

# ***Evidence Synthesis***

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## **Screening for Skin Cancer in Adults: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force**

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# Structured Abstract

**Background:** Melanoma is the leading cause of skin cancer mortality. Visual skin examination for skin cancer screening could impact disease incidence and mortality in U.S. adults and adolescents.

**Purpose:** We conducted a systematic evidence review of visual skin examination for skin cancer screening in primary care settings to support the U.S. Preventive Services Task Force (USPSTF) in updating its previous recommendation. Our review addressed five key questions in adults and adolescents age 15 years and older without a prior diagnosis of skin cancer: 1) What is the direct evidence that visual skin cancer screening by a primary care provider or dermatologist reduces skin cancer morbidity and mortality and all-cause-mortality? 2) What are the harms of skin cancer screening and diagnostic followup? 3) What are the test characteristics of visual skin cancer screening when performed by primary care providers or dermatologists? 4) Does visual skin cancer screening lead to earlier detection of skin cancer compared to usual care? and 5) What is the association between earlier detection of skin cancer and skin cancer morbidity and mortality and all-cause mortality?

**Data Sources:** We searched MEDLINE, PubMed, and the Cochrane Central Register of Controlled Trials for studies published from January 1, 1995 through June 1, 2015. We supplemented searches by examining bibliographies from previous systematic reviews, and retrieved articles and studies included in the previous USPSTF review for potential inclusion. We searched federal agency trial registries for ongoing and unpublished trials.

**Study Selection:** We conducted dual independent review of 12,514 abstracts. We reviewed 453 full-text articles, which two reviewers independently evaluated against well-defined inclusion/exclusion criteria and quality rated. Discrepancies were discussed with a third reviewer and resolved by consensus.

**Data Extraction and Analysis:** Four investigators abstracted data from 13 studies and 15 articles into evidence tables and a second reviewer checked these data. We qualitatively summarized the evidence for each key question, since data were insufficient in quantity or consistency for meta-analysis.

**Results:** *Key question 1. What is the direct evidence that visual skin cancer screening by a primary care provider or dermatologist reduces skin cancer morbidity and mortality and all-cause mortality?* One fair-quality ecologic study addressed the impact of physician visual skin cancer examination on melanoma mortality. The Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany (SCREEN study), conducted in the Schleswig-Holstein region of Germany, involved a multicomponent intervention including the following: 1) training nondermatologists and dermatologists in skin cancer screening; 2) a media campaign to encourage skin cancer screening in adults age 20 years and older; and 3) a followup dermatology referral protocol for nondermatologists to refer adults with either suspicious lesions or multiple risk factors for skin cancer. During the 1-year intervention period (2003 to 2004), nearly 361,000 adults (19% of the age-eligible adults) were screened with a visual skin cancer examination, mainly by nondermatologists. The majority of those screened were women (73.6%) and the

mean age was 49.7 years (standard deviation, 16.2 years). Using a pre-post design comparing melanoma mortality in the population in 1998 to 1999 and 2008 to 2009, the SCREEN study demonstrated a 48 percent reduction in melanoma mortality in the Schleswig-Holstein (intervention) region but no reductions in melanoma mortality were observed in the four neighboring (control) regions without an active skin cancer screening program or in Germany as a whole. The reduction in absolute mortality was a decline of 0.8 deaths due to melanoma per 100,000 persons in the intervention region. As an ecologic study, the results do not provide individual-level data about risk reduction associated with screening, and it is not possible to directly compare changes in mortality among those exposed versus not exposed to skin cancer screening and account for confounding.

*Key question 2. What are the harms of skin cancer screening and diagnostic followup?* Two fair-quality studies evaluated the harms of skin cancer screening by assessing biopsy yield and patient satisfaction with shave biopsy results. We found no studies that evaluated harms due to overdiagnosis, procedure-related adverse events, or psychosocial harms. The SCREEN study demonstrated variation by age in the number of skin excisions needed to detect one melanoma, squamous cell carcinoma, or basal cell carcinoma. For all cancers detected, fewer excisions were needed to detect one case in older adults age 65 years or older compared to younger adults. For melanoma, detecting one case in women age 65 years or older required 22 excisions compared to 41 excisions in women ages 20 to 34 years. Similar patterns were observed in men and for other skin cancer types. In a case series of 45 men and women who participated in skin cancer screening and underwent shave biopsy for suspected nonmelanoma skin cancer, 7.1 percent of patients expressed poor satisfaction with the cosmetic results from shave biopsy after 6 months compared to 16.1 percent of physicians rating the same site as poor.

*Key question 3. What are the test characteristics of visual skin cancer screening when performed by primary care providers versus dermatologists?* Two fair-quality observational studies reported test characteristics among screening-eligible populations. In the first study, primary care physicians conducted screenings in 16,383 adults in Queensland, Australia. Cancer outcomes were determined by pathology or biopsy reports. False-negative rates were estimated using published literature and population melanoma rates. Within 36 months of the first screening examination, sensitivity for melanoma detection was 40.2 percent (calculated) and specificity was 86.1 percent (95% confidence interval [CI], 85.6 to 86.6). The positive predictive value for melanoma was 1.4 percent. The second study evaluated the performance of volunteer dermatologists and plastic surgeons who conducted screening in Western Australia among 7,436 adult men and women. At 24 months, sensitivity for melanoma detection was 49.0 percent (95% CI, 34.4 to 63.7) and specificity was 97.6 percent (95% CI, 97.2 to 97.9), with an overall recall rate of 2.7 percent. The positive predictive value was 11.9 percent (95% CI, 7.8 to 17.2%). Different followup times for cancer outcomes prohibits direct comparison of screening accuracy between the two physician types.

*Key question 4. Does visual skin cancer screening lead to earlier detection of skin cancer compared to usual care?* One fair-quality case-control study from Queensland, Australia measured the association between whole-body skin examination by a physician in the previous 3 years among men and women ages 20 to 75 years with or without melanoma. Cases (n=3,762) were diagnosed with first primary melanoma between 2000 and 2003; controls (n=3,824) were

randomly selected from electoral rolls according to 5-year age categories and the sex distribution of the cases. Among controls, 28.3 percent reported receiving a whole-body skin examination by a physician within the previous 3 years compared to 35.3 percent of melanoma cases. In multivariate-adjusted models, cases diagnosed with thin melanoma ( $\leq 0.75$  mm) had a 38 percent higher odds (odds ratio [OR], 1.38 [95% CI, 1.22 to 1.56]) of receiving physician whole-body skin examination in the previous 3 years compared to controls. Further, cases diagnosed with thicker lesions ( $> 0.75$  mm) had a 14 percent reduced odds (OR, 0.86 [95% CI, 0.75 to 0.98]) of receiving physician skin examination compared to controls. The thickest melanoma lesion cases ( $\geq 3.00$  mm) had a 40 percent reduced odds of recent physician skin examination compared to controls (OR, 0.60 [95% CI, 0.43 to 0.83]). These results should be confirmed using a prospective study design.

*Key question 5. What is the association between earlier detection of skin cancer and skin cancer morbidity and mortality and all-cause mortality?* Eight fair- to good-quality studies evaluated the association between lesion thickness or stage at diagnosis and melanoma mortality and all-cause mortality. Four of the studies were conducted in U.S. populations, one in Germany, and three in Australia. All eight studies demonstrated a consistent statistically significant relationship between the degree of disease involvement at diagnosis and melanoma mortality, regardless of the characterization of the stage or lesion thickness. Thicker lesions ( $> 4.0$  mm) were associated with a 3.1- to 32.6-fold increased risk of melanoma mortality compared to thinner lesions. Similarly, advanced-stage melanomas (stage III or above) were associated with a 9.9- to 27.1-fold increased risk of melanoma mortality compared to early-stage melanomas. Stage at melanoma detection was associated with a statistically significant increase in all-cause mortality among melanoma cases identified from California SEER registries; compared to stage I disease at detection, the adjusted hazard ratio of all-cause mortality was 2.26 times higher for stage II disease (95% CI, 2.14 to 2.39), 4.27 for stage III disease (95% CI, 3.90 to 4.67), and 10.39 for stage IV disease (95% CI, 8.96 to 12.00).

**Limitations:** Very few screening studies met our inclusion criteria, and few were conducted in U.S. settings or with clear relevance to U.S. primary care.

**Conclusions:** On a population level, with limited evidence on skin cancer screening, a clear statement cannot be made about the benefit of skin cancer screening for melanoma mortality and all-cause mortality or association with thinner lesions. With few studies to confirm these results, the applicability for widespread skin cancer screening could be limited. Later stage at diagnosis of melanoma is associated with strong effect on melanoma mortality within 5 years of diagnosis. Future research on skin cancer screening should focus on evaluating the effectiveness of targeted screening in persons considered to be at higher risk for skin cancer.

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# Chapter 1. Introduction

## Scope and Purpose

This report will be used by the U.S. Preventive Services Task Force (USPSTF) to update the prior review of the effectiveness of skin cancer screening in average-risk persons. In 2009, the USPSTF concluded there was insufficient evidence to assess the balance of benefits and harms of screening for skin cancer by primary care clinicians or by patient skin self-examination (I statement).<sup>1</sup>

## Condition Definition

Skin cancer is among the most common cancers in men and women in the United States.<sup>2</sup> Skin cancer is classified as: 1) nonmelanoma skin cancer (NMSC), which includes basal cell and squamous cell cancers, and 2) melanoma skin cancer. NMSC represents the vast majority of skin cancers (>97%) and has very low mortality.<sup>2</sup> Melanoma skin cancer is less common than NMSC but has a higher mortality and case-fatality rate.<sup>3</sup> Detection of melanoma is the primary focus of skin cancer screening.

## Prevalence and Burden

### NMSC

Because NMSC is not a reportable cancer to the Surveillance, Epidemiology, and End Results Program (SEER) or state cancer registries, population estimates are based on care visits or skin procedures. An estimated 4.3 million cases of NMSC were treated in the United States based on U.S. and Australian population statistics.<sup>4</sup> The incidence of NMSC increases with age<sup>5-7</sup> and is more common in men than in women.<sup>5,7</sup> Among the Medicare-eligible population, approximately 2.1 million men and women are diagnosed with NMSC annually.<sup>8</sup> With the increasing use of tanning beds, there is growing concern about skin cancer in younger populations. The estimated age-adjusted incidence of basal cell carcinoma in persons younger than age 40 years in Olmsted County, Minnesota is 25.9 cases per 100,000 women and 20.9 cases per 100,000 men.<sup>9</sup> The incidence of squamous cell carcinoma in the same population was similar between men and women at 3.9 cases per 100,000 persons.<sup>9</sup>

The overall incidence of NMSC appears to be increasing over the past few decades; however, this observation could be the result of more evaluations and skin biopsies, leading to more diagnoses rather than a true increase in disease in the population.<sup>10</sup>

Mortality statistics are difficult to determine for NMSC but suggest that the case-fatality rate from NMSC is quite low.<sup>10</sup> From the state of Rhode Island, the age-adjusted NMSC mortality rate is estimated at 0.91 deaths per 100,000 person-years among residents.<sup>11</sup> While mortality is

low, the enduring impact of NMSC is reflected in the high recurrence rate of approximately 50 percent.<sup>12</sup>

## **Melanoma**

Malignant melanoma is the fifth- and seventh-leading cancer diagnosed in men and women, respectively.<sup>13</sup> In 2015, an estimated 73,870 persons were diagnosed with melanoma in the United States and 9,940 persons died from the disease.<sup>13</sup> Over the past nearly 40 years, melanoma incidence rates have increased and mortality rates have remained relatively stable. The increase in melanoma incidence is in part attributed to an increase in skin biopsies, which increased 2.5-fold in the SEER-Medicare population from 1986 to 2001.<sup>14</sup> Additional biopsies have resulted in increases in the number of early-stage melanoma cases detected, mainly melanoma in situ.<sup>14</sup>

### **Melanoma Incidence**

From 1975 to 2011, age-adjusted melanoma incidence rates increased 3-fold from 7.9 to 22.7 new cases per 100,000 persons.<sup>3</sup>

#### *Age*

Melanoma incidence increases with age. During 2007 to 2011, among persons younger than age 65 years, the incidence rate was 12.7 cases per 100,000 persons compared to 81.1 cases per 100,000 persons age 65 years and older.<sup>3</sup>

#### *Sex*

The age-adjusted melanoma incidence rate was higher in men than in women during 2007 to 2011, with 27.7 cases per 100,000 men versus 16.7 cases per 100,000 women.<sup>3</sup> However, this pattern is not consistent across all ages. Younger women, from teens to adults younger than age 50 years, have higher incidence rates than men.<sup>3</sup>

#### *Race*

Melanoma incidence varies by race. The age-adjusted melanoma incidence rate was 25.2 cases per 100,000 whites compared to 1.0 case per 100,000 blacks during 2007 to 2011.<sup>3</sup>

#### *Stage*

For cases diagnosed from 2004 to 2010, the distribution of stage at diagnosis was 84 percent localized, 9 percent regional, 4 percent distant, and 4 percent unstaged.<sup>3</sup>

### **Melanoma Mortality and Survival**

From 1975 to 2011, age-adjusted melanoma mortality rates increased slightly from 2.1 to 2.7 deaths per 100,000 persons.<sup>3</sup> Five-year relative survival among persons diagnosed during 2002 to

2009 was 93% overall.<sup>3</sup>

### *Age*

Melanoma mortality rates increase with age. During 2007 to 2011, among persons younger than age 65 years, the mortality rate was 1.2 deaths per 100,000 persons compared to 13.4 deaths per 100,000 persons age 65 years and older.<sup>3</sup>

### *Sex*

Age-adjusted melanoma mortality rates are higher in men than in women at 4.1 versus 1.7 deaths per 100,000 men and women, respectively, during 2007 to 2011.<sup>3</sup> Five-year relative survival was 91.1 percent in men and 95.0 percent in women among cases diagnosed during 2004 to 2010.<sup>3</sup>

### *Race*

Melanoma mortality rates are greater in whites than in blacks. During 2007 to 2011, the age-adjusted melanoma mortality rate was 3.1 deaths per 100,000 whites compared to 0.4 deaths per 100,000 blacks.<sup>3</sup> However, 5-year relative survival among persons diagnosed during 2004 to 2011 was lower in blacks (75.1%) than in whites (92.9%).<sup>3</sup> This difference in relative survival according to race has been attributed to a difference in the distribution of stage at diagnosis: among those diagnosed in 2004 to 2010, 19 percent of blacks were diagnosed with distant or unknown stage of disease compared to only 7 percent of whites.<sup>3</sup>

### *Stage*

For people diagnosed from 2004 to 2010, 5-year relative survival by stage was 98.1 percent for localized, 62.6 percent for regional, 16.1 percent for distant, and 78.3 percent for unstaged disease at diagnosis.<sup>3</sup> The vertical depth of melanoma is one of the strongest predictors of patient survival. Fifteen-year patient survival is 93 percent for depth less than 1 mm, 68 percent for depth 1 to 4 mm, and 42 percent for depth greater than 4 mm.<sup>15</sup>

## **Etiology and Natural History**

### **NMSC**

NMSC arises from keratinocytes or their precursors.<sup>10</sup> Basal cell carcinoma arises in the lower layers of the epidermis. Squamous cell carcinoma arises in the mid-layer of the epidermis, and can become invasive if left untreated. Actinic keratosis is thought to be the precursor lesion to squamous cell carcinoma and tends to occur in persons with fair skin and blond or red hair.<sup>2</sup>

Ultraviolet radiation from sun exposure or artificial sources damages DNA and leads to carcinogenesis of both basal and squamous cells.<sup>16</sup>

## Melanoma

Like all cancers, melanoma is described as a process of unregulated clonal growth.<sup>17</sup> Typically, melanocytes are found in the border of the epidermis and dermis layer. Melanocytes that grow in a horizontal lentiginous pattern appear on the skin as a freckle. Clusters of melanocytes can form to develop nevi. Mutations can result in nevi with pleomorphic features (i.e., variable cell and nuclei sizes and shapes) that have the potential to leave the epidermal border to locate in other areas of the skin.<sup>17</sup> The two most common types of melanoma are superficial spreading and nodular melanoma. The vertical depth of the melanoma is directly associated with prognosis. The common locations for melanoma to occur vary in men and women. In men, melanoma is more common on the back and in the head and neck areas. In women, melanoma is more common in the lower extremities, in particular, below the knee.<sup>18</sup>

## Risk Factors

Risk factors for melanoma and NMSC are similar, although there are some risk factors that are mainly associated with melanoma risk.

### Melanoma Only

Risk factors for melanoma are summarized in a recent meta-analysis of observational studies.<sup>19-21</sup>

#### *Family History of Melanoma*

Pooled estimates suggest a 74 percent increased risk of melanoma with family history of the disease (relative risk [RR], 1.7 [95% confidence interval (CI), 1.4 to 2.1]).<sup>21</sup>

#### *Dysplastic Nevi*

Increased total number of dysplastic nevi is associated with a 6.4-fold increased risk of melanoma (comparing 5 vs. 0 dysplastic nevi: RR, 6.4 [95% CI, 3.8 to 10.3]).<sup>19</sup>

#### *Multiple Nevi*

The presence of 101 to 120 nevi compared to fewer than 15 nevi is associated with a 6.9-fold increased risk of melanoma (RR, 6.9 [95% CI, 4.6 to 10.3]).<sup>19</sup>

#### *Sun Sensitivity*

Having skin that sunburns easily is associated with a 2-fold increased risk of melanoma compared to having skin that never burns (RR, 2.1 [95% CI, 1.7 to 2.6]).<sup>21</sup> Having natural red hair is associated with a 3.6-fold (RR, 3.6 [95% CI, 2.6 to 5.4]) increased risk of melanoma and natural blond hair is associated with a 2-fold (RR, 2.0 [95% CI, 1.4 to 2.7]) increased risk compared to having natural dark hair.<sup>21</sup>

### *History of Sunburns*

Sunburn history in the highest frequency category is associated with a 2-fold increased risk of melanoma (RR, 2.0 [95% CI, 1.7 to 2.4]).<sup>20</sup>

### *Indoor Tanning*

Ever use of tanning beds is associated with a 1.2-fold increased risk of melanoma (RR, 1.2 [95% CI, 1.0 to 1.3])<sup>22</sup> and first use before age 35 years is associated with a 1.8-fold increase in risk (RR, 1.8 [95% CI, 1.4 to 2.3]).<sup>23</sup>

### *History of NMSC*

A previous history of actinic keratosis or basal cell or squamous cell carcinoma is associated with a 4.3-fold increased risk of developing melanoma (RR, 4.3 [95% CI, 2.8 to 6.6]).<sup>21</sup>

## **NMSC**

Risks of developing basal cell and squamous cell carcinoma increase with exposure to ultraviolet radiation, either through sun exposure or use of indoor tanning beds. Similar to melanoma risk, persons who sunburn easily,<sup>24-26</sup> have natural red or blond hair,<sup>24-26</sup> have sustained a greater frequency of sunburns,<sup>27</sup> and have used indoor tanning beds<sup>22, 28</sup> are at increased risk of developing basal cell and squamous cell carcinoma.

## **Rationale for Screening**

The primary purpose of screening is to detect skin cancers earlier in their clinical course than would happen in usual care, allowing earlier and more effective treatment and thereby leading to a reduction in skin cancer morbidity and mortality.

## **Screening Strategies**

Visual skin cancer screening is either a whole or partial body skin examination conducted by a primary care provider or dermatologist. Visual skin cancer screening strategies are focused on the detection of melanoma but can also detect NMSC.

Visual inspection is guided by either the ABCDE mnemonic or the ugly duckling perspective. The ABCDE mnemonic<sup>29</sup> is an acronym of characteristics to detect melanoma: A) asymmetry (one half of nevus does not match the other half); B) border irregularity (edges of nevus are ragged, notched, or blurred); C) color (pigmentation of the nevus is not uniform, with variable degrees of tan, brown, or black); D) diameter greater than 6 mm; and E) evolving (nevus is changing over time). The ugly duckling approach assesses which nevus does not look like the others within a cluster of nevi.<sup>30</sup>

In addition to visual inspection of the skin, dermatologists often use a dermascope, a magnifying device, to further inspect the lesion or possibly whole body photography to assess changes in lesions.

Our review focused on clinical visual skin cancer screening by primary care or dermatology and distinct from skin self-examination, as conducted by the patient or partner.

## **Treatment Approaches**

### **Prevention/Intervention**

Primary prevention of skin cancer focuses on reducing exposure to sun or ultraviolet radiation exposure. Within primary care, physicians can be effective in counseling patients to avoid sun exposure and tanning beds and provide education on skin cancer risk factors.<sup>31, 32</sup> In an effort to reduce additional ultraviolet radiation exposure in adolescents, several U.S. states have initiated legislation to ban the use of tanning beds in persons younger than age 18 years.<sup>33</sup>

### **Treatment**

Definitive diagnosis of both NMSC and melanoma is through biopsy, including: 1) shave biopsy, 2) punch biopsy, or 3) excisional biopsy. The treatment options vary depending on the type of skin cancer.

#### **NMSC**

NMSC are removed by either surgical excision, Mohs micrographic surgery (i.e., tissue is removed in layers until microscopic examination of the layers indicates that the cancer has been completely removed), electrodesiccation and curettage (i.e., tissue destruction by electric current and removal by scraping with a curette), or cryosurgery (i.e., tissue destruction by freezing).<sup>2</sup> Radiation therapy and certain topical medications might be also be used.<sup>2</sup>

#### **Melanoma**

Primary tumor and surrounding normal tissue are removed and sometimes a sentinel lymph node is biopsied to determine stage.<sup>18</sup> There can be more extensive surgery if the sentinel lymph node is positive.<sup>18</sup> Melanomas with deep invasion or that have spread to lymph nodes might also be treated with immunotherapy, radiation therapy, chemotherapy, or a combination.<sup>18</sup> Advanced lesion thickness or later-stage melanoma cases may be treated with palliative surgery, immunotherapy, radiation therapy, chemotherapy, or a combination.<sup>18</sup>

## **Current Clinical Practice in the United States**

Dermatologists tend to perform more skin screening examinations than family practice physicians or internists<sup>34</sup> but lack the capacity to offer population screening.<sup>35</sup> Potentially, to

achieve skin screening of the general population, a two-step screening method with initial review of skin lesions in primary care and referral to dermatology for second review would be implemented. However, most primary care and general internists report not having sufficient training in skin cancer screening to feel confident in their skills to conduct whole body skin examinations on their patients.<sup>36</sup> Hence, skin cancer screening in the United States among primary care physicians remains quite low. Primary care physicians in two counties in Connecticut and Florida indicate that only 31 percent perform skin cancer screening on their adult patients. The primary barrier to screening was the physician's lack of confidence in identifying a suspected lesion.<sup>37</sup> While there are several educational interventions to improve knowledge of and confidence in skin cancer screening in primary care, few tools have been rigorously tested for measured changes in clinical practice.<sup>38</sup>

Currently, no U.S. professional organizations recommend clinician-performed skin cancer screening, including the American Academy of Family Physicians,<sup>39</sup> American College of Preventive Medicine,<sup>40</sup> American Academy of Dermatology (AAD),<sup>41</sup> and the American College of Physicians.<sup>42</sup> The American Academy of Family Physicians cites the 2009 USPSTF report<sup>43</sup> as the basis for its conclusion that there is insufficient evidence to evaluate the balance of benefits and harms of screening.<sup>39</sup> The American College of Preventive Medicine, AAD, and American College of Physicians do not have current guidance on whether or not to screen. The American Cancer Society has no specific recommendation for skin cancer screening, other than that persons age 21 years and older have a cancer-related checkup at their periodic health examination, including possibly an examination for skin cancer.<sup>44</sup> The recommendations from the Community Preventive Services Task Force focus on preventing skin cancer through various educational and policy approaches, such as promoting individual behaviors toward sun protection, and target populations in child-care centers, outdoor occupational settings, or primary and middle schools.<sup>45</sup>

Despite no current screening guidelines, AAD<sup>41</sup> has offered free skin cancer screening clinics since 1985, similar to its contemporary SPOTMe® screening campaign,<sup>46</sup> and conducted 2.4 million screenings to date.

## **Previous USPSTF Recommendations**

In 2009, the USPSTF concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening the adult general population by primary care clinicians or by patient skin self-examination for early detection of cutaneous melanoma, basal cell skin cancer, or squamous cell skin cancer (I statement).<sup>43</sup> The 2009 review found a lack of evidence about the influence of early detection on skin cancer mortality and morbidity and about the magnitude of harms from skin cancer screening.

The 2009 recommendation echoed findings from 2001, in which the USPSTF also concluded there was insufficient evidence to recommend for or against routine skin cancer screening by whole body skin examination for early detection of cutaneous melanoma, basal cell skin cancer, or squamous cell skin cancer (I statement).<sup>1</sup>

## Chapter 2. Methods

### Scope and Purpose

This systematic review was designed to update the prior 2009 review on the effectiveness of skin cancer screening in average-risk persons. For this review, we adapted the previous analytic framework and key questions (KQs) to address the benefits and harms of primary care screening for skin cancer. Since our review was focused on visual skin cancer screening within primary care settings, skin self-examination was considered to be outside the scope of this review.

### Analytic Framework and KQs

Using USPSTF methods (detailed in **Appendix A**), we developed an analytic framework (**Figure 1**) and five KQs:

1. What is the direct evidence that visual skin cancer screening by a primary care provider or dermatologist reduces skin cancer morbidity and mortality and all-cause mortality?
2. What are the harms of skin cancer screening and diagnostic followup?
3. What are the test characteristics of visual skin cancer screening when performed by primary care providers versus dermatologists?
4. Does visual skin cancer screening lead to earlier detection of skin cancer compared to usual care?
5. What is the association between earlier detection of skin cancer and skin cancer morbidity and mortality and all-cause mortality?

### Data Sources and Searches

We designed the review to be an extension of the 2009 systematic review.<sup>47</sup> The literature search for this systematic review covered MEDLINE, PubMed, and the Cochrane Central Register of Controlled Trials for studies published from January 1, 1995 through June 1, 2015. We worked with a medical librarian to develop our search strategy (**Appendix A**) and all searches were limited to English-language articles. We managed literature search results using version X5 of EndNote (Thomson Reuters, Philadelphia, PA), a bibliographic management software database, and an Access database (Microsoft, Redmond, WA).

To ensure comprehensiveness, we reviewed the reference lists of included studies, systematic reviews, and meta-analyses to identify relevant articles published before or not identified in our literature searches. We also supplemented our database searches with suggestions from experts and searched Clinicaltrials.gov to identify relevant ongoing trials (**Appendix B**).

All reviewed abstracts and full-text articles that might contain references of interest were marked, and references were assessed by the team. Articles identified through reference lists are included in the literature flow diagram (**Appendix A Figure 1**) as “identified through other



sources.” Articles that were not already identified in the original search results were evaluated using the inclusion/exclusion criteria described above.

## Study Selection

We developed an a priori set of inclusion and exclusion criteria (**Appendix A Table 1**). Two researchers independently reviewed 12,514 unique titles and abstracts to determine if the studies met the inclusion or exclusion criteria for design, population, intervention, and outcomes. We then reviewed the 453 full-text potentially relevant articles for inclusion using dual review. We resolved disagreements by consultation and consensus with a third reviewer, if necessary. We excluded articles that did not meet the inclusion criteria or were rated as poor quality, as described below. Excluded studies are listed in **Appendix C**. Systematic reviews were reviewed to identify potential included articles.

We included studies of asymptomatic adolescents and adults age 15 years and older. Included studies were required to be fair to good quality and conducted in countries with a United Nations Human Development Index score of 0.9 or greater.<sup>48</sup> We excluded studies that focused on nonskin cancers, populations under surveillance because of prior skin cancer diagnosis, skin self-screening or partner screening, intermediate or health outcomes relating clinician skin examination to other risk factors (e.g., sun protective behaviors), or measures of doctor-patient relationship quality.

For effectiveness and harms studies (KQs 1–4), acceptable screening tests were defined as whole or partial visual skin examination conducted by primary care providers (or related mid-level staff) or dermatologists with or without tools to aid examination (e.g., dermatoscopy, whole body photography). We excluded screening studies that focused on skin examinations in response to patient concerns for suspicious lesions, skin self-screening by individuals or partners, or physician counseling for self-screening. For studies focusing on morbidity and mortality (KQs 1 and 5), we reviewed studies that investigated skin cancer mortality, all-cause mortality, or morbidity associated with any skin cancer (including melanoma in situ, dysplastic nevi, and actinic keratosis), including quality of life. For test characteristic studies (KQ 3), we included studies that assessed cancer outcomes through cancer registry–based systems or pathology/biopsy reports within a defined period postscreening examination, and estimated false-negative rates for melanoma detection in participants who screened negative. For studies on early detection of skin cancer (KQs 4 and 5), we included studies that evaluated either American Joint Committee on Cancer (AJCC) stage<sup>49</sup> or Breslow lesion thickness at diagnosis.

We evaluated trials, cohort studies, other observational studies, and ecologic studies that reported clinical outcomes and included case series or case reports for identifications of harms in KQ 2.

## Quality Assessment and Data Abstraction

Two reviewers independently appraised all articles that met the inclusion criteria for this review as good, fair, or poor quality. Appraisal criteria were adapted from the USPSTF design-specific

quality criteria (**Appendix A Table 2**). The final quality rating in the evidence tables is based on a combination of criteria adapted from the USPSTF methods,<sup>50</sup> Dufault 2011,<sup>51</sup> and Tu 2008.<sup>52</sup> In general, a good-quality study met all criteria well. A fair-quality study did not clearly meet at least one criterion but had no known issues that would invalidate its results. Poor-quality studies had severe limitations, including one or more of the following risks of bias: unclear study population, unclear screening strategy, lack of defined followup, and lack of accounting for confounders or reporting of baseline characteristics.

Four researchers extracted data from all included studies rated as fair to good quality into evidence tables. A second reviewer checked the data for accuracy. The reviewers abstracted study characteristics (e.g., population, purpose, exposure, and outcomes), study design elements (e.g., recruitment procedures, inclusion/exclusion criteria, followup duration and attrition), outcomes for screening studies (e.g., true positives, diagnostic yield, positive predictive value), health outcomes (e.g., skin cancer morbidity and mortality), and harms.

## **Data Synthesis and Analysis**

For the body of evidence defined by the KQs, we created summary evidence tables to capture key study characteristics and sources of heterogeneity (e.g., study quality, sample size, geographic location, age, and sex). Further, for each KQ, we present results summarized qualitatively in the absence of data available to pool across studies.

## **Expert Review and Public Comment**

A draft research plan that included the analytic framework, KQs, and inclusion criteria was available for public comment from May 15 to June 11, 2014. We made no substantive changes to our review methods based on comments received. A draft version of this report was reviewed by four invited content experts and federal partners from the Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, National Institutes of Health, Veterans Health Administration, and the Military Health Service. Comments received during this process were presented to the USPSTF during its deliberation of the evidence and were addressed in the final version of the report. Additionally, a draft of the full report was posted on the USPSTF Web site from November 30 to December 28, 2015. A few comments were received during this public comment period. We made clarifications and additions to the Introduction and Discussion sections to incorporate important points noted by commenters.

## **USPSTF Involvement**

The authors worked with USPSTF liaisons at key points throughout the review process to refine inclusion criteria, address methodological decisions on applicable evidence, and resolve issues around scope for the final evidence synthesis. The Agency for Healthcare Research and Quality funded this research under a contract to support USPSTF work. Agency staff provided oversight for the project and assisted in external review of the draft evidence report.

## Chapter 3. Results

### Description of Included Studies

Our literature search yielded 12,514 unique abstracts; 453 met the criteria for full-text review (**Appendix A Figure 1**). We included 13 unique studies (k=13) of fair to good quality reported in 15 articles (n=15) that answered one or more of our five KQs as follows: KQ 1 (n=3 articles, k=1 study), KQ 2 (n=3, k=2), KQ 3 (n=2, k=2), KQ 4 (n=1, k=1) and KQ 5 (n=8, k=8) (**Table 1**).

Of the 13 unique studies, most study designs (k=10) were observational cohort studies. The study designs for the remaining three studies were case-control, ecologic, and case series. The most relevant included study was the Skin Cancer Research to Provide Evidence for the Effectiveness of Screening (SCREEN) study conducted in the Schleswig-Holstein region of Germany. The SCREEN study provided data on outcomes including mortality (KQ 1) and number of excisions needed to detect one case of skin cancer (KQ 2).

### Included Populations

Of the 13 included studies, five were included for screening questions (KQs 1–4) and eight for the association between stage at melanoma detection and skin cancer mortality (KQ 5).

In the five screening studies (**Table 2**), four evaluated skin cancer screening in populations and one evaluated skin cancer screening as an exposure using a case-control design. Study population size ranged from 45 to 360,288 individuals. The reported mean age ranged from 32 to 58 years. When reported, the prevalence of more than one skin cancer risk factor ranged from 47.7 to 62.4 percent of the populations.

In the eight studies that included the association between stage at melanoma detection and skin cancer mortality, all had a sample size of more than 4,000 individuals. Mean age ranged from 48.3 to 58 years, when reported, and the majority of populations were between ages 40 and 64 years. One study was conducted in a Medicare only population. Four studies were conducted with data from the United States, three from Australia, and one from Germany.

### Included Screening Programs

Three different screening programs were described by five articles (**Table 2**).<sup>53-57</sup> The screening interventions were aimed at asymptomatic populations and included screening by primary care physicians only, primary care physicians and other nondermatology specialists, or volunteer dermatologists and plastic surgeons. All screening interventions were multicomponent and included physician education; media campaigns or outreach to encourage individuals to participate in screening; and access to visual skin examinations with a medical provider with planned followup for the participants who screen positive. None of the screening programs

encouraged biopsy of lesions at the time of the first visual examination.

