuracy

Author, Year	Study Sample and Setting	Recruitment Focus	Patients (n)	Index Test	P or D	Defn. of Susp. Lesion	Suspicious Lesions (n)	(%)	Probability of Cancer	BCC/ Skin Cancer %	MM/ Skin Cancer %	SCC/ Skin Cancer %	Positive Predictive Value (Low)	(High)	Biopsy Rate*	Likelihood Ratio**
Screening for All Skin Cancer																
de Rooij et al.,[33] 1995 Rampen et al.,[37] 1995	Volunteers for skin cancer screening in the Netherlands	Patients who have skin cancer risks	1,961	Lesion-specific exam or TSE	d	Skin cancer	93	4.7%	0.031	85.1%	12.8%	2.1%	0.51	0.54	0.935	37.32
Limpert,[31] 1995	Free skin cancer clinic at family physician's office	Not reported	247	TSE	p	Skin cancer	51	20.6%	0.057	92.9%	7.1%	0.0%	0.27	0.42	0.647	12.26
de Rooij et al.,[32] 1997	Vounteer melanoma screenings in the Netherlands following a public campaign on melanoma and risk factors	Patients who have melanoma risks	4,146	Lesion-specific exam or TSE	d	Skin cancer	173	4.2%	0.011	73.5%	26.5%	0.0%	0.28	0.30	0.912	37.95
Jonna et al.,[34] 1998	Free skin cancer screening in San Diego for self-selected high risk	Patients who have skin cancer risks	464	TSE	d	Skin cancer	132	28.4%	0.060	85.2%	11.1%	3.7%	0.21	0.58	0.364	21.80
Screening for Melanoma																
Koh et al.,[36] 1996	Volunteer skin cancer education and screenings by the American Academy of Dermatology	Not targeted	282,555	Not reported	d	Suspected Melanoma	763	0.3%	0.001				0.17	0.19	0.890	183.57
Koh et al.,[36] 1996	Volunteer skin cancer education and screenings by the American Academy of Dermatology	Not targeted	282,555	Not reported	d	Rule-out melanoma	3,695	1.3%	0.001				0.06	0.09	0.690	78.33

MM, malignant melanoma; BCC, basal cell carcinoma; SCC, squamous cell carcinoma; TSE, total-skin examination, p, Primary care provider; d, dermatologist;

Defn. of Susp. Lesion, Definition of suspicious lesion. The overall probability of cancer was calculated as the total number of cancers diagnosed divided by the number of patients screened.

For the first group of studies, all skin cancers are included in the numerator. For the Koh et al. studies, only melanomas are included.

Methods for calculating the high and low estimates of predictive value and likelihood ratios are described in the text.
* Proportion of patients referred for biopsy who actually had one.
** Method for estimating likelihood ratio of a positive test is described in the text.

Table 2: Studies of Screening for Skin Cancer

Author, Year	Population/Setting/Recruitment	Screening Test, Examiner	Media Target; Reported Risk Factors	Referral Procedure (Patient's PCP, Pt's dermatologist, Study PCP/Derm, Reminder, No Reminder)	Referral (probability)	Suspected melanoma	Confirmed melanoma	Confirmed Melanoma In Situ	Suspected basal cell/ squamous cell carcinoma	Suspected actinic keratosis	Negative Screen	Biopsy	Melanoma|Biopsy Suspected Melanoma Only	Melanoma| Biopsy All Suspicious Lesions
Mass Screening														
Jonna et al.,[34] 1998	464 volunteers, hospital, US; 72% <65, 94% white, 43% male	TSE, dermatologists	Targeted high risk	Patient's PCP or dermatologist, no reminder		0.08	0.002	0.002	0.21		0.42	0.21	0.15	0.04
Limpert,[31] 1995	247 volunteers, PCP clinic, US; mean age 53.5 (range 4-84), 100% white, 38% male	TSE, family physician	Not targeted	Patient's PCP, Patient's dermatologist, or study PCP, reminder			0.004				0.57	0.18		0.02
Rampen et al.,[37] 1995	1961 volunteers, hospital, Netherlands	TSE or Partial skin exam, dermatologists	Targeted high risk	Not specified	0.1	0.003	0.003	0.001	0.02		0.9			
McGee et al.,[66] 1994	279 volunteers, New Zealand; 41% age 40-59, 29% >/= age 60	Not specified, general medical practitioners	42% came because of a "worrying mark," 25% fair skin, 53% history of severe sunburn, 22% fair or red hair, 8% personal history squamous cell carcinoma, 20% family history squamous cell carcinoma	Patient's PCP, no reminder	0.2	0.03			0.08					
Koh et al.,[36] 1996	282 555 volunteers, hospitals, US	Not specified	Not targeted	Patient's PCP or dermatologist, no reminder		0.02	0.001	0.001					0.11	
de Rooij et al.,[33] 1995	2463 volunteers, hospital, Netherlands; 53% >age 50	Lesion-specific TSE	Not targeted	Patient's PCP, no reminder		0.01	0.003	0.001	0.04	0.06				
de Rooij et al.,[32] 1997	4146 volunteers, hospital, Netherlands; 34% >age 50	Lesion-specific TSE	Targeted high risk	Patient's PCP, no reminder	0.12	0.02	0.001	0.002	0.02	0.02		0.08	0.17	0.03
Hourani et al.,[67] 1995	351 volunteers, hospital, US; 30% > age 50	Not specified	Not targeted; 36% reported possible change in mole; residents of county considered to be at extremely high risk for squamous cell carcinoma	Patient's PCP or study PCP	0.34	0.001			0.1	0.1	0.52			
Katris et al.,[68] 1996	3379 volunteers, hospital and community, Australia; 35% >/= age 50, 16% >/= age 60	TSE	Targeted high risk	Not specified		0.02	0.08	0.038	0.13		0.83		0.08	
Katris et al.,[69] 1998	256 volunteers, hospital and community, Australia	TSE, nurses and plastic surgeons	Targeted high risk	Not specified	0.05				Surgeon: 0.10 Nurse: 0.07	Nurse: .03	Surgeon: 0.70 Nurse: 0.60			
Rivers and Gallagher[70] 1995	1681 volunteers, community, Canada; 16% >/= age 65	TSE partial skin exam, lesion specific, dermatolotists	Beachgoers; 33% had 2 or more risk factors (blond or red hair, blue or green eyes, propensity to sunburn)	Patient's PCP	0.005									
Dozier et al.,[71] 1997	1) 49 volunteers, community, US; mean age 29.7 2) 53 volunteers, hospital, US; mean age 35.4	1) partial skin exam 2) TSE dermatologists	1) Surfers 2) Not targeted	1) Patient's PCP, reminder 2) Patient's PCP, no reminder		1) 0.0 2) 0.0			1) 0.16 2) 0.02	1) 0.41 2) 0.15				

PCP, primary care physician; TSE, total skin examination; NA, not applicable

Table 2: Studies of Screening for Skin Cancer

Author, Year	Population/Setting/Recruitment	Screening Test, Examiner	Media Target; Reported Risk Factors	Referral Procedure (Patient's PCP, Pt's dermatologist, Study PCP/Derm, Reminder, No Reminder)	Referral (probability)	Suspected melanoma	Confirmed melanoma	Confirmed Melanoma In Situ	Suspected basal cell/squamous cell carcinoma	Suspected actinic keratosis	Negative Screen	Biopsy	Melanoma|Biopsy Suspected Melanoma Only	Melanoma|Biopsy All Suspicious Lesions
Population-Based Screening														
Harvey et al.,[72,73] 1996a, 1996b	560 random population sample, community, UK; 100% >/= age 60	Partial skin exam, dermatologists	NA	Patient's PCP, reminder	0.02	0.004			0.02	0.23	0.75			
Ichihashi et al.,[74] 1995	4736 consecutive attendees at regional health exam, Japan	Partial skin exam, dermatologists	NA	Study dermatologist, no reminder		0			0.0004	0.01				
Tornberg et al.,[75] 1996	1654 random sample, hospital, Sweden; 100% age 40-54	Not specified, nurses, dermatolotist, oncologist	NA	Study dermatologist, no reminder	0.05	0.09	0				0.91	0.04	0	
Bergenmar et al.,[76] 1997	501 random sample, hospital, Sweden; 100% age 40-54	NA												
Casefinding														
Ruskiewicz,[77] 1998	1000 consecutive patients, optometrist office, US; mean age 66.3 (range 35-96)	Partial skin exam, optometrist	NA; 0.096 had prior diagnosis of squamous cell carcinoma or actinic keratosis	Dermatologist		0			0.1	0.003	0.9			
Whited et al.,[78] 1997	190 consecutive patients,PCP and specialty clinic, US	Partial skin exam, dermatologists, internists, physician assistants	NA									0.31		0