## Quality

We included four good- and 11 fair-quality articles. In general, the limitations for fair-quality studies included: response rates for followup, study design, outcome assessment, complete data presented, and specifications of model adjustment.

### **KQ 1. What Is the Direct Evidence That Visual Screening for Skin Cancer by a Primary Care Provider or Dermatologist Reduces Skin Cancer Morbidity and Mortality and All-Cause Mortality?**

#### **Summary of Results**

We identified no trials that assessed skin cancer morbidity or all-cause mortality associated with physician visual skin screening. We identified one fair-quality ecologic study (the SCREEN study) that compared trends in melanoma mortality in the population over 10 years in the Schleswig-Holstein region of Germany, where there was a population-based visual skin cancer screening program, compared to melanoma mortality trends in surrounding regions, where there was no population-based skin cancer screening program (**Table 3**).

The SCREEN study introduced a statewide skin cancer screening program in 2003,<sup>54</sup> including a multicomponent intervention: 1) training nondermatologists and dermatologists in skin cancer screening, 2) a media campaign to encourage skin cancer screening in adults age 20 years and older, and 3) a followup dermatology referral protocol for nondermatologists to refer adults with either suspicious lesions or multiple risk factors for skin cancer. During the 1-year intervention period (2003 to 2004), nearly 361,000 adults (19% of the age-eligible adults) were screened with a visual skin cancer examination, mainly by nondermatologists. The majority of those screened were women (73.6%), and the mean age was 49.7 years (standard deviation, 16.2 years). Changes in melanoma mortality pre- and postintervention were compared to four surrounding geographic regions and Germany as a whole (excluding the intervention region). Between 1998 and 1999 (prescreening) and 2003 and 2004 (screening program initiation), melanoma mortality remained constant in the intervention region and the five comparison regions. Between 1998 and 1999 (prescreening) and 2008 and 2009 (postscreening), age- and sex-adjusted melanoma mortality decreased from 1.7 to 0.9 deaths per 100,000 persons. The change in melanoma mortality decreased by 48 percent in the SCREEN region, resulting in an overall absolute mortality difference of 0.8 melanoma deaths per 100,000 persons. By comparison, in the other five regions the absolute change in melanoma mortality remained stable or increased by 0.1 to 0.3 deaths due to melanoma per 100,000 persons. Percent change in mortality over 10 years increased from 2 to 32 percent. As an ecologic study, the results do not provide individual-level data about risk reduction associated with screening, and it is not possible to directly compare changes in mortality among those exposed versus not exposed to skin cancer screening and

account for confounding. The results should be viewed cautiously.

## Detailed Results

### The SCREEN Study (Germany)

The SCREEN study was conducted to determine the feasibility of a population-based skin cancer screening program in the German primary care health system. Germany had a nationally mandated but previously unorganized early skin cancer detection program.<sup>55</sup> In 1989, analysis of the feasibility of the pilot program and data collection components began. In 2001, pilot intervention activities occurred on a small scale with 200 physicians and 6,000 screened patients in the Schleswig-Holstein region of northern Germany. Pilot activities included physician training sessions, a limited screening program within clinical practice, and public awareness campaigns. The pilot activities helped to draft protocol for full implementation.

Between 2003 and 2004, the SCREEN project implemented population-based skin cancer screening with a component intervention (**Table 2**), including the following:

1. **Provider education and training.** From April 2003 to September 2003, nondermatologists (defined as general practitioners in primary care, obstetricians and gynecologists, and urologists) (n=1,673) and dermatologists (n=116) participated in an 8-hour training course. The course focused on detecting all skin cancers and included training in the epidemiology and etiology of skin cancer, training and practice in standardized whole body visual examination, strategies for actively recruiting patients for screening, and program documentation and referral procedures. All providers were evaluated at the end of training for accuracy in visual diagnosis of skin cancer and demonstrated improvement in knowledge.<sup>55</sup> Training participation rates were 64 percent for nondermatology providers and 98 percent for dermatologists practicing in the region.
2. **Public outreach.** The intervention encouraged residents of Schleswig-Holstein age 20 years and older to seek skin cancer screening by a nondermatology physician. Communication channels included health insurers, physicians, and mass media campaigns via print, Internet, and telephone resources. Outreach efforts provided information about the screening procedure, program eligibility criteria, and how to get screened.
3. **Screening procedure.** Screening examinations were conducted from July 2003 to June 2004. The main screening pathway was a whole-body visual skin examination conducted by a nondermatology provider. Referrals to dermatology were made on identification of a suspicious skin lesion or for patients with risk factors for skin cancer. Alternatively, participants could choose to be initially screened by a dermatologist. Upon documentation of the screening episode using a standardized paper form that included risk factor information, physicians were reimbursed about \$20 per screening examination. From dermatology, all tentative clinical diagnoses were followed by biopsy and histopathologic evaluation. All detected cancers were reported to the state tumor registry.

Neither the surrounding German regions to the east, west, and south, nor Denmark, the country sharing Schleswig-Holstein's northern border, implemented population-based skin cancer screening activities during the same time frame. These areas were used as comparison

populations for melanoma mortality.

### *Participation*

Of a total population of 2.8 million, 1.9 million persons age 20 years and older comprised the eligible screening population. During the project period, 360,288 persons completed visual skin examinations, representing 19.1 percent of the eligible population in the region. Screening participation rates varied by age, with 20 to 22 percent of adults ages 35 to 69 years participating in screening compared to 14.9 percent of adults older than age 70 years. Almost three quarters of screened participants were women (73.6%).

### *Conduct of Screening*

Of the initial screening examinations, 77.4 percent were conducted by nondermatology providers and 22.6 percent were conducted by dermatologists. Among the 73,710 persons referred to dermatology after screening by nondermatology providers, 36.8 percent were lost to followup and did not see a dermatology provider for a second clinical examination.

### *Skin Lesion Results*

During the SCREEN study period from 2003 to 2004, 1,169 incident melanoma cases were reported to the state cancer registry, 585 of which were detected via the SCREEN study.<sup>54, 55</sup> Of the melanomas detected by the SCREEN study, 31 percent were melanoma in situ and 69 percent were invasive melanoma diagnoses. The SCREEN study also detected 1,961 basal cell carcinomas, 392 squamous cell carcinomas (including Bowen carcinoma), and 165 other skin cancers.

As anticipated, incidence of melanoma, basal cell carcinoma, squamous cell carcinoma, and melanoma in situ all increased statistically significantly by 15 to 48 percent during the SCREEN study (**Appendix D Table 3**). Age-adjusted melanoma incidence rates (per 100,000 persons) in the prescreening (2001 to 2003) versus during-screening period (2003 to 2004) increased 27 percent, from 14.2 (95% CI, 13.3 to 15.1) to 18.0 (95% CI, 16.6 to 19.4) cases, respectively. Age-adjusted melanoma in situ incidence rates (per 100,000 persons) in the prescreening versus during-screening period increased 48 percent, from 5.8 (95% CI, 5.2 to 6.4) to 8.5 (95% CI, 7.5 to 9.5) cases, respectively. Age-adjusted squamous cell carcinoma incidence rates (per 100,000 persons) in the prescreening versus during-screening period increased 15 percent from 11.2 (95% CI, 10.6 to 11.8) to 12.9 (95% CI, 12.0 to 13.8) cases, respectively. Age-adjusted basal cell carcinoma incidence rates (per 100,000 persons) in the prescreening versus during-screening period increased 29 percent, from 60.5 (95% CI, 59.0 to 62.1) to 78.4 (95% CI, 75.9 to 80.8) cases, respectively.

### *Melanoma Mortality*

Age- and sex-adjusted melanoma mortality rates in Schleswig-Holstein declined 48 percent in 2008 to 2009, 5 years after the SCREEN study began, compared to 1998 to 1999, 5 years before the SCREEN study (**Table 3**). From 5 years prescreening (1998 to 1999) to 5 years

postscreening (2008 to 2009), melanoma mortality declined by 0.8 melanoma deaths per 100,000 persons within the intervention region. Declines in melanoma mortality were not observed in the same time period in regions to the north, south, east, or west or in Germany overall (excluding Schleswig-Holstein). During the study period, melanoma mortality changes in other regions were: 2 percent increase in Hamburg (south), 7 percent increase in Lower Saxony (west), 32 percent increase in Mecklenburg-Vorpommern (east), 4 percent increase in Denmark (north), and 10 percent increase in Germany (excluding the intervention region). Melanoma mortality reductions in the intervention region were similar for men and women (**Appendix D Tables 1 and 2**).

As an ecologic study, the results from SCREEN do not provide information about individual risk reduction associated with skin cancer screening to directly compare changes in mortality among persons exposed versus not exposed to skin cancer screening and to account for confounding (through randomization or multivariate adjustment), which limits the ability to infer a causal relationship between the SCREEN program and melanoma mortality. The results should be viewed cautiously.

## **KQ 2. What Are the Harms of Screening for Skin Cancer and Diagnostic Followup?**

### **Summary of Results**

We assessed harms due to screening, including overdiagnosis, psychosocial harms, and procedure-related adverse events. We did not identify any studies that directly reported on procedure-related adverse events or psychosocial harms, such as skin infections or scar revisions in screened populations. Further, we did not identify any studies that specifically identified overdiagnosis in screened populations. We identified two fair-quality studies conducted in Germany that assessed the number of excisions needed to detect one melanoma, basal cell carcinoma, or squamous cell carcinoma (the SCREEN study) and cosmetic acceptance of shave biopsy in a screened population (**Tables 4 and 5**).<sup>54, 58</sup>

The number of excisions needed to detect one melanoma, basal cell carcinoma, or squamous cell carcinoma varied by age and sex. For all cancers, fewer excisions were needed to detect a single case in individuals age 65 years or older compared to younger individuals. For example, detecting one melanoma in women age 65 years or older required 22 excisions compared to 41 excisions in women ages 20 to 34 years. Similar patterns were observed in men and for other cancer types. In a population of 46 adults who underwent cancer screening subsequent to shave biopsy for removal of potential NMSC, 7.1 percent of patients reported their cosmetic results as poor (mean score 1.7, between excellent and good) compared to 16.1 percent of physicians who rated the results as poor (mean score 2.5, between good and fair). Few studies evaluated harms of screening.

## Detailed Results

### Excision Rates per Melanoma, Basal Cell Cancer, or Squamous Cell Cancer Detected

The fair-quality SCREEN study evaluated the impact of skin cancer screening on the overall number of excisions needed for melanoma detection by number of melanomas detected (**Table 4**). The study included 15,983 total excisions performed in 360,288 adults screened for skin lesions suspicious for melanoma, squamous cell carcinoma, or basal cell carcinoma. Calculations were based on only one excision per person and one malignant finding per tumor per person.

Comparing men and women, similar numbers of excisions were needed to detect any melanoma (1 per 28 excisions) or any basal cell carcinoma (1 per 9 to 10 excisions). However, 28 additional excisions occurred in women compared to men to detect a single squamous cell carcinoma (56 in women vs. 28 in men). Large differences were seen in diagnostic yield analyzed by age, with younger women and men undergoing more excisions for a lower yield compared to older adults. Compared to women age 65 years and older, women ages 20 to 34 years experienced 19 additional excisions to detect one melanoma and 134 additional excisions to detect one basal cell carcinoma. The number needed to excise additional squamous cell lesions could not be calculated with the available data in young women. However, 565 additional excisions were needed to detect one squamous cell carcinoma in women ages 35 to 49 years compared to women older than age 65 years. Compared to men age 65 years and older, men ages 20 to 34 years experienced 24 additional excisions per one melanoma, 898 additional excisions per one squamous cell carcinoma, and 109 additional excisions per one basal cell carcinoma. Based on these excision rates, the estimated false-positive rate for melanoma or NMSC can be quite high in a screened population with a younger age distribution.

### Cosmetic Harms

In one fair-quality study<sup>59</sup> of routine outpatient cancer screening, cosmetic harms were evaluated by 45 patients and a single physician at 6 days and at 6 months after shave biopsy (**Table 5**). Participants were identified during routine skin cancer screening but the study authors did not further describe the screening process. Only patients who underwent razor-blade shave excision for suspected NMSC and did not have subsequent skin cancer were included. In 5 percent of shave sites, delayed healing and infection were postoperatively observed by the physician. Among the 60 percent of patients evaluated at 6 months, physicians reported shave site outcomes, including 52 percent hypopigmentation, 32 percent marginal hyperpigmentation, 23 percent erythema, 7 percent hypertrophic scarring, 4 percent hypotrophic scarring, and 13 percent recurrent nevus. At 6 months, the physician and the patients assessed patient outcomes at the excision site based on a four-point physical judgment scale of excellent, good, moderate, or poor. The mean patient evaluation score was higher (1.7, between excellent and good) than the mean physician score (2.5, between good and moderate). As such, 7.1 percent of patients expressed poor satisfaction with the cosmetic results from shave biopsy 6 months later compared to 16.1 percent of their physicians regarding the same lesion removal. The results do not directly assess cosmetic results from excisional biopsies needed for melanoma diagnosis, which are more invasive procedures.



# **KQ 3. What Are the Test Characteristics of Visual Screening for Skin Cancer When Performed by Primary Care Providers Versus Dermatologists?**

## **Summary of Results**

We identified two fair-quality cohort studies with data on the test characteristics of skin cancer screening performed by primary care physicians or dermatologists in Australia. Skin cancer outcomes were obtained through either cancer registry data<sup>57</sup> or pathology and biopsy reports and an estimate of false-negative screening rates (**Table 6**).<sup>56</sup> In the first study in Queensland, Australia, primary care physicians conducted screenings among 16,383 adults. Cancer outcomes were determined by pathology or biopsy reports for positive screens. False-negative rates for melanoma were estimated using prior literature and population melanoma rates. The recall rate was 14.1 percent for those who screened positive and were referred to their usual primary care physicians for followup. Based on the number of melanomas detected within 3 years of the first screening examination, sensitivity for melanoma detection was 40.2 percent (calculated) and specificity was 86.1 percent (95% CI, 85.6 to 86.6). The positive predictive value for melanoma was 1.4 percent. The second study evaluated the performance of volunteer dermatologists and plastic surgeons who conducted screening in 7,436 adults in suburban and rural areas in Western Australia. With followup to 24 months for melanoma through a cancer registry system, the sensitivity was 49.0 percent (95% CI, 34.4 to 63.7) and the specificity was 97.6 percent (95% CI, 97.2 to 97.9), with an overall recall rate of 2.7 percent. The positive predictive value was 11.9 percent (95% CI, 7.8 to 17.2). Different followup times for cancer outcomes prohibited direct comparison of screening accuracy between the two physician types.

## **Detailed Results**

### **Screening by Primary Care Physicians**

One fair-quality study of skin cancer screening within nine communities in Queensland, Australia allowed assessment of test characteristics of screening conducted by primary care physicians. The intervention, a pilot study intended to precede a randomized, controlled trial, had three components: 1) a community education program; 2) a physician education program, including a full day with dermatology specialists to review skin cancer epidemiology, early diagnosis, management, and patient communication aimed at encouraging primary care physicians to offer their patients whole-body skin examinations; and 3) free patient access to skin cancer screening clinics in the intervention regions. Whole-body skin examinations were provided by primary care physicians who practiced within the communities and by primary care physicians from outside the community employed by the research study. The research team sent personalized letters to men and women in the community ages 30 to 79 years to encourage participation in skin cancer screening. Positive screens were defined as a skin lesion suspected to be cancerous at the screening examination, and persons with positive screens were referred to their usual primary care physicians for diagnosis and management of the lesion.

Pathology reports from biopsy were used to ascertain cancer outcomes for patients who screened positive. Patients with negative screens were not linked to cancer registry data; instead, the negative screening rate for melanoma was estimated using the number of false-negative results from the literature<sup>60</sup> and population-based estimates of melanoma incidence. Using a false-negative rate of 0.2 percent and an adjusted age distribution for screening participants, an estimated 49 participants would screen negative but subsequently be diagnosed with melanoma within 3 years of the examination, if the entire sample had been linked to cancer registry data. Because the false-negative rate was estimated only for melanoma and not for all skin cancers, test accuracy for sensitivity and specificity for all skin cancers could not be estimated.

The total sample included 16,383 adults. About 52 percent of the study population were women and the average age of those screened was 46.5 years (standard deviation, 16.4). Of those referred for further evaluation, 79.1 percent followed up with their physician.

During the screening program, 33 melanomas (including 13 in situ melanomas), 259 basal cell carcinomas, and 97 squamous cell carcinomas were detected. Other benign skin conditions were also detected. Calculated sensitivity of screening examinations conducted by primary care physicians for melanoma detection was 40.2 percent (33 melanomas detected within 3 years/[33 melanomas plus 49 estimated false-negative melanomas]) and specificity was 86.1 percent (95% CI, 85.6 to 86.6). The recall rate was 14.1 percent of all screening examinations referred for additional workup among 2,302 persons. The positive predictive value for melanoma detection among those with a positive screening examination was 1.4 percent, and the overall cancer detection rate was 0.2 percent.

No information was provided on the false-negative rate for NMSC, so we were not able to calculate sensitivity and specificity. Some study data were available to calculate the positive predictive value for all skin cancer, including melanoma and NMSC in this population, which was 16.9 percent. The cancer detection rate was 2.4 percent.

### **Screening by Dermatologists**

From 1994 to 2002, the Lions Cancer Institute offered whole-body skin examinations to men and women age 20 years and older in rural and suburban areas of Western Australia. Advertisements in local papers recruited individuals to screening clinics. From 1996, the advertisements directly targeted persons with the following eight risk factors: 1) family history of melanoma; 2) five or more moles on the forearm; 3) previous removal of a benign nevus; 4) previous skin cancer; 5) lesion changing in size, color, or shape; 6) lesion that does not heal; 7) fair skin that burns rather than tans; and 8) episodes of severe burns as a child. Volunteer dermatologists and plastic surgeons performed the whole-body skin examinations on patients, referring participants to their usual primary care physicians for further evaluation of suspected lesions. All participants regardless of screening outcome were linked to the Lions Cancer Registry for detection of melanoma at 1 and 2 years postscreening examination. Data were only provided for melanoma outcomes, and there were no data on all skin cancers or NMSC.

Over the 13 years of the screening program, 9,808 persons were screened, of whom 7,436 met the study inclusion criteria. About 56 percent of the population were women and 50.6 percent

were older than age 50 years at the time of the screening examination.

There were 33 melanoma lesions diagnosed within 1 year of the screening examination and 16 additional melanomas diagnosed within 2 years of the screening examination, a total of 49 melanomas. Sensitivity for melanoma at 1 year was 69.7 percent (95% CI, 51.3 to 84.4), declining at 2 years to 49.0 percent (95% CI, 34.4 to 63.7). Specificity was 97.6 percent (95% CI, 97.2 to 97.9). Calculated recall rates for the screening examinations was 2.7 percent. The positive predictive value ranged from 11.4 to 11.9 percent for cancers detected within 1 and 2 years, respectively. In this population, the cancer detection rate was 0.31 percent for cancers diagnosed within 1 year and 0.32 percent for cancers diagnosed within 2 years.

## **KQ 4. Does Visual Screening for Skin Cancer Lead to Earlier Detection of Skin Cancer Compared to Usual Care?**

### **Summary of Results**

We identified one fair-quality case-control study that measured the association between whole-body skin examinations performed by a physician during the 3 years before melanoma diagnosis for cases or referent date for controls and risk of invasive melanoma according to lesion thickness at diagnosis (**Table 7**). The study was conducted among 3,762 cases with incident melanoma in Queensland, Australia and 3,824 controls randomly selected through electoral rolls. Among the controls, 28.3 percent reported receiving a clinical skin examination by a physician within 3 years of their reference date compared to 35.3 percent of melanoma cases. In multivariate-adjusted models, cases diagnosed with thin melanoma ( $\leq 0.75$  mm) had a 38 percent higher odds (odds ratio [OR], 1.38 [95% CI, 1.22 to 1.56]) of receiving a clinical skin examination by a physician in the previous 3 years compared to controls. Further, cases diagnosed with thicker lesions ( $> 0.75$  mm) had a 14 percent reduced odds (OR, 0.86 [95% CI, 0.75 to 0.98]) of recent physician skin examination compared to controls. When thick lesions were further stratified by lesion size, the thickest melanoma lesion cases ( $\geq 3.00$  mm) had 40 percent reduced odds of recent physician skin examination compared to controls (OR, 0.60 [95% CI, 0.43 to 0.83]). As a case-control study with self-reported exposure, there is the potential for recall bias. Medical record review of patient skin cancer screening history to confirm self-report would strengthen future research.

### **Detailed Results**

A case-control study in Queensland, Australia examined melanoma thickness and receipt of a physician clinical skin examination in the 3 years prior to melanoma diagnosis for cases ( $n=3,762$ ) and controls ( $n=3,824$ ).<sup>61</sup> Cases were men and women ages 20 to 75 years with a histologically confirmed first primary invasive cutaneous melanoma diagnosed between January 2000 and December 2003 who were identified through the Queensland Cancer Registry. Recruitment letters were mailed to cases' treating physicians explaining the research study and seeking permission to contact the patients. After physicians provided permission, cases were invited by letter to participate in the study. Controls were randomly selected from the

Queensland Electoral Rolls and matched to 5-year age categories and the sex distribution of the cases. Controls were also contacted by letter about study participation.

In telephone interviews, information was obtained on demographics and melanoma risk factors, including ethnicity, natural hair color at age 21 years, eye color, color of skin before tanning, tendency to burn when exposed to sun for an hour without protection, number of moles on the back, childhood sunburn history, and age when arriving in Australia. Participation rates in the telephone interviews were 78.0 percent for cases and 50.4 percent for controls.

Among controls, 58 percent were male and 49 percent were ages 50 to 69 years. The frequency of sun exposure factors for controls included: 93 percent with a tendency to burn after sun exposure; 60 percent with a heavy to very heavy average lifetime sun exposure; 19.2 percent with previous diagnosis of NMSC; and 14.5 percent with family history of melanoma in a blood relative.

Information on skin cancer screening collected in telephone interviews included self-screening, screening by partners and other lay people, and screening by a doctor, referred to as a clinical skin examination. For cases, screening history was collected only until the time of first awareness of melanoma signs and symptoms. Controls were assigned a reference date to evaluate skin cancer screening exposure. Reference dates were based on the distribution of cases for time from first symptom awareness to date of telephone interview, so the time frame for recollection would be similar between cases and controls. Clinical skin examinations were determined in telephone interviews by asking the question, “During the last 3 years before (you believed something was wrong [cases]/reference date [controls]), had a doctor deliberately checked all or nearly all of your whole body for early signs of skin cancer?” The self-reported receipt of screening by cases and controls was not confirmed by medical record review. However, the question as phrased had been validated in prior work, and test-retest reliability in a sample of participants 1 to 3 months after the interview indicated good agreement for both the cases and the controls.<sup>62</sup>

Among the controls, 28.3 percent reported receiving a clinical skin examination by a physician within the 3 years before their reference date compared to 35.3 percent of melanoma cases. When further stratified by lesion thickness, case report of receiving a clinical skin examination declined as lesion thickness increased: 38.7 percent for lesions smaller than 0.75 mm, 30.3 percent for lesions 0.76 to 1.49 mm, 28.0 percent for lesions 1.5 to 2.99 mm, and 22.5 percent for lesions 3.00 mm or larger.

Multivariate models adjusted for confounders, including age group, sex, education, employment status, marital status, eye color, hair color, skin color, degree of freckling, number of moles on back, age of arrival in Australia, average lifetime sun exposure, family history of melanoma, family history of NMSC, and ethnicity. In multivariate-adjusted models, cases diagnosed with thin melanoma lesions ( $\leq 0.75$  mm) had 38 percent higher odds (95% CI, 1.22 to 1.56) of receiving a physician clinical skin examination in the past 3 years compared to controls. Further, cases diagnosed with thicker lesions ( $> 0.75$  mm) had 14 percent reduced odds (95% CI, 0.75 to 0.98) of recent physician skin examination compared to controls.

When thick lesions were further stratified by size, the odds of having a clinical skin examination by a physician decreased as thickness increased: 7 percent decreased odds for lesions 0.76 to 1.49 mm (95% CI, 0.79 to 1.10); 17 percent decreased odds for lesions 1.50 to 2.99 mm (95% CI, 0.66 to 1.05); and 40 percent decreased odds for lesions 3.0 mm or larger (95% CI, 0.43 to 0.83).

As a case-control study, there is the potential for recall bias due to differential reporting prior to physician skin screening examination by cases compared to controls. However, the potential for cases to recall examinations differentially by lesion size seems unlikely. Nonetheless, medical record review of patient skin cancer screening history to confirm self-report would strengthen future research using case-control study designs, as would cohort studies with clear exposure categories.

## **KQ 5. What Is the Association Between Earlier Detection of Skin Cancer and Skin Cancer Morbidity and Mortality and All-Cause Mortality?**

### **Summary of Results**

We identified eight fair- or good-quality observational cohort studies that included more than 200,000 persons. The studies examined the association between lesion thickness or stage at diagnosis (either AJCC or SEER stage) and either melanoma-specific or all-cause mortality (**Tables 8–10**). We identified one good-quality study that evaluated cancer stage and all-cause mortality. We did not identify any studies that evaluated lesion thickness or stage at diagnosis associated with skin cancer morbidity.

All studies demonstrated a consistent linear increase in risk of melanoma mortality with increasing tumor thickness or stage, regardless of categorization. Tumor thickness larger than 4.0 mm was associated with a 3.1 to 32.6 increased risk of melanoma mortality compared to thinner lesions in multivariate-adjusted models. In the largest study of 68,495 melanoma cases diagnosed from 1992 to 2006 and identified through 13 SEER registries, each 1.0-mm increase in tumor thickness was associated with a subsequent increase in melanoma mortality. Compared to thin lesions (<1 mm), increased risk of melanoma mortality by thickness were: 2.89 (95% CI, 2.62 to 3.18) for tumors 1.01 to 2.00 mm; 4.69 (95% CI, 4.24 to 5.02) for tumors 2.01 to 4.00 mm; and 5.71 (95% CI, 5.10 to 6.39) for tumors larger than 4.00 mm. Using the same study population and categorizing by SEER summary stage, tumors in the distant stage were associated with an 18.66-fold increased risk of melanoma mortality compared to localized disease. Finally, results in a cohort of 39,049 California residents with a diagnosis of melanoma demonstrated that late stage at diagnosis was associated with a 10.4-fold increased risk of all-cause mortality in adjusted hazard ratio (HR) models.

## Detailed Results

### Stage at Diagnosis and Melanoma Mortality

Three fair- to good-quality cohort studies evaluated the association between stage at diagnosis and melanoma mortality and also reported measures of risk of melanoma death according to stage at diagnosis using either AJCC or SEER stages (**Table 8**). The three studies had similar consistent, linear results.<sup>63-65</sup> In one study that used AJCC stage I disease as the comparison, stage II melanoma had a 4.96-fold increased relative risk of mortality (95% CI, 4.51 to 5.56); stage III melanoma had a 9.99-fold increased relative risk (95% CI, 8.84 to 11.29); and stage IV melanoma had a 27.1-fold increased relative risk (95% CI, 22.4 to 32.8).<sup>64</sup>

Two studies used the SEER stages of local, regional, distant, and unknown.<sup>63, 65</sup> One study used in situ melanoma as the reference category. Two study populations potentially overlap but likely minimally. One study evaluated 13 SEER regions from 1992 to 2006 for all ages. The second study used SEER-Medicare data from 11 SEER regions from 1988 to 2000. Using in situ melanoma as the reference category, the HR of risk of melanoma death was 8.83 (localized), 23.2 (regional), and 94.0 (distant).<sup>63</sup> Using localized stage as the reference category, risk of melanoma death was 3.62 for regional and 18.66 for distant.<sup>65</sup> All estimates in the three studies reached statistical significance.

### Lesion Thickness at Diagnosis and Melanoma Mortality

Seven studies using tumor thickness as a main exposure found that the risk of melanoma death increased linearly with increasing tumor thickness at diagnosis (**Table 9**).<sup>63, 65-70</sup> Reference categories ranged from 0.25 mm or smaller to 1.0 mm or smaller. Maximum tumor thickness categories ranged from 1.0 mm to 6 mm or larger.

Because of changes in reference category, actual estimates of melanoma mortality varied. In three studies using tumor thickness of 1.0 mm or smaller as the reference category and risk groups consistent with the AJCC staging system,<sup>49</sup> HR risk of melanoma death for a tumor thickness of 1.01 to 2.00 mm ranged from 2.06<sup>63</sup> to 4.13.<sup>68</sup> Tumors with a thickness of 2.01 to 4.00 mm had risk of melanoma death ranging from 3.11<sup>63</sup> to 6.88.<sup>68</sup> Tumors with a thickness larger than 4.0 mm reported associated risks of 5.71<sup>65</sup> and 9.52.<sup>68</sup> In two studies using a lesion thickness of 0.50 mm or smaller as the reference category, risk estimates increased with increasing lesion thickness, from 3.9 for thickness of 0.76 to 1.0 mm to 23.08 for thickness larger than 6.0 mm.<sup>70</sup> One study used lesion thickness of 1 to 1.5 mm as the reference category and found incrementally decreasing risk of melanoma mortality for tumors 0.75 to 1.00 mm (RR, 0.55) and 0.75 mm or smaller (RR, 0.28), and risk increasing to 3.88 for tumors larger than 4.00 mm.<sup>66</sup>

### Stage at Diagnosis and All-Cause Mortality

We identified one good-quality study that evaluated the association between stage at melanoma diagnosis and all-cause mortality (**Table 10**). A study of 39,049 California residents with a median age of 58.0 years (95% CI, 29 to 84) who were diagnosed with melanoma from 1993 to

2003 found increased HR of all-cause mortality was associated with increased melanoma stage at detection, with estimates of 2.26 (95% CI, 2.14 to 2.39) for stage II melanoma, 4.27 (95% CI, 3.90 to 4.67) for stage III melanoma, and 10.39 (95% CI, 8.96 to 12.0) for stage IV melanoma, compared to stage I disease.<sup>64</sup>

## Chapter 4. Discussion

### Summary of Evidence

We conducted this systematic review to assist the USPSTF in updating its previous skin cancer screening recommendation.<sup>47</sup> Thirteen unique studies met our inclusion criteria. The prior review did not explicitly evaluate lesion thickness, harms of screening, or the relationship between mortality outcomes and melanoma thickness or stage at diagnosis.

No firm conclusions on skin cancer screening and melanoma mortality can be made from the evidence reviewed. Results from a single population-based ecologic study suggested skin cancer screening may be associated with reductions in population-level melanoma mortality rates, based on pre- versus postintervention comparisons in one German region implementing a 1-year multicomponent skin cancer screening program compared to surrounding regions that did not implement the screening program. However, as an ecologic study, the measures of association were drawn from population-level changes in mortality, not individual-level data, which cannot account for confounding or assess comparisons between exposed and nonexposed participants. While data demonstrating unchanged or increased melanoma mortality in control regions are promising, the ecologic study design limits assessment of causal inference. Further, the large relative mortality reduction translated to an absolute mortality reduction of 0.8 melanoma deaths per 100,000 persons, after screening only 19 percent of the target population. The context of the results must also be considered among the following: 1) the high proportion of younger women screened who were at lower risk of melanoma incidence and mortality compared to older men, suggesting a healthy screenee bias; 2) the high proportion of persons with suspicious findings who did not receive followup by a dermatologist; and 3) the impact of the other components of the screening program, including education in the community, which cannot be differentiated from visual skin cancer screening. Nonetheless, the results and challenges from the SCREEN study likely reflect real-world population-based screening programs when implemented.

We found limited data on harms of visual screening examinations, except for biopsy yields and cosmetic harms. The included evidence suggested that cosmetic results of shave biopsy are acceptable to most adults. Most screen-positive lesions, particularly to detect one malignant melanoma, require additional excisional biopsies as diagnostic workup. When the ratio of excisions required per malignant melanoma identified was evaluated by type of lesion, age, and sex, younger adults (age <35 years) required about twice as many excisions of suspicious lesions than older adults (age >64 years). The pretest probability of melanoma is lower in young adults than in older adults. Although these data do not clearly define overdiagnosis, they demonstrate a potential excess burden of excisions for nonmalignant lesions in younger adults participating in community skin cancer screening programs, where the incidence of NMSC and melanoma is lowest.

We were not able to directly compare screening accuracy between dermatologists and primary care clinicians due to differences in time to ascertainment of cancer outcomes that affect screening examination performance measures. Only one study linked participants to cancer registry data, the gold standard for cancer detection and the only way to assess cancer outcomes



in screen-negatives within the population. Relying on biopsy or pathology reports could have underestimated the number of melanomas detected in the population rather than through cancer registry rates, and the estimation of false-negative rates could be an overestimate of the number of cancers missed. Nonetheless, whether visual skin cancer examination can detect skin cancer 24 to 36 months from examination might not be a reasonable time frame. Sensitivity is reduced as the length of followup time to observe cancers is extended. Sensitivity was also affected by the inclusion of both incident melanoma and melanoma in situ in the screening examinations conducted by primary care physicians,<sup>56</sup> compared to the inclusion of only invasive melanoma cases as positive findings in dermatology and plastic surgery examinations.<sup>57</sup> Not affected by cancer ascertainment followup, recall rates were lower for dermatology providers than primary care physicians, consistent with higher specificity as might be expected for a specialist examination.

Self-report of skin cancer screening within the prior 3 years was associated with reduced risk of thicker melanoma lesions compared to controls with melanoma who did not report skin cancer screening.<sup>61</sup> In the case-control study, cases may have recalled receipt of a recent screening examination differentially than controls without a melanoma diagnosis. To minimize potential recall bias, the study ascertained history of skin screening examinations using a well-tested and reliable question documented to have high validity compared to medical record review.<sup>62</sup> The study did not further validate self-report with medical record review. While cases might have recalled their screening history differently than controls, differences within cases are unlikely to have aligned according to lesion thickness to produce a spurious trend of decreasing risk with increasing lesion thickness. Data from cohort studies will be important to confirm this finding and its magnitude.

There is consistent evidence that later stage or thicker lesions at melanoma detection is highly related to increased risk of melanoma mortality and may be associated with all-cause mortality.<sup>64</sup> It is unlikely that future research in this area will change the overall conclusions of this body of current evidence based on lesion thickness alone.

## **Challenges in Demonstrating Benefits of Visual Screening for Skin Cancer**

Despite efforts to conduct true population-based screening, the challenges faced by other countries attempting such programs may be instructive for the United States. First, for population-based screening, the high proportion of well women who received skin cancer screening and represent a group at lower risk of melanoma compared to older men suggests that healthy screenee bias should be addressed in future skin cancer screening studies. Second, in studies of diagnostic accuracy, the high proportion of persons with several skin cancer risk factors within the screened population suggests that the participating population might not represent an average-risk population.<sup>53,71</sup> The need to increase the pretest probability of melanoma detection is the likely driver of encouraging skin cancer screening participation, but might not reflect the population observed in primary care settings. Hence, further studies should attempt to address inclusion of study populations representing average-risk persons.

Based on the results of the SCREEN study, the German health care system launched a

nationwide skin cancer screening program in 2008. However, a recent evaluation comparing age-adjusted mortality data from before the nationwide screening program in 2008 to 5-year followup data found increases in melanoma mortality rates in men and no change in melanoma mortality rates in women.<sup>72</sup> Further, the initial decrease in mortality reported from the SCREEN study in the Schleswig-Holstein region appeared to be transient, and melanoma mortality rates returned to preintervention baseline rates. The only randomized, controlled trial to evaluate skin cancer screening began as a pilot study in Queensland, Australia in the early 2000s, but a full trial following the pilot was not able to be conducted. At the time of this report, there are no anticipated results for mortality outcomes from these pilot data.<sup>73</sup>

Both studies of diagnostic accuracy were conducted in Australia, where overall general knowledge of skin protection habits and sun safety is high and primary care physicians routinely diagnose and manage skin cancer lesions.<sup>74</sup> Physician training in detecting and diagnosing skin cancers in primary care was part of both studies and is likely important for improving performance, whether for screening alone or responding to patient concerns. In a different Australian population presenting for both skin cancer screening and due to concern about a skin lesion, sensitivity was statistically significantly different for melanoma detection between general practitioners with and without skin cancer medicine training (60% vs. 29%;  $p < 0.001$ ).<sup>74</sup> Specificity was similar for both provider types; however, due to low sensitivity, general practitioners without specific skin cancer training also had lower positive predictive values than those with specialized skin cancer training (18% vs. 25%). Currently, U.S.-based primary care physicians are not confident in their skills to conduct skin cancer screening,<sup>36</sup> and could require additional training to achieve skin cancer screening goals.

Potential harms of skin cancer screening include cosmetic harms, overdiagnosis, overtreatment, and psychosocial harms related to diagnostic workup. The evidence on these harms is very limited. Risk for excision-related harms could be greater in younger persons, based on a greater number of excisions required for each melanoma or NMSC case detected.<sup>58</sup> For melanoma, excision-related harms are important because initial management with biopsy alone is not sufficient for removing the entire lesion. Subsequent excisions are usually necessary for clear margins, even for small lesions, particularly if the first biopsy is a shave or punch biopsy.<sup>75</sup> No identified studies addressed overdiagnosis in a screening setting, but there is potential for overdiagnosis: melanoma incidence has increased 3-fold since 1975 while melanoma mortality has remained stable, suggesting increased detection of clinically insignificant cancers rather than earlier detection of invasive tumors.<sup>14, 76</sup> An important consideration for the 2.1 million Medicare enrollees diagnosed with NMSC annually<sup>8</sup> is the increase in the detection and treatment of basal cell carcinoma in adults that likely has limited impact on life expectancy.<sup>77</sup> Further, patient-relevant definitions and outcomes of melanoma overdiagnosis and overtreatment are not well understood and should be further explored.

The effectiveness of screening depends on effective treatment of identified lesions, and there have been several trends in the surgical treatment of skin cancer. In the late 1990s, clinical practice adopted sentinel lymph node biopsy in the diagnostic workup of melanoma, even in persons diagnosed with thin lesions. Based on SEER data (1995 to 2001), the proportion of thin lesions that received sentinel lymph node biopsy has statistically significantly increased. The proportion of thin melanomas smaller than 0.69 mm and 0.70 to 1.00 mm with sentinel lymph

node biopsy increased from 1.6 and 6.3 percent, respectively, in 1995 to 7.8 and 42.4 percent, respectively, in 2001.<sup>78</sup> More contemporary biopsy data has not yet been reported, and it is unclear whether the proportion of surgeons using lymph node biopsy has changed. In 2012, the clinical guidelines from the American Society for Clinical Oncology and the American College of Surgeons recommended sentinel lymph node biopsy for lesions of 1 to 4 mm, but the organizations felt evidence was insufficient to create guidelines for lesions smaller than 1.0 mm.<sup>79, 80</sup>

We were unable to describe the proportion of lesions smaller than 1.0 mm detected on the trunk or extremities that were treated with Mohs micrographic surgery, which is currently not recommended for basal cell or squamous cell carcinoma, lentigo maligna, and melanoma in situ on the trunk or extremities. The surgery is only appropriate for particularly large or aggressive types of skin cancer.<sup>81</sup> As part of the AAD Choosing Wisely campaign, clinicians are advised not to treat uncomplicated NMSC smaller than 1.0 mm on the trunk and extremities with Mohs micrographic surgery.<sup>82</sup> Although data on the use of Mohs micrographic surgery for these types of small skin cancers on the trunk or extremities could indicate potential overtreatment of screen-detected skin cancers, we found no relevant published data at the time of this report.

## Future Directions

The balance in favor of screening for skin cancer is likely to be greatest among subgroups of the population that are the most likely to develop fatal melanoma, which is yet to be distinguished. However, several algorithms use melanoma risk factors to qualify risk of melanoma and could have utility for screening programs in identifying persons who might benefit most from screening.<sup>83-86</sup> The algorithms vary by whether ascertainment of the risk factor information is meant to be done by a health care provider, whether the target population includes persons with a family history of melanoma and/or a history of NMSC; and whether the algorithm has been validated. Most existing algorithms have been developed using only information on melanoma risk among persons of white race.<sup>83-86</sup>

One algorithm intended for use by health care providers during clinical care and developed using data from a large melanoma case-control study estimates 5-year risk of developing melanoma in non-Hispanic white persons ages 20 to 70 years.<sup>83</sup> The algorithm includes demographic information (sex, age, and region of residence), history of blistering sunburn (men)/propensity for skin to become tanned (women), and presence of nevi on the back.<sup>83</sup> The area under the receiver operating characteristic curve—a measure of the accuracy of the algorithm, where 0.5 indicates inability to predict who will and will not develop melanoma<sup>87</sup>—ranged from 0.7 to 0.8 depending on sex and age group.<sup>83</sup> The algorithm was not validated in an external population.<sup>83</sup> There is no evidence to suggest that these algorithms have been adopted in U.S. clinical practice. If externally validated, risk assessment tools might lead to research testing a targeted screening approach. Similar to other cancer risk assessment tools, they may also provide guidance to individuals on their risk of developing melanoma.

## Review Limitations

Our review focused on the clinical skin examination to screen for skin cancer, not the self-

detection of skin cancer by an individual. The nature of skin cancer makes this review unique. In contrast to breast, colorectal, or lung cancers, where a provider-administered screening modality and access to specialty followup are essential for early detection, individuals can and do identify concerning lesions on their own skin. Thus, community education about skin cancer and improved access to physician review of suspicious lesions is a critically important part of any skin cancer early detection program. These components have been reviewed by the Community Preventive Services Task Force.<sup>88</sup> Further, studies conducted outside of primary care (e.g., the workplace, “screening days,” or “pigmented lesion clinics”) were outside the scope of this review, as were studies of patients referred for diagnostic workup from a source population that could not be defined. For these reasons, the role of physician screening in primary care may appear as isolated in this review.

## **Study Limitations and Future Research Needs**

The bulk of the literature considered in this review was from international settings, specifically Australia, where skin cancer screening and outcomes have been a research focus and the burden of melanoma is much higher compared to the United States or other countries.<sup>89</sup>

A main limitation of this review is the lack of rigorous studies on skin cancer screening conducted in the United States with an application in primary care or internal medicine settings. Our focus was on fair- or good-quality studies that met our inclusion criteria. Among U.S. studies, very few had longitudinal followup for cancer outcomes, limiting their applicability. Participants in most screening studies tended to be younger women with a perceived increased risk of skin cancer, even though the incidence of skin cancer is highest in older men.<sup>90</sup>

Further research on skin cancer screening should:

- Conduct followup of sufficient length to assess individual melanoma mortality in screened and unscreened persons, with ascertainment of cancer outcomes based on registry systems
- Examine the impact of targeted, risk-based screening versus average-risk population screening for clinical effectiveness and clearly document the risk factors of the screened population for potential self-selection
- Study the relative impact of primary care–based screening relative to other components of a screening program, such as public education and improved access to skin examinations
- Advance knowledge about the potential for overtreatment and overdiagnosis, including the psychosocial consequences, of population-based skin cancer screening to help fully understand the benefits of screening in the context of potential harms

## **Conclusion**

On a population level, with limited evidence on skin cancer screening, a clear statement cannot be made about the benefit of skin cancer screening for melanoma mortality and all-cause

mortality or association with thinner lesions. With few studies to confirm these results, the applicability for widespread skin cancer screening could be limited. Later stage at diagnosis of melanoma is associated with strong effect on melanoma mortality within 5 years of diagnosis. Future research on skin cancer screening should focus on targeted screening in persons considered to be at higher risk for skin cancer.

## References

1. U. S. Preventive Services Task Force. Screening for skin cancer: recommendations and rationale. *Am J Prev Med.* 2001;20(3 Suppl):44-6. PMID: 11306231.
2. Thomas VD, Aasi SZ, Wilson LD, et al. Cancer of the skin. In: DeVita VT, Lawrence TS, Rosenberg SA, DePinho RA, Weinberg RA, editors. *DeVita, Hellman and Rosenberg's Cancer: Principles and Practice of Oncology.* 8th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008. p. 1863-87.
3. Howlander N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2011. Bethesda, MD: National Cancer Institute [2015 April 1]. [http://seer.cancer.gov/csr/1975\\_2011/](http://seer.cancer.gov/csr/1975_2011/).
4. Perera E, Sinclair R. An estimation of the prevalence of nonmelanoma skin cancer in the U.S. *F1000Research.* 2013;2:107. PMID: 24358841.
5. Harris RB, Griffith K, Moon TE. Trends in the incidence of nonmelanoma skin cancers in southeastern Arizona, 1985-1996. *J Am Acad Dermatol.* 2001;45(4):528-36. PMID: 11568742.
6. Karagas MR, Greenberg ER, Spencer SK, et al. 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(4):555-9. PMID: 10225444.
7. Eisemann N, Waldmann A, Geller AC, et al. Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence. *J Invest Dermatol.* 2014;134(1):43-50. PMID: 23877569.
8. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. *Arch Dermatol.* 2010;146(3):283-7. PMID: 20231499.
9. Christenson LJ, Borrowman TA, Vachon CM, et al. Incidence of basal cell and squamous cell carcinomas in a population younger than 40 years. *JAMA.* 2005;294(6):681-90. PMID: 16091570.
10. Karagas MR, Weinstock MA, Nelson HH. Keratinocyte Carcinomas (Basal and Squamous Cell Carcinomas of the Skin). In: Schottenfeld D, Fraumeni JF, editors. *Cancer Epidemiology and Prevention, Third Edition.* Oxford: Oxford University Press; 2006. p. 1230-50.
11. Lewis KG, Weinstock MA. Nonmelanoma skin cancer mortality (1988-2000): the Rhode Island follow-back study. *Arch Dermatol.* 2004;140(7):837-42. PMID: 15262694.
12. Corona R. Epidemiology of nonmelanoma skin cancer: a review. *Ann Ist Super Sanita.* 1996;32(1):37-42. PMID: 8804184.
13. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin.* 2015;65(1):5-29. PMID: 25559415.
14. Welch HG, Woloshin S, Schwartz LM. Skin biopsy rates and incidence of melanoma: population based ecological study. *BMJ.* 2005;331(7515):481. PMID: 16081427.
15. Rigel DS, Russak J, Friedman R. The evolution of melanoma diagnosis: 25 years beyond the ABCDs. *CA Cancer J Clin.* 2010;60(5):301-16. PMID: 20671054.
16. de Gruijl FR, van Kranen HJ, Mullenders LH. UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer. *J Photochem Photobiol B.* 2001;63(1-3):19-27. PMID: 11684448.

17. Gruber SB, Armstrong BK. Cutaneous and Ocular Melanoma. In: Schottenfeld D, Fraumeni JF, editors. *Cancer Epidemiology and Prevention*, Third Edition. Oxford: Oxford University Press; 2006. p. 1196-229.
18. Slingluff Jr CL, Flaherty KT, Rosenberg SA, et al. Melanoma Section 2 Cutaneous Melanoma. In: deVita VT, Lawrence TS, Rosenberg SA, dePinho RA, Weinberg RA, editors. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia: Wolters, Kluwer Health/Lippencourt Williams & Wilkins; 2008. p. 1897-951.
19. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. *Eur J Cancer*. 2005;41(1):28-44. PMID: 15617989.
20. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. *Eur J Cancer*. 2005;41(1):45-60. PMID: 15617990.
21. Gandini S, Sera F, Cattaruzza MS, et al. Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. *Eur J Cancer*. 2005;41(14):2040-59. PMID: 16125929.
22. Colantonio S, Bracken MB, Beecker J. The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. *J Am Acad Dermatol*. 2014;70(5):847-57 e1-18. PMID: 24629998.
23. International Agency for Research on Cancer Working Group on artificial ultraviolet light and skin cancer. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. *Int J Cancer*. 2007;120(5):1116-22. PMID: 17131335.
24. Veierod MB, Couto E, Lund E, et al. Host characteristics, sun exposure, indoor tanning and risk of squamous cell carcinoma of the skin. *Int J Cancer*. 2013. PMID: 24408678.
25. Khalesi M, Whiteman DC, Tran B, et al. A meta-analysis of pigmentary characteristics, sun sensitivity, freckling and melanocytic nevi and risk of basal cell carcinoma of the skin. *Cancer Epidemiol*. 2013;37(5):534-43. PMID: 23849507.
26. Olsen CM, Carroll HJ, Whiteman DC. Estimating the attributable fraction for melanoma: a meta-analysis of pigmentary characteristics and freckling. *Int J Cancer*. 2010;127(10):2430-45. PMID: 20143394.
27. van Dam RM, Huang Z, Rimm EB, et al. Risk factors for basal cell carcinoma of the skin in men: results from the health professionals follow-up study. *Am J Epidemiol*. 1999;150(5):459-68. PMID: 10472945.
28. Zhang M, Qureshi AA, Geller AC, et al. Use of tanning beds and incidence of skin cancer. *J Clin Oncol*. 2012;30(14):1588-93. PMID: 22370316.
29. Abbasi NR, Shaw HM, Rigel DS, et al. Early diagnosis of cutaneous melanoma: revisiting the ABCD criteria. *JAMA*. 2004;292(22):2771-6. PMID: 15585738.
30. Grob JJ, Bonerandi JJ. The 'ugly duckling' sign: identification of the common characteristics of nevi in an individual as a basis for melanoma screening. *Arch Dermatol*. 1998;134(1):103-4. PMID: 9449921.
31. Rat C, Quereux G, Riviere C, et al. Targeted melanoma prevention intervention: a cluster randomized controlled trial. *Ann Fam Med*. 2014;12(1):21-8. PMID: 24445100.
32. Norman GJ, Adams MA, Calfas KJ, et al. A randomized trial of a multicomponent intervention for adolescent sun protection behaviors. *Arch Pediatr Adolesc Med*. 2007;161(2):146-52. PMID: 17283299.

33. Pan M, Geller L. Update on indoor tanning legislation in the United States. *Clin Dermatol*. 2015;33(3):387-92. PMID: 25889141.
34. Oliveria SA, Heneghan MK, Cushman LF, et al. Skin cancer screening by dermatologists, family practitioners, and internists: barriers and facilitating factors. *Arch Dermatol*. 2011;147(1):39-44. PMID: 21242390.
35. Kimball AB, Resneck JS, Jr. The US dermatology workforce: a specialty remains in shortage. *J Am Acad Dermatol*. 2008;59(5):741-5. PMID: 18723242.
36. Wise E, Singh D, Moore M, et al. Rates of skin cancer screening and prevention counseling by US medical residents. *Arch Dermatol*. 2009;145(10):1131-6. PMID: 19841400.
37. Kirsner RS, Mukherjee S, Federman DG. Skin cancer screening in primary care: prevalence and barriers. *J Am Acad Dermatol*. 1999;41(4):564-6. PMID: 10495376.
38. Goulart JM, Quigley EA, Dusza S, et al. Skin cancer education for primary care physicians: a systematic review of published evaluated interventions. *J Gen Intern Med*. 2011;26(9):1027-35. PMID: 21472502.
39. American Academy of Family Physicians (AAFP). Skin Cancer. Clinical Preventive Service Recommendation Leawood, KS: American Academy of Family Physicians (AAFP) [2015 May 15]. <http://www.aafp.org/patient-care/clinical-recommendations/all/skin-cancer.html>.
40. American College of Preventive Medicine. ACPM Position Statements. Washington, DC: American College of Preventive Medicine [2015 May 15]. [http://www.acpm.org/?page=Policy\\_Statements](http://www.acpm.org/?page=Policy_Statements).
41. American Academy of Dermatology. Clinical Guidelines. Schaumburg, IL: American Academy of Dermatology [2015 May 15]. <https://www.aad.org/education/clinical-guidelines>.
42. American College of Physicians. Guidelines: ACP Clinical Recommendations. Philadelphia: American College of Physicians, [2015 May 22]. [http://www.acponline.org/clinical\\_information/guidelines/](http://www.acponline.org/clinical_information/guidelines/).
43. U. S. Preventive Services Task Force. Screening for skin cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009;150(3):188-93. PMID: 19189908.
44. American Cancer Society. American Cancer Society Guidelines for the Early Detection of Cancer Atlanta, GA: American Cancer Society [2015 May 15]. <http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer>.
45. Guide to Community Preventive Services. Preventing skin cancer: interventions in outdoor recreational and tourism settings. Washington, DC: Department of Health and Human Services [2015 September 17]. <http://www.thecommunityguide.org/cancer/skin/education-policy/outdoorrecreation.html>.
46. American Academy of Dermatology. SPOTme. Schaumburg, IL: American Academy of Dermatology [2015 May 22]. <https://www.aad.org/spot-skin-cancer/community-programs-events/spotme-skin-cancer-screenings>.
47. Wolff T, Tai E, Miller T. Screening for skin cancer: an update of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2009;150(3):194-8. PMID: 19189909.
48. United Nations Development Programme. Human Development Reports: Data. Human Development Reports: United Nations [2015 May 22]. <http://hdr.undp.org/en/data>.

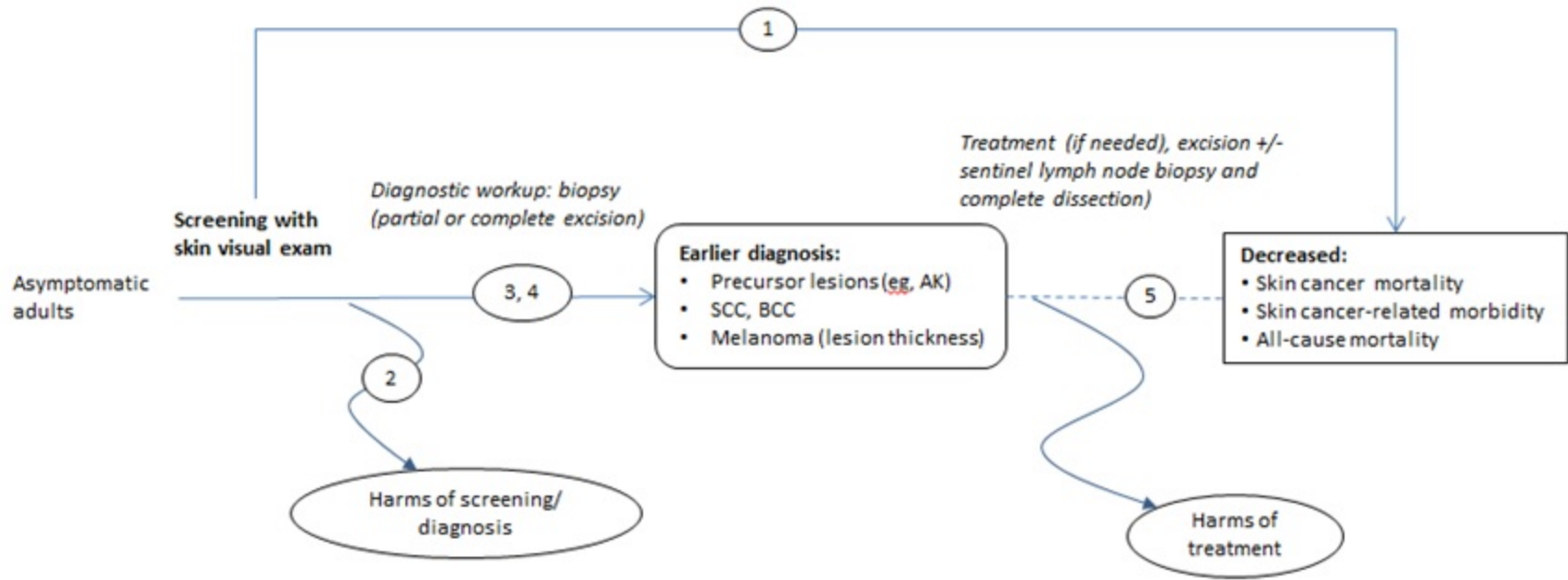


49. Byrd D, Compton CC, Fritz AG, et al. *AJCC cancer staging manual (Vol 649)*. New York: Springer; 2010.
50. U.S. Preventive Services Task Force. *U.S. Preventive Services Task Force Procedure Manual*. AHRQ Publication Number 08-05118-EF. Rockville, MD: U.S. Preventive Services Task Force; 2008.
51. Dufault B, Klar N. The quality of modern cross-sectional ecologic studies: a bibliometric review. *Am J Epidemiol*. 2011;174(10):1101-7. PMID: 21940800.
52. Tu JV, Ko DT. Ecological studies and cardiovascular outcomes research. *Circulation*. 2008;118(24):2588-93. PMID: 19064693.
53. Katalinic A, Waldmann A, Weinstock MA, et al. Does skin cancer screening save lives?: an observational study comparing trends in melanoma mortality in regions with and without screening. *Cancer*. 2012;118(21):5395-402. PMID: 22517033.
54. Waldmann A, Nolte S, Weinstock MA, et al. Skin cancer screening participation and impact on melanoma incidence in Germany--an observational study on incidence trends in regions with and without population-based screening. *Br J Cancer*. 2012;106(5):970-4. PMID: 22294187.
55. Breitbart EW, Waldmann A, Nolte S, et al. Systematic skin cancer screening in Northern Germany. *J Am Acad Dermatol*. 2012;66(2):201-11. PMID: 22074699.
56. Aitken JF, Janda M, Elwood M, et al. Clinical outcomes from skin screening clinics within a community-based melanoma screening program. *J Am Acad Dermatol*. 2006;54(1):105-14. PMID: 16384764.
57. Fritschi L, Dye SA, Katris P. Validity of melanoma diagnosis in a community-based screening program. *Am J Epidemiol*. 2006;164(4):385-90. PMID: 16760225.
58. Waldmann A, Nolte S, Geller AC, et al. Frequency of excisions and yields of malignant skin tumors in a population-based screening intervention of 360,288 whole-body examinations. *Arch Dermatol*. 2012;148(8):903-10. PMID: 22911184.
59. Gambichler T, Senger E, Rapp S, et al. Deep shave excision of macular melanocytic nevi with the razor blade biopsy technique. *Dermatol Surg*. 2000;26(7):662-6. PMID: 10886275.
60. Rampen RH. Point-counterpoint. Mass population skin cancer screening is not worthwhile. *J Cutan Med Surg*. 1998;2(3):128-9. PMID: 9556369.
61. Aitken JF, Elwood M, Baade PD, et al. Clinical whole-body skin examination reduces the incidence of thick melanomas. *Int J Cancer*. 2010;126(2):450-8. PMID: 19609948.
62. Aitken JF, Youl PH, Janda M, et al. Validity of self-reported skin screening histories. *Am J Epidemiol*. 2004;159(11):1098-105. PMID: 15155295.
63. Reyes-Ortiz CA, Goodwin JS, Freeman JL, et al. Socioeconomic status and survival in older patients with melanoma. *J Am Geriatr Soc*. 2006;54(11):1758-64. PMID: 17087705.
64. Zell JA, Cinar P, Mobasher M, et al. Survival for patients with invasive cutaneous melanoma among ethnic groups: the effects of socioeconomic status and treatment. *J Clin Oncol*. 2008;26(1):66-75. PMID: 18165642.
65. Pollack LA, Li J, Berkowitz Z, et al. Melanoma survival in the United States, 1992 to 2005. *J Am Acad Dermatol*. 2011;65(5 Suppl 1):S78-86. PMID: 22018071.
66. Owen SA, Sanders LL, Edwards LJ, et al. Identification of higher risk thin melanomas should be based on Breslow depth not Clark level IV. *Cancer*. 2001;91(5):983-91. PMID: 11251950.

67. Luke CG, Coventry BJ, Foster-Smith EJ, et al. A critical analysis of reasons for improved survival from invasive cutaneous melanoma. *Cancer Causes Control*. 2003;14(9):871-8. PMID: 14682444.
68. Marashi-Pour S, Morrell S, Cooke-Yarborough C, et al. Competing risk analysis of mortality from invasive cutaneous melanoma in New South Wales: a population-based study, 1988-2007. *Aust N Z J Public Health*. 2012;36(5):441-5. PMID: 23025365.
69. Green AC, Baade P, Coory M, et al. Population-based 20-year survival among people diagnosed with thin melanomas in Queensland, Australia. *J Clin Oncol*. 2012;30(13):1462-7. PMID: 22412152.
70. Leiter U, Buettner PG, Eigentler TK, et al. Prognostic factors of thin cutaneous melanoma: an analysis of the central malignant melanoma registry of the German dermatological society. *J Clin Oncol*. 2004;22(18):3660-7. PMID: 15302905.
71. Aitken JF, Elwood JM, Lowe JB, et al. A randomised trial of population screening for melanoma. *J Med Screen*. 2002;9(1):33-7. PMID: 11943795.
72. Boniol M, Autier P, Gandini S. Melanoma mortality following skin cancer screening in Germany. *BMJ Open*. 2015;5(9):e008158. PMID: 26373399.
73. Aitken J, (Epidemiology Unit, Queensland Cancer Fund, et al. Personal email to. In: Wernli KJ, (Group Health Research Institute, Seattle WA), editors. 2015.
74. Youl PH, Baade PD, Janda M, et al. Diagnosing skin cancer in primary care: how do mainstream general practitioners compare with primary care skin cancer clinic doctors? *Med J Aust*. 2007;187(4):215-20. PMID: 17708723.
75. Stell VH, Norton HJ, Smith KS, et al. Method of biopsy and incidence of positive margins in primary melanoma. *Ann Surg Oncol*. 2007;14(2):893-8. PMID: 17119869.
76. Welch HG, Black WC. Overdiagnosis in cancer. *J Natl Cancer Inst*. 2010;102(9):605-13. PMID: 20413742.
77. Linos E, Schroeder SA, Chren MM. Potential overdiagnosis of basal cell carcinoma in older patients with limited life expectancy. *JAMA*. 2014;312(10):997-8. PMID: 25203077.
78. Harlan LC, Lynch CF, Ballard-Barbash R, et al. Trends in the treatment and survival for local and regional cutaneous melanoma in a US population-based study. *Melanoma Res*. 2011;21(6):547-54. PMID: 21897302.
79. Wong SL, Balch CM, Hurley P, et al. Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. *J Clin Oncol*. 2012;30(23):2912-8. PMID: 22778321.
80. Wong SL, Balch CM, Hurley P, et al. Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. *Ann Surg Oncol*. 2012;19(11):3313-24. PMID: 22766987.
81. American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. *Dermatol Surg*. 2012;38(10):1582-603. PMID: 22958088.
82. Choosing Wisely. American Academy of Dermatology five things physicians and patients should question. Philadelphia: ABIM Foundation [2015 March 30]. <http://www.choosingwisely.org/doctor-patient-lists/american-academy-of-dermatology/>.

83. Fears TR, Guerry Dt, Pfeiffer RM, et al. Identifying individuals at high risk of melanoma: a practical predictor of absolute risk. *J Clin Oncol*. 2006;24(22):3590-6. PMID: 16728488.
84. Cho E, Rosner BA, Feskanich D, et al. Risk factors and individual probabilities of melanoma for whites. *J Clin Oncol*. 2005;23(12):2669-75. PMID: 15837981.
85. Williams LH, Shors AR, Barlow WE, et al. Identifying persons at highest risk of melanoma using self-assessed risk factors. *J Clin Exp Dermatol Res*. 2011;2(6):pii: 1000129. PMID: 22229112.
86. Davies JR, Chang YM, Bishop DT, et al. Development and validation of a melanoma risk score based on pooled data from 16 case-control studies. *Cancer Epidemiol Biomarkers Prev*. 2015;24(5):817-24. PMID: 25713022.
87. Weiss NS, Koepsell TD. *Epidemiologic methods*. New York: Oxford; 2014.
88. Community Preventive Services Task Force. *Cancer Prevention and Control. Publications about the Community Guide* Washington, DC: US Department of Health and Human Services [2015 May 22]. <http://www.thecommunityguide.org/library/pubstopic.htm#cancer>.
89. International Agency for Research on Cancer. *GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence worldwide in 2012*. Lyon, France: World Health Organization [2015 May 22]. <http://globocan.iarc.fr/Pages/Map.aspx>.
90. Collins MK, Secrest AM, Ferris LK. Screening for melanoma. *Melanoma Res*. 2014;24(5):428-36. PMID: 24999755.

Figure 1. Analytic Framework



**Abbreviations:** AK = actinic keratosis; BCC = basal cell carcinoma; SCC = squamous cell carcinoma.

**Table 1. Description of Included Studies for KQs 1–5**

Author, Year Quality	Country	Study Design	N	Population	Mean Age, Years (SD or Range) or Category	% Female	Dates of Data Collection	Length of Followup	KQ
Katalinic, 2012 <sup>53</sup> Fair Waldmann, 2012 <sup>58</sup> Fair Breitbart, 2012 <sup>55</sup> Good  SCREEN	Germany	Ecologic <sup>53</sup>	87.46 <i>million</i>	Inhabitants of Germany and Denmark from 1998 to 2009	NR	50.9%	1998–2009	5 years after intervention	1
		Cohort <sup>55,58</sup>	360,288	Residents of Schleswig-Holstein, Germany age ≥20 years with whole-body skin cancer screening exam between July 2003 and June 2004	49.7 (16.2)	73.6%	2003–2004	12 months	1, 2
Gambichler, 2000 <sup>59</sup> Fair	Germany	Case series	45	Routine skin cancer screening outpatients not suspected of melanoma with a shave biopsy	32 (range, 15–54)	51.1%	NR	6 months after biopsy	2
Aitken, 2006 <sup>56</sup> Fair	Australia	Cohort	16,383	Residents in a community-based pilot randomized, clinical trial of skin cancer screening program	46.5 (16.4)	51.5%	1998–2001	Up to 3 years after the initial screening exam	3
Fritschi, 2006 <sup>57</sup> Fair	Australia	Cohort	7,436	Adults who attended Lions Cancer Institute weekend mobile screening clinics in rural and suburban locations in Western Australia	<40: 26.2% 40–59: 46.2% ≥60: 27.6%	56.0%	1994–2002	2 years after the initial screening exam	3
Aitken, 2010 <sup>61</sup> Fair	Australia	Population-based case-control	3,762 cases 3,824 controls	Queensland residents ages 20 to 75 years; cases identified from cancer registry and controls selected through stratified random sampling from Queensland Electoral Roll	<40: 16.4% 40–69: 69.6% ≥70: 14.0%*	42.4%*	NR	N/A	4
Marashi-Pour, 2012 <sup>68</sup> Good	Australia	Retrospective cohort study	52,330	Cases of cutaneous melanoma from the New South Wales Central Cancer Registry diagnosed between 1988 and 2007	<40: 14% 40–69: 54% ≥70: 31	42%	1988–2007	Followup time was calculated from the date of diagnosis until death or end of the study period (December 31, 2007)	5
Pollack, 2011 <sup>65</sup> Good	U.S.	Retrospective cohort study	68,495	Cases of melanoma (excluding in situ disease) in the 13 SEER registries in persons age >15 years with no previous cancer diagnosis	<40: 19.5% 40–64: 48.9% ≥65: 31.5%	45.1%	1992–2006	First primary melanoma cases diagnosed from 1992 to 2001. Followed up through 2006.	5

**Table 1. Description of Included Studies for KQs 1–5**

Author, Year Quality	Country	Study Design	N	Population	Mean Age, Years (SD or Range) or Category	% Female	Dates of Data Collection	Length of Followup	KQ
Reyes-Ortiz, 2006 <sup>63</sup> Fair	U.S.	Retrospective cohort study	23,068	23,068 Medicare beneficiaries age ≥65 years residing in 1 of 11 SEER regions, diagnosed with melanoma between 1988 and 1999, and ethnicity information complete	<39: 0% 40–64: 0% ≥65: 100%	40.0%	1988–1999	Survival defined as the period between diagnosis and death from melanoma. Censored at death from other causes or December 31, 2000. Followup through December 31, 2000.	5
Leiter, 2004 <sup>70</sup> Fair	Germany	Retrospective cohort study	12,728	Persons with thin incident primary invasive melanoma between 1976 and 2000 in the German-based Central Malignant Melanoma Registry	50 (15.7)	58.6%	1976–2000	Data obtained from the Central Malignant Melanoma registry. Patients were examined every 3 to 6 months for 10 years. All included patients had a followup time of at least 3 months and at most 10 years.	5
Luke, 2003 <sup>67</sup> Fair	Australia	Retrospective cohort study	9,519	Residents of the state of South Australia diagnosed with invasive cutaneous melanoma	<39: 21% 40–69: 53% ≥70: 26%	49.9%	1980–2000	1994 to 2000 diagnostic period identified through cancer registry; dates censored at death from other causes or December 31, 2000	5
Zell, 2008 <sup>64</sup> Good	U.S.	Retrospective cohort study	39,049	Incident patient cases of cutaneous melanoma reported between 1993 and 2003 in the California Cancer Registry <sup>†</sup>	58 <sup>†</sup> (95% CI, 29.0 to 84.0)	43.1%	1993–2003	Hospital registrars contacted cases annually and Registry staff annually reviewed death certificates. The last date of followup was either date of death or the last date of contact.	5
Owen, 2001 <sup>66</sup> Fair	U.S.	Retrospective cohort study	4,560	Registered patients at the Duke University Melanoma Clinic who began treatment within 3 months before or after excision of a primary melanoma (in situ excluded)	48.3 (14.2) <sup>§</sup>	45.5%	1970–1995	Patients registered at Duke University Melanoma clinic between January 1, 1970 and December 31, 1995. Followup was limited to 10 years by censoring all observations for patients still alive at 10 years after surgery (also death from other causes and LTFU resulted in censoring).	5

**Table 1. Description of Included Studies for KQs 1–5**

Author, Year Quality	Country	Study Design	N	Population	Mean Age, Years (SD or Range) or Category	% Female	Dates of Data Collection	Length of Followup	KQ
Green 2012 <sup>69</sup> Fair	Australia	Retrospective cohort study	26,736	Queensland residents with a single thin invasive melanoma ( $\leq 1.00$ mm) diagnosed between 1982 and 2006	52.7 (range, 15 to 89)	46.4%	1982–2006	Minimum 1 year followup (survival assessed up to December 31, 2007). Average length of followup NR.	5

Numbers in italics represent calculated numbers.