PCP, primary care physician; TSE, total skin examination; NA, not applicable

Table 2: Studies of Screening for Skin Cancer

Author, Year	Population/Setting/Recruitment	Screening Test, Examiner	Media Target; Reported Risk Factors	Referral Procedure (Patient's PCP, Pt's dermatologist, Study PCP/Derm, Reminder, No Reminder)	Referral (probability)	Suspected melanoma	Confirmed melanoma	Confirmed Melanoma In Situ	Suspected basal cell/squamous cell carcinoma	Suspected actinic keratosis	Negative Screen	Biopsy	Melanoma|Biopsy Suspected Melanoma Only	Melanoma|Biopsy All Suspicious Lesions
													Results (probability)	
Worksite Screening														
Friedman et al.,[79] 1995	421 hospital employees, identified as high risk and invited, US; mean age 41 (standard deviation 10.6)	Not specified, dermatologists	Targeted high risk	Patient's dermatologist or study dermatologist	0.32	0.002			0.02	0.09				
Schneider et al.,[61] 1994	3889 laboratory employees, 9% of employees age 20-24, 56% of employees age 70 and older	Not specified, dermatologist	NA; participants classified according to number of atypical moles: 64% none, 29% possible or probable, 7% clear pattern of marked atypical moles											
Other														
Herd et al.,[80] 1995	421 patients who have suspected melanoma, specialty clinic, UK	TSE, dermatologists	NA	Study dermatologist									0.036	
Marghoob et al.,[81] 1995	298 patients who have basal cell or squamous cell carcinoma, dermatology practice, US	TSE (melanoma only), dermatologists	All had basal cell and/or squamous cell carcinoma	Study dermatologist		0.22	0.034						0.15	
van der Spek-Keijser et al.,[82] 1997	Pathology study of all melanomas diagnosed from 1980-92 after regional preventive skin cancer campaign, Netherlands, 95% Caucasians	NA	NA	NA										
Veierod et al.,[83] 1997	Follow-up study of 50, 759 participants in health screening from 1977-83, Norway, age 16-56	NA	NA	NA		0.002								

PCP, primary care physician; TSE, total skin examination; NA, not applicable

Table 3. Thickness of Malignant Melanoma Lesions Found in Screening Studies
N (p) in mm

Study	0.5 – 1	1.0 – 1.5	1.5 – 2	2 – 2.5	2.5 – 3	3 – 3.5	3.5 – 4	4
De Rooij et al.,[32] 1997	12 (0.92)	1 (0.08)						
Herd et al.,[80] 1995	82 (0.76)		26 (0.24)					
Katris et al.,[68] 1998	4 (1.0)	0 (0)						
Jonna et al.,[34] 1998	1 (1.0)	0 (0)						
Schneider et al.,[61] 1994	9 (1.0)	0 (0)						
Koh et al.,[36] 1996	180 (0.87)		22 (0.11)					4 (0.02)
Marghoob et al.,[81] 1995	10 (1.0)	0 (0)						
van der Spek Keijser et al.,[82] 1997	1451 (0.67)		506 (0.23)				206 (0.10)	

Table 4. Summary of Evidence for Screening for Skin Cancer

Linkage in Analytic Framework.	Evidence Code*	Quality of Evidence
1a. Accuracy of total-body skin examination: evidence that total-body skin examination can detect skin cancer.	II-2	Fair: The accuracy of a total-body skin examination by primary care physicians in unselected patients may be low. Reliability of pathologic diagnosis in community practice in the U.S. is not clear.
1b. Accuracy of risk assessment: evidence that in selected patients, a questionnaire or interview, followed by exam, can detect skin cancer.	II-2	Fair: Mole counts and other factors predict elevated risk over time, but no study has determined the accuracy of risk stratification followed by total-body skin examination in selected patients as a screening method.
2. Adverse effects of screening: evidence that screening causes significant harms.	III	Poor: Most postulated adverse effects have not been evaluated in studies.
3. Effectiveness of early detection: evidence that persons detected through screening have better outcomes than those who are not screened.	II-3	Poor: No studies directly link screening to lower mortality and morbidity. Most well-done population-based studies concern promotion of self-care behaviors such as self-examination rather than universal screening.
4a. Effectiveness of treatment of nonmelanoma skin cancer found by screening.	III	Poor: The hypothesis that early detection by screening could reduce mortality and morbidity is plausible but has not been examined in studies.
4b. Effectiveness of treatment of melanoma found by screening.	II-1, III	Fair: There are no controlled studies of treatment in patients found by screening to have thin melanomas, but epidemiologic studies, studies of skin health behaviors, and studies of factors associated with advanced melanoma suggest that elderly men are at high risk and are unlikely to benefit from health promotion efforts. Studies of delay in diagnosis have conflicting results, and the ability of screening to reach individuals at high risk and to find aggressive tumors while they are still curable have not been established.

* I, randomized controlled trial; II-1, controlled trial without randomization; II-2, cohort or case-control analytic studies; II-3, multiple time series, dramatic uncontrolled experiments; III, opinions of respected authorities, descriptive epidemiology.