\*These data refer to control participants only.

†California Cancer Registry is part of SEER.

‡Median age.

§Mean age at surgery.

**Abbreviations:** SD = standard deviation; KQ = key question; NR = not reported, N/A = not applicable; SEER = Surveillance, Epidemiology, and End Results Program; LTFU = lost to followup.

**Table 2. Description of Screening Interventions of Included Studies (KQs 1–4)**

Author, Year Quality Location	Target Population	N	% Female Mean Age (SD)	Skin Cancer Risk Factors	Provider	Setting and Skin Cancer Screening Program	Followup of Identified Lesions
Katalinic, 2012 <sup>53</sup> Fair (KQ 1)  Waldmann, 2012 <sup>58</sup> Fair (KQs 1, 2)  Breitbart, 2012 <sup>55</sup> Good (KQs 1, 2)  SCREEN study Germany	Residents of Schleswig- Holstein, Germany 1998– 2009	360,288	73.6% 49.7 (16.2)	NR; among people with referral to dermatology, report of skin conditions included: Multiple melanocytic nevi: 9.8% Clinically atypical nevi: 9.0% UV-damaged skin: 4.8% Actinic keratosis: 2.1%	Nondermatologists and dermatologists	1. Physician education (training of 64.0% nondermatologists and 98.3% dermatologists who practice in this region) 2. Public awareness campaign 3. Whole-body skin exam conducted by nondermatologist and dermatologists	Referred to dermatologist
Gambichler, 2000 <sup>59</sup> Fair (KQ 2)  Germany	Patients undergoing shave excision biopsy for suspicion of NMSC	45	51.1% 32 (15–54)	NR	Dermatologists	Routine outpatient skin cancer screening (not further specified) followed by razor blade shave excision	Assessed by physician after 6 months
Aitken, 2006 <sup>56</sup> Fair (KQ 3)  Australia	9 intervention communities All primary care patients (adult)	16,383	51.5% 46.5 (16.4)	≥1 risk factor*: 47.7%	Primary care physicians	1. Physician education 2. Community education program 3. Free access to screening clinics for whole-body skin exam, excluding areas covered by underwear	Referred to personal primary care physician; those not completing referral sent a reminder at 2 and 5 months
Fritschi, 2006 <sup>57</sup> Fair (KQ 3)  Australia	Residents in rural and suburban locations, Western Australia	7,436	56.0% <40: 26.2% 40–59: 46.2% ≥60: 27.6%	0–2 risk factors†: 37.7% 3–5: 55.8% 6–8: 6.6%	Dermatologists and plastic surgeons	1. Earned media providing education on 8 risk factors and number to call for appointment 2. Mobile clinic staffed by physician volunteers 3. Whole-body skin exam	Referred to primary care physician. Cancer outcomes were ascertained from national cancer registry as gold standard.

\*Fair skin, a tendency to burn after 1 hour of sun exposure, or >10 moles on the body.

†Risk factors included: family history of melanoma; ≥5 moles on the forearms; previous removal of benign nevi; previous skin cancer; a lesion that is changing in size, color, or shape; a lesion that does not heal; fair skin that burns rather than tans; and episodes of severe sunburn as a child.

**Abbreviations:** KQ = key question; SD = standard deviation; NR = not reported; UV = ultraviolet; NMSC = nonmelanoma skin cancer.



**Table 3. Melanoma Mortality Associated With Visual Skin Cancer Screening (KQ 1)**

Katalinic, 2012 <sup>53</sup>	Total Population 2009 (Millions)	Prescreening (1998–1999) Melanoma Deaths (n)	Prescreening (1998–1999) WASR (95% CI)	Screening Program (2003–2004) Melanoma Deaths (n)	Screening Program (2003–2004) WASR (95% CI)	Postscreening (2008–2009) Melanoma Deaths (n)	Postscreening (2008–2009) WASR (95% CI)	Absolute Change in WASR From 1998–1999 to 2008–2009	% Change in Mortality Rate 1998–1999 to 2008–2009
<b>Intervention region</b>									
Schleswig-Holstein (360,288 persons screened)	2.83	86	1.7 (1.4–2.0)	82	1.4 (1.2–1.6)	50	0.9 (0.7–1.1)	-0.8	-48%
<b>Comparison regions</b>									
South: Hamburg	1.78	41	1.2 (0.9–1.5)	52	1.5 (1.2–1.8)	46	1.2 (1.0–1.5)	0	+2%
West: Lower-Saxony	7.94	224	1.4 (1.3–1.6)	239	1.5 (1.3–1.6)	253	1.5 (1.4–1.7)	+0.1	+7%
East: Mecklenburg-Vorpommern	1.66	32	1.0 (0.8–1.3)	43	1.3 (1.0–1.6)	50	1.3 (1.0–1.6)	+0.3	+32%
North: Denmark	5.53	203	2.3 (2.0–2.5)	221	2.3 (2.0–2.5)	252	2.5 (2.2–2.7)	+0.2	+4%
Germany*	79.1	1,940	1.3 (1.3–1.4)	2,213	1.4 (1.3–1.4)	2,529	1.4 (1.4–1.5)	+0.1	+10%

\*Excludes Schleswig-Holstein region.

**Abbreviations:** KQ = key question; CI = confidence interval; WASR = world age-standardized mortality rate (per 100,000).

**Table 4. Number of Excisions Needed to Detect One Case of Melanoma or Squamous Cell or Basal Cell Carcinoma (KQ 2)**

<b>Number of Excisions Needed to Detect 1 Case</b>	<b>Melanoma</b>	<b>Squamous Cell Carcinoma</b>	<b>Basal Cell Carcinoma</b>
Waldmann, 2012 <sup>58</sup> Fair Germany			
<b>Overall</b>	<b>28</b>	<b>41</b>	<b>9</b>
<b>Female</b>			
Age, years			
20–34	41	N/A	138
35–49	30	579	34
50–64	24	72	8
≥65	22	14	4
<b>Total</b>	<b>28</b>	<b>56</b>	<b>10</b>
<b>Male</b>			
Age, years			
20–34	52	926	116
35–49	55	435	35
50–64	22	48	7
≥65	20	12	4
<b>Total</b>	<b>28</b>	<b>28</b>	<b>7</b>

**Abbreviations:** KQ = key question,; N/A = not applicable.

**Table 5. Measured Cosmetic Harms From Participating in Screening and Diagnostic Workup (KQ 2)**

<b>Study</b>	<b>N</b>	<b>Procedure and Provider Type</b>	<b>Harms Assessment</b>	<b>Reported Harms</b>
Gambichler, 2000 <sup>59</sup> Fair Germany	45 patients who had been identified by skin cancer screening with 77 nevi and received biopsy	Deep shave excision with razor blade biopsy	Assessed by physician* and patient on a 4-point scale 6 months after excision (1=excellent, 4=poor)	Physician-reported poor: 16.1% (mean score, 2.5) Patient-reported poor: 7.1% (mean score, 1.7)

\*Cosmetic harms defined as: erythema, hyperpigmentation, hypopigmentation, hypertrophic scarring, and hypotrophic scarring.

**Abbreviation:** KQ = key question.

**Table 6. Diagnostic Accuracy of Primary Care Providers and Dermatologists for Diagnosing Melanoma Through Visual Skin Examination (KQ 3)**

Study, Year Quality	Who Performed Screening?	Comparison/Gold Standard	Followup	Sensitivity (95% CI)*	Specificity (95% CI)*	Recall Rate†	PPV (95% CI)*‡	Cancer Detection Rate	Cancer Rate
Fritschi, 2006 <sup>57</sup> Fair Australia	Volunteer dermatologists or plastic surgeons	Cancer diagnosis in regional cancer registry within 2 years of screening	12 months melanoma	69.7% (51.3 to 84.4)	97.6% (97.2 to 97.9)	2.7%	11.4 (7.4 to 16.7)	0.3%	0.4%
			24 months melanoma	49.0% (34.4 to 63.7)	97.6% (97.2 to 97.9)	2.7%	11.9 (7.8 to 17.2)	0.3%	0.7%
Aitken, 2006 <sup>56</sup> Fair Australia	Primary care physicians	For positive screen: pathology and biopsy reports  Estimated the number of false-negatives based on prior literature <sup>60</sup> and Queensland melanoma incidence rates	36 months melanoma only	40.2%	86.1% (85.6 to 86.6)	14.1%	1.4%	0.2%	0.5%
			36 months any skin cancer	<i>Cannot be calculated</i>	<i>Cannot be calculated</i>	14.1%	16.9%	2.4%	<i>Cannot be calculated</i>

Values that are italicized were calculated using available data from the study results.

\*Confidence intervals reported for measures calculated by study authors.

†Recall rate = the number of skin examinations that resulted in a recommendation for followup with a dermatologist divided by the number of screened individuals; the recall rate is the same regardless whether followup is 1 or 2 years.

‡Skin cancer diagnosis among those recalled for further examination.

**Abbreviations:** KQ = key question; CI = confidence interval; PPV = positive predictive value.

**Table 7. Association Between Physician Clinical Skin Examination and Lesion Thickness at Melanoma Detection (KQ 4)**

Study	Total N	Study Population	Exposure	Main Analysis and Adjusted Confounders	Main Result OR (95% CI)
Aitken, 2010 <sup>61</sup> Fair Queensland, Australia	Controls: 3,824 Cases: 3,762	Controls: Randomly selected from Queensland Electoral Roll, based on 5-year groups and sex distribution of cases Cases: Men and women ages 20 to 75 years with histologically confirmed primary melanoma diagnosed between January 2000 and December 2003	During the last 3 years before (you first believed something was wrong [cases]/reference date [controls]), had a doctor deliberately checked all or nearly all of your whole body for early signs of skin cancer?	Logistic regression adjusted for age group, sex, education, employment status, marital status, eye color, hair color, skin color, degree of freckling, number of moles on back, age of arrival in Australia, average lifetime sun exposure, family history of melanoma, family history of nonmelanoma skin cancer, and ethnicity	Controls: Referent  Lesion thickness (mm) ≤0.75: 1.38 (1.22–1.56) >0.75: 0.86 (0.75–0.98)  Stratification of thicker lesions 0.76–1.49: 0.93 (0.79–1.10) 1.50–2.99: 0.83 (0.66–1.05) ≥3.00: 0.60 (0.43–0.83)

**Abbreviations:** KQ = key question; OR = odds ratio; CI = confidence interval.

**Table 8. Association Between Stage at Melanoma Diagnosis and Melanoma-Related Mortality (KQ 5)**

Study, Year Quality Country	N	% Female Age (Years)	Stage Distribution	Melanoma Deaths (n)	Primary Analysis	Confounders for Adjustment	Melanoma-Related Mortality Adjusted HR (95% CI)
Pollack, 2011 <sup>65</sup> Good U.S. (13 SEER regions)  1992–2006	68,495	45.1% female  <40: (19.5%) 40–64: (48.9%) ≥65: (31.5%)	Localized: 82.5% Regional: 10.8% Distant: 3.3% Unstaged: 3.5%	NR	Cox regression restricted to 5- year followup after diagnosis	Stratified on histologic subtype and anatomic site and adjusted for sex, age at diagnosis, race/ethnicity, stage, and depth.	Localized: Referent Regional: 3.62 (3.35–3.91) Distant: 18.66 (16.54–21.06)
Zell, 2008 <sup>64</sup> Good U.S. (California)  1993–2003	39,049	43.1% female  Median age: 58 (95% CI, 29.0– 84.0)	Stage IA: 58.7% IB: 21.0% IIA: 8.6% IIB: 5.0% IIC: 1.2% IIIB: 13.1% IIIC: 1.7% IV: 0.7%	2,842	Cox proportional hazards	Age, sex, race/ethnicity, AJCC stage, histologic subtype, anatomic tumor site, tumor ulceration, SES quintile, radiation therapy, chemotherapy, and immunotherapy.	I: Referent II: 4.96 (4.51–5.56) III: 9.99 (8.84–11.29) IV: 27.1 (22.4–32.8)
Reyes-Ortiz, 2006 <sup>63</sup> Fair U.S. (11 SEER regions)  1988–2000	23,068	40.0% female  <39: 0 (0%) 40–64: 0 (0%) ≥65: (100%)	In situ: 32.8% Localized: 45.7% Regional: 8.5% Distant: 3.0% Unknown: 10.0%	NR	Kaplan-Meier product limit Cox proportional hazards	Census tract median income, race/ethnicity, age, sex, marital status, years of diagnosis (1988– 1993, 1994–1999), stage, tumor thickness, histology, site, and comorbidity (Charlson score of 0, 1, or 2+)	In situ: Referent Localized: 8.83 (6.0–12.9) Regional: 23.2 (15.7–34.3) Distant: 94.0 (63.3–139.5) Unknown: 19.1(13.1–27.8)

**Abbreviations:** KQ = key question; HR = hazard ratio; CI = confidence interval; SEER = Surveillance, Epidemiology, and End Results Program; NR = not reported; AJCC = American Joint Committee on Cancer; SES = socioeconomic status.

**Table 9. Association Between Breslow Lesion Thickness of Melanoma at Diagnosis and Melanoma Mortality (KQ 5)**

Study, Year Quality Country	N	% Female Age	Distribution of Breslow Thickness (mm) at Detection	Melanoma Deaths (n)	Primary Analysis	Confounders for Adjustment	Melanoma-Related Mortality Adjusted HR* (95% CI)
Marashi-Pour, 2012 <sup>68</sup> Good Australia 1988–2007	52,330	42% female  <40: 7,813 (15%) 40–69: 28,132 (54%) ≥70: 16,374 (31%) Missing: 11 (0%)	≤1: 61% 1.01–2: 16% 2.01–4: 10% ≥4.01: 6% Missing: 7%	5,291 melanoma deaths (13,581 from all causes)	Fine and Gray competing risk regression with backward modeling	Sex, age at diagnosis, histological type, body site, year and season of diagnosis, tumor thickness, and degree of spread at diagnosis	≤1.0 mm: Referent 1.01–2.0 mm: 4.13 (3.74–4.56) 2.01–4.0 mm: 6.88 (6.18–7.65) ≥4.01 mm: 9.52 (8.42–10.77) Missing: 6.37 (5.57–7.29)
Green, 2012 <sup>69</sup> Fair Australia 1982–2006	26,736	46.4% female  Mean age: 52.7	<0.25: 2,372 (8.9%) 0.25–0.49: 11,552 (43.2%) 0.50–0.74: 8,366 (31.3%) 0.75–1.00: 4,446 (16.6%)	Total: 592 <0.25: 24 (4.1%) 0.25–0.49: 127 (21.5%) 0.50–0.74: 174 (29.4%) 0.75–1.00: 267 (45.1%)	Multivariate Cox proportional hazard models	Year, sex, time after diagnosis, sex*time after diagnosis (interaction), age group, site, level, morphology	<0.25 mm: Referent 0.25–0.49 mm: 1.14 (0.7–1.7) 0.50–0.74 mm: 1.84 (1.2–2.9) 0.75–1.00 mm: 4.33 (2.8–6.8)
Pollack, 2011 <sup>65</sup> Good U.S. (13 SEER regions) 1992–2006	68,495	45.1% female  <40: 19.5% 40–64: 48.9% ≥65y: 31.5%	0.01–1.00: 59.8% 1.01–2.00: 13.9% 2.01–4.00: 7.6% >4: 4.3% Unknown: 13.7% No tumor found: 0.7%	NR	Cox regression restricted to 5- year followup. 56,886 cases of 68,495 in multivariate analyses (missing data)	Stratified on histologic subtype and anatomic site. Adjusted for sex, age at diagnosis, race/ethnicity, stage, and depth	≤1.0 mm: Referent 1.01–2.0 mm: 2.89 (2.62–3.18) 2.01–4.0 mm: 4.69 (4.24–5.02) >4.0 mm: 5.71 (5.10–6.39) No tumor found: 3.03 (1.98– 4.64)
Reyes-Ortiz, 2006 <sup>63</sup> Fair U.S. (11 SEER regions) 1988–1999 to 2000	23,068	40% female  <39: 0 (0%) 40–64: 0 (0%) ≥65: 23,068 (100%)	<1.00: 30.7% 1.01–2.00: 8.8% 2.01–4.00: 6.6% >4.00: 3.9% Unknown: 50.0%	NR	Kaplan-Meier product limit Cox proportional hazards	Census tract median income, race/ethnicity, age, sex, marital status, years of diagnosis (1988–1993, 1994– 1999), stage, tumor thickness, histology, site, and comorbidity (Charlson score of 0, 1, or 2+)	≤1.00 mm: Referent 1.01–2.0 mm: 2.06 (1.69–2.50) 2.01–4.0 mm: 3.11 (2.57–3.76) >4.0 mm: 3.17 (2.56–3.92) Unknown: 2.05 (1.70–2.47)
Leiter, 2004 <sup>70</sup> Fair Germany 1976–2000	12,728	59% female  Mean age: 50 (SD, 15.7)	≤0.25: 8.4% 0.26–0.50: 36.3% 0.51–0.75: 29.7% 0.76–1.00: 25.6%	162	Multivariate Cox proportional hazard models	Adjusted by age, sex, Breslow tumor thickness, Clark level of invasion, ulceration, regression, histologic subtypes, and body sites	≤0.50 mm: Referent 0.51–0.75 mm: 1.9 (1.2–2.9) 0.76–1.00 mm: 3.9 (2.6–5.8)

**Table 9. Association Between Breslow Lesion Thickness of Melanoma at Diagnosis and Melanoma Mortality (KQ 5)**

Study, Year Quality Country	N	% Female Age	Distribution of Breslow Thickness (mm) at Detection	Melanoma Deaths (n)	Primary Analysis	Confounders for Adjustment	Melanoma-Related Mortality Adjusted HR* (95% CI)
Luke, 2003 <sup>67†</sup> Fair Australia 1980–2000	9,519	50% female  <39: 1,999 (21%) 40–69: 5,015 (53%) ≥70: 2,505 (26%)	≤0.50: 35.1% 0.51–1.00: 31.8% 1.01–1.50: 11.1% 1.51–2.00: 5.9% 2.01–2.50: 3.9% 2.51–3.00: 2.7% 3.01–3.50: 1.9% 3.51–4.00: 1.8% 4.01–4.50: 1.9% 4.51–5.00: 1.2% 5.01–5.50: 0.5% 5.51–6.00: 0.8% ≥6.01: 1.4%	NR	Cox proportional hazard regression (relative risk of case fatality)	Diagnostic period, Breslow thickness, Clark level, body site, age at diagnosis, and sex	≤0.50 mm: Referent 0.51–1.00 mm: 2.81 (1.81–4.35) 1.01–1.50 mm: 6.18 (3.75–10.20) 1.51–2.00 mm: 8.53 (5.05–14.43) 2.01–2.50 mm: 13.89 (8.16–23.64) 2.51–3.00 mm: 15.44 (8.90–26.80) 3.01–3.50 mm: 20.74 (11.83–36.34) 3.51–4.00 mm: 27.39 (15.71–47.73) 4.01–4.50 mm: 32.62 (18.78–56.63) 4.51–5.00 mm: 21.09 (11.38–39.09) 5.01–5.50 mm: 22.1 (10.62–45.99) 5.51–6.00 mm: 33.99 (18.13–63.73) ≥6.01: 23.08 (12.70–41.95)
Owen, 2001 <sup>66</sup> Fair U.S. 1970–1995	4,560	46% female  Mean age at surgery: 48.3 (14.2)	<0.75: 10.5% 0.75–1.0: 13.2% 1.0–1.5: 26.1% 1.5–3.0: 32.8% 3.0–4.0: 7.3% >4.0: 10.0%	867	Cox proportional hazards	Age, sex, and site of primary lesion	≤0.75 mm: 0.28 (0.17–0.44) 0.75–1.0 mm: 0.55 (0.4–0.76) 1.0–1.5 mm: Referent 1.5–3.0 mm: 1.93 (1.6–2.34) 3.0–4.0 mm: 3.02 (2.37–3.86) >4.0 mm: 3.88 (3.12–4.83)

\*Leiter 2004 and Owen 2001 reported relative risks, not hazard ratios.

†Missing data n=1,103; percentages based off of n=8,416.

**Abbreviations:** KQ = key question; HR = hazard ratio; CI = confidence interval; SEER = Surveillance, Epidemiology, and End Results Program; NR = not reported; SD = standard deviation.



**Table 10. Association Between Melanoma AJCC Stage and All-Cause Mortality (KQ 5)**

Study, Year Quality Country	Dates of Data Collection	N	Age % Female	All-Cause Deaths	Primary Analysis	Adjustment Variables	All-Cause Mortality HR (95% CI)
Zell, 2008 <sup>64</sup> Good California, U.S.	1993–2003	39,049	Median: 58 years (95% CI, 29.0–84.0) 43.1%	6,706	Cox proportional hazard ratio	Age, sex, race/ethnicity, AJCC stage, histologic subtype, anatomic tumor site, surgery stage, SES quintile, radiation therapy, chemotherapy, and immunotherapy	I: Referent II: HR, 2.26 (95% CI, 2.14–2.39) III: HR, 4.27 (95% CI, 3.9–4.67) IV: HR, 10.39 (95% CI, 8.96–12.0)

**Abbreviations:** AJCC = American Joint Committee on Cancer; KQ = key question; HR = hazard ratio; CI = confidence interval; SES = socioeconomic status.

**Table 11. Summary of Evidence**

Key Question	Population	No. of Studies (k), No. of Observations (n)	Design	Major Limitations	Consistency	Applicability	Overall Quality	Summary of Findings
KQ 1. What is the direct evidence that visual screening for skin cancer by a primary care provider or dermatologist reduces skin cancer morbidity and mortality and all-cause mortality?	Residents of Schleswig-Holstein Germany age ≥20 years with whole-body skin cancer screening exam between July 2003 and June 2004	k=1 study (3 articles) n=360,288	Ecologic (1)	In the main study, an ecologic study design permitted only population-level analysis of mortality rates compared to those in the surrounding areas, not individual-level data. 2 related publications using observational designs described skin cancer incidence after the screening program and participation in the program. The physician screening component was part of a multimodal screening program involving physician education, dermatologist referral for screen-detected lesions, public outreach, and access to physician review of patient-identified suspicious lesions.	N/A (1 study included)	The screening program made considerable efforts to be truly population-based and screen the entire adult population in the study area. However, the screened population (19% of total) had a high proportion of younger women screened, who are at low risk for melanoma.	Fair	In the SCREEN study in Germany, melanoma mortality decreased 48% from 1.7 to 0.9 melanoma deaths per 100,000 persons 5 years after the screening program. Absolute reduction was 0.8 melanoma deaths per 100,000 persons. There were no mortality reductions in the surrounding geographic areas.

**Table 11. Summary of Evidence**

Key Question	Population	No. of Studies (k), No. of Observations (n)	Design	Major Limitations	Consistency	Applicability	Overall Quality	Summary of Findings
KQ 2. What are the harms of screening for skin cancer and diagnostic followup?	Routine skin cancer screening outpatients in Germany	k=2 (3 articles) n=360,333	Cohort (1), Case series (1)	Data from the SCREEN study presented the false-positive rates and number of excisions needed to detect 1 melanoma during the screening program. Overdiagnosis could not be assessed directly. A small study of 45 people assessed the acceptability of cosmetic scars from shave biopsy for suspected NMSC, which is not the major approach to melanomas.	Low (different harms assessed in each study and 1 per outcome)	The SCREEN data suggest potential for very high number of false-positives that could be relevant to other screening programs. Patient-reported data on cosmetic harms is important.	Fair	The number of excisions needed to detect 1 skin cancer varied by age and sex. Fewer excisions were needed to detect a single case in older adults and in men. After shave biopsy for removal of potential NMSC detected through cancer screening, 7% of patients viewed their scar outcomes poorly at 6 months after biopsy
KQ 3. What are the test characteristics of visual screening for skin cancer when performed by primary care providers versus dermatologists?	Australian residents who either participated in a community-based pilot randomized, clinical trial of skin screening program or attended Lions Cancer Institute weekend mobile screening clinics in rural and suburban locations in Western Australia	k=2 (2 articles) n=23,819	Cohort (2)	An Australian cohort study assessed performance of dermatologists in a mobile screening program. An unrelated cohort study, also Australian, assessed performance of primary care providers. Missed cancers were detected through registry and medical record linkages, but ascertainment bias is likely due to differential followup time periods.	Low (followup times prohibit direct comparison of studies)	These results may not apply to U.S. settings.	Fair	Sensitivity for melanoma detection was 40.2% at 36 months for primary care providers and 49.0% at 24 months for dermatologists. Specificity was 86.1% at 36 months for primary care providers and 97.6% at 24 months for dermatologists. Recall rate was 14.1% for primary care and 2.7% for dermatologists. Melanoma detection rates were <1% in both studies.

**Table 11. Summary of Evidence**

Key Question	Population	No. of Studies (k), No. of Observations (n)	Design	Major Limitations	Consistency	Applicability	Overall Quality	Summary of Findings
KQ 4. Does visual screening for skin cancer lead to earlier detection of skin cancer compared to usual care?	Queensland residents ages 20 to 75 years; cases identified from cancer registry and controls selected through stratified random sampling from Queensland Electoral Roll	k=1 (1 article) n=7,586	Case control (1)	1 Australian case-control study compared receipt of physician whole-body skin exam in the previous 3 years and the association of melanoma thickness (in cases) with physician skin exam. Potential for recall bias.	N/A (1 study included)	The ability of physician skin exam to detect lesions earlier than through usual care or self-identification is important to establishing an effect of physician screening in the context of multimodal skin cancer early detection programs.	Fair	28.3% of controls reported receiving a clinical skin exam in the previous 3 years compared to 35.3% of melanoma cases. Cases with thin melanoma lesions ( $\leq 0.75$ mm) had 38% higher odds of clinical skin exam than controls. Cases with thicker lesions ( $> 0.75$ mm) had 14% reduced odds of recent physician skin exam compared to controls.
KQ 5. What is the association between earlier detection of skin cancer and skin cancer morbidity and mortality and all-cause mortality?	Cases of melanoma identified through registries in Australia, Germany, and the U.S.	k=8 (8 articles) n= 236,485	Cohort (8)	3 good- and 5 fair-quality observational studies included $> 200,000$ persons with melanoma in the U.S., Germany, and Australia. The studies examined the association between melanoma-specific mortality and lesion thickness or stage at diagnosis. 1 of the good-quality studies also assessed all-cause mortality and stage at diagnosis.	High	The association of melanoma or all-cause mortality with earlier stage or lesion thickness at detection is relevant to screening programs.	Good	All studies demonstrated a consistent linear increase in risk of melanoma mortality with increasing tumor thickness or stage. Tumor thickness $> 4.0$ mm was associated with a 3.1- to 32.6-fold increased risk of melanoma mortality compared to thinner lesions in multivariate-adjusted models.

**Abbreviations:** KQ = key question; N/A = not applicable; SCREEN = Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany; NMSC = nonmelanoma skin cancer.

## Appendix A. Detailed Methods

### Search Strategy

Sources Searched
MEDLINE
PUBMED
Cochrane Central Register of Controlled Clinical Trials

Key:

/ = MeSH subject heading

\$ = truncation

\* = truncation

? = wildcard

ab = word in abstract

ae = adverse effects

adj# = adjacent within x number of words

near/# = adjacent within x number of words

kw = keyword

mo = mortality

su = surgery

ti = word in title

### Cochrane Central Register of Controlled Clinical Trials

- #1 (skin or derm\* or cutaneous or epithelial or epithelium or epiderm\*):ti,ab,kw near/3 (cancer\* or neoplasm\* or carcinoma\* or tumor\* or tumour\* or malignan\* or lesion\* or metasta\* or dysplas\*):ti,ab,kw #2 melanoma\*:ti,ab,kw
- #3 (naevoid or nevoid):ti,ab,kw near/3 syndrome\*:ti,ab,kw
- #4 (dysplastic or malignant):ti,ab,kw near/2 (nevus or naevus or nevi or naevi):ti,ab,kw
- #5 "Hutchinson's Melanotic Freckle":ti,ab,kw
- #6 "lentigo maligna":ti,ab,kw
- #7 basal:ti,ab,kw next cell:ti,ab,kw next (carcinoma\* or neoplasm\* or carcinoma\* or tumor\* or tumour\* or malignan\* or lesion\* or metasta\* or epithelioma\*):ti,ab,kw
- #8 (basocellular\* or basosquamous):ti,ab,kw next carcinoma\*:ti,ab,kw
- #9 squamous:ti,ab,kw next cell:ti,ab,kw next (carcinoma\* or neoplasm\* or carcinoma\* or tumor\* or tumour\* or malignan\* or lesion\* or metasta\* or epithelioma\*):ti,ab,kw
- #10 merkel:ti,ab,kw next cell:ti,ab,kw next (carcinoma\* or neoplasm\* or carcinoma\* or tumor\* or tumour\* or malignan\* or lesion\* or metasta\* or epithelioma\*):ti,ab,kw
- #11 "actinic keratosis":ti,ab,kw
- #12 bowen\*:ti,ab,kw next disease:ti,ab,kw
- #13 cutaneous:ti,ab,kw near/2 lymphoma\*:ti,ab,kw
- #14 {or, #1-#13}
- #15 screen\*:ti,ab,kw
- #16 (skin or body or physical):ti,ab,kw near/3 (exam\* or inspect\*):ti,ab,kw
- #17 (dermoscop\* or dermatoscop\*):ti,ab,kw
- #18 visual\*:ti,ab,kw next inspect\*:ti,ab,kw
- #19 photography:ti,ab,kw
- #20 {or #15-#19}
- #21 #14 and #20 Publication Year from 1995 to 2015, in Trials
- #22 (biopsy\* or biopsies or biopsied):ti,ab,kw
- #23 (excise\* or excision\*):ti,ab,kw

## Appendix A. Detailed Methods

- #24 rebiops\*:ti,ab,kw
- #25 #22 or #23 or #24
- #26 (harm or harms or harmful or harmed):ti,ab,kw
- #27 (death or deaths):ti,ab,kw
- #28 (adverse or negative or unintended):ti,ab,kw next (effect\* or event\* or outcome\* or reaction\*):ti,ab,kw
- #29 complication\*:ti,ab,kw
- #30 side:ti,ab,kw next effect\*:ti,ab,kw
- #31 safety:ti,ab,kw
- #32 false:ti,ab,kw next negative\*:ti,ab,kw
- #33 misdiagnos\*:ti,ab,kw
- #34 overdiagnos\*:ti,ab,kw
- #35 (unneeded or unnecessary):ti,ab,kw near/5 (treat\* or therap\* or surg\* or procedure\*):ti,ab,kw
- #36 label\*:ti,ab,kw
- #37 psychological:ti,ab,kw next effect\*:ti,ab,kw
- #38 (cicatrix or scar\*):ti,ab,kw
- #39 {or #26-#38}
- #40 #14 and #25 and #39 Publication Year from 1995 to 2015, in Trials
- #41 (detect\* or diagnos\* or biops\*):ti,ab,kw near/5 stage:ti,ab,kw
- #42 (late\* or distant or advanced or end):ti,ab,kw next stage:ti,ab,kw
- #43 (early or earlier):ti,ab,kw next (diagnos\* or detect\* or discovery or findings):ti,ab,kw
- #44 #41 or #42 or #43
- #45 #14 and #44 Publication Year from 1995 to 2015, in Trials
- #46 (surger\* or surgical):ti
- #47 curettage:ti,ab,kw
- #48 dessicat\*:ti,ab,kw
- #49 electrodessicat\*:ti,ab,kw
- #50 cryosurg\*:ti,ab,kw
- #51 "laser ablation":ti,ab,kw
- #52 mohs:ti,ab,kw
- #53 metastasectom\*:ti,ab,kw
- #54 lymphadenectom\*:ti,ab,kw
- #55 ("lymph node" or "lymph nodes" or lymphoid):ti,ab,kw near/3 (remov\* or dissect\* or resect\*):ti,ab,kw
- #56 {or #46-#55}
- #57 (lymphedema or lymphoedema):ti,ab,kw
- #58 (surg\* or postsurg\* or post-surg\*):ti,ab,kw near/2 infect\*:ti,ab,kw
- #59 {or #26-#31, #38, #57-#58}
- #60 #14 and #56 and #59 Publication Year from 1995 to 2015, in Trials 1
- #61 #21 or #40 or #45 or #60

### MEDLINE search strategy

Database: Ovid MEDLINE(R) <1946 to July Week 3 2015>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <June 1, 2015>, Ovid MEDLINE(R) Daily Update <June 1, 2015>

Search Strategy:

- 
- 1 Skin Neoplasms/
  - 2 Melanoma/

## Appendix A. Detailed Methods

- 3 Melanoma, Amelanotic/
- 4 Nevus/
- 5 Dysplastic Nevus Syndrome/
- 6 Hutchinson's Melanotic Freckle/
- 7 Carcinoma, Basal Cell/
- 8 Carcinoma, Squamous Cell/
- 9 Carcinoma, Merkel Cell/
- 10 Neoplasms, Basal Cell/
- 11 Neoplasms, Squamous Cell/
- 12 "Neoplasms, Adnexal and Skin Appendage"/
- 13 Actinic keratosis/
- 14 Bowen disease/
- 15 Lymphoma, T-Cell, Cutaneous/
- 16 ((skin or derm\$ or cutaneous or epithelial or epithelium or epiderm\$) adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or dysplas\$)).ti.
- 17 melanoma\$.ti.
- 18 ((naevoid or nevoid) adj3 syndrome\$).ti.
- 19 ((dysplastic or malignant) adj2 (nevus or naevus or nevi or naevi)).ti.
- 20 Hutchinson\$ Melanotic Freckle.ti.
- 21 lentigo maligna.ti.
- 22 (basal cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti.
- 23 ((basocellular\$ or basosquamous) adj carcinoma\$).ti.
- 24 (squamous cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti.
- 25 (merkel cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti.
- 26 actinic keratosis.ti.
- 27 bowen\$ disease.ti.
- 28 (cutaneous adj2 lymphoma\$).ti.
- 29 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
- 30 ((skin or derm\$ or cutaneous or epithelial or epithelium or epiderm\$) adj3 (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or dysplas\$)).ti,ab.
- 31 melanoma\$.ti,ab.
- 32 ((naevoid or nevoid) adj3 syndrome\$).ti,ab.
- 33 ((dysplastic or malignant) adj2 (nevus or naevus or nevi or naevi)).ti,ab.
- 34 Hutchinson\$ Melanotic Freckle.ti,ab.
- 35 lentigo maligna.ti,ab.
- 36 (basal cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti,ab.
- 37 ((basocellular\$ or basosquamous) adj carcinoma\$).ti,ab.
- 38 (squamous cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti,ab.
- 39 (merkel cell adj (cancer\$ or neoplas\$ or carcinoma\$ or tumo?r\$ or malignan\$ or lesion\$ or metasta\$ or epithelioma\$)).ti,ab.
- 40 actinic keratosis.ti,ab.
- 41 bowen\$ disease.ti,ab.

## Appendix A. Detailed Methods

42 (cutaneous adj2 lymphoma\$.ti,ab.  
43 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42  
44 limit 43 to ("in data review" or in process or "pubmed not medline")  
45 29 or 44  
46 Mass screening/  
47 Early detection of Cancer/  
48 (screen\$ or detect\$.ti,ab.  
49 46 or 47 or 48  
50 Physical Examination/  
51 Dermoscopy/  
52 Photography/  
53 ((skin or body or physical) adj3 (exam\$ or inspect\$)).ti,ab.  
54 visual\$ inspect\$.ti,ab.  
55 dermoscop\$.ti,ab.  
56 dermatoscop\$.ti,ab.  
57 photography.ti,ab.  
58 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57  
59 45 and 49 and 58  
60 screen\$.ti.  
61 45 and 60  
62 59 or 61  
63 limit 62 to (english language and yr="1995 -Current")  
64 remove duplicates from 63  
65 Biopsy/  
66 Biopsy, Needle/  
67 Biopsy, Large-Core Needle/  
68 Sentinel Lymph Node Biopsy/  
69 (biopsy\$ or biopsies or biopsied).ti,ab.  
70 (excise\* or excision\$.ti,ab.  
71 rebiopsy.ti,ab.  
72 65 or 66 or 67 or 68 or 69 or 70 or 71  
73 (harm or harms or harmful or harmed).ti,ab.  
74 (adverse effects or mortality).fs.  
75 Mortality/  
76 Morbidity/  
77 death/  
78 (death or deaths).ti,ab.  
79 ((adverse or negative or unintended) adj (effect\$ or event\$ or outcome\$ or reaction\$)).ti,ab.  
80 complication\$.ti,ab.  
81 side effect\$.ti,ab.  
82 safety.ti,ab.  
83 false negative\$.ti,ab.  
84 misdiagnos\$.ti,ab.  
85 overdiagnos\$.ti,ab.  
86 ((unneeded or unnecessary) adj5 (treat\$ or therap\$ or surg\$ or procedure\$)).ti,ab.  
87 label\$.ti,ab.  
88 psychological effect\$.ti,ab.  
89 Cicatrix/



## Appendix A. Detailed Methods

- 90 (cicatrix or scar\$.ti,ab.
- 91 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90
- 92 45 and 72 and 91
- 93 limit 92 to (english language and yr="1995 -Current")
- 94 remove duplicates from 93
- 95 Neoplasm Staging/
- 96 ((detect\$ or diagnos\$ or biops\$) adj5 stage).ti,ab.
- 97 ((late\$ or distant or advanced or end) adj stage).ti,ab.
- 98 ((early or earlier) adj (diagnos\$ or detect\$ or discovery or findings)).ti,ab.
- 99 95 or 96 or 97 or 98
- 100 Registries/
- 101 Survival Analysis/
- 102 SEER program/
- 103 Morbidity/
- 104 Mortality/
- 105 Death/
- 106 mo.fs.
- 107 (registr\$ or register\$.ti,ab.
- 108 SEER.ti,ab.
- 109 "Surveillance epidemiology and end results".ti,ab.
- 110 morbidit\$.ti,ab.
- 111 mortalit\$.ti,ab.
- 112 (death or deaths).ti,ab.
- 113 survival.ti,ab.
- 114 110 or 111 or 112 or 113
- 115 limit 114 to ("in data review" or in process or "pubmed not medline")
- 116 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 115
- 117 45 and 99 and 116
- 118 limit 117 to (english language and yr="1995 -Current")
- 119 remove duplicates from 118
- 120 Dermatologic Surgical Procedures/ ]
- 121 Curettage/
- 122 Dessication/
- 123 Cryosurgery/
- 124 Laser Therapy/
- 125 Mohs Surgery/
- 126 Lymph Node Excision/
- 127 (surger\$ or surgical).ti.
- 128 curettage.ti,ab.
- 129 dessicat\$.ti,ab.
- 130 electrodessicat\$.ti,ab.
- 131 cryosurg\$.ti,ab.
- 132 laser ablation.ti,ab.
- 133 mohs.ti,ab.
- 134 metastasectom\$.ti,ab.
- 135 lymphadenectom\$.ti,ab.
- 136 ((lymph node\$ or lymphoid) adj3 (remov\$ or dissect\$ or resect\$)).ti,ab.

## Appendix A. Detailed Methods

- 137 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136  
 138 limit 137 to ("in data review" or in process or "pubmed not medline")  
 139 120 or 121 or 122 or 123 or 124 or 125 or 126 or 138  
 140 45 and 139  
 141 Skin Neoplasms/su  
 142 Melanoma/su  
 143 Melanoma, Amelanotic/su  
 144 Nevus/su  
 145 Dysplastic Nevus Syndrome/su  
 146 Hutchinson's Melanotic Freckle/su  
 147 Carcinoma, Basal Cell/su  
 148 Carcinoma, Squamous Cell/su  
 149 Carcinoma, Merkel Cell/su  
 150 Neoplasms, Basal Cell/su  
 151 Neoplasms, Squamous Cell/su  
 152 "Neoplasms, Adnexal and Skin Appendage"/su  
 153 Actinic keratosis/su  
 154 Bowen disease/su  
 155 Lymphoma, T-Cell, Cutaneous/su  
 156 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155  
 157 Lymphedema/  
 158 Lymph?edema.ti,ab.  
 159 Surgical wound infection/  
 160 ((surg\$ or postsurg\$ or post-surg\$) adj2 infect\$.ti,ab.  
 161 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 89 or 90 or 157 or 158 or 159 or 160  
 162 156 and 161  
 163 limit 162 to (english language and yr="1995 -Current")  
 164 64 or 94 or 119 or 163  
 165 Animal/ not (Animal/ and Human/)  
 166 164 not 165  
 167 (oral or tongue or larynx or laryng\$ or hypolaryng\$ or oropharyng\$ or pharynx or pharyng\$ or esophag\$ or oesophag\$ or gastric or ovary or ovaries or ovarian or cervical or cervix or endometrium or endometrial or lung or breast or ocular or vulva\$ or anus or anal or mucosal).ti.  
 168 166 not 167

### PubMed search strategy [publisher-supplied references only]

Search	Query
<a href="#">#62</a>	Search (((#61) AND publisher[sb]) AND English[Language]) AND ("1995"[Date - Publication] : "3000"[Date - Publication])
<a href="#">#61</a>	Search #12 AND #60
<a href="#">#60</a>	Search #17 OR #34 OR #44 OR #59
<a href="#">#59</a>	Search #55 AND #58
<a href="#">#58</a>	Search #22 OR #23 OR #24 OR #25 OR #26 OR #32 OR #56 OR #57
<a href="#">#57</a>	Search (surg*[tiab] OR postsurg*[tiab] OR post surg*[tiab]) AND infect*[tiab]
<a href="#">#56</a>	Search lymphedema[tiab] OR lymphoedema[tiab]

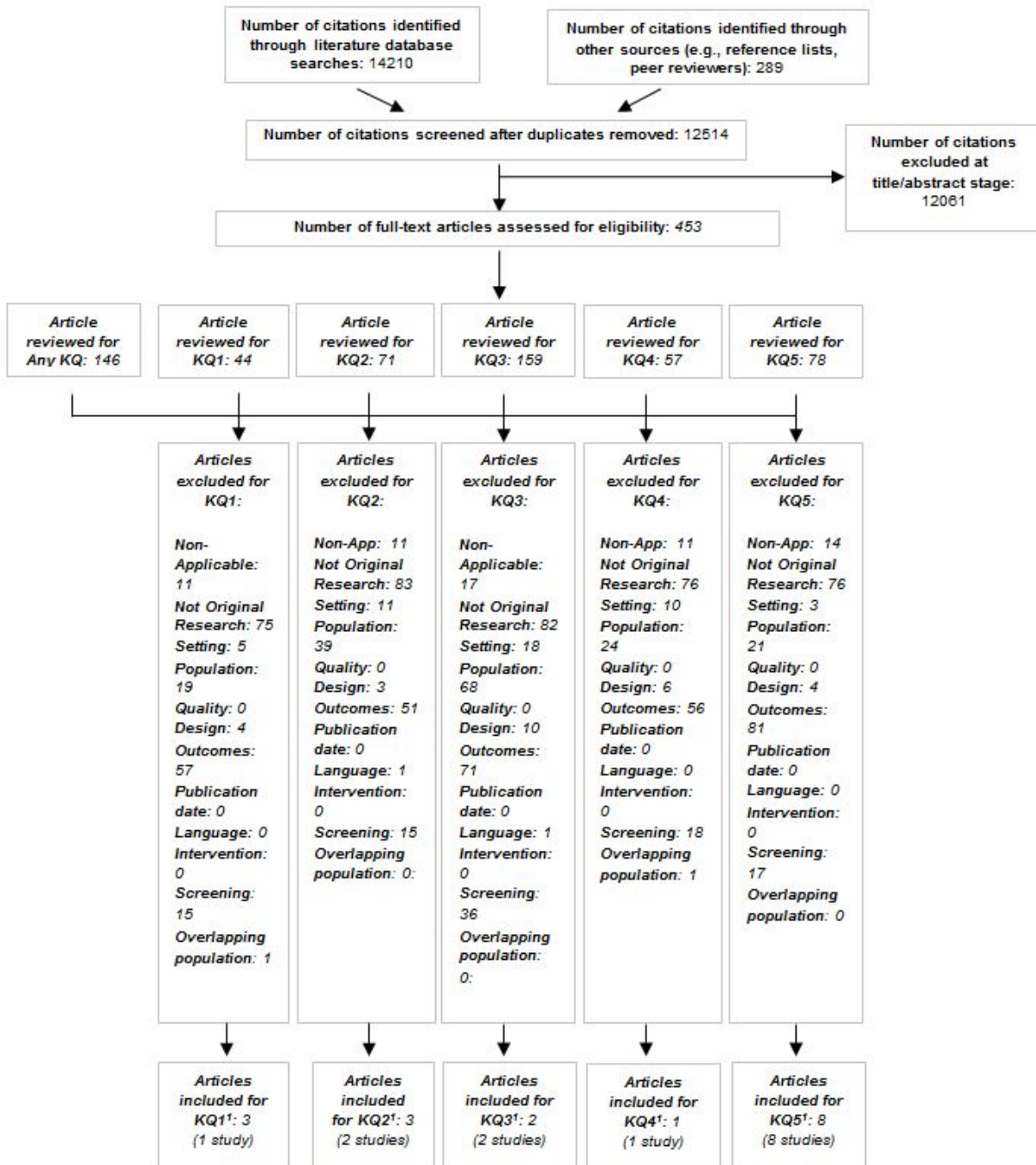
## Appendix A. Detailed Methods

Search	Query
<a href="#">#55</a>	Search #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54
<a href="#">#54</a>	Search (lymph node*[tiab] OR lymphoid[tiab]) AND (remov*[tiab] OR dissect*[tiab] OR resect*[tiab])
<a href="#">#53</a>	Search lymphadenectomy*[tiab]
<a href="#">#52</a>	Search metastasectom*[tiab]
<a href="#">#51</a>	Search mohs[tiab]
<a href="#">#50</a>	Search laser ablation[tiab]
<a href="#">#49</a>	Search cryosurg*[tiab]
<a href="#">#48</a>	Search electrodessicat*[tiab]
<a href="#">#47</a>	Search dessicat*[tiab]
<a href="#">#46</a>	Search curettage[tiab]
<a href="#">#45</a>	Search surger*[ti] OR surgical[ti]
<a href="#">#44</a>	Search #38 AND #43
<a href="#">#43</a>	Search #39 OR #40 OR #41 OR #42
<a href="#">#42</a>	Search survival[tiab]
<a href="#">#41</a>	Search morbidity[tiab] OR mortality[tiab] OR death[tiab] OR deaths[tiab]
<a href="#">#40</a>	Search SEER[tiab] OR surveillance epidemiology[tiab]
<a href="#">#39</a>	Search registr*[tiab] OR register*[tiab]
<a href="#">#38</a>	Search #35 OR #36 OR #37
<a href="#">#37</a>	Search early diagnos*[tiab] OR early detection[tiab] OR earlier diagnos*[tiab] OR earlier detection[tiab] OR diagnosed earl*[tiab] OR detected earl*[tiab]
<a href="#">#36</a>	Search late stage[tiab] OR distant stage[tiab]
<a href="#">#35</a>	Search (detect*[tiab] OR diagnos*[tiab] OR biops*[tiab]) AND stage[tiab]
<a href="#">#34</a>	Search #21 AND #33
<a href="#">#33</a>	Search #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32
<a href="#">#32</a>	Search scar*[tiab] OR cixatrix[tiab]
<a href="#">#31</a>	Search psychological effect*[tiab]
<a href="#">#30</a>	Search label*[tiab]
<a href="#">#29</a>	Search ((unneeded[tiab] OR unnecessary[tiab]) AND (treat*[tiab] OR therap*[tiab] OR surg*[tiab] OR procedure*[tiab]))
<a href="#">#28</a>	Search misdiagnos*[tiab] OR overdiagnos*[tiab]
<a href="#">#27</a>	Search false negative[tiab]
<a href="#">#26</a>	Search safety[tiab]
<a href="#">#25</a>	Search side effect*[tiab]
<a href="#">#24</a>	Search complication*[tiab]
<a href="#">#23</a>	Search adverse effect*[tiab] OR adverse event*[tiab] OR adverse outcome*[tiab] OR adverse reaction*[tiab]
<a href="#">#22</a>	Search death[tiab] OR deaths[tiab] OR harm[tiab] OR harms[tiab] OR harmful[tiab] OR harmed[tiab]

## Appendix A. Detailed Methods

Search	Query
<a href="#">#21</a>	Search #18 OR #19 OR #20
<a href="#">#20</a>	Search rebiopsy[tiab]
<a href="#">#19</a>	Search excise*[tiab] OR excision*[tiab]
<a href="#">#18</a>	Search biopsy*[tiab] OR biopsies[tiab] OR biopsied[tiab]
<a href="#">#17</a>	Search #13 OR #14 OR #15 OR #16
<a href="#">#16</a>	Search dermoscop*[tiab] OR dermatoscop*[tiab] OR photography[tiab]
<a href="#">#15</a>	Search visual inspect*[tiab] OR visually inspect[tiab]
<a href="#">#14</a>	Search skin exam*[tiab] OR body exam*[tiab] OR physical exam*[tiab]
<a href="#">#13</a>	Search screen*[tiab]
<a href="#">#12</a>	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
<a href="#">#11</a>	Search cutaneous[ti] AND lymphoma*[ti]
<a href="#">#10</a>	Search bowen disease[ti]
<a href="#">#9</a>	Search actinic keratosis[ti]
<a href="#">#8</a>	Search basocellular carcinoma*[ti] OR basosquamous carcinoma*[ti]
<a href="#">#7</a>	Search (basal[ti] OR squamous[ti] OR merkel[ti]) AND (cancer*[ti] OR neoplasm*[ti] OR carcinoma*[ti] OR tumor*[ti] OR tumour*[ti] OR malignan[ti] OR lesion[ti] OR metasta*[ti] OR epithelioma*[ti])
<a href="#">#6</a>	Search "lentigo maligna"[ti]
<a href="#">#5</a>	Search "hutchinson's melanotic freckle"[ti]
<a href="#">#4</a>	Search (dysplastic[ti] or malignant[ti]) AND (nevus[ti] OR naevus[ti] OR nevi[ti] OR naevi[ti])
<a href="#">#3</a>	Search (naevoid[ti] or nevoid[ti]) AND syndrome*[ti]
<a href="#">#2</a>	Search melanoma*[ti]
<a href="#">#1</a>	Search (skin[ti] or derm*[ti] or cutaneous[ti] or epithelial[ti] or epiderm*[ti]) AND (cancer*[ti] or neoplasm*[ti] or carcinoma*[ti] or tumor*[ti] or tumour*[ti] or malignan*[ti] or lesion*[ti] or metasta*[ti])

# Appendix A Figure 1. Literature Flow Diagram



<sup>1</sup> Number of articles that were not included in prior review: KQ1=3; KQ2=3; KQ3=1; KQ4=1; KQ5=8

**Appendix A Table 1. Inclusion and Exclusion Criteria**

	<b>Include</b>	<b>Exclude</b>
<b>Population</b>	Asymptomatic adults age 15 years and older	<ul style="list-style-type: none"> <li>• Persons younger than age 15 years</li> <li>• People already under surveillance for skin cancer due to previous skin or other cancer</li> </ul>
<b>Settings</b>	Primary care-relevant, countries with a United Nations Human Development Index score of $\geq 0.9$	
<b>Screening tests</b>	Total or partial visual skin examination conducted by primary care providers or dermatologists with or without tools to aid examination (for example but not limited to, dermatoscopy; whole body photography)	<ul style="list-style-type: none"> <li>• Diagnostic skin examinations in response to patient concern</li> <li>• Skin self-screening by individuals or partners</li> <li>• Physician counseling for self-screening</li> </ul>
<b>Comparison</b>	<p><b>KQs 1, 2:</b> No visual skin examination</p> <p><b>KQ 3:</b> Biopsy</p> <p><b>KQ 4:</b> Usual care</p> <p><b>KQ 5:</b> Stage at detection</p>	
<b>Outcomes</b>	<p><b>KQs 1, 5:</b> Morbidity associated with any skin cancer (including melanoma in situ, dysplastic nevi, actinic keratosis) including quality of life; skin cancer mortality; or all-cause mortality</p> <p><b>KQ 2:</b> Any harm from screening, biopsy, or excision including over-diagnosis, psychosocial harms, or procedure-related adverse events</p> <p><b>KQ 3:</b> Sensitivity, specificity, positive predictive value, false positive, false negative, cancer detection rates</p> <p><b>KQ 4:</b> Lesion thickness or stage at diagnosis</p>	<p>Non-skin location</p> <p>Intermediate or health outcomes relating clinician skin examination to other risk behaviors (e.g., self-screening, sun protective behaviors) or measures of doctor-patient relationship quality</p>
<b>Study design</b>	<p>Fair- to good-quality studies published since January 1, 1995 to March 31, 2015.</p> <p>Systematic reviews (of included study designs); randomized, controlled trials; selected well-designed controlled clinical trials; observational studies including cohort and case-control studies; ecologic studies</p> <p><b>KQs 2:</b> Same as above and including harms of screening case series</p>	Poor-quality studies with a fatal flaw; studies outside of the publication window; case reports and case series (except as noted for KQs 2 and 6); decision analyses

## Appendix A Table 2. Quality Assessment Criteria

Study Design	Adapted Quality Criteria
Randomized controlled trials, adapted from the USPSTF methods <sup>50</sup>	<ul style="list-style-type: none"> <li>• Valid random assignment?</li> <li>• Was allocation concealed?</li> <li>• Was eligibility criteria specified?</li> <li>• Were groups similar at baseline?</li> <li>• Were measurements equal, valid and reliable?</li> <li>• Was there intervention fidelity?</li> <li>• Was there adequate adherence to the intervention?</li> <li>• Were outcome assessors blinded?</li> <li>• Was there acceptable followup?</li> <li>• Were the statistical methods acceptable?</li> <li>• Was the handling of missing data appropriate?</li> <li>• Was there evidence of selective reporting of outcomes?</li> <li>• Was the device calibration and/or maintenance reported?</li> </ul>
Ecologic studies adapted from Dufault 2011 <sup>51</sup> and Tu 2008 <sup>52</sup>	<ul style="list-style-type: none"> <li>• A priori information: is the identified ecological relationship between the exposure and the outcomes biologically plausible and consistent with what is already known about a given topic at an individual subject level?</li> <li>• Adequate sample size</li> <li>• Level of aggregation appropriate / are the subjects in the ecologic study representative of the group, place or population of interest?</li> <li>• Level of inference (individual, ecologic, unclear)</li> <li>• Pre-specification of ecologic units</li> <li>• Classification of primary outcomes; were the exposure and outcome variables measured and defined in a similar or same way across the different populations or groups that are being studied?</li> <li>• Analytic methodology: would it be practical to conduct alternative ways of studying the same question? Or was the ecologic study the only alternative?</li> <li>• Validity of regression</li> <li>• Use of covariates; have the data been collected on important confounding variables that might also explain the exposure-outcome relationship and have they been statistically adjusted for? If data are not available on key factors, is it reasonable to assume that their prevalence is similar in the different groups or populations being compared?</li> <li>• Discussion of cross-level bias / have the investigators interpreted their data with appropriate caveats? Did they acknowledge the possibility of an ecological fallacy? Were alternative explanations for the association between the exposure and outcomes considered by the investigators?</li> <li>• Have the study data been collected at multiple levels? If yes, was multilevel modeling considered or used for analyzing the data?</li> </ul>

Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but do not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using a priori quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

## Appendix B. Ongoing Studies

We identified 4 potentially relevant ongoing randomized controlled clinical trials through four registries: ClinicalTrials.gov (<http://clinicaltrials.gov>), Current Controlled Trials (<http://www.controlled-trials.com>), Australian New Zealand Clinical Trials Registry (<http://www.anzctr.org.au>), and the World Health Organization's International Clinical Trials Registry Platform (<http://www.who.int/ictpr>). We restricted our searches to “skin cancer” AND screening.

Four studies regarding skin cancer screening were identified from ClinicalTrials.gov. These four studies focused on skin cancer screening efficacy and range from not yet recruiting to recently completed. Two of the studies<sup>91,92</sup> focus on training and education for physicians regarding skin cancer screening. Of these two screening education projects the Skin Cancer Screening Education Study (SCSES) just began recruitment in February 2015. In addition to the two skin cancer screening education trials there are two other potentially relevant ongoing studies: One study addresses the attitudes and barriers<sup>93</sup> to skin cancer screening in an academic dermatology clinic and depending on the demographics of the population, may not be considered included (those in dermatologist waiting room may not represent asymptomatic population). The beach based controlled trial<sup>94</sup> represents an evaluation of a skin cancer and education program delivered at beaches. This intervention also includes skin cancer prevention education and therefore, depending on the actual methods may not contain the relevant population.

We also used NIH Research portfolio online reporting tools (RePORTer)<sup>95</sup> to identify ongoing projects that are currently funded through NIH. From RePORTer we found one potentially relevant currently funded work on skin cancer screening. Comparative Assessments of **screening** Strategies for Melanoma (5R21CA182241) led by Dr. Sandra J. Lee at the Dana-Farber Cancer Institute, Harvard Medical School. The proposal is centered around research problems arising in the early detection of malignant melanoma with an emphasis on sex-based differences in the early diagnosis of melanoma. The principal research areas include: (i) Investigate the natural history of melanoma and develop stochastic models for early detection of melanoma, (ii) Evaluate the mortality benefit of potential screening programs in the general and high-risk populations, (iii) Establish a pilot database of individuals at high-risk of developing melanoma and evaluate the factors associated with the risk of developing melanoma and of fatal melanoma.

During our bridge search and expert review two additional screening efforts were brought to our attention. These include one US based training program for increasing effectiveness of primary care provider screening.<sup>96</sup> This web-based training program aims to increase appropriate diagnosis and management of skin cancer screening. The second screening effort that would be of interest to future research is a French screening campaign.<sup>31</sup> This cluster randomized controlled trial was a targeted melanoma prevention intervention. This particular paper focused on patient prevention behavior, there may be relevant data from future papers that pertain to effectiveness of skin cancer screening by primary care physicians.



## Appendix C. Excluded Studies

Code	Reason for Exclusion
E1	Not English
E2	Not original research in a peer-reviewed journal
E3	Publication date not 1995-present
E4	Ineligible SETTING (a) non-generalizable to primary care; (b) low HDI country
E5	Ineligible POPULATION
E6	Ineligible OUTCOMES
E7	Ineligible screening strategy
E8	Ineligible treatment
E9	Ineligible study design
E10	Study rated as poor quality
E11	Overlapping study population
E12	N/A

**Abbreviations:** HDI = Human Development Index, N/A = not applicable.

1. Screening for melanoma. *Med Lett Drugs Ther.* 2011;53-1372:72. PMID: 21897350. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
2. Do I need an annual skin check to screen for cancer? *Mayo Clin Womens Healthsource.* 2009;13-6:8. PMID: 19415051. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
3. New tools aid in diagnosing and detecting skin cancer in earliest stages. *Dermatol Nurs.* 2009;21-4:222-3. PMID: 19691242. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
4. Early detection of melanoma plus regular skin exams is vital for beating disease. *Dermatol Nurs.* 2009;21-6:363-4. PMID: 20102024. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
5. How to decrease morbidity and mortality of skin cancer: primary prevention of skin cancer/screening of skin cancer. Report of a workshop held under the auspices of the Society of Dermatological Prevention (ADP e.V.), Commission of Early Detection and Prevention of Skin Cancer. 11 May 1994, Hamburg, Germany. *Eur J Cancer Prev.* 1996;5-4:297-9. PMID: 8894567. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
6. Abbas Q, Celebi ME, Fondon I. Computer-aided pattern classification system for dermoscopy images. *Skin Res Technol.* 2012;18-3:278-89. PMID: 22093020. **KQ3E9.**
7. Abbas Q, Garcia IF, Emre Celebi M et al. Unified approach for lesion border detection based on mixture modeling and local entropy thresholding. *Skin Res Technol.* 2013;19-3:314-9. PMID: 23573804. **KQ3E9.**
8. Abbas Q, Garcia IF, Rashid M. Automatic skin tumour border detection for digital dermoscopy using a new digital image analysis scheme. *Br J Biomed Sci.* 2010;67-4:177-83. PMID: 21294444. **KQ3E4.**
9. Affleck AG, Varma S. A case of do-it-yourself Mohs' surgery using bloodroot obtained from the internet. *Br J Dermatol.* 2007;157-5:1078-9. PMID: 17854372. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
10. Aitken JF, Elwood JM, Lowe JB et al. A randomised trial of population screening for melanoma. *J Med Screen.* 2002;9-1:33-7. PMID: 11943795. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
11. Aitken JF, Youl PH, Janda M et al. Increase in skin cancer screening during a community-based randomized intervention trial. *Int J Cancer.* 2006;118-4:1010-6. PMID: 16152577. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
12. Alam M, Ratner D. Cutaneous squamous-cell carcinoma. *N Engl J Med.* 2001;344-13:975-83. PMID: 11274625. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
13. Aldridge RB, Naysmith L, Ooi ET et al. The importance of a full clinical examination: assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. *Acta Derm Venereol.* 2013;93-6:689-92. PMID: 23695107. **KQ2E5, KQ3E5.**
14. Altamura D, Menzies SW, Argenziano G et al. Dermatoscopy of basal cell carcinoma: morphologic variability of global and local features and accuracy of diagnosis. *J Am Acad Dermatol.* 2010;62-1:67-75. PMID: 19828209. **KQ3E7.**

## Appendix C. Excluded Studies

15. Amrock SM, Meydani A. Trends and disparities in total-body skin examination: evaluating the National Health Interview Survey, 2000-2010. *JAMA Dermatol.* 2013;149-3:363-4. PMID: 23552730. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
16. Andersson AP, Dahlstrom KK, Drzewiecki KT. Prognosis of thin cutaneous head and neck melanoma (<1mm). *Eur J Surg Oncol.* 1996;22-1:55-7. PMID: 8846868. **KQ5E6.**
17. Andersson TM, Eriksson H, Hansson J et al. Estimating the cure proportion of malignant melanoma, an alternative approach to assess long term survival: a population-based study. *Cancer Epidemiol.* 2014;38-1:93-9. PMID: 24447700. **KQ5E6.**
18. Andreeva VA, Cockburn MG. Cutaneous melanoma and other skin cancer screening among Hispanics in the United States: a review of the evidence, disparities, and need for expanding the intervention and research agendas. *Arch Dermatol.* 2011;147-6:743-5. PMID: 21690545. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
19. Annessi G, Bono R, Sampogna F et al. Sensitivity, specificity, and diagnostic accuracy of three dermoscopic algorithmic methods in the diagnosis of doubtful melanocytic lesions: the importance of light brown structureless areas in differentiating atypical melanocytic nevi from thin melanomas. *J Am Acad Dermatol.* 2007;56-5:759-67. PMID: 17316894. **KQ3E7.**
20. Anzai S, Anan T, Kai Y et al. Skin cancer screening on a fishing island and in an inland agricultural area of Japan. *J Dermatol.* 2005;32-11:875-82. PMID: 16361747. **KQ1E6, KQ2E6, KQ3E9, KQ4E9, KQ5E6.**
21. Argenziano G, Puig S, Zalaudek I et al. Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *J Clin Oncol.* 2006;24-12:1877-82. PMID: 16622262. **KQ3E7.**
22. Argenziano G, Zalaudek I, Hofmann-Wellenhof R et al. Total body skin examination for skin cancer screening in patients with focused symptoms. *J Am Acad Dermatol.* 2012;66-2:212-9. PMID: 21757257. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
23. Augustin M, Stadler R, Reusch M et al. Skin cancer screening in Germany - perception by the public. *J Dtsch Dermatol Ges.* 2012;10-1:42-9. PMID: 21923730. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
24. Austin JR, Byers RM, Brown WD et al. Influence of biopsy on the prognosis of cutaneous melanoma of the head and neck. *Head Neck.* 1996;18-2:107-17. PMID: 8647675. **KQ2E5.**
25. Averbook BJ, Fu P, Rao JS et al. A long-term analysis of 1018 patients with melanoma by classic Cox regression and tree-structured survival analysis at a major referral center: Implications on the future of cancer staging. *Surgery.* 2002;132-4:589-602; discussion 602-4. PMID: 12407342. **KQ5E6.**
26. Averbook BJ, Lee SJ, Delman KA et al. Pediatric melanoma: analysis of an international registry. *Cancer.* 2013;119-22:4012-9. PMID: 24022819. **KQ5E6.**
27. Averbook BJ, Russo LJ, Mansour EG. A long-term analysis of 620 patients with malignant melanoma at a major referral center. *Surgery.* 1998;124-4:746-55; discussion 755-6. PMID: 9780997. **KQ5E6.**
28. Azzarello LM, Jacobsen PB. Factors influencing participation in cutaneous screening among individuals with a family history of melanoma. *J Am Acad Dermatol.* 2007;56-3:398-406. PMID: 17184873. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
29. Baade P, Coory M. Trends in melanoma mortality in Australia: 1950-2002 and their implications for melanoma control. *Aust N Z J Public Health.* 2005;29-4:383-6. PMID: 16222938. **KQ1E13.**
30. Baade P, Meng X, Youlden D et al. Time trends and latitudinal differences in melanoma thickness distribution in Australia, 1990-2006. *Int J Cancer.* 2012;130-1:170-8. PMID: 21344376. **KQ4E7.**
31. Badertscher N, Meier M, Rosemann T et al. The role of skin self-examination at the Swiss skin cancer day. *BMC Health Serv Res.* 2014;14:581. PMID: 25408258. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
32. Baehner FL, Li R, Jenkins T et al. The impact of primary melanoma thickness and microscopic tumor burden in sentinel lymph nodes on melanoma patient survival. *Ann Surg Oncol.* 2012;19-3:1034-42. PMID: 21989664. **KQ5E7.**

## Appendix C. Excluded Studies

33. Bafounta ML, Beauchet A, Aegerter P et al. Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. *Arch Dermatol.* 2001;137-10:1343-50. PMID: 11594860. **KQ3E13.**
34. Balch CM, Soong SJ, Gershenwald JE et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. *J Clin Oncol.* 2001;19-16:3622-34. PMID: 11504744. **KQ5E6.**
35. Balch CM, Soong SJ, Smith T et al. Long-term results of a prospective surgical trial comparing 2 cm vs. 4 cm excision margins for 740 patients with 1-4 mm melanomas. *Ann Surg Oncol.* 2001;8-2:101-8. PMID: 11258773. **KQ2E5, KQ5E6.**
36. Balch CM, Soong S, Ross MI et al. Long-term results of a multi-institutional randomized trial comparing prognostic factors and surgical results for intermediate thickness melanomas (1.0 to 4.0 mm). Intergroup Melanoma Surgical Trial. *Ann Surg Oncol.* 2000;7-2:87-97. PMID: 10761786. **KQ5E6.**
37. Baldwin BT, Cherpelis BS, Sondak V et al. Sentinel lymph node biopsy in melanoma: Facts and controversies. *Clin Dermatol.* 2010;28-3:319-23. PMID: 20541686. **KQ2E2, KQ6.**
38. Bambara M, Magnano M, Castelli G et al. 0109 Study on diseases of the skin in an industrial population of a petrochemical site in Sicily. *Occup Environ Med.* 2014:A74. PMID: 25018467. **KQ1E6.**
39. Banky JP, Kelly JW, English DR et al. Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. *Arch Dermatol.* 2005;141-8:998-1006. PMID: 16103329. **KQ1E7.**
40. Barzegari M, Ghaninezhad H, Mansoori P et al. Computer-aided dermoscopy for diagnosis of melanoma. *BMC Dermatol.* 2005;5:8. PMID: 16000171. **KQ3E4.**
41. Barzilai DA, Cooper KD, Neuhauser D et al. Geographic and patient variation in receipt of surveillance procedures after local excision of cutaneous melanoma. *J Invest Dermatol.* 2004;122-2:246-55. PMID: 15009702. **KQ2E5.**
42. Bataille V. Early detection of melanoma improves survival. *Practitioner.* 2009;253-1722:29-32, 3. PMID: 19938560. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
43. Bauer AM. Current trends of surgical management of head and neck carcinomas. *Nurs Clin North Am.* 2001;36-3:501-6, x. PMID: 11532664. **KQ2E2.**
44. Bauer P, Cristofolini P, Boi S et al. Digital epiluminescence microscopy: usefulness in the differential diagnosis of cutaneous pigmentary lesions. A statistical comparison between visual and computer inspection. *Melanoma Res.* 2000;10-4:345-9. PMID: 10985668. **KQ3E13.**
45. Bello DM, Chou JF, Panageas KS et al. Prognosis of acral melanoma: a series of 281 patients. *Ann Surg Oncol.* 2013;20-11:3618-25. PMID: 23838913. **KQ5E6.**
46. Benelli C, Roscetti E, Pozzo VD et al. The dermoscopic versus the clinical diagnosis of melanoma. *Eur J Dermatol.* 1999;9-6:470-6. PMID: 10491506. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
47. Bennassar A, Ishioka P, Vilalta A. Surgical treatment of primary melanoma. *Dermatol Ther.* 2012;25-5:432-42. PMID: 23046022. **KQ2E7.**
48. Ben-Porat L, Panageas KS, Hanlon C et al. Estimates of stage-specific survival are altered by changes in the 2002 American Joint Committee on Cancer staging system for melanoma. *Cancer.* 2006;106-1:163-71. PMID: 16331596. **KQ5E6.**
49. Berwick M, Armstrong BK, Ben-Porat L et al. Sun exposure and mortality from melanoma. *J Natl Cancer Inst.* 2005;97-3:195-9. PMID: 15687362. **KQ1E7, KQ2E5, KQ3E5, KQ4E6, KQ5E7.**
50. Beyeler M, Dummer R. Cutaneous melanoma: uncommon presentations. *Clin Dermatol.* 2005;23-6:587-92. PMID: 16325067. **KQ1E9, KQ2E6, KQ3E9, KQ4E9, KQ5E9.**
51. Bhattacharyya N, Nayak VK. Survival outcomes for second primary head and neck cancer: a matched analysis. *Otolaryngol Head Neck Surg.* 2005;132-1:63-8. PMID: 15632911. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
52. Boi S, Cristofolini M, Micciolo R et al. Incidence and mortality data from cutaneous melanoma in Trentino: registry-based study. *J Cutan Med Surg.* 2008;12-2:59-63. PMID: 18346401. **KQ1E7.**

## Appendix C. Excluded Studies

53. Bong JL, Perkins W. Shave excision of benign facial melanocytic naevi: a patient's satisfaction survey. *Dermatol Surg.* 2003;29-3:227-9. PMID: 12614413. **KQ2E5.**
54. Bono A, Bartoli C, Cascinelli N et al. Melanoma detection. A prospective study comparing diagnosis with the naked eye, dermatoscopy and telespectrophotometry. *Dermatology.* 2002;205-4:362-6. PMID: 12444332. **KQ3E5.**
55. Bono A, Ferrari A. Early diagnosis remains the most reliable way to cure children with melanoma. *Pediatr Blood Cancer.* 2005;45-3:355; author reply 356. PMID: 15809990. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
56. Bono A, Tolomio E, Trincone S et al. Micro-melanoma detection: a clinical study on 206 consecutive cases of pigmented skin lesions with a diameter < or = 3 mm. *Br J Dermatol.* 2006;155-3:570-3. PMID: 16911283. **KQ3E7.**
57. Borden EC. Reducing primary melanoma mortality. *Curr Oncol Rep.* 2000;2-4:289-91. PMID: 11122855. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
58. Bordoni A, Leoni-Parvex S, Peverelli S et al. Opportunistic screening strategy for cutaneous melanoma does not change the incidence of nodular and thick lesions nor reduce mortality: a population-based descriptive study in the European region with the highest incidence. *Melanoma Res.* 2013;23-5:402-7. PMID: 23839077. **KQ1E7, KQ5E7.**
59. Boulos S, Fiala K, Butler DF. Free skin cancer screening provides access to care. *J Am Acad Dermatol.* 2012;67-4:787-8. PMID: 22980248. **KQ1E6, KQ2E6, KQ3E4, KQ4E6, KQ5E6.**
60. Bourne P, Rosendahl C, Keir J et al. BLINCK-A diagnostic algorithm for skin cancer diagnosis combining clinical features with dermatoscopy findings. *Dermatol Pract Concept.* 2012;2-2:202a12. PMID: 23785600. **KQ3E7.**
61. Bowns IR, Collins K, Walters SJ et al. Telemedicine in dermatology: a randomised controlled trial. *Health Technol Assess.* 2006;10-43:iii-iv, ix-xi, 1-39. PMID: 17049140. **KQ3E7.**
62. Bradford PT, Goldstein AM, McMaster ML et al. Acral lentiginous melanoma: incidence and survival patterns in the United States, 1986-2005. *Arch Dermatol.* 2009;145-4:427-34. PMID: 19380664. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
63. Brandt TP. Skin cancer screening. *Med Clin North Am.* 1996;80-1:99-114. PMID: 8569303. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
64. Breuninger H, Schlagenhauff B, Stroebel W et al. Patterns of local horizontal spread of melanomas: consequences for surgery and histopathologic investigation. *Am J Surg Pathol.* 1999;23-12:1493-8. PMID: 10584702. **KQ2E6.**
65. Brown JE, Butow PN, Culjak G et al. Psychosocial predictors of outcome: time to relapse and survival in patients with early stage melanoma. *Br J Cancer.* 2000;83-11:1448-53. PMID: 11076652. **KQ5E6.**
66. Bruce AJ, Brodland DG. Overview of skin cancer detection and prevention for the primary care physician. *Mayo Clin Proc.* 2000;75-5:491-500. PMID: 10807078. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
67. Brunner M, Veness MJ, Ch'ng S et al. Distant metastases from cutaneous squamous cell carcinoma--analysis of AJCC stage IV. *Head Neck.* 2013;35-1:72-5. PMID: 22266877. **KQ5E6.**
68. Buckley D, McMonagle C. Melanoma in primary care. The role of the general practitioner. *Ir J Med Sci.* 2014;183-3:363-8. PMID: 24091614. **KQ1E7, KQ3E5.**
69. Buettner PG, Leiter U, Eigentler TK et al. Development of prognostic factors and survival in cutaneous melanoma over 25 years: An analysis of the Central Malignant Melanoma Registry of the German Dermatological Society. *Cancer.* 2005;103-3:616-24. PMID: 15630700. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
70. Bulliard JL, Maspoli M, Panizzon RG et al. Evaluation of the Euromelanoma skin cancer screening campaign: the Swiss experience. *J Eur Acad Dermatol Venereol.* 2008;22-3:365-6. PMID: 18269606. **KQ1E6, KQ2E6, KQ3E7, KQ4E6, KQ5E6.**
71. Bursa V, Pizinger K, Solc J et al. Our experience with operative treatment of malignant melanoma. *Acta Chir Plast.* 1996;38-1:21-3. PMID: 8771806. **KQ2E5.**

## Appendix C. Excluded Studies

72. Burton RC, Howe C, Adamson L et al. General practitioner screening for melanoma: sensitivity, specificity, and effect of training. *J Med Screen.* 1998;5-3:156-61. PMID: 9795877. **KQ3E5, KQ4E6.**
73. Butler JM. Playing detective. Assessing skin lesions in primary care. *Adv Nurse Pract.* 1997;5-8:41-3. PMID: 9459955. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
74. Carducci M, Betti R. Basal cell carcinoma: surgical margin detection using digital dermoscopy. *Dermatol Surg.* 2012;38-6:964-5. PMID: 22642455. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
75. Carli P, Balzi D, de Giorgi V et al. Results of surveillance programme aimed at early diagnosis of cutaneous melanoma in high risk Mediterranean subjects. *Eur J Dermatol.* 2003;13-5:482-6. PMID: 14693495. **KQ1E5.**
76. Carli P, Chiarugi A, De Giorgi V. Examination of lesions (including dermoscopy) without contact with the patient is associated with improper management in about 30% of equivocal melanomas. *Dermatol Surg.* 2005;31-2:169-72. PMID: 15762209. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
77. Carli P, De Giorgi V, Argenziano G et al. Pre-operative diagnosis of pigmented skin lesions: in vivo dermoscopy performs better than dermoscopy on photographic images. *J Eur Acad Dermatol Venereol.* 2002;16-4:339-46. PMID: 12224689. **KQ2E6, KQ3E7.**
78. Carli P, De Giorgi V, Chiarugi A et al. Effect of lesion size on the diagnostic performance of dermoscopy in melanoma detection. *Dermatology.* 2003;206-4:292-6. PMID: 12771468. **KQ3E5.**
79. Carli P, de Giorgi V, Chiarugi A et al. Addition of dermoscopy to conventional naked-eye examination in melanoma screening: a randomized study. *J Am Acad Dermatol.* 2004;50-5:683-9. PMID: 15097950. **KQ3E5.**
80. Carli P, De Giorgi V, Crocetti E et al. Diagnostic and referral accuracy of family doctors in melanoma screening: effect of a short formal training. *Eur J Cancer Prev.* 2005;14-1:51-5. PMID: 15677895. **KQ3E7.**
81. Carli P, De Giorgi V, Crocetti E et al. Improvement of malignant/benign ratio in excised melanocytic lesions in the 'dermoscopy era': a retrospective study 1997-2001. *Br J Dermatol.* 2004;150-4:687-92. PMID: 15099364. **KQ3E5.**
82. Carli P, De Giorgi V, Giannotti B. Dermoscopy as a second step in the diagnosis of doubtful pigmented skin lesions: how great is the risk of missing a melanoma? *J Eur Acad Dermatol Venereol.* 2001;15-1:24-6. PMID: 11451316. **KQ2E6, KQ3E6.**
83. Carli P, De Giorgi V, Giannotti B et al. Skin cancer day in Italy: method of referral to open access clinics and tumor prevalence in the examined population. *Eur J Dermatol.* 2003;13-1:76-9. PMID: 12609788. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
84. Carli P, De Giorgi V, Massi D et al. The role of pattern analysis and the ABCD rule of dermoscopy in the detection of histological atypia in melanocytic naevi. *Br J Dermatol.* 2000;143-2:290-7. PMID: 10951135. **KQ3E6.**
85. Carli P, De Giorgi V, Nardini P et al. Melanoma detection rate and concordance between self-skin examination and clinical evaluation in patients attending a pigmented lesion clinic in Italy. *Br J Dermatol.* 2002;146-2:261-6. PMID: 11903237. **KQ3E7.**
86. Carli P, de Giorgi V, Palli D et al. Preoperative assessment of melanoma thickness by ABCD score of dermoscopy. *J Am Acad Dermatol.* 2000;43-3:459-66. PMID: 10954657. **KQ3E6.**
87. Carli P, De Giorgi V, Palli D et al. Dermatologist detection and skin self-examination are associated with thinner melanomas: results from a survey of the Italian Multidisciplinary Group on Melanoma. *Arch Dermatol.* 2003;139-5:607-12. PMID: 12756097. **KQ4E5.**
88. Carli P, de Giorgi V, Salvini C et al. The gold standard for photographing pigmented skin lesions for diagnostic purposes: contact versus distant imaging. *Skin Res Technol.* 2002;8-4:255-9. PMID: 12423545. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
89. Carli P, Ghigliotti G, Gnone M et al. Baseline factors influencing decisions on digital follow-up of melanocytic lesions in daily practice: an Italian multicenter survey. *J Am Acad Dermatol.* 2006;55-2:256-62. PMID: 16844508. **KQ2E6, KQ3E6.**
90. Carli P, Mannone F, De Giorgi V et al. The problem of false-positive diagnosis in melanoma screening: the impact of dermoscopy. *Melanoma Res.* 2003;13-2:179-82. PMID: 12690302. **KQ2E5, KQ3E5.**

## Appendix C. Excluded Studies

91. Carli P, Massi D, de Giorgi V et al. Clinically and dermoscopically featureless melanoma: when prevention fails. *J Am Acad Dermatol.* 2002;46-6:957-9. PMID: 12063500. **KQ2E5.**
92. Carli P, Nardini P, Crocetti E et al. Frequency and characteristics of melanomas missed at a pigmented lesion clinic: a registry-based study. *Melanoma Res.* 2004;14-5:403-7. PMID: 15457097. **KQ2E5, KQ3E5.**
93. Carlos-Ortega B, Sanchez-Alva ME, Ysita-Morales A et al. [Correlation among simple observation and dermoscopy in the study of pigmented lesions of the skin]. *Rev Med Inst Mex Seguro Soc.* 2007;45-6:541-8. PMID: 18593536. **KQ3E1.**
94. Cavalcanti PG, Scharcanski J. Automated prescreening of pigmented skin lesions using standard cameras. *Comput Med Imaging Graph.* 2011;35-6:481-91. PMID: 21489751. **KQ3E6.**
95. Celebi ME, Iyatomi H, Schaefer G et al. Lesion border detection in dermoscopy images. *Comput Med Imaging Graph.* 2009;33-2:148-53. PMID: 19121917. **KQ3E2.**
96. Celebi ME, Iyatomi H, Schaefer G et al. Approximate lesion localization in dermoscopy images. *Skin Res Technol.* 2009;15-3:314-22. PMID: 19624428. **KQ3E13.**
97. Cha HC, Harting M, Cha KB et al. Effects of contiguous scars in dermatoscopic evaluation of clinically atypical melanocytic nevi. *J Am Acad Dermatol.* 2012;66-5:e179-80. PMID: 22507589. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
98. Chagpar RB, Ross MI, Reintgen DS et al. Factors associated with improved survival among young adult melanoma patients despite a greater incidence of sentinel lymph node metastasis. *J Surg Res.* 2007;143-1:164-8. PMID: 17950088. **KQ5E6.**
99. Chang AE, Karnell LH, Menck HR. The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer.* 1998;83-8:1664-78. PMID: 9781962. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
100. Chartier T, Bigby M. Rational follow-up recommendations for patients with melanoma. *Arch Dermatol.* 2000;136-9:1145-7. PMID: 10987873. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
101. Cherian P, Tait CP. Melanoma in private practice: do dermatologists make a difference? *Australas J Dermatol.* 2009;50-4:257-60. PMID: 19916968. **KQ1E6, KQ2E6, KQ3E5, KQ4E6, KQ5E6.**
102. Chintamani, Shankar M, Singhal V, Singh JP et al. Squamous cell carcinoma developing in the scar of Fournier's gangrene--case report. *BMC Cancer.* 2004;4:16. PMID: 15113443. **KQ2E5.**
103. Choudhury K, Volkmer B, Greinert R et al. Effectiveness of skin cancer screening programmes. *Br J Dermatol.* 2012;94-8. PMID: 22881593. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
104. Civantos F Jr, Zitsch R et al. Sentinel node biopsy for squamous cell carcinoma of the head and neck. *J Surg Oncol.* 2008;97-8:683-90. PMID: 18493916. **KQ3E2.**
105. Clark GS, Pappas-Politis EC, Cherpelis BS et al. Surgical management of melanoma in situ on chronically sun-damaged skin. *Cancer Control.* 2008;15-3:216-24. PMID: 18596673. **KQ2E2.**
106. Cokkinides VE, Geller AC, Jemal A. Trends in melanoma mortality among non-Hispanic whites by educational attainment, 1993-2007. *Arch Dermatol.* 2012;148-5:587-91. PMID: 22250192. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
107. Collins MK, Secrest AM, Ferris LK. Screening for melanoma. *Melanoma Res.* 2014;24-5:428-36. PMID: 24999755. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
108. Commens C. Skin screening in health promotion. *Australas J Dermatol.* 1995;36-2:103. PMID: 7646388. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
109. Conti EM, Cercato MC, Gatta G et al. Childhood melanoma in Europe since 1978: a population-based survival study. *Eur J Cancer.* 2001;37-6:780-4. PMID: 11311654. **KQ5E7.**
110. Coory M, Baade P, Aitken J et al. Trends for in situ and invasive melanoma in Queensland, Australia, 1982-2002. *Cancer Causes Control.* 2006;17-1:21-7. PMID: 16411049. **KQ5E6.**

## Appendix C. Excluded Studies

111. Coory M, Smithers M, Aitken J et al. Urban-rural differences in survival from cutaneous melanoma in Queensland. *Aust N Z J Public Health*. 2006;30-1:71-4. PMID: 16509022. **KQ5E6.**
112. Cordova KB, Weinstock MA. Skin cancer prevention and detection--melanoma and beyond. *Med Health R I*. 2005;88-3:92-5. PMID: 15915783. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
113. Coups EJ, Stapleton JL, Hudson SV et al. Skin cancer screening among Hispanic adults in the United States: results from the 2010 National Health Interview Survey. *Arch Dermatol*. 2012;148-7:861-3. PMID: 22801634. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
114. Curiel-Lewandrowski C, Kim CC, Swetter SM et al. Survival is not the only valuable end point in melanoma screening. *J Invest Dermatol*. 2012;132-5:1332-7. PMID: 22336950. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
115. Dal Pozzo V, Benelli C, Roscetti E. The seven features for melanoma: a new dermoscopic algorithm for the diagnosis of malignant melanoma. *Eur J Dermatol*. 1999;9-4:303-8. PMID: 10356410. **KQ3E4.**
116. Day GR, Barbour RH. Automated skin lesion screening--a new approach. *Melanoma Res*. 2001;11-1:31-5. PMID: 11254113. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
117. De Giorgi V, Grazzini M, Rossari S et al. Adding dermatoscopy to naked eye examination of equivocal melanocytic skin lesions: effect on intention to excise by general dermatologists. *Clin Exp Dermatol*. 2011;36-3:255-9. PMID: 21091756. **KQ3E5.**
118. De Giorgi V, Grazzini M, Rossari S et al. Total body photography versus digital dermoscopic follow-up in the diagnosis of pigmented lesions. *Dermatol Surg*. 2011;37-3:406-7. PMID: 21410826. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
119. de Lima Vazquez V, Sachetto T, Perpetuo NM et al. Prognostic factors for lymph node metastasis from advanced squamous cell carcinoma of the skin of the trunk and extremities. *World J Surg Oncol*. 2008;6:73. PMID: 18601735. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
120. De Rooij MJ, Rampen FH, Schouten LJ et al. Total skin examination during screening for malignant melanoma does not increase the detection rate. *Br J Dermatol*. 1996;135-1:42-5. PMID: 8776357. **KQ3E6.**
121. de Rooij MJ, Rampen FH, Schouten LJ et al. Skin cancer screening focusing on melanoma yields more selective attendance. *Arch Dermatol*. 1995;131-4:422-5. PMID: 7726583. **KQ3E4.**
122. de Vries E, Coebergh JW. Cutaneous malignant melanoma in Europe. *Eur J Cancer*. 2004;40-16:2355-66. PMID: 15519506. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
123. de Vries M, Vonkeman WG, van Ginkel RJ et al. Morbidity after inguinal sentinel lymph node biopsy and completion lymph node dissection in patients with cutaneous melanoma. *Eur J Surg Oncol*. 2006;32-7:785-9. PMID: 16806794. **KQ5E7.**
124. Del Mar CB, Green AC. Aid to diagnosis of melanoma in primary medical care. *BMJ*. 1995;310-6978:492-5. PMID: 7888887. **KQ1E6, KQ3E6, KQ5E6.**
125. Dhiwakar M, Khan NA, McClymont LG. Surgery for head and neck skin tumors in the elderly. *Head Neck*. 2007;29-9:851-6. PMID: 17427964. **KQ2E4.**
126. Dolan NC, Martin GJ, Robinson JK et al. Skin cancer control practices among physicians in a university general medicine practice. *J Gen Intern Med*. 1995;10-9:515-9. PMID: 8523156. **KQ3E13.**
127. Douglas NC, Baillie L, Soyer HP. Skin cancer screening of outdoor workers in Queensland. *Med J Aust*. 2011;195-2:100-1. PMID: 21770887. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
128. Dozier S, Wagner RF Jr et al. Beachfront screening for skin cancer in Texas Gulf coast surfers. *South Med J*. 1997;90-1:55-8. PMID: 9003825. **KQ1E6.**
129. Drugge RJ, Nguyen C, Drugge ED et al. Melanoma screening with serial whole body photographic change detection using Melanoscan technology. *Dermatol Online J*. 2009;15-6:1. PMID: 19723475. **KQ3E5, KQ4E5, KQ5E5.**
130. Drugge RJ, Nguyen C, Gliga L et al. Clinical pathway for melanoma detection using comprehensive cutaneous analysis with Melanoscan. *Dermatol Online J*. 2010;16-8:1. PMID: 20804678. **KQ3E5.**
131. Duff CG, Melsom D, Rigby HS et al. A 6 year prospective analysis of the diagnosis of malignant melanoma in a pigmented-lesion clinic: even the experts miss malignant melanomas, but not often. *Br J Plast Surg*. 2001;54-4:317-21. PMID: 11355986. **KQ3E9.**

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132. Durbec F, Vitry F, Granel-Brocard F et al. The role of circumstances of diagnosis and access to dermatological care in early diagnosis of cutaneous melanoma: a population-based study in France. *Arch Dermatol.* 2010;146-3:240-6. PMID: 20231493. **KQ1E6, KQ2E6, KQ3E6, KQ4E7, KQ5E6.**
133. Edman RL, Klaus SN. Is routine screening for melanoma a benign practice? *JAMA.* 2000;284-7:883-6. PMID: 10938180. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
134. Edmondson PC, Curley RK, Marsden RA et al. Screening for malignant melanoma using instant photography. *J Med Screen.* 1999;6-1:42-6. PMID: 10321371. **KQ1E6, KQ4E7.**
135. Eide MJ, Weinstock MA, Dufresne RG et al. Relationship of treatment delay with surgical defect size from keratinocyte carcinoma (basal cell carcinoma and squamous cell carcinoma of the skin). *J Invest Dermatol.* 2005;124-2:308-14. PMID: 15675948. **KQ2E5.**
136. Eisemann N, Waldmann A, Geller AC et al. Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence. *J Invest Dermatol.* 2014;134-1:43-50. PMID: 23877569. **KQ1E11, KQ4E6, KQ5E6.**
137. Elsheikh TM, Kirkpatrick JL, Fischer D et al. Does the time of day or weekday affect screening accuracy? A pilot correlation study with cytotechnologist workload and abnormal rate detection using the ThinPrep Imaging System. *Cancer Cytopathol.* 2010;118-1:41-6. PMID: 20099317. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
138. Elwood JM. Screening for melanoma. *Cancer Treat Res.* 1996;86:129-47. PMID: 8886443. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
139. Engelberg D, Gallagher RP, Rivers JK. Follow-up and evaluation of skin cancer screening in British Columbia. *J Am Acad Dermatol.* 1999;41-1:37-42. PMID: 10411408. **KQ3E5.**
140. English DR, Burton RC, del Mar CB et al. Evaluation of aid to diagnosis of pigmented skin lesions in general practice: controlled trial randomised by practice. *BMJ.* 2003;327-7411:375. PMID: 12919990. **KQ3E6.**
141. Essner R. Surgical treatment of malignant melanoma. *Surg Clin North Am.* 2003;83-1:109-56. PMID: 12691453. **KQ2E2, KQ6.**
142. Estrada JG. Non-melanoma skin cancer in Catalonia. A community-based prevalence study. *Int J Dermatol.* 2005;44-11:922-4. PMID: 16336524. **KQ1E6, KQ3E4.**
143. Faries M. Survival and the sentinel lymph node in melanoma. *Ann Surg Oncol.* 2010;17-1:18-20. PMID: 19885700. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
144. Fawzy FI, Canada AL, Fawzy NW. Malignant melanoma: effects of a brief, structured psychiatric intervention on survival and recurrence at 10-year follow-up. *Arch Gen Psychiatry.* 2003;60-1:100-3. PMID: 12511177. **KQ2E6, KQ5E7.**
145. Federman DG, Concato J, Kirsner RS. Screening for skin cancer: absence of evidence. *Arch Dermatol.* 2009;145-8:926-7. PMID: 19687426. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
146. Federman DG, Kravetz JD, Tobin DG et al. Full-body skin examinations: the patient's perspective. *Arch Dermatol.* 2004;140-5:530-4. PMID: 15148096. **KQ1E6, KQ2E5, KQ3E7, KQ4E7, KQ5E6.**
147. Feit NE, Dusza SW, Marghoob AA. Melanomas detected with the aid of total cutaneous photography. *Br J Dermatol.* 2004;150-4:706-14. PMID: 15099367. **KQ1E7, KQ2E7, KQ3E7, KQ4E7.**
148. Fernandez CA, McClure LA, LeBlanc WG et al. A comparison of Florida skin cancer screening rates with those in the rest of the United States. *Arch Dermatol.* 2012;148-3:393-5. PMID: 22431787. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
149. Ferrandiz L, Moreno-Ramirez D, Camacho FM. Shave excision of common acquired melanocytic nevi: cosmetic outcome, recurrences, and complications. *Dermatol Surg.* 2005;31(9 Pt 1):1112-5. PMID: 16164859. **KQ2E7.**
150. Ferrara G, Argenziano G, Cerroni L et al. A pilot study of a combined dermoscopic-pathological approach to the teleradiology of melanocytic skin neoplasms. *J Telemed Telecare.* 2004;10-1:34-8. PMID: 15006214. **KQ3E4.**
151. Ferrara G, Argenziano G, Giorgio CM et al. Dermoscopic-pathologic correlation: apropos of six equivocal cases. *Semin Cutan Med Surg.* 2009;28-3:157-64. PMID: 19782939. **KQ3E5.**
152. Ferrini R. Screening for skin cancer. *Am Fam Physician.* 2002;65-7:1401-2. PMID: 11996425. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**



## Appendix C. Excluded Studies

153. Fisher M, Vines HH, Hasora P. Clinical inquiries. Which technique for removing nevi is least scarring? *J Fam Pract.* 2007;56-9:743-4, 746. PMID: 17764646. **KQ2E2.**
154. Fisher NM, Schaffer JV, Berwick M et al. Breslow depth of cutaneous melanoma: impact of factors related to surveillance of the skin, including prior skin biopsies and family history of melanoma. *J Am Acad Dermatol.* 2005;53-3:393-406. PMID: 16112344. **KQ2E6, KQ4E4.**
155. Forsea AM. Melanoma staging and sentinel lymph node biopsy. *Acta Dermatovenerol Croat.* 2010;18-4:279-88. PMID: 21251448. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
156. Friedman RJ, Gutkowitz-Krusin D, Farber MJ et al. The diagnostic performance of expert dermoscopists vs a computer-vision system on small-diameter melanomas. *Arch Dermatol.* 2008;144-4:476-82. PMID: 18427041. **KQ3E5.**
157. Fueyo-Casado A, Vazquez-Lopez F, Sanchez-Martin J et al. Evaluation of a program for the automatic dermoscopic diagnosis of melanoma in a general dermatology setting. *Dermatol Surg.* 2009;35-2:257-9; discussion 260-2. PMID: 19215265. **KQ3E6.**
158. Futoryan T, Grande D. Postoperative wound infection rates in dermatologic surgery. *Dermatol Surg.* 1995;21-6:509-14. PMID: 7773598. **KQ1E13, KQ2E5, KQ3E6, KQ4E13, KQ5E13.**
159. Gajda M, Kaminska-Winciorek G. Do not let to be late: overview of reasons for melanoma delayed diagnosis. *Asian Pac J Cancer Prev.* 2014;15-9:3873-7. PMID: 24935566. **KQ4E2.**
160. Garcia Arroyo JL, Garcia Zapirain B. Detection of pigment network in dermoscopy images using supervised machine learning and structural analysis. *Comput Biol Med.* 2014;44:144-57. PMID: 24314859. **KQ3E4.**
161. Garcia C, Holman J, Poletti E. Mohs surgery: commentaries and controversies. *Int J Dermatol.* 2005;44-11:893-905. PMID: 16336520. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
162. Garg A, Geller A. Need to improve skin cancer screening of high-risk patients: Comment on "Skin cancer screening by dermatologists, family practitioners, and internists". *Arch Dermatol.* 2011;147-1:44-5. PMID: 21242391. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
163. Garnavi R, Aldeen M, Celebi ME et al. Border detection in dermoscopy images using hybrid thresholding on optimized color channels. *Comput Med Imaging Graph.* 2011;35-2:105-15. PMID: 20832992. **KQ3E6.**
164. Geller AC. Screening for melanoma. *Dermatol Clin.* 2002;20-4:629-40, viii. PMID: 12380050. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
165. Geller AC, Greinert R, Sinclair C et al. A nationwide population-based skin cancer screening in Germany: proceedings of the first meeting of the International Task Force on Skin Cancer Screening and Prevention (September 24 and 25, 2009). *Cancer Epidemiol.* 2010;34-3:355-8. PMID: 20381443. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
166. Geller AC, Sober AJ, Zhang Z et al. Strategies for improving melanoma education and screening for men age  $\geq$  50 years: findings from the American Academy of Dermatological National Skin Cancer Screening Program. *Cancer.* 2002;95-7:1554-61. PMID: 12237925. **KQ1E6, KQ4E6.**
167. Geller AC, Zhang Z, Sober AJ et al. The first 15 years of the American Academy of Dermatology skin cancer screening programs: 1985-1999. *J Am Acad Dermatol.* 2003;48-1:34-41. PMID: 12522368. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
168. Goldsmith SM. Cost analysis suggests overemphasis on biopsy rate for melanoma diagnosis. *J Am Acad Dermatol.* 2013;68-3:517-9. PMID: 23394922. **KQ1E4.**
169. Goodson AG, Florell SR, Hyde M et al. Comparative analysis of total body and dermatoscopic photographic monitoring of nevi in similar patient populations at risk for cutaneous melanoma. *Dermatol Surg.* 2010;36-7:1087-98. PMID: 20653722. **KQ3E4.**
170. Goto M, Kai Y, Arakawa S et al. Analysis of 256 cases of basal cell carcinoma after either one-step or two-step surgery in a Japanese institution. *J Dermatol.* 2012;39-1:68-71. PMID: 21951151. **KQ2E6.**
171. Grange F, Woronoff AS, Bera R et al. Efficacy of a general practitioner training campaign for early detection of melanoma in France. *Br J Dermatol.* 2014;170-1:123-9. PMID: 23937244. **KQ1E6.**

## Appendix C. Excluded Studies

172. Grann AF, Froslev T, Olesen AB et al. The impact of comorbidity and stage on prognosis of Danish melanoma patients, 1987-2009: a registry-based cohort study. *Br J Cancer*. 2013;109-1:265-71. PMID: 23681188. **KQ5E6.**
173. Greinert R, Boniol M. Skin cancer--primary and secondary prevention (information campaigns and screening)--with a focus on children & sunbeds. *Prog Biophys Mol Biol*. 2011;107-3:473-6. PMID: 21906618. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
174. Griffiths RW, Feeley K, Suvarna SK. Audit of clinical and histological prognostic factors in primary invasive squamous cell carcinoma of the skin: assessment in a minimum 5 year follow-up study after conventional excisional surgery. *Br J Plast Surg*. 2002;55-4:287-92. PMID: 12160533. **KQ5E7.**
175. Grimaldi L, Silvestri A, Brandi C et al. Digital epiluminescence dermoscopy for pigmented cutaneous lesions, primary care physicians, and teliagnosis: a useful tool? *J Plast Reconstr Aesthet Surg*. 2009;62-8:1054-8. PMID: 18547883. **KQ3E5.**
176. Grob JJ, Bonerandi JJ. The 'ugly duckling' sign: identification of the common characteristics of nevi in an individual as a basis for melanoma screening. *Arch Dermatol*. 1998;134-1:103-4. PMID: 9449921. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
177. Guillen DR, Cockerell CJ. Accurate diagnosis of cutaneous keratinocytic neoplasms: the importance of histological step sections (and other factors). *Arch Dermatol*. 2000;136-4:535-7. PMID: 10768653. **KQ3E2.**
178. Gurgun J, Gatti M. Epiluminescence microscopy (dermoscopy) versus visual inspection during Mohs microscopic surgery of infiltrative basal cell carcinoma. *Dermatol Surg*. 2012;38(7 Pt 1 ):1066-9. PMID: 22676346. **KQ3E5.**
179. Guther S, Ramrath K, Dyall-Smith D et al. Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. *J Eur Acad Dermatol Venereol*. 2012;26-1:86-94. PMID: 21371132. **KQ3E6.**
180. Haenssle HA, Korpas B, Hansen-Hagge C et al. Seven-point checklist for dermoscopy: performance during 10 years of prospective surveillance of patients at increased melanoma risk. *J Am Acad Dermatol*. 2010;62-5:785-93. PMID: 20226567. **KQ3E5.**
181. Hajdarevic S, Hornsten A, Sundbom E et al. Health-care delay in malignant melanoma: various pathways to diagnosis and treatment. *Dermatol Res Pract*. 2014;2014:294287. PMID: 24516469. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
182. Haniffa MA, Lloyd JJ, Lawrence CM. The use of a spectrophotometric intracutaneous analysis device in the real-time diagnosis of melanoma in the setting of a melanoma screening clinic. *Br J Dermatol*. 2007;156-6:1350-2. PMID: 17535234. **KQ3E6.**
183. Harrison PV, Kirby B, Dickinson Y et al. Teledermatology--high technology or not? *J Telemed Telecare*. 1998;31-2. PMID: 9640726. **KQ3E7.**
184. Hauschild A, Chen SC, Weichenthal M et al. To excise or not: impact of MelaFind on German dermatologists' decisions to biopsy atypical lesions. *J Dtsch Dermatol Ges*. 2014;12-7:606-14. PMID: 24944011. **KQ3E7.**
185. Hayashi K, Uhara H, Okuyama R. Detection of the tumor margin of basal-cell carcinoma using dermoscopy and high-frequency ultrasound with narrow pieces of surgical tape as skin markers. *Dermatol Surg*. 2014;40-6:704-6. PMID: 24852480. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
186. Hazan C, Melzer K, Panageas KS et al. Evaluation of the proliferation marker MIB-1 in the prognosis of cutaneous malignant melanoma. *Cancer*. 2002;95-3:634-40. PMID: 12209757. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
187. Heckman CJ. Enhancing skin cancer screening through behavioral intervention. *JAMA Dermatol*. 2014;150-4:363-5. PMID: 24553600. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
188. Helfand M, Mahon SM, Eden KB et al. Screening for skin cancer. *Am J Prev Med*. 2001;20(3 Suppl ):47-58. PMID: 11306232. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**

## Appendix C. Excluded Studies

189. Helfand M, Mahon S, Eden K. Screening for Skin Cancer. 2001. PMID: 20722115. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
190. 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;132-4:563-70. PMID: 7748747. **KQ1E6, KQ4E6, KQ5E6.**
191. Hernandez C, Kim H, Mauleon G et al. A pilot program in collaboration with community centers to increase awareness and participation in skin cancer screening among Latinos in Chicago. *J Cancer Educ.* 2013;28-2:342-5. PMID: 23378167. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
192. Hernandez C, Mermelstein R, Robinson JK et al. Assessing students' ability to detect melanomas using standardized patients and moulage. *J Am Acad Dermatol.* 2013;68-3:e83-8. PMID: 22196980. **KQ3E5.**
193. Herschorn A. Dermoscopy for melanoma detection in family practice. *Can Fam Physician.* 2012;58-7:740-5, e372-8. PMID: 22859635. **KQ3E2.**
194. Hershock D. Genetics, prevention and screening for melanoma. *Cancer Chemother Biol Response Modif.* 2005;22:707-28. PMID: 16110635. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
195. Hinton D. Strategies for skin cancer screening. *Dermatol Nurs.* 2008;20-6:475. PMID: 19241746. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
196. Hocutt JE Jr, Morgan LO. Dermatoscopic screening in family practice. *Del Med J.* 2001;73-6:227-34. PMID: 11449929. **KQ3E6.**
197. Hoffmann K, Gambichler T, Rick A et al. Diagnostic and neural analysis of skin cancer (DANAOS). A multicentre study for collection and computer-aided analysis of data from pigmented skin lesions using digital dermoscopy. *Br J Dermatol.* 2003;149-4:801-9. PMID: 14616373. **KQ3E6.**
198. Hohnheiser AM, Gefeller O, Gohl J et al. Malignant melanoma of the skin: long-term follow-up and time to first recurrence. *World J Surg.* 2011;35-3:580-9. PMID: 21125274. **KQ4E7, KQ5E6.**
199. Holme SA, Varma S, Chowdhury MM et al. Audit of a melanoma screening day in the U.K.: clinical results, participant satisfaction and perceived value. *Br J Dermatol.* 2001;145-5:784-8. PMID: 11736902. **KQ1E6, KQ3E5.**
200. Hossain D, Qian J, Adupe J et al. Differentiation of melanoma and benign nevi by fluorescence in-situ hybridization. *Melanoma Res.* 2011;21-5:426-30. PMID: 21900793. **KQ3E13.**
201. Hu S, Kirsner RS. Suboptimal skin cancer screening and delayed melanoma diagnosis in Hispanics: comment on "Cutaneous melanoma and other skin cancer screening among Hispanics in the United States". *Arch Dermatol.* 2011;147-6:745-6. PMID: 21690546. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
202. Hu S, Soza-Vento RM, Parker DF et al. Comparison of stage at diagnosis of melanoma among Hispanic, black, and white patients in Miami-Dade County, Florida. *Arch Dermatol.* 2006;142-6:704-8. PMID: 16785372. **KQ2E5.**
203. Hunger RE, Della Torre R, Serov A et al. Assessment of melanocytic skin lesions with a high-definition laser Doppler imaging system. *Skin Res Technol.* 2012;18-2:207-11. PMID: 22092722. **KQ3E7.**
204. Hussussian CJ. Surgical treatment of advanced melanoma. *Clin Plast Surg.* 2010;37-1:161-8. PMID: 19914466. **KQ2E2, KQ6.**
205. Iyatomi H, Celebi M, Oka H et al. An Internet-based melanoma screening system with acral volar lesion support. *Conf Proc IEEE Eng Med Biol Soc.* 2008;2008:5156-9. PMID: 19163878. **KQ3E13.**
206. Iyatomi H, Norton KA, Celebi M et al. Classification of melanocytic skin lesions from non-melanocytic lesions. *Conf Proc IEEE Eng Med Biol Soc.* 2010;2010:5407-10. PMID: 21096271. **KQ3E5.**
207. Iyatomi H, Oka H, Celebi ME et al. An improved Internet-based melanoma screening system with dermatologist-like tumor area extraction algorithm. *Comput Med Imaging Graph.* 2008;32-7:566-79. PMID: 18703311. **KQ3E5.**
208. Iyatomi H, Oka H, Celebi ME et al. Computer-based classification of dermoscopy images of melanocytic lesions on acral volar skin. *J Invest Dermatol.* 2008;128-8:2049-54. PMID: 18323788. **KQ3E5.**

## Appendix C. Excluded Studies

209. Jackson AM, Morgan DR, Ellison R. Diagnosis of malignant melanoma by general practitioners and hospital specialists. *Postgrad Med J.* 2000;76-895:295-8. PMID: 10775284. **KQ3E5.**
210. Jackson A. 'Is this mole all right'? Practitioner. 1998;242-1585:254-6, 260-2, 264 passim. PMID: 10492981. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
211. Jackson A, Wilkinson C, Ranger M et al. 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;316-7124:34-8; discussion 38-9. PMID: 9451264. **KQ3E6.**
212. Janda M, Lowe JB, Elwood M et al. Do centralised skin screening clinics increase participation in melanoma screening (Australia)? *Cancer Causes Control.* 2006;17-2:161-8. PMID: 16425094. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
213. Janda M, Youl P, Neale R et al. Clinical skin examination outcomes after a video-based behavioral intervention: analysis from a randomized clinical trial. *JAMA Dermatol.* 2014;150-4:372-9. PMID: 24553807. **KQ1E6, KQ3E7.**
214. Jonna BP, Delfino RJ, Newman WG et al. Positive predictive value for presumptive diagnoses of skin cancer and compliance with follow-up among patients attending a community screening program. *Prev Med.* 1998;27-4:611-6. PMID: 9672956. **KQ1E6, KQ3E5, KQ4E6.**
215. Kansal AR, Shaul AJ, Stern S et al. Cost-effectiveness of a FISH assay for the diagnosis of melanoma in the USA. *Expert Rev Pharmacoecon Outcomes Res.* 2013;13-3:371-80. PMID: 23672374. **KQ3E5.**
216. Kantor J, Kantor DE. Routine dermatologist-performed full-body skin examination and early melanoma detection. *Arch Dermatol.* 2009;145-8:873-6. PMID: 19687416. **KQ3E6, KQ4E6.**
217. Kanzler MH. The current status of evaluation and treatment of high-risk cutaneous melanoma: therapeutic breakthroughs remain elusive. *Arch Dermatol.* 2007;143-6:785-7. PMID: 17576947. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
218. Karampoiki V, Flores FJ, Altinoz H et al. Screening Evaluation System--Europe (SESy\_Europe) met skin cancer screening. *Cent Eur J Public Health.* 2007;15-2:71-3. PMID: 17645221. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
219. Karim RZ, Scolyer RA, Li W et al. False negative sentinel lymph node biopsies in melanoma may result from deficiencies in nuclear medicine, surgery, or pathology. *Ann Surg.* 2008;247-6:1003-10. PMID: 18520228. **KQ2E5.**
220. Katris P. Results from a skin cancer screening program in Western Australia. *Med J Aust.* 1995;163-10:557. PMID: 8538531. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
221. 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 N Z J Surg.* 1996;66-2:101-4. PMID: 8602803. **KQ1E6, KQ3E6, KQ4E6, KQ5E6.**
222. Katris P, Donovan RJ, Gray BN. Nurses screening for skin cancer: an observation study. *Aust N Z J Public Health.* 1998;22(3 Suppl ):381-3. PMID: 9629826. **KQ3E5.**
223. Keeley D. Screening for melanoma risk is misguided. *BMJ.* 1995;310-6984:916. PMID: 7719185. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
224. Kelly JW, Yeatman JM, Regalia C et al. A high incidence of melanoma found in patients with multiple dysplastic naevi by photographic surveillance. *Med J Aust.* 1997;167-4:191-4. PMID: 9293264. **KQ3E5.**
225. Kirsner RS, Wilkinson JD, Ma F et al. The association of Medicare health care delivery systems with stage at diagnosis and survival for patients with melanoma. *Arch Dermatol.* 2005;141-6:753-7. PMID: 15967922. **KQ5E6, KQ6.**
226. Kitchener SJ, McMaster S, Nasveld P. Who attends skin cancer screening in the suburbs? *Aust N Z J Public Health.* 2006;30-3:290-1. PMID: 16800212. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
227. Kitchener S, McMaster S, Nasveld P. Dermoscopy in primary care for detection of melanoma. *Int J Dermatol.* 2009;48-12:1397-8. PMID: 20415681. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**

## Appendix C. Excluded Studies

228. Koh HK. Melanoma screening: focusing the public health journey. *Arch Dermatol.* 2007;143-1:101-3. PMID: 17224549. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
229. 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;34-6:971-8. PMID: 8647990. **KQ1E6, KQ4E6, KQ3E5.**
230. Konstadoulakis MM, Messaris E, Zografos G et al. Common prognostic factors for stage III melanoma patients and for stage I and II melanoma patients with recurrence to their regional lymph nodes. *Melanoma Res.* 2002;12-4:357-64. PMID: 12170185. **KQ5E6.**
231. Kovalyshyn I, Dusza SW, Siamas K et al. The impact of physician screening on melanoma detection. *Arch Dermatol.* 2011;147-11:1269-75. PMID: 21768448. **KQ3E5.**
232. Kretschmer L, Starz H, Thoms KM et al. Age as a key factor influencing metastasizing patterns and disease-specific survival after sentinel lymph node biopsy for cutaneous melanoma. *Int J Cancer.* 2011;129-6:1435-42. PMID: 21064111. **KQ5E6.**
233. Krickler A, Armstrong B, Hansen V et al. Basal cell carcinoma and squamous cell carcinoma growth rates and determinants of size in community patients. *J Am Acad Dermatol.* 2014;70-3:456-64. PMID: 24373780. **KQ5E6.**
234. Kroemer S, Fruhauf J, Campbell TM et al. Mobile teledermatology for skin tumour screening: diagnostic accuracy of clinical and dermoscopic image tele-evaluation using cellular phones. *Br J Dermatol.* 2011;164-5:973-9. PMID: 21219286. **KQ3E9.**
235. Kyrgidis A, Tzellos T, Mocellin S et al. Sentinel lymph node biopsy followed by lymph node dissection for localised primary cutaneous melanoma. *Cochrane Database Syst Rev.* 2015;5:CD010307. PMID: 25978975. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
236. Lai SM, King JB, Garimella S et al. Effect of the staging schema on melanoma cancer reporting, 1999 to 2006. *J Am Acad Dermatol.* 2011;65(5 Suppl 1):S95-103. PMID: 22018073. **KQ1E4, KQ2E4, KQ3E4, KQ4E4, KQ5E4.**
237. Lallas A, Argenziano G, Kyrgidis A et al. Dermoscopy uncovers clinically undetectable pigmentation in basal cell carcinoma. *Br J Dermatol.* 2014;170-1:192-5. PMID: 24117444. **KQ3E6.**
238. Lamel SA, Haldeman KM, Ely H et al. Application of mobile teledermatology for skin cancer screening. *J Am Acad Dermatol.* 2012;67-4:576-81. PMID: 22243769. **KQ3E6.**
239. Lane JE, Dalton RR, Sanguenza OP. Cutaneous melanoma: detecting it earlier, weighing management options. *J Fam Pract.* 2007;56-1:18-28. PMID: 17217894. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
240. Lasithiotakis KG, Leiter U, Eigentler T et al. Improvement of overall survival of patients with cutaneous melanoma in Germany, 1976-2001: which factors contributed? *Cancer.* 2007;109-6:1174-82. PMID: 17265520. **KQ1E5, KQ4E5, KQ5E5.**
241. Laub DR Jr. Death from metastatic basal cell carcinoma: herbal remedy or just unlucky? *J Plast Reconstr Aesthet Surg.* 2008;61-7:846-8. PMID: 18472318. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
242. Lee EH, Busam KJ. Desmoplastic melanoma presenting after laser treatment: a case report and tale of caution. *Dermatol Surg.* 2011;37-11:1689-92. PMID: 21790855. **KQ1E9, KQ2E4, KQ3E9, KQ4E9, KQ5E9.**
243. Lehto US, Ojanen M, Dyba T et al. Baseline psychosocial predictors of survival in localized melanoma. *J Psychosom Res.* 2007;63-1:15-Sep. PMID: 17586333. **KQ2E6.**
244. Lejeune FJ. The impact of surgery on the course of melanoma. *Recent Results Cancer Res.* 2002;160:151-7. PMID: 12079209. **KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
245. Limpert GH. Skin-cancer screening: a three-year experience that paid for itself. *J Fam Pract.* 1995;40-5:471-5. PMID: 7730771. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
246. Lin KW, Sharangpani R. Screening for skin cancer. *Am Fam Physician.* 2010;81-12:1435-6; quiz 1429. PMID: 20540480. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
247. Linos E, Wehner MR, Frosch DL et al. Patient-reported problems after office procedures. *JAMA Intern Med.* 2013;173-13:1249-50. PMID: 23689235. **KQ2E6.**

## Appendix C. Excluded Studies

248. Little P, Keefe M, White J. Screening for melanoma. *BMJ*. 1995;311-7001:389-90. PMID: 7640558. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
249. Livingstone E, Windemuth-Kieselbach C, Eigentler TK et al. A first prospective population-based analysis investigating the actual practice of melanoma diagnosis, treatment and follow-up. *Eur J Cancer*. 2011;47-13:1977-89. PMID: 21612915. **KQ4E5.**
250. Lowe M, Hill N, Page A et al. The impact of shave biopsy on the management of patients with thin melanomas. *Am Surg*. 2011;77-8:1050-3. PMID: 21944522. **KQ2E4, KQ3E4, KQ4E4.**
251. MacKie RM, Fleming C, McMahon AD et al. The use of the dermatoscope to identify early melanoma using the three-colour test. *Br J Dermatol*. 2002;146-3:481-4. PMID: 11952549. **KQ3E6.**
252. Malvey J, Hauschild A, Curiel-Lewandrowski C et al. Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multicentre, prospective and blinded clinical trial on efficacy and safety. *Br J Dermatol*. 2014;171-5:1099-107. PMID: 24841846. **KQ3E5.**
253. Marks R. Positive predictive value of skin cancer screening. *J Am Acad Dermatol*. 2006;55-3:544-5; author reply 545-6. PMID: 16908378. **KQ3E2.**
254. Marks R. Squamous cell carcinoma. *Lancet*. 1996;347-9003:735-8. PMID: 8602006. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
255. Massone C, Maak D, Hofmann-Wellenhof R et al. Teledermatology for skin cancer prevention: an experience on 690 Austrian patients. *J Eur Acad Dermatol Venereol*. 2014;28-8:1103-8. PMID: 24372877. **KQ3E5.**
256. Matteucci P, Pinder R, Magdum A et al. Accuracy in skin lesion diagnosis and the exclusion of malignancy. *J Plast Reconstr Aesthet Surg*. 2011;64-11:1460-5. PMID: 21741335. **KQ4E6, KQ4E6.**
257. Mauad EC, Silva TB, Latorre MR et al. Opportunistic screening for skin cancer using a mobile unit in Brazil. *BMC Dermatol*. 2011;11:12. PMID: 21645347. **KQ1E5, KQ4E5.**
258. Mayer JE, Swetter SM, Fu T et al. Screening, early detection, education, and trends for melanoma: current status (2007-2013) and future directions: Part II. Screening, education, and future directions. *J Am Acad Dermatol*. 2014;71-4:611 e1-611 e10; quiz 621-2. PMID: 25219717. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
259. Mayer JE, Swetter SM, Fu T et al. Screening, early detection, education, and trends for melanoma: current status (2007-2013) and future directions: Part I. Epidemiology, high-risk groups, clinical strategies, and diagnostic technology. *J Am Acad Dermatol*. 2014;71-4:599 e1-599 e12; quiz 610, 599 e12. PMID: 25219716. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
260. Melia J. Early detection of cutaneous malignant melanoma in Britain. *Int J Epidemiol*. 1995:S39-44. PMID: 7558550. **KQ1E6.**
261. 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;132-3:414-21. PMID: 7718458. **KQ1E6, KQ3E6, KQ4E7.**
262. Melia J, Harland C, Moss S et al. Feasibility of targeted early detection for melanoma: a population-based screening study. *Br J Cancer*. 2000;82-9:1605-9. PMID: 10789732. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
263. Melia J, Moss S, Coleman D et al. The relation between mortality from malignant melanoma and early detection in the Cancer Research Campaign Mole Watcher Study. *Br J Cancer*. 2001;85-6:803-7. PMID: 11556828. **KQ1E6.**
264. Menzies SW, Emery J, Staples M et al. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *Br J Dermatol*. 2009;161-6:1270-7. PMID: 19747359. **KQ3E7, KQ4E6.**
265. Mills JK, White I, Diggs B et al. Effect of biopsy type on outcomes in the treatment of primary cutaneous melanoma. *Am J Surg*. 2013;205-5:585-90; discussion 590. PMID: 23592167. **KQ2E13, KQ3E13, KQ4E13.**

## Appendix C. Excluded Studies

266. Moore P, Hundley J, Hundley J et al. Does shave biopsy accurately predict the final breslow depth of primary cutaneous melanoma? *Am Surg.* 2009;75-5:369-73; discussion 374. PMID: 19445285. **KQ2E4, KQ4E4.**
267. Moran B, McDonald I, Wall D et al. Complete skin examination is essential in the assessment of dermatology patients: findings from 483 patients. *Br J Dermatol.* 2011;165-5:1124-6. PMID: 21711328. **KQ1E6, KQ3E5, KQ4E5.**
268. Moreno-Ramirez D, Ferrandiz L, Galdeano R et al. Teledermatology as a triage system for pigmented lesions: a pilot study. *Clin Exp Dermatol.* 2006;31-1:13-8. PMID: 16309470. **KQ3E7.**
269. Moreno-Ramirez D, Ferrandiz L, Nieto-Garcia A et al. Store-and-forward teledermatology in skin cancer triage: experience and evaluation of 2009 teleconsultations. *Arch Dermatol.* 2007;143-4:479-84. PMID: 17438180. **KQ3E5.**
270. Mosterd K, Thissen MR, van Marion AM et al. Correlation between histologic findings on punch biopsy specimens and subsequent excision specimens in recurrent basal cell carcinoma. *J Am Acad Dermatol.* 2011;64-2:323-7. PMID: 21238826. **KQ2E5.**
271. Munoz C, Vazquez-Botet M. Melanoma in situ in Puerto Rico: clinical characteristics and detection patterns. *P R Health Sci J.* 2004;23-3:179-82. PMID: 15631171. **KQ4E5.**
272. Murali R, Doubrovsky A, Watson GF et al. Diagnosis of metastatic melanoma by fine-needle biopsy: analysis of 2,204 cases. *Am J Clin Pathol.* 2007;127-3:385-97. PMID: 17276948. **KQ3E13.**
273. Nagano T, Ueda M, Suzuki T et al. Skin cancer screening in Okinawa, Japan. *J Dermatol Sci.* 1999;19-3:161-5. PMID: 10215187. **KQ3E7.**
274. Nathansohn N, Orenstein A, Trau H et al. Pigmented lesions clinic for early detection of melanoma: preliminary results. *Isr Med Assoc J.* 2007;9-10:708-12. PMID: 17987757. **KQ3E6.**
275. Nichols AC, Bhattacharyya N. Racial differences in stage and survival in head and neck squamous cell carcinoma. *Laryngoscope.* 2007;117-5:770-5. PMID: 17473666. **KQ5E13.**
276. Nikkels AF, Nikkels-Tassoudji N, Jerusalem-Noury E et al. Skin cancer screening campaign in the German speaking Community of Belgium. *Acta Clin Belg.* 2004;59-4:194-8. PMID: 15597726. **KQ3E6.**
277. Oivanen T, Kojo K, Pylkkanen L et al. Early detection of skin cancer as public health policy: comparison of campaign and routine activity. *Prev Med.* 2008;46-2:160-5. PMID: 17919714. **KQ3E7.**
278. O'Leary JA, Berend KR, Johnson JL et al. Subungual melanoma. A review of 93 cases with identification of prognostic variables. *Clin Orthop Relat Res.* 2000;-378:206-12. PMID: 10986996. **KQ5E5.**
279. Orfaniotis G, Mennie JC, Fairbairn N et al. Findings of computed tomography in stage IIB and IIC melanoma: a six-year retrospective study in the South-East of Scotland. *J Plast Reconstr Aesthet Surg.* 2012;65-9:1216-9. PMID: 22525255. **KQ5E13.**
280. Osborne JE. Skin cancer screening and surveillance. *Br J Dermatol.* 2002;146-5:745-54. PMID: 12000369. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
281. Osborne JE, Bourke JF, Graham-Brown RA et al. False negative clinical diagnoses of malignant melanoma. *Br J Dermatol.* 1999;140-5:902-8. PMID: 10354030. **KQ2E4, KQ6.**
282. Osborne JE, Chave TA, Hutchinson PE. Comparison of diagnostic accuracy for cutaneous malignant melanoma between general dermatology, plastic surgery and pigmented lesion clinics. *Br J Dermatol.* 2003;148-2:252-8. PMID: 12588376. **KQ3E6.**
283. Pacifico MD, Grover R, Sanders R. Use of an early-detection strategy to improve disease control in melanoma patients. *Br J Plast Surg.* 2004;57-2:105-11. PMID: 15037164. **KQ1E13, KQ4E7.**
284. Pacifico MD, Pearl RA, Grover R. The UK Government two-week rule and its impact on melanoma prognosis: an evidence-based study. *Ann R Coll Surg Engl.* 2007;89-6:609-15. PMID: 18201477. **KQ1E6, KQ2E2, KQ3E13, KQ4E13, KQ5E13.**
285. Paoli J, Danielsson M, Wennberg AM. Results of the 'Euromelanoma Day' screening campaign in Sweden 2008. *J Eur Acad Dermatol Venereol.* 2009;23-11:1304-10. PMID: 19522711. **KQ3E5.**

## Appendix C. Excluded Studies

286. Penel N, Fournier C, Lefebvre D et al. Multivariate analysis of risk factors for wound infection in head and neck squamous cell carcinoma surgery with opening of mucosa. Study of 260 surgical procedures. *Oral Oncol.* 2005;41-3:294-303. PMID: 15743692. **KQ2E5.**
287. Pennie ML, Soon SL, Risser JB et al. Melanoma outcomes for Medicare patients: association of stage and survival with detection by a dermatologist vs a nondermatologist. *Arch Dermatol.* 2007;143-4:488-94. PMID: 17438181. **KQ1E7, KQ3E7, KQ5E7.**
288. Petit JY, Avril MF, Margulis A et al. Evaluation of cosmetic results of a randomized trial comparing surgery and radiotherapy in the treatment of basal cell carcinoma of the face. *Plast Reconstr Surg.* 2000;105-7:2544-51. PMID: 10845311. **KQ2E7.**
289. Pilko G, Besic N, Zgajnar J et al. Prognostic heterogeneity after the excision of lymph node metastases in patients with cutaneous melanoma. *Surg Oncol.* 2011;20-1:26-34. PMID: 19900803. **KQ5E7.**
290. Plym A, Ullenhag GJ, Breivald M et al. Clinical characteristics, management and survival in young adults diagnosed with malignant melanoma: A population-based cohort study. *Acta Oncol.* 2014;53-5:688-96. PMID: 24369746. **KQ5E6.**
291. Pollitt RA, Clarke CA, Shema SJ et al. California Medicaid enrollment and melanoma stage at diagnosis: a population-based study. *Am J Prev Med.* 2008;35-1:13-Jul. PMID: 18482824. **KQ5E6.**
292. Poo-Hwu WJ, Ariyan S, Lamb L et al. Follow-up recommendations for patients with American Joint Committee on Cancer Stages I-III malignant melanoma. *Cancer.* 1999;86-11:2252-8. PMID: 10590365. **KQ5E6.**
293. Posther KE, Selim MA, Mosca PJ et al. Histopathologic characteristics, recurrence patterns, and survival of 129 patients with desmoplastic melanoma. *Ann Surg Oncol.* 2006;13-5:728-39. PMID: 16538415. **KQ5E6.**
294. Poulsen M, Round C, Keller J et al. Factors influencing relapse-free survival in Merkel cell carcinoma of the lower limb--a review of 60 cases. *Int J Radiat Oncol Biol Phys.* 2010;76-2:393-7. PMID: 19515508. **KQ5E6.**
295. Poziomczyk CS, Koche B, Dornelles Mde A et al. Pain evaluation in the cryosurgery of actinic keratoses. *An Bras Dermatol.* 2011;86-4:645-50. PMID: 21987127. **KQ2E7, KQ6.**
296. Printz C. Target: melanoma: skin cancer screenings hold promise to reduce mortality rates, but usage of widespread screening lags. *Cancer.* 2013;119-13:2359-60. PMID: 23775430. **KQ1E2.**
297. Puig S, Argenziano G, Zalaudek I et al. Melanomas that failed dermoscopic detection: a combined clinicodermoscopic approach for not missing melanoma. *Dermatol Surg.* 2007;33-10:1262-73. PMID: 17903162. **KQ2E6.**
298. Purdue MP, Freeman LE, Anderson WF et al. Recent trends in incidence of cutaneous melanoma among US Caucasian young adults. *J Invest Dermatol.* 2008;128-12:2905-8. PMID: 18615112. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7.**
299. Quereux G, N'Guyen JM, Cary M et al. Validation of the Self-Assessment of Melanoma Risk Score for a melanoma-targeted screening. *Eur J Cancer Prev.* 2012;21-6:588-95. PMID: 22555198. **KQ3E5.**
300. Rademaker M, Oakley A. Digital monitoring by whole body photography and sequential digital dermoscopy detects thinner melanomas. *J Prim Health Care.* 2010;2-4:268-72. PMID: 21125066. **KQ2E6, KQ3E6, KQ4E6.**
301. Rajpara SM, Botello AP, Townend J et al. Systematic review of dermoscopy and digital dermoscopy/ artificial intelligence for the diagnosis of melanoma. *Br J Dermatol.* 2009;161-3:591-604. PMID: 19302072. **KQ3E9.**
302. Rampen FH, Casparie-van Velsen JI, van Huystee BE et al. False-negative findings in skin cancer and melanoma screening. *J Am Acad Dermatol.* 1995;33-1:59-63. PMID: 7601947. **KQ2E6, KQ3E6.**
303. Rampen RH. Point-counterpoint. Mass population skin cancer screening is not worthwhile. *J Cutan Med Surg.* 1998;2-3:128-9. PMID: 9556369. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
304. Ravin AG, Pickett N, Johnson JL et al. Melanoma of the ear: treatment and survival probabilities based on 199 patients. *Ann Plast Surg.* 2006;57-1:70-6. PMID: 16799312. **KQ5E6.**



## Appendix C. Excluded Studies

305. Reintgen C, Shivers S, Reintgen M et al. The changing face of malignant melanoma. *J Surg Oncol*. 2010;101-6:443-6. PMID: 20401913. **KQ5E6.**
306. Reisenauer A, Lee BJ, Akamine K et al. Management of melanoma in a patient population: using electronic health records to enhance postdiagnosis surveillance. *JAMA Dermatol*. 2013;149-3:365-6. PMID: 23552748. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
307. Resnik KS, DiLeonardo M, Gibbons G. Clinically occult cutaneous metastases. *J Am Acad Dermatol*. 2006;55-6:1044-7. PMID: 17110220. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
308. Retsas S, Henry K, Mohammed MQ et al. Prognostic factors of cutaneous melanoma and a new staging system proposed by the American Joint Committee on Cancer (AJCC): validation in a cohort of 1284 patients. *Eur J Cancer*. 2002;38-4:511-6. PMID: 11872343. **KQ5E6.**
309. Rex J, Paradelo C, Mangas C et al. Management of primary cutaneous melanoma of the hands and feet: a clinicoprognostic study. *Dermatol Surg*. 2009;35-10:1505-13. PMID: 19686364. **KQ5E6.**
310. Rhodes AR. Prognostic usefulness of sentinel lymph node biopsy for patients who have clinically node negative, localized, primary invasive cutaneous melanoma: a Bayesian analysis using informative published reports. *Arch Dermatol*. 2011;147-4:408-15. PMID: 21173300. **KQ5E2, KQ6.**
311. Richtig E, Ambros-Rudolph CM, Trapp M et al. Melanoma markers in marathon runners: increase with sun exposure and physical strain. *Dermatology*. 2008;217-1:38-44. PMID: 18367839. **KQ3E7.**
312. Richtig E, Santigli E, Fink-Puches R et al. Assessing melanoma risk factors: how closely do patients and doctors agree? *Public Health*. 2008;122-12:1433-9. PMID: 18752818. **KQ3E7.**
313. Rigel DS. Is the ounce of screening and prevention for skin cancer worth the pound of cure? *CA Cancer J Clin*. 1998;48-4:236-8. PMID: 9676538. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
314. Rissin Y, Fodor L, Ishach H et al. Patient satisfaction after removal of skin lesions. *J Eur Acad Dermatol Venereol*. 2007;21-7:951-5. PMID: 17659005. **KQ2E9.**
315. Robati RM, Toossi P, Karimi M et al. Screening for skin cancer: a pilot study in Tehran, Iran. *Indian J Dermatol*. 2014;59-1:105. PMID: 24470679. **KQ2E4, KQ3E4, KQ4E4.**
316. Robinson JK, McGaghie WC. Skin cancer detection in a clinical practice examination with standardized patients. *J Am Acad Dermatol*. 1996;34-4:709-11. PMID: 8601670. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6.**
317. Roder DM, Luke CG, McCaul KA et al. Trends in prognostic factors of melanoma in South Australia, 1981-1992: implications for health promotion. *Med J Aust*. 1995;162-1:25-9. PMID: 7845294. **KQ5E6.**
318. Roetzheim RG, Lee JH, Ferrante JM et al. The influence of dermatologist and primary care physician visits on melanoma outcomes among Medicare beneficiaries. *J Am Board Fam Med*. 2013;26-6:637-47. PMID: 24204060. **KQ1E7, KQ3E7.**
319. Roetzheim RG, Pal N, van Durme DJ et al. Increasing supplies of dermatologists and family physicians are associated with earlier stage of melanoma detection. *J Am Acad Dermatol*. 2000;43(2 Pt 1 ):211-8. PMID: 10906640. **KQ3E6.**
320. Rosenblatt L, Marks R. Deaths due to squamous cell carcinoma in Australia: is there a case for a public health intervention? *Australasian Journal of Dermatology*. 1996;37-1:26-9. PMID: 8936067. **KQ5E6.**
321. Rosendahl C, Williams G, Eley D et al. The impact of subspecialization and dermatoscopy use on accuracy of melanoma diagnosis among primary care doctors in Australia. *J Am Acad Dermatol*. 2012;67-5:846-52. PMID: 22325462. **KQ3E6.**
322. Rossi CR, De Salvo GL, Bonandini E et al. Factors predictive of nonsentinel lymph node involvement and clinical outcome in melanoma patients with metastatic sentinel lymph node. *Ann Surg Oncol*. 2008;15-4:1202-10. PMID: 18165880. **KQ5E13.**
323. Rossi CR, Vecchiato A, Bezze G et al. Early detection of melanoma: an educational campaign in Padova, Italy. *Melanoma Res*. 2000;10-2:181-7. PMID: 10803719. **KQ1E6, KQ2E6, KQ3E7, KQ4E6.**
324. Rouhani P, Arheart KL, Kirsner RS. Differences in melanoma outcomes among Hispanic Medicare enrollees. *J Am Acad Dermatol*. 2010;62-5:768-76. PMID: 20219264. **KQ5E6.**

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325. Rowbotham MC, Leong SP. How to reduce the incidence of neuropathic pain: sentinel node biopsy for diagnosis of metastatic malignant melanoma. *Pain*. 2011;152-12:2681-2. PMID: 21983239. **KQ2E2, KQ6.**
326. Rubegni P, Cevenini G, Burroni M et al. Objective follow-up of atypical melanocytic skin lesions: a retrospective study. *Arch Dermatol Res*. 2010;302-7:551-60. PMID: 20411393. **KQ3E6.**
327. Rueth NM, Groth SS, Tuttle TM et al. Conditional survival after surgical treatment of melanoma: an analysis of the Surveillance, Epidemiology, and End Results database. *Ann Surg Oncol*. 2010;17-6:1662-8. PMID: 20165985. **KQ5E6.**
328. Rughani MG, Swan MC, Adams TS et al. Sentinel node status predicts survival in thick melanomas: the Oxford perspective. *Eur J Surg Oncol*. 2012;38-10:936-42. PMID: 22617251. **KQ5E6.**
329. Rughani MG, Swan MC, Adams TS et al. Sentinel lymph node biopsy in melanoma: The Oxford ten year clinical experience. *J Plast Reconstr Aesthet Surg*. 2011;64-10:1284-90. PMID: 21612993. **KQ5E6, KQ6.**
330. Russell L. Patient's page. Malignant melanoma and the importance of screening. *South Med J*. 2008;101-5:455. PMID: 18414149. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
331. Rutkowski P, Nowecki ZI, Nasierowska-Guttmejer A et al. Lymph node status and survival in cutaneous malignant melanoma--sentinel lymph node biopsy impact. *Eur J Surg Oncol*. 2003;29-7:611-8. PMID: 12943629. **KQ2E7.**
332. Sahn RE, Lang PG. Sentinel lymph node biopsy for high-risk nonmelanoma skin cancers. *Dermatol Surg*. 2007;33-7:786-92; discussion 792-3. PMID: 17598843. **KQ2E7, KQ6.**
333. Saida T, Miyazaki A, Oguchi S et al. Significance of dermoscopic patterns in detecting malignant melanoma on acral volar skin: results of a multicenter study in Japan. *Arch Dermatol*. 2004;140-10:1233-8. PMID: 15492186. **KQ3E5.**
334. Salerni G, Carrera C, Lovatto L et al. Characterization of 1152 lesions excised over 10 years using total-body photography and digital dermatoscopy in the surveillance of patients at high risk for melanoma. *J Am Acad Dermatol*. 2012;67-5:836-45. PMID: 22521205. **KQ3E6.**
335. Salerni G, Carrera C, Lovatto L et al. Benefits of total body photography and digital dermatoscopy ("two-step method of digital follow-up") in the early diagnosis of melanoma in patients at high risk for melanoma. *J Am Acad Dermatol*. 2012;67-1:e17-27. PMID: 21683472. **KQ3E5.**
336. Salerni G, Lovatto L, Carrera C et al. Melanomas detected in a follow-up program compared with melanomas referred to a melanoma unit. *Arch Dermatol*. 2011;147-5:549-55. PMID: 21242346. **KQ3E5.**
337. Salerni G, Teran T, Puig S et al. Meta-analysis of digital dermatoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. *J Eur Acad Dermatol Venereol*. 2013;27-7:805-14. PMID: 23181611. **KQ3E6.**
338. Salvio AG, Assumpcao Junior A, Segalla JG et al. One year experience of a model for melanoma continuous prevention in the city of Jau (Sao Paulo), Brazil. *An Bras Dermatol*. 2011;86-4:669-74. PMID: 21987131. **KQ1E4, KQ2E4, KQ3E4, KQ4E4, KQ5E4.**
339. Sankaran N. A call for stepped-up melanoma screening. *Ann Intern Med*. 1997;126-4:160-1. PMID: 9446503. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
340. Sanlorenzo M, Ribero S, Osella-Abate S et al. Prognostic differences across sexes in melanoma patients: what has changed from the past? *Melanoma Res*. 2014;24-6:568-76. PMID: 24892954. **KQ5E6.**
341. Sargeran K, Murtomaa H, Safavi SM et al. Survival after lip cancer diagnosis. *J Craniofac Surg*. 2009;20-1:248-52. PMID: 19165039. **KQ5E13.**
342. Satorres Nieto M, Gargallo Albiol J, Gay Escoda C. Surgical management of actinic cheilitis. *Med Oral*. 2001;6-3:205-17. PMID: 11500638. **KQ2E1.**
343. Schaefer I, Rustenbach SJ, Zimmer L et al. Prevalence of skin diseases in a cohort of 48,665 employees in Germany. *Dermatology*. 2008;217-2:169-72. PMID: 18525204. **KQ3E4.**
344. Schiffner R, Schiffner-Rohe J, Landthaler M et al. Long-term dermoscopic follow-up of melanocytic naevi: clinical outcome and patient compliance. *Br J Dermatol*. 2003;149-1:79-86. PMID: 12890198. **KQ2E5.**

## Appendix C. Excluded Studies

345. Schmid-Wendtner MH, Baumert J, Eberle J et al. Disease progression in patients with thin cutaneous melanomas (tumour thickness < or = 0.75 mm): clinical and epidemiological data from the Tumour Center Munich 1977-98. *Br J Dermatol*. 2003;149-4:788-93. PMID: 14616371. **KQ5E6.**
346. Schmid-Wendtner MH, Berking C, Baumert J et al. Cutaneous melanoma in childhood and adolescence: an analysis of 36 patients. *J Am Acad Dermatol*. 2002;46-6:874-9. PMID: 12063484. **KQ5E6.**
347. Schmitt J, Seidler A, Heinisch G et al. Effectiveness of skin cancer screening for individuals age 14 to 34 years. *J Dtsch Dermatol Ges*. 2011;9-8:608-16. PMID: 21501381. **KQ3E6, KQ4E13.**
348. Schneider JS, Moore DH 2nd, Mendelsohn ML. Screening program reduced melanoma mortality at the Lawrence Livermore National Laboratory, 1984 to 1996. *J Am Acad Dermatol*. 2008;58-5:741-9. PMID: 18068264. **KQ1E4, KQ3E4, KQ4E4.**
349. Schneider R. Dermoscopy in melanoma screening. *Arch Dermatol*. 2002;138-10:1378-9. PMID: 12374550. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
350. Schumacher H, Huang S. A 20-year-old basal cell carcinoma. *Plast Reconstr Surg*. 2005;115-2:668-9. PMID: 15692395. **KQ1E9, KQ2E9, KQ3E9, KQ4E9, KQ5E9.**
351. Schwartz JL, Wang TS, Hamilton TA et al. Thin primary cutaneous melanomas: associated detection patterns, lesion characteristics, and patient characteristics. *Cancer*. 2002;95-7:1562-8. PMID: 12237926. **KQ4E7.**
352. Scoggins CR, Bowen AL, Martin RC et al. Prognostic information from sentinel lymph node biopsy in patients with thick melanoma. *Arch Surg*. 2010;145-7:622-7. PMID: 20644123. **KQ5E6, KQ6.**
353. Seetharamu N, Tu TJ, Christos P et al. Enrollment in clinical trials correlates with improved survival in metastatic melanoma. *Oncology*. 2011;81-42130:403-9. PMID: 22270052. **KQ5E6.**
354. Seidenari S, Arginelli F, Dunsby C et al. Multiphoton laser tomography and fluorescence lifetime imaging of melanoma: morphologic features and quantitative data for sensitive and specific non-invasive diagnostics. *PLoS One*. 2013;8-7:e70682. PMID: 23923016. **KQ3E7.**
355. Seidenari S, Bellucci C, Bassoli S et al. High magnification digital dermoscopy of basal cell carcinoma: a single-centre study on 400 cases. *Acta Derm Venereol*. 2014;94-6:677-82. PMID: 24682274. **KQ3E6.**
356. Seidenari S, Benati E, Ponti G et al. Italian Euromelanoma Day Screening Campaign (2005-2007) and the planning of melanoma screening strategies. *Eur J Cancer Prev*. 2012;21-1:89-95. PMID: 22001916. **KQ3E5.**
357. Seidenari S, Longo C, Giusti F et al. Clinical selection of melanocytic lesions for dermoscopy decreases the identification of suspicious lesions in comparison with dermoscopy without clinical preselection. *Br J Dermatol*. 2006;154-5:873-9. PMID: 16634889. **KQ3E5.**
358. Seo SH, Son SW, Kim IH. Round excisions lead to shorter scars and better scar positioning than traditional elliptical excisions. *Dermatology*. 2008;217-3:276-80. PMID: 18688169. **KQ2E6.**
359. Seregard S. To biopsy or not to biopsy? *Acta Ophthalmol*. 2009;87-6:586-7. PMID: 19719803. **KQ2E13, KQ6.**
360. Seretis K, Thomaidis V, Karpouzis A et al. Epidemiology of surgical treatment of nonmelanoma skin cancer of the head and neck in Greece. *Dermatol Surg*. 2010;36-1:15-22. PMID: 19912277. **KQ2E13.**
361. Sewell LD, Marks VJ. Excision of a peristomal basal cell carcinoma using Mohs micrographic surgery. *Dermatol Surg*. 2008;34-7:971-3. PMID: 18384605. **KQ1E9, KQ2E9, KQ3E9, KQ4E9, KQ5E9.**
362. Shalom A, Klein D, Friedman T et al. Lack of complications in minor skin lesion excisions in patients taking aspirin or warfarin products. *Am Surg*. 2008;74-4:354-7. PMID: 18453305. **KQ2E5.**
363. Shalom A, Wong L. Outcome of aspirin use during excision of cutaneous lesions. *Ann Plast Surg*. 2003;50-3:296-8. PMID: 12800908. **KQ2E5.**
364. Shields CL, Kaliki S, Al-Dahmash SA et al. American Joint Committee on Cancer (AJCC) clinical classification predicts conjunctival melanoma outcomes. *Ophthalmol Plast Reconstr Surg*. 2012;28-5:313-23. PMID: 22965011. **KQ5E5, KQ6.**
365. Siao D, Velayos F. Avoiding rash decision making: skin cancer screening of patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol*. 2014;12-2:274-6. PMID: 24183955. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**

## Appendix C. Excluded Studies

366. Sibson L, Dunn R, Evans J et al. The virtual mole clinic: preliminary results from the Plymouth skin cancer screening study using telemedicine. *Med Inform Internet Med*. 1999;24-3:189-99. PMID: 10654813. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
367. Simpson CL. The ABCs of Melanoma: Expanding Basic Screening and Education. *Virtual Mentor*. 2006;8-8:517-9. PMID: 23234690. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
368. Singh S, Stevenson JH, McGurty D. An evaluation of Polaroid photographic imaging for cutaneous-lesion referrals to an outpatient clinic: a pilot study. *Br J Plast Surg*. 2001;54-2:140-3. PMID: 11207125. **KQ3E5.**
369. Slater LJ. Brush biopsy: false negative results. *J Oral Maxillofac Surg*. 2004;62-6:764. PMID: 15181904. **KQ2E13.**
370. Smeets NW, Krekels GA, Ostertag JU et al. Surgical excision vs Mohs' micrographic surgery for basal-cell carcinoma of the face: randomised controlled trial. *Lancet*. 2004;364-9447:1766-72. PMID: 15541449. **KQ2E6, KQ6.**
371. Smith LC, Cox NH, Dawn G. Shave biopsy without local anaesthetic to diagnose basal cell carcinoma and other skin tumours prior to definitive treatment: analysis of 109 lesions. *Br J Dermatol*. 2009;160-1:180-2. PMID: 18795923. **KQ2E4.**
372. Smith Y, Weinberg A, Klauss S et al. Improving screening for melanoma by measuring similarity to pre-classified images. *Melanoma Res*. 2000;10-3:265-72. PMID: 10890381. **KQ3E5.**
373. Sneyd MJ. Skin Phenotype and the Impact of Surveillance on Melanoma in New Zealand. *Asian Pac J Cancer Prev*. 2001;2-1:49-55. PMID: 12718654. **KQ1E6.**
374. Sneyd M, Cox B. The control of melanoma in New Zealand. *N Z Med J*. 2006;119-1242:U2169. PMID: 16998570. **KQ1E6.**
375. Soufir N, Grandchamp B, Basset-Seguain N. New trends in the susceptibility to melanoma. *Cancer Treat Res*. 2009;146:213-23. PMID: 19415206. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
376. Soyer HP. Dermoscopy and recently developed imaging techniques. Introduction. *Semin Cutan Med Surg*. 2009;28-3:141. PMID: 19782936. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
377. Soyer HP, Argenziano G, Zalaudek I et al. Three-point checklist of dermoscopy. A new screening method for early detection of melanoma. *Dermatology*. 2004;208-1:27-31. PMID: 14730233. **KQ3E5.**
378. Soyer HP, Smolle J, Leitinger G et al. Diagnostic reliability of dermoscopic criteria for detecting malignant melanoma. *Dermatology*. 1995;190-1:25-30. PMID: 7894091. **KQ3E5.**
379. Stang A. Genital and nongenital nonmelanoma skin cancer: more epidemiological studies are needed. *J Invest Dermatol*. 2007;127-10:2296-9. PMID: 17853917. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
380. Stang A, Stang K, Stegmaier C et al. Skin melanoma in Saarland: incidence, survival and mortality 1970-1996. *Eur J Cancer Prev*. 2001;10-5:407-15. PMID: 11711755. **KQ5E6.**
381. Stratman EJ. Overscreening and underscreening for melanoma: comment on "the influence of age and sex on reasons for seeking and expected benefits of skin cancer screening". *Arch Dermatol*. 2010;146-10:1102. PMID: 20956640. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
382. Swetter SM, Geller AC. Perspective: catch melanoma early. *Nature*. 2014;515-7527:S117. PMID: 25407708. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
383. Swetter SM, Pollitt RA, Johnson TM et al. Behavioral determinants of successful early melanoma detection: role of self and physician skin examination. *Cancer*. 2012;118-15:3725-34. PMID: 22179848. **KQ4E9.**
384. Swetter SM, Waddell BL, Vazquez MD et al. Increased effectiveness of targeted skin cancer screening in the Veterans Affairs population of Northern California. *Prev Med*. 2003;36-2:164-71. PMID: 12590991. **KQ1E6, KQ2E6, KQ3E7, KQ4E6, KQ5E6.**
385. Tas F, Keskin S, Karadeniz A et al. Noncutaneous melanoma have distinct features from each other and cutaneous melanoma. *Oncology*. 2011;81-42130:353-8. PMID: 22248874. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**

## Appendix C. Excluded Studies

386. Tavaloni Braga JC, Gomes E, Macedo MP et al. Early detection of melanoma arising within nevus spilus. *J Am Acad Dermatol*. 2014;70-2:e31-2. PMID: 24438974. **KQ1E13, KQ2E13, KQ3E13, KQ4E13, KQ5E13.**
387. Thomas JM. Lymphoedema in the observation and biopsy arms of MSLT-1. *Ann Surg Oncol*. 2011:S311; author reply S312-4. PMID: 21773841. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
388. Thomas JM. Sentinel-node biopsy in melanoma. *N Engl J Med*. 2007;356-4:418; author reply 419-21. PMID: 17251542. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
389. Thomas JM. The place of sentinel node biopsy in melanoma after the Multicenter Selective Lymphadenectomy Trial. *ANZ J Surg*. 2006;76-3:98-9. PMID: 16626339. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
390. Thomas JM. Time to re-evaluate sentinel node biopsy in melanoma post-multicenter selective lymphadenectomy trial. *J Clin Oncol*. 2005;23-36:9443-4. PMID: 16361650. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
391. Thompson JF. The value of sentinel node biopsy in patients with primary cutaneous melanoma. *Dermatol Surg*. 2008;34-4:550-4; discussion 554-5. PMID: 18261107. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
392. Thompson LD. Skin basal cell carcinoma. *Ear Nose Throat J*. 2010;89-9:418-20. PMID: 20859866. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
393. Tiplica GS, Olteanu R, Chiriac A et al. Skin cancer screening campaigns in a Bucharest dermatology clinic. *J Eur Acad Dermatol Venereol*. 2014;28-3:388-9. PMID: 23676085. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
394. Tornberg S, Mansson-Brahme E, Linden D et al. Screening for cutaneous malignant melanoma: a feasibility study. *J Med Screen*. 1996;3-4:211-5. PMID: 9041488. **KQ3E6.**
395. Toth V, Somlai B, Hatvani Z et al. Melanoma screening in a Hungarian nuclear power plant. *Pathol Oncol Res*. 2013;19-2:323-8. PMID: 23242566. **KQ1E4, KQ2E4, KQ3E4, KQ4E4, KQ5E4.**
396. Tromme I, Sacre L, Hammouch F et al. Availability of digital dermoscopy in daily practice dramatically reduces the number of excised melanocytic lesions: results from an observational study. *Br J Dermatol*. 2012;167-4:778-86. PMID: 22564185. **KQ3E4, KQ4E4.**
397. Tryggvadottir L, Gislum M, Hakulinen T et al. Trends in the survival of patients diagnosed with malignant melanoma of the skin in the Nordic countries 1964-2003 followed up to the end of 2006. *Acta Oncol*. 2010;49-5:665-72. PMID: 20491525. **KQ5E7.**
398. Valachis A, Mauri D, Karampoiki V et al. Time-trend of melanoma screening practice by primary care physicians: a meta-regression analysis. *Ups J Med Sci*. 2009;114-1:32-40. PMID: 19242870. **KQ3E6.**
399. Valery PC, Neale R, Williams G et al. The effect of skin examination surveys on the incidence of basal cell carcinoma in a Queensland community sample: a 10-year longitudinal study. *J Investig Dermatol Symp Proc*. 2004;9-2:148-51. PMID: 15083782. **KQ4E6.**
400. van der Eerden PA, Lohuis PJ, Hart AA et al. Secondary intention healing after excision of nonmelanoma skin cancer of the head and neck: statistical evaluation of prognostic values of wound characteristics and final cosmetic results. *Plast Reconstr Surg*. 2008;122-6:1747-55. PMID: 19050527. **KQ2E4, KQ4E6, KQ6.**
401. van der Leest RJ, de Vries E, Bulliard JL et al. The Euromelanoma skin cancer prevention campaign in Europe: characteristics and results of 2009 and 2010. *J Eur Acad Dermatol Venereol*. 2011;25-12:1455-65. PMID: 21951235. **KQ1E6, KQ2E6, KQ3E5, KQ4E6.**
402. van der Leest RJ, Nijsten T, de Vries E. Screening for second primary melanomas: is it efficient? Reply from authors. *Br J Dermatol*. 2013;168-5:1135. PMID: 23614564. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
403. Vandaele MM, Richert B, Van der Endt JD et al. Melanoma screening: results of the first one-day campaign in Belgium ('melanoma Monday'). *J Eur Acad Dermatol Venereol*. 2000;14-6:470-2. PMID: 11444268. **KQ1E6, KQ2E6, KQ3E6, KQ4E6.**

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404. Varma S. Mobile teledermatology for skin tumour screening. *Br J Dermatol.* 2011;164-5:939-40. PMID: 21518326. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
405. Venna SS, Lee D, Stadecker MJ et al. Clinical recognition of actinic keratoses in a high-risk population: how good are we? *Arch Dermatol.* 2005;141-4:507-9. PMID: 15837871. **KQ1E5, KQ2E5, KQ3E5, KQ4E5, KQ5E5.**
406. Veronesi A, Pizzichetta MA, De Giacomi C et al. A two-year regional program for the early detection of cutaneous melanoma. *Tumori.* 2003;89-1:5-Jan. PMID: 12729352. **KQ1E6, KQ2E6, KQ3E6, KQ4E6.**
407. Viola KV, Tolpinrud WL, Gross CP et al. Outcomes of referral to dermatology for suspicious lesions: implications for teledermatology. *Arch Dermatol.* 2011;147-5:556-60. PMID: 21576574. **KQ3E5.**
408. Vogt V, Siegel M, Sundmacher L. Examining regional variation in the use of cancer screening in Germany. *Soc Sci Med.* 2014;110:74-80. PMID: 24727534. **KQ3E6.**
409. Voigt H, Classen R. Topodermatographic image analysis for melanoma screening and the quantitative assessment of tumor dimension parameters of the skin. *Cancer.* 1995;75-4:981-8. PMID: 7842419. **KQ3E7.**
410. Waldmann A, Nolte S, Weinstock MA et al. Skin cancer screening participation and impact on melanoma incidence in Germany--an observational study on incidence trends in regions with and without population-based screening. *Br J Cancer.* 2012;106-5:970-4. PMID: 22294187. **KQ1E6, KQ2E6, KQ3E6, KQ4E6.**
411. Wanat KA, Kist J, Jambusaria-Pahlajani A et al. Improving students' ability to perform skin examinations and detect cutaneous malignancies using standardized patients and moulage. *J Am Acad Dermatol.* 2013;69-5:816-7. PMID: 24124813. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
412. Wang SQ, Kopf AW, Koenig K et al. Detection of melanomas in patients followed up with total cutaneous examinations, total cutaneous photography, and dermoscopy. *J Am Acad Dermatol.* 2004;50-1:15-20. PMID: 14699359. **KQ3E6, KQ4E6.**
413. Weary PE. Skin cancer screening. *J Cutan Med Surg.* 1998;3-1:49. PMID: 10026013. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
414. Weatherhead SC, Lawrence CM. Melanoma screening clinics: are we detecting more melanomas or reassuring the worried well? *Br J Dermatol.* 2006;154-3:539-41. PMID: 16445788. **KQ1E6, KQ2E6, KQ3E6, KQ4E7.**
415. Weinstock MA. Progress and prospects on melanoma: the way forward for early detection and reduced mortality. *Clin Cancer Res.* 2006;12(7 Pt 2 ):2297s-2300s. PMID: 16609048. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
416. Weinstock MA. Point-counterpoint. Mass population skin cancer screening can be worthwhile--(if it's done right). *J Cutan Med Surg.* 1998;2-3:129-32. PMID: 9556370. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2.**
417. Welch HG, Woloshin S, Schwartz LM. Skin biopsy rates and incidence of melanoma: population based ecological study. *BMJ.* 2005;331-7515:481. PMID: 16081427. **KQ2E5, KQ4E5, KQ5E5.**
418. Westerhoff K, McCarthy WH, Menzies SW. Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. *Br J Dermatol.* 2000;143-5:1016-20. PMID: 11069512. **KQ3E5.**
419. Whited JD, Grichnik JM. The rational clinical examination. Does this patient have a mole or a melanoma? *JAMA.* 1998;279-9:696-701. PMID: 9496989. **KQ3E2.**
420. Wilde M, Jones B, Lewis BK et al. Skin cancer screening in the homeless population. *Dermatol Online J.* 2013;19-1:14. PMID: 23374956. **KQ1E6, KQ3E6, KQ4E6.**
421. Wilkes D. The use of dermoscopy in medical photography for the early detection of skin cancer. *J Vis Commun Med.* 2010;33-4:169-73. PMID: 21087188. **KQ3E2.**
422. Williams HA, Fritschi L, Reid A et al. Who attends skin cancer screening in Western Australia? Results from the Lions Cancer Institute Skin Cancer Screening Program. *Aust N Z J Public Health.* 2006;30-1:75-80. PMID: 16502955. **KQ1E13, KQ3E6, KQ4E6.**
423. Wilson RL, Yentzer BA, Isom SP et al. How good are US dermatologists at discriminating skin cancers? A number-needed-to-treat analysis. *J Dermatolog Treat.* 2012;23-1:65-9. PMID: 21756146. **KQ3E4, KQ4E4.**

## Appendix C. Excluded Studies

424. Wilson R, Jackson J, Rassekh C. A study of squamous cell carcinoma of the lip at West Virginia University Hospitals from 1980-2000. *W V Med J*. 2005;101-5:217-9. PMID: 16422271. **KQ5E6**.
425. Wolf IH, Smolle J, Soyer HP et al. Sensitivity in the clinical diagnosis of malignant melanoma. *Melanoma Res*. 1998;8-5:425-9. PMID: 9835456. **KQ3E5**.
426. Wolf JA, Moreau JF, Akilov O et al. Diagnostic inaccuracy of smartphone applications for melanoma detection. *JAMA Dermatol*. 2013;149-4:422-6. PMID: 23325302. **KQ1E2, KQ2E2, KQ3E2, KQ4E2, KQ5E2**.
427. Wollina U, Burroni M, Torricelli R et al. Digital dermoscopy in clinical practise: a three-centre analysis. *Skin Res Technol*. 2007;13-2:133-42. PMID: 17374053. **KQ3E5, KQ4E6**.
428. Xing Y, Chang GJ, Hu CY et al. Conditional survival estimates improve over time for patients with advanced melanoma: results from a population-based analysis. *Cancer*. 2010;116-9:2234-41. PMID: 20187100. **KQ4E6, KQ5E6**.
429. Yiannias JA, Laman SD, Stevens R et al. Skin cancer prevention in annual performance of total skin examination, photoprotection counseling, and patient instruction of self-skin examination. *Int J Dermatol*. 2014;53-8:981-4. PMID: 24134438. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6**.
430. Youl PH, Baade PD, Parekh S et al. Association between melanoma thickness, clinical skin examination and socioeconomic status: results of a large population-based study. *Int J Cancer*. 2011;128-9:2158-65. PMID: 20607832. **KQ4E11**.
431. Youl PH, Coxeter PD, Whiteman DC et al. Screening for skin cancer in Queensland: who attends, and why and where do they attend? *Med J Aust*. 2009;190-1:45. PMID: 19120011. **KQ1E7, KQ2E7, KQ3E7, KQ4E7, KQ5E7**.
432. Youl PH, Janda M, Elwood M et al. Who attends skin cancer clinics within a randomized melanoma screening program? *Cancer Detect Prev*. 2006;30-1:44-51. PMID: 16457967. **KQ4E6**.
433. Youl PH, Janda M, Lowe JB et al. Does the type of promotional material influence men's attendance at skin screening clinics? *Health Promot J Austr*. 2005;16-3:229-32. PMID: 16375040. **KQ1E6, KQ2E6, KQ3E6, KQ4E6, KQ5E6**.
434. Zager JS, Hochwald SN, Marzban SS et al. Shave biopsy is a safe and accurate method for the initial evaluation of melanoma. *J Am Coll Surg*. 2011;212-4:454-60; discussion 460-2. PMID: 21463767. **KQ2E7, KQ3E7**.
435. Zalaudek I, Schmid K, Niederkorn A et al. Proposal for a clinical-dermoscopic classification of scalp naevi. *Br J Dermatol*. 2014;170-5:1065-72. PMID: 24641327. **KQ3E13**.
436. Zhu JJ, Padillo O, Duff J et al. Cavernous sinus and leptomeningeal metastases arising from a squamous cell carcinoma of the face: case report. *Neurosurgery*. 2004;54-2:492-8; discussion 498-9. PMID: 14744296. **KQ2E5**.
437. Zogakis TG, Essner R, Wang HJ et al. Natural history of melanoma in 773 patients with tumor-negative sentinel lymph nodes. *Ann Surg Oncol*. 2007;14-5:1604-11. PMID: 17333418. **KQ5E6, KQ6**.
438. Zogakis TG, Essner R, Wang HJ et al. Melanoma recurrence patterns after negative sentinel lymphadenectomy. *Arch Surg*. 2005;140-9:865-71; discussion 871-2. PMID: 16172295. **KQ5E13**.

**Appendix D Table 1. Melanoma Mortality Associated With Visual Skin Cancer Screening in Men (KQ 1)**

Katalinic, 2012 <sup>53</sup> Fair	Total Population 2009 (Millions)	Prescreening (1998–1999) Melanoma Deaths (n)	Prescreening (1998–1999) WASR (95% CI)	Screening Program (2003–2004) Melanoma Deaths (n)	Screening Program (2003–2004) WASR (95% CI)	Postscrening (2008–2009) Melanoma Deaths (n)	Postscrening (2008–2009) WASR (95% CI)
<b>Intervention region</b>							
Schleswig-Holstein (360,288 persons screened)	1.39	42	1.9 (1.5–2.4)	43	1.6 (1.2–1.9)	28	1.0 (0.7–1.3)
<b>Comparison regions</b>							
South: Hamburg	0.87	19	1.3 (0.9–1.8)	29	2.0 (1.5–2.5)	24	1.4 (1.0–1.8)
West: Lower- Saxony	3.90	112	1.7 (1.5–1.9)	123	1.8 (1.5–2.0)	151	2.0 (1.8–2.3)
East: Mecklenburg- Vorpommern	0.82	15	1.1 (0.7–1.5)	23	1.6 (1.1–2.2)	28	1.6 (1.2–2.1)
North: Denmark	2.74	117	2.9 (2.4–3.3)	118	2.7 (2.4–3.1)	150	3.2 (2.8–3.5)
Germany*	38.8	1,000	1.6 (1.6–1.7)	1,229	1.8 (1.7–1.9)	1,382	1.8 (1.7–1.9)

\*Excludes Schleswig-Holstein region.

**Abbreviations:** CI = confidence interval; KQ = key question; WASR = world age-standardized mortality rate (per 100,000).



**Appendix D Table 2. Melanoma Mortality Associated With Visual Skin Cancer Screening in Women (KQ 2)**

Katalinic, 2012 <sup>53</sup> Fair	Total Population 2009 (Millions)	Prescreening (1998–1999) Melanoma Deaths (n)	Prescreening (1998–1999) WASR (95% CI)	Screening Program (2003–2004) Melanoma Deaths (n)	Screening Program (2003–2004) WASR (95% CI)	Postscrening (2008–2009) Melanoma Deaths (n)	Postscrening (2008–2009) WASR (95% CI)
<b>Intervention region</b>							
Schleswig-Holstein (360,288 persons screened)	1.44	45	1.4 (1.1–1.8)	39	1.3 (0.9–1.6)	22	0.7 (0.5–1.0)
<b>Comparison regions</b>							
South: Hamburg	0.91	22	1.2 (0.8–1.6)	23	1.1 (0.7–1.4)	23	1.1 (0.7–1.5)
West: Lower- Saxony	4.04	112	1.3 (1.1–1.4)	116	1.2 (1.0–1.4)	102	1.1 (0.9–1.3)
East: Mecklenburg- Vorpommern	0.84	17	0.8 (0.5–1.2)	20	1.0 (0.6–1.3)	23	1.1 (0.7–1.5)
North: Denmark	2.79	86	1.8 (1.5–2.1)	103	1.8 (1.5–2.1)	103	1.9 (1.6–2.1)
Germany*	40.3	940	1.1 (1.0–1.1)	984	1.1 (1.0–1.1)	1,148	1.2 (1.1–1.2)

\*Excludes Schleswig-Holstein region.

**Abbreviations:** CI = confidence interval; KQ = key question; WASR = world age-standardized mortality rate (per 100,000).

**Appendix D Table 3. Impact of Screening on Detection of Melanoma in Situ, Squamous Cell Carcinoma, and Basal Cell Carcinoma**

Study Year Quality Location	N Screened	Age-Adjusted Incidence Rates per 100,000 (95% CI)	In situ Melanoma	Malignant Melanoma	In situ SCC	SCC	BCC
<b>Breitbart 2012<sup>55</sup></b> Good Schleswig- Holstein, Germany	360,288	Baseline (2001–2003)	5.8 (5.2–6.4)	14.2 (13.3–15.1)	6.7 (6.3–7.2)	11.2 (10.6–11.8)	60.5 (59.0–62.1)
		SCREEN (2003–2004)	8.5 (7.5–9.5)	18.0 (16.6–19.4)	8.8 (8.1–9.6)	12.9 (12.0–13.8)	78.4 (75.9–80.8)
		% change	48% increase	27% increase	31% increase	15% increase	29% increase

**Abbreviations:** CI = confidence interval; SCC = squamous cell carcinoma; BCC = basal cell carcinoma; SCREEN = Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany.