Abstract

The purpose of this study was to estimate the cost-effectiveness of melanoma screening programs. A decision analysis model was used to estimate the cost-effectiveness of a hypothetical melanoma screening program by dermatologists in 1998 in a self-selected (higher-than-average-risk) population by comparing data on melanomas diagnosed in screenings by the American Academy of Dermatology (AAD) screenings with data on melanomas diagnosed by current care (largely without special screenings) as reported to the Surveillance, Epidemiology, and End Results (SEER) program. The analysis was performed from a societal perspective and the results were reported as cost per year-of-life-saved (YLS). Further analyses evaluated screens in specific sub-groups at varying risk for melanoma and another analysis modeled mass screening of the entire Caucasian population. A sensitivity analysis was performed to determine the influence of varying key estimates on the cost per YLS. The results showed that a one-time melanoma screening costs $51,481 per YLS. If the additional costs of evaluating and treating non-melanoma skin cancers as part of the melanoma screening were included in the analysis, the cost increased to $64,646 per YLS, but there would be additional non-life-saving benefits of early diagnosis and treatment of non-melanoma skin cancers. For a one-time screen of a self-selected population age
fifty or above the cost-effectiveness ratio was $18,904 per YLS for men and $30,888 per YLS for women. A one-time mass screening of the entire Caucasian population cost $172,276 per YLS. Patients with screen-detected melanomas had an 87.8% ten-year survival versus an 83.6% ten-year survival for melanomas detected by the status quo and an expected benefit of 7.76 lives not lost to melanoma per 100,000 patients over ten years when compared to current care. The cost of providing the initial screen was a major determinant of the cost of the program. The cost-effectiveness of many of these melanoma screening scenarios fall within the range of other currently funded cancer screening programs. A trial of melanoma screening with prospective data collection on cost effectiveness should be performed.

**Introduction**

Melanoma (MM) is the eighth most common US malignancy and accounts for 1% of all cancer deaths. In addition, the incidence of melanoma has been rising. In recent years over 7,000 deaths per year have been reported due to melanoma. In 1935 the lifetime risk of melanoma was 1 in 1500, whereas now it is 1 in 75, an approximate 5% increase per year. The increase is due not only to earlier detection, but represents a true increase in the incidence of the disease. Each melanoma death has been reported to result in an average of 17.1 years of potential life lost, which is one of the highest rates for adult-onset cancers. Because survival differences between early disease and late disease in patients with melanoma correlate very well with stage at diagnosis, it is believed that earlier diagnosis and treatment interventions should yield improved survival. Early lesions may take months or even years to progress to a late lesion, and
thus screening programs which may detect lesions at an earlier stage are often touted as a means by which melanoma outcomes may be improved. In fact, melanoma has many traits that might make it suitable to screening. The disease burden is high. The screening exam is non-invasive, easy to perform, and inexpensive. The sensitivity of the exam is good when performed by dermatologists. Detected early, the disease has an excellent prognosis, while detected late the prognosis is dismal. Other aspects of the disease such as the natural history are not known with certainty.

However, prudent health policy regarding melanoma screening is difficult to formulate at this time because of a lack of comprehensive research on the effectiveness and cost-effectiveness (CE) of such programs. Indeed, authoritative opinions vary as to the value of routine screening for melanoma. While the American Academy of Dermatology (AAD) and the American Cancer Society recommend regular skin examinations, the US Preventive Services Task Force, Australian Cancer Society, and the International Union Against Cancer do not recommend routine screening for melanoma. The Canadian Task Force on the Periodic Health Examination recommends skin examinations only for high-risk patients.

Measurements of the cost-effectiveness of melanoma screening programs, such as cost per year-of-life-saved (YLS), are not available in any comprehensive manner and no randomized controlled trials of melanoma screening programs exist. Since funds spent on melanoma screening could also be spent on various interventions including other cancer screening programs, it is important to determine and compare the cost-effectiveness of melanoma screening to the cost-effectiveness of other screening
programs and perhaps the best comparisons are with screening programs for colon, breast, cervical, and prostate cancers. While recommendations regarding screening remain controversial at this time, screening programs may be a cost-effective way to reduce the mortality and morbidity from this disease. If so, one can argue they be funded in much the same manner as other currently funded cancer screening programs. Eventually, a large-scale, prospective, randomized screening trial may be conducted to estimate the cost-effectiveness of melanoma screening. Such a trial should be considered ethical given that the current default standard is not to screen for melanoma. However, such a costly and lengthy trial could be better planned and a better case made for such a trial if a decision analysis model determines screening is likely to be effective and cost-effective.

**Previous Studies**

There have been no randomized controlled trials, relatively few reports of the results of melanoma screening programs in general, and no studies on the cost-effectiveness of melanoma screening programs aside from a recent study by Freedberg et al\textsuperscript{31} and another in Australia by Grigis et al\textsuperscript{37}.

Freedberg et al\textsuperscript{31}, in an interesting study calculated a cost-effectiveness ratio of $29,170 per YLS for a one-time screening program of self-selected, high-risk patients with a mean age of 48 years. This estimate included the induced costs of the detection and treatment of non-melanoma skin cancer (NMSCA) during the melanoma screening. Cost estimates came from 1993 HCFA reimbursements and parameters for the
effectiveness of screening came from an analysis of AAD screening programs for the screened branch and 1990 SEER data for the non-screened branch. The screened group was self-selected and at higher-than-average risk\textsuperscript{31,36,56}. Because the population who received AAD screenings were self-selected, it is possible that differences seen in the stage of distribution of melanomas between the screened AAD group and “unscreened” SEER group were due in part to differences in the groups besides the screening itself. Screening remained below $50,000/YLS if the prevalence of melanoma in the screened population remained at least 90 per 100,000, 98.4% of detected melanomas were localized, and the cost of the initial screen was below $57.

In this model, screening made a difference for those 5 percent of patients (by the authors’ assumptions and calculations) who if screened, would have been detected with localized disease, but if not screened would have developed metastatic disease. The authors did not examine the results in a model that evaluated a step-wise progression through the Breslow stages of localized disease into regional and metastatic disease and the authors only evaluated a one-time screen. From the methods section, it is not clear if their model directly accounts for potential age-and gender-related differences in melanoma incidence and survival and benefits from screening across a spectrum of ages. The authors did not calculate age-or gender-specific cost-effectiveness estimates for melanoma screening in their study. Such estimates would be useful in determining a coherent screening strategy, which may use age or gender as or factor when deciding who should be screened. Regarding costs, the authors appear to have considered direct medical costs of evaluation and treatment but not costs for terminal care or increased future care because of lives saved. The cost estimates the authors used for
melanoma patients are low compared with a recently published article estimating the
costs of melanoma evaluation and treatment\textsuperscript{88}. Despite some drawbacks however, this
paper appears to provide the best estimate of the cost-effectiveness of melanoma
screening available to-date.

Girgis et al\textsuperscript{37} in 1996 published a cost-effectiveness study of melanoma screening in
Australians age 50 or older by family practitioners every five years and found a cost of
Aust. $6,853 and Aust. $11,102 per year of life saved for men and women, respectively.
If the screening was performed every other year, the cost per year of life saved was
Aust. $12,137 and Aust. $20,877 for men and women respectively. Very few details of
the model are described and thus the analysis is difficult to critique and no further work
from this group has been published on the cost-effectiveness of melanoma screening
since this study.

Cristofolini et al\textsuperscript{14} in 1992 evaluated the cost-effectiveness of a health education
campaign for the early diagnosis of melanoma in Trentino, Italy from 1977-1985. In this
study the educational campaign actually saved lives and resulted in savings, though this
was not a study on melanoma screening.

The American Academy of Dermatology AAD has sponsored adult skin cancer
screenings since 1985, resulting in more than one million screenings\textsuperscript{56}. Of those screened, approximately 50,000 possible non-melanoma skin cancers and 10,000
possible melanomas have been discovered. Koh et al\textsuperscript{54-56} have reviewed two AAD
melanoma screening programs and these will be discussed further when determining parameters to be used in the model. Epstein et al\textsuperscript{26} in a retrospective study of patients presenting for treatment of melanoma found that just over one half of the cancers were patient-detected (55%), but physicians were more likely to detect thinner melanomas (median thickness 0.23 mm vs. 0.9 mm; \(p<0.001\)). Koh et al\textsuperscript{55} previously found that women are more likely to discover their own melanomas versus men and Epstein’s study findings are in agreement with this. Studies such as these imply that often a physician or someone other than the individual with a melanoma is often needed to detect earlier-stage melanomas.

**Methods**

**Description of the Model**

The model used for the analysis was a decision tree. This model describes two comparable hypothetical populations in 1998, one group screened for melanoma by dermatologists in an outpatient clinic setting by visual inspection of the entire skin of the body and the other group representing the status quo, without a screening intervention. Figures 4.1A depicts the two populations in the model within a tree diagram of events up to a confirmed diagnosis of melanoma and Figure 4.1B continues from there. The unscreened group depicts the usual costs and life expectancies associated with this population for a given prevalence of melanoma. The screened group depicts a comparable population with the same prevalence but with somewhat different costs and life expectancies due to having been screened for melanoma. Melanoma screening if effective, results in the discovery of melanomas with a different and more favorable
distribution of stages due to earlier detection. With a complete model and a
determination of all the relevant streams of costs and life expectancies associated with
each group, a cost-effectiveness ratio was calculated. We calculated the cost-
effectiveness of a “reference case” defined by the Panel on Cost-Effectiveness in Health
and Medicine\textsuperscript{38} as a baseline analysis, which uses a standard set of methodological
practices outlined by the panel to improve comparability of cost-effectiveness analyses.
Table 4.1 depicts some important model parameters used in the analysis.

**Figure 4.1A. Melanoma screening tree.**
Figure 4.1B. Confirmed melanoma: Melanoma screening tree.

Table 4.1. Model parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability positive screen for melanoma</td>
<td>0.016</td>
<td>AAD data(^{56})</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.85</td>
<td>Estimate from AAD data(^{56})</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.99</td>
<td>Estimate from AAD data(^{56})</td>
</tr>
<tr>
<td>Prevalence</td>
<td>184 per 100,000</td>
<td>AAD data(^{56}), adjusted to 1997</td>
</tr>
<tr>
<td>Probability positive screen for NMSC</td>
<td>0.06</td>
<td>Helfand et al(^{45})</td>
</tr>
<tr>
<td>Probability true positive, given positive screen for NMSC</td>
<td>0.3</td>
<td>Helfand et al(^{45})</td>
</tr>
</tbody>
</table>
Population Estimates

The population for the screened group in the reference case was a high-risk group with a prevalence derived from 1992-94 AAD screenings\textsuperscript{56}. When not otherwise specified in this paper a “high-risk population” refers to a self-selected population that would likely choose to take advantage of a voluntary screening similar to the AAD screenings, whose stage distribution of disease has been described\textsuperscript{31,56}. The AAD screened group has been described by Koh et al\textsuperscript{56} and Geller et al\textsuperscript{36} as adults greater than twenty years old who are at relatively high risk for melanoma, light-skinned people who burn easily and tan poorly or those with a family history of skin cancer, extensive sun exposure, or a higher than average number of nevi. For a comparable unscreened group representing the status quo, we used data on Caucasians in 1998 from the nationally representative SEER database\textsuperscript{83} age- and gender- matched to the AAD screened population to derive the stage distribution of disease, but attributed to this group the same prevalence of disease as found in the AAD screenings.

The SEER Program is the most authoritative source of information on cancer incidence and survival in the United States and is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and survival rates within each stage\textsuperscript{83}. The mortality data reported by SEER are provided by the National Center for Health Statistics. The population covered by SEER is comparable to the general US population with regard to measures of poverty and education, but tends to be somewhat more urban and has a higher proportion of foreign-born persons than the general US population\textsuperscript{83}.
An “average-risk population” in this paper refers to a group whose incidence and prevalence is similar to the population from which the SEER database is derived. Our analysis is of a screening assumed to have taken place in 1998. The incidence of melanoma increased between 1992-94 and 1998. We adjusted the prevalence from the 1992-94 AAD screenings by a factor of 1.21 to approximate the incidence increases between 1992-94 and 1997. We adjusted to 1997 rather than 1998 to account for lead time, which we estimated to be approximately one year. Lead time is discussed further on page 22 under “Effects/Life Expectancy”. The 1992-94 AAD screening prevalence adjusted to 1997 is 6.8 times the incidence in the SEER population in 1998. The prevalence of melanoma in the general population is not known with certainty, thus exactly how much higher-at-risk this screened population is than the age-adjusted general population is not known. If one assumes the prevalence in the AAD group is three times higher than the average U.S. prevalence, which seems reasonable given the description of this population from Geller et al\textsuperscript{36}, then an estimate of the prevalence-to-annual incidence ratio in the general US population would be approximately two\textsuperscript{3}. This implies a preclinical period\textsuperscript{4} for melanoma of about two years. One can use the prevalence-to-incidence ratio to estimate the preclinical period duration as was done by Zelen and Feinlieb\textsuperscript{97} for breast cancer. The length of the preclinical period has significant implications for the ability of screening to be effective, with a short preclinical

\textsuperscript{3} The formulae for this calculation are: $PIR = \frac{P_s}{I_s}$ and $I_s = I_u \cdot k$, where $PIR$ = the prevalence-to-incidence ratio, $P_s$ and $I_s$ are the prevalence and incidence in screened individuals respectively, $I_u$ is the incidence in unscreened individuals derived from SEER and $k$ is the estimate of the ratio of the prevalence of melanoma in the screened group to an average-risk group (a.k.a. relative risk). In the example given, $P_s/I_u = 6.8$ and $k = 3$ (estimated). Thus, the $PIR = P_s/I_s = 2.27$.\textsuperscript{4} Defined as the time from when a melanoma is first present and potentially detectable by a skin exam, to the time when it would be discovered without a screening exam.
period making screening less likely to be effective, and a long preclinical period making screening more likely to be effective, ceteris parebus. While a long preclinical period makes initial screenings more effective, it also implies that a relatively longer interval between the initial and recurrent screens may be optimal.

In an effort to determine the cost-effectiveness ratio of melanoma screening for populations at different levels of risk, the cost-effectiveness analysis (CEA) was performed using different prevalence rates in the sensitivity analysis.

The age and gender (thirty-nine percent males and sixty-one percent females) distributions of the population were derived from data on the AAD 1992-94 screenings. This gender distribution is comparable to the distribution reported in an AAD screening performed in Massachusetts in 1987\(^5\). This allowed for a determination of 5- and 10-year age, stage-, and gender-specific survival and life expectancy from SEER databases and life tables.

Effects/Life Expectancy

Life expectancy was the only effect of interest for the cost-effectiveness analysis. QALYs have not been studied in any depth relating to melanoma in general and thus were not part of the analysis. It is likely that QALYs and YLS are of somewhat similar value for many of those diagnosed and cured from early localized disease with minor surgery alone in non-cosmetic areas, not requiring lymph node dissection. However, for disease requiring chemotherapy, lymph node dissection, or requiring major or
disfiguring surgery, QALYs could be a better measure of effectiveness than YLS alone.

Life expectancy gains in the screened arm of the analysis were determined by the improvement in stage distribution of disease with screening (Table 4.2) and thus improvement in probability of survival and life expectancy (Table 4.3A & 4.3B). The stage distribution for the screened group was primarily derived from a report by Koh et al\textsuperscript{56} on AAD screenings from 1992-1994 and further stage delineations were estimated from published data by Balch et al\textsuperscript{3-4}. The stage distribution for the non-screened group was derived from Caucasians in the1998 SEER database, age- and gender-matched to the AAD population. An assumption of the model is that detection of melanoma at an earlier stage will result in an improved probability of survival. This assumption is based on the numerous studies showing that stage at time of diagnosis is the best independent predictor of survival\textsuperscript{3-4}.

### Table 4.2. Comparison of stage distribution of melanomas, screened versus non-screened.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Screened</th>
<th>Non-screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma in Situ</td>
<td>0.414</td>
<td>0.364</td>
</tr>
<tr>
<td>Localized Breslow Level 1 Thickness</td>
<td>0.352</td>
<td>0.334</td>
</tr>
<tr>
<td>Localized Breslow Level 2 Thickness</td>
<td>0.151</td>
<td>0.115</td>
</tr>
<tr>
<td>Localized Breslow Level 3 Thickness</td>
<td>0.061</td>
<td>0.075</td>
</tr>
<tr>
<td>Localized Breslow Level 4 Thickness</td>
<td>0.011</td>
<td>0.024</td>
</tr>
<tr>
<td>Regional Metastases</td>
<td>0.008</td>
<td>0.063</td>
</tr>
<tr>
<td>Distant Metastases</td>
<td>0.003</td>
<td>0.026</td>
</tr>
</tbody>
</table>
Table 4.3A. Stage-specific probability of ten-year survival, age- and gender-adjusted*.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma in Situ</td>
<td>Not applicable*</td>
</tr>
<tr>
<td>Localized Breslow Level 1 Thickness</td>
<td>86%</td>
</tr>
<tr>
<td>Localized Breslow Level 2 Thickness</td>
<td>78%</td>
</tr>
<tr>
<td>Localized Breslow Level 3 Thickness</td>
<td>63%</td>
</tr>
<tr>
<td>Localized Breslow Level 4 Thickness</td>
<td>59%</td>
</tr>
<tr>
<td>Regional Metastases</td>
<td>47%</td>
</tr>
<tr>
<td>Distant Metastases</td>
<td>12%</td>
</tr>
</tbody>
</table>


Table 4.3B. Stage-specific life expectancy, age- and gender-adjusted to screening data*.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Expected value of life years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma in Situ</td>
<td>30.0</td>
</tr>
<tr>
<td>Localized Breslow Level 1 Thickness</td>
<td>28.8</td>
</tr>
<tr>
<td>Localized Breslow Level 2 Thickness</td>
<td>26.6</td>
</tr>
<tr>
<td>Localized Breslow Level 3 Thickness</td>
<td>22.6</td>
</tr>
<tr>
<td>Localized Breslow Level 4 Thickness</td>
<td>20.7</td>
</tr>
<tr>
<td>Regional Metastases</td>
<td>17.1</td>
</tr>
<tr>
<td>Distant Metastases</td>
<td>4.8</td>
</tr>
</tbody>
</table>


In the model, the expected value of life-years for melanoma patients was based on the stage-specific probability of ten-year survival or death and the life expectancy (LE) given ten-year survival or death.

< [p(survival > 10 yrs|stage) * (LE|survival > 10 yrs)]+[(p(death ≤10yrs|stage) * LE(death ≤ 10 yrs))] >
Life expectancy was calculated separately for patients in each decade of life for each gender and was stage-specific. We assumed life expectancy for those surviving melanoma ten years (hereafter referred to as melanoma survivors) was the same as cohorts without melanoma, based on an analysis of SEER\textsuperscript{83} survival data (analysis not shown). Age- and gender-specific life expectancy values for melanoma survivors and those without melanoma came from 1996 National Vital Statistics (NVS) life tables. Life expectancy values for those not surviving melanoma were derived from SEER 1988-98 cumulative databases. The undiscounted life expectancy derived from SEER and NVS was then used to calculate a discounted life expectancy using an approach known as the mixed declining exponential approximation to life expectancy or “mixed DEALE” as described by Keeler and Bell\textsuperscript{52}. This formulation allows for increasing chances of dying with age. In contrast, a constant hazard spreads death over too wide a range for all but the severely ill\textsuperscript{5}.

The lead time of screening is the difference between the time a patient would seek medical care in the absence of screening and the time that the disease is detected by screening. Lead time bias occurs when not accounting for the fact that screening picks up lesions earlier in time than they would have been diagnosed without screening. Thus, survival from the time of diagnosis is not an appropriate comparison for screened patients.

\begin{equation}
LE = p \left(1 - \exp\left(-\frac{d}{L}\right)\right) + \frac{1-p}{d + \left(\frac{1}{L}\right)}
\end{equation}

\textsuperscript{5} The life expectancy for a diseased person using the mixed DEALE is the weighted sum of life expectancies for the original DEALE formula and the fixed lifetime approximation of life expectancy (FLALE). $L$ is life expectancy without disease, $d$ is a constant hazard, and $p$ equals the proportion of the population living exactly $L$ more years (see Keeler and Bell, 1992\textsuperscript{52}).
and unscreened patients. One method of accounting for lead time is to compare survival for screened patients to lead time plus survival for unscreened patients and this was the method we chose in our analysis. Since melanoma (ten-year) survivors were assumed to have a normal life expectancy, lead time bias was not pertinent to this group. Lead time was pertinent to those dying from melanoma, however. We accounted for lead time by adding an additional 1.14 years to the stage-specific life expectancy of patients who were not screened and died from melanoma. The value for lead time was estimated after deriving the value of the preclinical period as previously described. Average lead time was estimated to be one-half the value of the preclinical period, by assuming that lesions are diagnosed in a random distribution over the preclinical period.

Costs
Weinstein and Stason\textsuperscript{94} have defined the net health care costs in cost-effectiveness analysis as “all direct medical and health care costs [including] costs of hospitalization, physician time, medications, laboratory services, counseling, and other ancillary services.” Also included in their definition are costs associated with adverse side effects of treatment, the offsetting costs from savings in health care, rehabilitation and custodial costs due to the prevention or alleviation of disease. Opportunity costs such as the costs of missing work to attend a screening exam were not included in the analysis, since the screen described could be either one of convenience such as in a mall, or a scheduled screen requiring travel time and time off from work. It is controversial whether to include the costs of treating diseases that occur as a result of living longer
because of the intervention\textsuperscript{34,38,94}. Some suggest counting future medical costs associated with living longer because research has shown that analyses that omit future costs are biased in favor of interventions in the elderly that extend life, over interventions that improve quality of life\textsuperscript{34,47,71-72,95}. Costs that arise solely from living longer were not included in the reference case, but a separate analysis was performed on the reference case when such future health costs were included in the total costs and results of both analyses are presented. Future age-specific health costs were derived from two sources, the 1998 Medicare Current Beneficiary Survey\textsuperscript{70} and the 1998 Medical Expenditure Panel Survey\textsuperscript{69}. Table 4.4 outlines the costs attributed to each step of the analysis as described below.

Costs in this analysis included the discounted streams of costs related to melanoma screening and melanoma once detected. The cost of the screening exam itself ($43.46 per screen) was derived from the median salary for dermatologists ($181,774; 1998 estimate by the Medical Group Management Association, MGMA), the average percentage of clinic costs attributable to the dermatologist’s salary (54% by Medicare estimates) and an estimate of the number of screenings that could be performed per year (7717.5; estimate based on a survey of local dermatologists, calculated as five patients per hour, seven hours per day of direct patient care, four and a half days per week, 49 weeks per year). Of note, the estimated number of screens per year is 46% higher than the average number of patients seen per year by dermatologists as reported by the MGMA (5293). However, it is assumed that a screen would take less time than the average dermatologist’s clinic visit, which often involves multiple problems, complex
medical decision-making, or procedures. In addition, no biopsies or extensive evaluations would take place during such a screen, nor would prescriptions be written.

Had I used the estimated number of patients seen by a dermatologist per year from MGMA (5293), the cost of the screen would have increased to $63.36. An estimate of the cost of a melanoma screen in an Institute of Medicine funded study\(^ {19} \) on the costs of covering skin cancer screening by Medicare came up with a very similar estimate as the

### Table 4.4. Costs.

<table>
<thead>
<tr>
<th>Event</th>
<th>Cost</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen</td>
<td>$43</td>
<td>Estimated</td>
</tr>
<tr>
<td>Total biopsy cost</td>
<td>$206</td>
<td>CMS*</td>
</tr>
<tr>
<td>Follow-up visit</td>
<td>$99</td>
<td>Estimated</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>$53</td>
<td>Estimated</td>
</tr>
<tr>
<td>Laboratory studies (CBC &amp; Comprehensive Panel)</td>
<td>$71</td>
<td>Estimated</td>
</tr>
<tr>
<td>Non-screen dermatologist visit</td>
<td>$99</td>
<td>CMS*</td>
</tr>
<tr>
<td>Screen-detected NMSCA** treatment</td>
<td>$1,442</td>
<td>Estimated</td>
</tr>
<tr>
<td>Non-screen-detected NMSCA** treatment</td>
<td>$1,580</td>
<td>CMS*</td>
</tr>
<tr>
<td>Yearly cost of follow-up visit after detection of NMSCA**</td>
<td>$99</td>
<td>CMS*</td>
</tr>
<tr>
<td>Undiscounted final year of life cost</td>
<td>$43,443</td>
<td>Hogan et al</td>
</tr>
<tr>
<td>Discount rate: Base (Range)</td>
<td>5% (3-7%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>Discounted expected value of costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma in Situ</td>
<td>$13,543</td>
</tr>
<tr>
<td>Localized Breslow Level 1 Thickness</td>
<td>$15,588</td>
</tr>
<tr>
<td>Localized Breslow Level 2 Thickness</td>
<td>$17,796</td>
</tr>
<tr>
<td>Localized Breslow Level 3 Thickness</td>
<td>$23,488</td>
</tr>
<tr>
<td>Localized Breslow Level 4 Thickness</td>
<td>$25,897</td>
</tr>
<tr>
<td>Regional Metastases</td>
<td>$67,639</td>
</tr>
<tr>
<td>Distant Metastases</td>
<td>$43,946</td>
</tr>
</tbody>
</table>

*Centers for Medicare and Medicaid Services
**Non-melanoma skin cancer
one used in this study ($40 per screen) based on a resource-based relative value scale (RVRBS) analysis. The impact of potential differences in the estimated screen cost on the cost- effectiveness estimate is substantial and is discussed in the sensitivity analysis.

The costs for all patients in the screened arm of the model included the cost of the screening examination itself as previously described. Patients with a positive screen incur the costs of a follow-up visit and biopsy with histopathologic processing and evaluation by a dermatopathologist. The costs in the first year of diagnosis for patients with a diagnosis of melanoma in both the screened and non-screened branch of the analysis were based on a report of the stage-specific annual cost of melanoma by Tsao et al\textsuperscript{88}. To this amount was added the discounted yearly cost of follow-up based on recent published recommendations for melanoma follow-up\textsuperscript{10} for the stage-specific life expectancy. A final-year-of-life cost\textsuperscript{46} appropriately discounted based on life expectancy was also added to the cost calculation for those with melanoma and melanoma in situ. Future costs were age-specific and included in the costs for one analysis referred to previously. All costs were discounted at a rate of three percent and a sensitivity analysis was performed varying the discount rate from zero to five percent.

Screening Exam Parameter Estimates

Screening exam parameter estimates were based primarily on a study of melanoma screening exams by Koh et al\textsuperscript{55} and adjusted to the prevalence of disease used in this study. These screen parameters for the reference case are shown in Table 4.1. A
range of parameters whose values were derived from other studies was tested in the sensitivity analysis.

Cost-Effectiveness

Cost-effectiveness was calculated as the sum of the costs for screening arm less the costs for the non-screening arm, divided by the sum of the life expectancy of the screening arm less the life expectancy of the non-screening arm.

\[
\text{Cost-Effectiveness} = \frac{\sum \text{Costs (screen)} - \sum \text{Costs (no screen)}}{\sum \text{L.E. (screen)} - \sum \text{L.E. (no screen)}}
\]

Non-melanoma Skin Cancer (NMSCA)

Because non-melanoma skin cancer is much more common than melanoma, melanoma screening exams are likely to find many times more suspected and actual NMSCA than melanomas. A separate analysis was performed adding the costs of screening, evaluating, and treating NMSCA to the reference case. Modeling NMSCA screening requires more assumptions with substantially more uncertainty than in the reference case due to a paucity of adequate data on which to develop the NMSCA model. Unless one chooses to ignore non-melanoma lesions during the screening exam, the impact of evaluating, excluding, and detecting these lesions on the overall costs could be substantial, while the impact on life expectancy is likely negligible. When diagnosed with NMSCA, some form of treatment such as local surgical excision is almost always performed and is the standard of care. One could argue that the value of treating NMSCA is greater to or equal to the cost since it is almost invariably treated once
diagnosed and thus has no negative impact on melanoma screening cost-effectiveness. On the other hand, routine screening for NMSCA in the general population is not currently recommended and screening would certainly be associated with significant costs associated with excluding skin cancer in benign but suspicious lesions detected during the exam. Rarely do NMSCA result in death as attested by the >99% survival in most studies and moreover, early detection is of unknown value. Typically there are cosmetic and functional consequences to NMSCA lesions, which are improved by early treatment of smaller lesions. Thus, including NMSCA screening as part of a melanoma screening program should increase costs without increasing effectiveness (when effectiveness is defined as life years saved as it is in this analysis).

Several assumptions were made in the NMSCA model. First, it was assumed early detection and treatment did not affect life expectancy. This may be overly conservative because it is possible there is some small benefit to life expectancy from screening for NMSCA, but it is almost certainly very small and has never been proven. Thus including improved life expectancy from NMSCA screening did not seem prudent. Second, I assumed NMSCA tumors were detected one year earlier on average with screening than they would have been detected without screening. This is an estimate based on my own professional experience treating patients with NMSCA. The exact accuracy of this estimate has little practical impact on the analysis. I derived the cost for treating NMSCA not detected by screening from a 1993 estimate from The Centers for Medicare and Medicaid Services⁹ (CMS, formerly HCFA,) and adjusted this cost to 1998 values. For NMSCA detected by screening I assumed a cost of 15% less since
the lesion would be smaller in size. This cost would be incurred one year earlier in accordance with the previous assumption. I assumed 6% of screened patients would have a suspected NMSCA based on review of screening for nonmelanoma skin cancer by Helfand et al. Of those with suspected lesions, I assumed 30% had an actual NMSCA while 70% had false positives (i.e. lesions suspected of being NMSCA that resulted in a negative work up based on a review of the available literature). A cost of $354 was included for false positives to cover the costs of subsequent biopsy, pathology preparation and reading. Also in the model, patients who developed a NMSCA subsequently incurred a cost of a screening exam each year for their remaining years of life.

Results

Life Expectancy and Survival

In the reference case, individuals with melanoma detected by screening had an 87.8% ten-year survival versus an 83.6% for those not screened. Thus, those screened had a 5.0 percent greater chance of ten-year survival than those not screened. With a prevalence of 186 melanomas per 100,000 people and a sensitivity rate of 84.6%, screening results in an expected benefit of 7.68 lives not lost to melanoma in ten years and an additional eighty-seven life-years per 100,000 patients screened.

Costs

In the reference case, the incremental cost per person was $42 higher in those screened than in those not screened after all discounted costs and savings resulting.
from screening were calculated. The total cost per person screened was $79 versus $37 in those not screened. Since the screening exam itself without regard to any subsequent downstream costs or savings was $43, one can see that: 1) the screening exam cost is a major determinant of the difference in cost per person between those screened and not screened and that, 2) there are some modest net savings in costs per person diagnosed with melanoma if screened.

Cost-Effectiveness
The calculated cost-effectiveness ratios for the screening programs modeled are summarized in Table 4.5. The cost per YLS of melanoma screening in the reference case, a one-time screening of self-selected moderately high-risk men and women, was $51,481. If the additional induced costs of evaluating and treating non-melanoma skin cancers were included in the analysis, the cost per YLS increased to $64,646. If future health costs were incorporated into the reference case, the cost per YLS increased from $51,481 to $57,639. If the one-time screening program is limited to these same self-selected, high-risk men and women, but only to those aged 50 or older, the cost per YLS was reduced to $22,368. If the one-time screen in this population was restricted to only women age 50 or older, the cost per YLS was $30,888, while if limited to men older than age 50, the cost per YLS was $18,904. A one-time screen in an entire cross section of the Caucasian population at average risk was modeled and the cost-effectiveness ratio was $172,276\textsuperscript{6}.

\textsuperscript{6} This calculation assumed that the prevalence for the “average” Caucasian population was 2.3 times the incidence in Caucasians in SEER data. This estimate was derived by assuming the previously modeled self-selected, moderately high-risk AAD population had a prevalence three times as high as “average”, based on published descriptions of risk factors\textsuperscript{36,56}.
Table 4.5. Cost-effectiveness estimates.

<table>
<thead>
<tr>
<th>Screen characteristics</th>
<th>Cost per YLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference Case:</td>
<td></td>
</tr>
<tr>
<td>One-time screen in self-selected (moderately high-risk)</td>
<td>$51,481</td>
</tr>
<tr>
<td>population of all ages</td>
<td></td>
</tr>
<tr>
<td>One-time screen in self-selected population of all ages</td>
<td>$64,646</td>
</tr>
<tr>
<td>including costs for non-melanoma skin cancer</td>
<td></td>
</tr>
<tr>
<td>One-time screen in self-selected population of all ages</td>
<td>$57,639</td>
</tr>
<tr>
<td>including future health care costs</td>
<td></td>
</tr>
<tr>
<td>One-time screen in self-selected, 50+ year old men and women</td>
<td>$22,368</td>
</tr>
<tr>
<td>One-time screen in self-selected, 50+ year old women</td>
<td>$30,888</td>
</tr>
<tr>
<td>One-time screen in self-selected, 50+ year old men</td>
<td>$18,904</td>
</tr>
<tr>
<td>One-time screen in average-risk Caucasian population of all ages</td>
<td>$172,276</td>
</tr>
</tbody>
</table>

Sensitivity Analysis

Parameters in this decision analysis model were varied over reasonable ranges to determine the robustness of the cost effectiveness estimate and to determine which parameters were the most important determinants in the model.

*Prevalence*. The prevalence of melanoma in the screened population was varied over a range from 10 per 100,000 people to 910 per 100,000 people. The cost-effectiveness ratio declines exponentially with increasing prevalence over this range (see Figure 4.2). A prevalence of greater than 189 per 100,000 people, yields a cost-effectiveness ratio less than $50,000. A prevalence of twice that of the reference case (i.e. 376 per
100,000 people) yields a cost-effectiveness ratio of $21,901 per YLS. As the prevalence of melanoma in the screened population is reduced below 110 per 100,000 people, the cost-effectiveness ratio increases rapidly.

**Figure 4.2. Sensitivity analysis: Prevalence.**

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**Screen Cost.** The cost-effectiveness ratio varied linearly with the screen cost. As a rough rule of thumb the cost-effectiveness ratio is slightly higher than 1000 times the screen cost (see Figure 4.3). A screen cost of $20 yielded a cost-effectiveness of $23,015 and a screen cost of $60 yielded a cost-effectiveness ratio of $71,558. Thus, in the reference case, each 1000 screens yield approximately one extra year-of-life.

Table 4.6 depicts the results of a two-way analysis on the impact of changing the two most important parameters affecting cost-effectiveness, prevalence and the cost of the screen. From $253,000 to $713,825 can be seen as bounds on screening the average risk population with recurrent screens annually and $7,036 to $29,404 can be seen as bounds on screening a very high-risk population once.
Figure 4.3. Sensitivity analysis: Screen cost.

Table 4.6. Two-way analysis of variations in screen cost and prevalence of disease on cost-effectiveness.

<table>
<thead>
<tr>
<th>Cost/Screen</th>
<th>400 melanomas per 100k population</th>
<th>20 melanomas per 100k population</th>
</tr>
</thead>
<tbody>
<tr>
<td>$20</td>
<td>$7,036</td>
<td>$266,465</td>
</tr>
<tr>
<td>$60</td>
<td>$29,404</td>
<td>$713,825</td>
</tr>
</tbody>
</table>

*Screen Exam Sensitivity.* Changes in screen sensitivity alter the cost-effectiveness ratio as depicted in Figure 4.4. The cost-effectiveness of screening remains below $50,000 in the reference case as long as the sensitivity is greater than or equal to 86%. Figure 4.5 depicts screen sensitivity and screen cost tradeoffs, which yield a constant cost-effectiveness ratio of $52,000. Over the range of sensitivities evaluated in Figure 4.5, if
every $8 decrease in cost per screen is associated with a decrease in sensitivity of the examination by less than 10%, the cost-effectiveness will improve. Thus, if a screener other than a dermatologist costs $35 per screen rather than $43, and had a sensitivity of better than 75%, the cost-effectiveness would be improved.

![Figure 4.4. Sensitivity analysis: screening examination sensitivity.](image)

Discount Rate. Figure 4.6 shows the effect of changing the discount rate in the analysis of the reference case. The cost-effectiveness ratio ranges from $20,563 at a 0% discount rate, to $61,616 at a rate of 7%.
Figure 4.5. Sensitivity analysis: Tradeoff needed between screen sensitivity and cost to keep CEA of $48,000/YLS.

Figure 4.6. Sensitivity analysis: Discount rate.
Discussion

In this decision analysis of melanoma screening, the cost per YLS was $51,481 in the reference case, a one-time screening for melanoma in a self-selected population by dermatologists. If one includes the costs associated with the screening, detection, and treatment of non-melanoma skin cancer, then the cost of the program was $64,646 per YLS. These costs are in line with or better than estimates of many cancer screening programs (Table 4.7). According to our estimates, one-time melanoma screening in the setting of the reference case costs approximately the same as screening for cervical cancer with a PAP smear every three years ($48,000, Eddy\textsuperscript{22}). It produces more years of life per dollar spent than annual fecal occult blood testing plus sigmoidoscopy every 5 years from age 50 to 85 years\textsuperscript{7} ($92,900/YLS, Frazier et al\textsuperscript{30}) and more years of life per dollar spent than screening for prostate cancer with a prostate-specific antigen at age 60 ($158,129/YLS, Krahn et al\textsuperscript{59}), but less than biennial mammography for women aged 50 to 79 years ($16,000/YLS, Lindfors\textsuperscript{61}, JAMA 1995). These findings are important since melanoma screening programs are not currently routine and opinions on whether screenings should be performed are contradictory. This study suggests that screening of a relatively high-risk population such as described in the reference case will likely save lives and have a cost-effectiveness in line with many other life-saving medical interventions. As should be expected, the estimates of cost-effectiveness of the different screening programs analyzed in this paper differ significantly, from $18,904 per YLS for a one-time screen of self-selected men age fifty or older to $172,276 per YLS for a one-time screen in an average-risk Caucasian population of all ages. The range of

\textsuperscript{7} Followed by colonoscopy if either a low- or high-risk polyp was found
estimates corroborates the impressions of many that targeted screening may be warranted and that screening the entire general population would be expensive.

We estimate that a recurrent screen could be performed in the range of three to six years with a reasonably similar cost effectiveness as a one-time screen, based on the previously noted assumptions on prevalence-to-incidence ratios. However, determining the actual cost-effectiveness of recurrent screens and the optimal interval between screenings requires more knowledge of the rate of interval cancers, defined as the rate of cancers developing after a screening.

Table 4.7. Cost-effectiveness estimates of other various cancer screening programs.

<table>
<thead>
<tr>
<th>Screen</th>
<th>Cost/YLS</th>
<th>Reference</th>
<th>Adjusted from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate-specific antigen, age 60, for prostate cancer</td>
<td>$158,129</td>
<td>Krahn et al</td>
<td>1996</td>
</tr>
<tr>
<td>Annual fecal occult blood testing plus sigmoidoscopy every 5 years from age 50 to 85 years, followed by colonoscopy for low- or high-risk polyp, for colon cancer</td>
<td>$92,000</td>
<td>Frazier et al</td>
<td>2000</td>
</tr>
<tr>
<td>Dermatologist one-time screening of self-selected group for melanoma</td>
<td>$51,569</td>
<td>Current study</td>
<td>1998</td>
</tr>
<tr>
<td>PAP smear every three years for cervical cancer</td>
<td>$48,139</td>
<td>Eddy</td>
<td>1996</td>
</tr>
<tr>
<td>Biennial mammography for women aged 50-79 years, for breast cancer</td>
<td>$17,193</td>
<td>Lindfors et al</td>
<td>1995</td>
</tr>
</tbody>
</table>

* All estimates converted to 1998 dollars using the Medical CPI, Bureau of Labor Statistics, U.S. Dept. of Labor

If the distribution of prevalence-to-incidence ratios were known or could be estimated from recurrent screens, one could approximate the time in years after a screening when the prevalence of a cancer would return to the pre-screening rate in the absence of further screening. Studies involving computer simulations or a trial of screening with
data on interval cancers collected after screening could provide a better estimate of interval cancers and the prevalence-to-incidence ratios. Such estimates would be useful in determining the most appropriate interval between screens and should be the goal of future research efforts.

The cost-effectiveness estimate in this study is in line with but somewhat higher than that of Freedberg et al who also modeled the use of dermatologists for mass melanoma screening. Freedberg’s\textsuperscript{31} cost-effectiveness estimate at a cost of $30.00 per screen including the effect of NMSCA was $29,170 per YLS for a one-time screen, versus this study’s estimate of $64,646 per YLS (when we accounted for NMSCA as Freedberg did). Freedberg also used AAD screening data to arrive at the estimate of screening effectiveness. Approximately one-half of the difference in the estimates of cost-effectiveness between Freedberg’s estimate and ours can be accounted for by the difference in the estimate of the cost of the initial screening exam. The cost of the initial screening exam was shown in our sensitivity analysis to be a dominating factor on the cost-side of the cost-effectiveness ratio for melanoma screening. Freedberg used $30 as an estimate of the cost of the initial screening exam, while we used an estimate of $43. Their estimate of the cost of the screen was based on the charge and cost-to-charge ratio at their university for a physician visit at the time of their study (personal communication, co-author Allan Geller), while our screen cost was calculated from 1998 national estimates of the median annual dermatologist salary, the Medicare overhead rate, and an estimate of the number of screens likely to be performed per year. A recent study sponsored by the Institute of Medicine estimated the cost of screening for
Our estimate is substantially higher than that by Grigis et al who have also estimated the cost-effectiveness of melanoma screening. However, their model used general practitioners not dermatologists to screen for melanomas in Australia, not the United States, in people over the age of fifty only, and the screen was performed every two to five years rather than just once. They found it cost Aust. $6,853 to $20,877 per YLS. Though we did not model a recurrent screen due to a lack of information on interval cancer rates, we found the cost-effectiveness of screening for melanomas by a dermatologist’s one-time screen in a moderately high-risk, self-selected group over age fifty was $22,368 per YLS. For a one-time screen restricted to self-selected men older than fifty, the cost-effective ratio decreased further to $18,904. Thus, using age-specific
and/or gender-specific criteria for entry into the screening appears to be a simple manner by which one could fairly dramatically reduce the cost-effectiveness ratio of a planned melanoma screening program. With cost-effectiveness ratios of approximately $50,000 per YLS for a one-time self-selected mass screening and approximately $20,000 per YLS for a one-time self-selected mass screening of those older than fifty, the cost-effectiveness of these programs fall in line with or are better than many currently funded life-saving medical interventions\textsuperscript{86-87}.

There are several interesting results from the sensitivity analysis, which deserve further review. In the reference case, the screen must be fairly sensitive (greater than or equal to 86\%) \textit{ceteris paribus}, for the cost-effectiveness to remain below $50,000/YLS. Our estimate of a screen sensitivity of 85\% is not unreasonable for a dermatologist, based on the currently available evidence\textsuperscript{31,40,56-57,79-80}. However, a screener with a lower sensitivity could be used while maintaining or lowering the cost-effectiveness ratio if the screen cost was concurrently decreased. Thus, a less sensitive but less costly screener might be a potentially useful strategy for a screening program. A less costly professional such as a highly and specifically trained nurse or nurse practitioner may result in a similar or potentially even more cost-effective melanoma screening or could be used for sequential screening where only select people with a positive nurse/nurse practitioner screen is referred to a dermatologist. Specifically trained nurse practitioners have been reported to have a sensitivity in the range of 67-100\%\textsuperscript{75}, though such a wide range clearly needs further study. Assuming a sensitivity of 70\%, a screen cost of less than $35 per screen would be more cost-effective than the reference case. Employing
a screener other than a dermatologist would almost certainly be a necessary strategy to consider if one’s goal was to provide a screen for a large portion of the population both from a cost-effectiveness standpoint and a practical standpoint. Screening the entire US population would require the full-time efforts of every dermatologist and leave no time for the provision of any other dermatologic services. Recent advances in computer-assisted digital photography and automated pigmented lesion analysis may have implications for melanoma screening and may allow technicians to perform an initial screen, followed by a referral of positive screens. Of course, for melanoma screening, cost-effectiveness is not the only issue. For example, people may be unwilling to settle for an examination that was insensitive, due to the higher number of false negatives that would occur. Part of the benefit of participating in a screening examination is the reassurance the screen provides and an examination with a sensitivity of for instance 70%, may not be adequate to provide such reassurance to the average patient. This study suggests that various issues surrounding screening such as involving other screeners besides dermatologists alone are important to determine and in need of further study.

The sensitivity analysis shows that targeted screening of a high-risk, high-prevalence group of individuals (such as older males or first-degree relatives of family members of melanoma patients) is important to consider for cost-effectiveness. Others have suggested Medicare recipients may be a good target group for melanoma screening programs\textsuperscript{35-36,45}. The majority of Medicare recipients see a physician each year and could easily be screened by the primary care physician or could be referred to a
dermatologist for this purpose. The marginal cost of having the primary care physician or a specially trained nurse/nurse practitioner screening during the primary care visit may be relatively small (an Institute of Medicine study\textsuperscript{19} estimate was $20). In addition to the increased prevalence in older individuals, there appears to be a worse stage distribution of melanomas in older individuals especially men, which suggests screening may be even more effective in this group.

On the other hand, limiting the screening to very high-risk individuals rather than doing population-based screening program, while being more cost-effective, would also lower the total impact of screening on melanoma mortality. If the prevalence of the screened population in the reference case were only 70 per 100,000 people rather than 186 per 100,000 people, the cost would increase to $146,361 per YLS. Thus, accurate targeting of the population in such a screening program is likely to be quite important, but there remains a tension between targeting to improve cost-effectiveness and mass screening to achieve a greater impact on overall morbidity and mortality.

There are limitations to this study. First, ideally a study on the cost-effectiveness of melanoma screening should be based on prospectively collected data from randomized controlled trial of screening. This is not the case for our study because no such study is available. Thus, for a study such as this, the parameters used come from a variety of different sources and are brought together with the aim of approximating a clinical trial. Clearly, people may have different opinions on what are the appropriate parameters. Moreover, combining parameters from different settings can cause problems if
parameters co-vary with each other. For this reason, we chose to take values for many of the parameters from a single source, the AAD screenings. Thus, the co-varying relationship between these parameters should be valid. In so doing, we increased the internal validity of the results. More credence should be given to the estimate for the reference case than for the scenario of screening the entire average Caucasian population where the prevalence was estimated. Because the patients in the AAD screening were self-selected and at higher-than-average risk, it is possible that they are different than the population from which the SEER data came. It is possible that differences seen in the stage of distribution of melanomas between the screened and unscreened group were due in part to differences in the groups besides screening. However, until a randomized or population-based screening trial is attempted, this problem will be difficult to overcome.

One potential problem not addressed by our study design is that screens in general may be more likely to detect the less aggressive, slower-growing lesions rather than the faster-growing, more aggressive ones. This may happen since slower growing lesions, which tend to be less aggressive by the nature of their slower growth, have a longer window (preclinical period) during which they may be detected. This criticism is lessened by our study design. We controlled for this to a certain degree by the noting the percentages of each stage of the lesions detected in the AAD screenings. The results of the AAD screens suggest that screening does find metastatic lesions and localized lesions of higher Breslow levels, not just thin, non-aggressive lesions.
This study did not evaluate opportunity costs of patients for participating in the screen (e.g. time lost from work, etc...), which could be substantial or minimal depending on how the screen was organized. Exams taking place at places such as malls or at annual primary care provider exams reduce the opportunity costs but select for people who visit those places. This study did not evaluate QALYs. Given the sparse data on QALYs and melanoma, it was felt that such an analysis would not add valuable information to the analysis at this point in time. As shown in this study’s sensitivity analysis, a targeted approached to screening may be the best way to ensure a highly cost-effective program. Age, gender, and the general risk of the population to be screened were shown to be important in this analysis. In fact, using age as a criterion for screening may result in an even better cost-effectiveness than estimated here if one accounts for the worsened stage distribution of disease in older individuals, which our analyses did not. The main limitation of targeted screening, using a criterion such as age greater than 50 for entry, is that an age-limited screening design would obviously not affect those outside the screening age and there is in fact, significant morbidity in the U.S. from melanomas in people under age 50. Thus, the main goal of melanoma screening programs should not necessarily be to maximize cost-effectiveness per se. Rather, it may be to minimize melanoma mortality, given certain cost-effectiveness constraints. Further analysis could determine the optimal age, gender, or other risk-stratifying strategy for reducing mortality, given an accepted cost-effectiveness constraint. One could imagine a combined strategy such as doing mass screening of people over a certain age and only screening people under that age who have a given
set of risk factors. In order to determine an optimal strategy, more age- and risk-factor-specific prevalence data is needed.

A one-time screen was used for the reference case because the AAD screenings were for most people (roughly 20%, Geller et al\textsuperscript{36}) a one-time screen. Furthermore, if we had found that a one-time screening had a cost-effectiveness ratio that was too high to be considered worthwhile, a recurrent screen would be even less likely to be worth pursuing. However, melanomas may develop at any age and unlike cervical cancer probably do not have a dramatically long average preclinical stage. Unfortunately, a one-time screen will have a limited impact on the total mortality from melanoma, because one would only have one to six years (estimated) in a person’s lifetime during which to detect a preclinical melanoma. Clearly, a one-time screen is most likely not to fall in that window of time for most people and thus, a majority of melanomas would not be detected by such a screening program. A recurrent screen is more likely to have a major impact on morbidity and mortality and will be less cost-effective than (or at best almost equal to) a one-time screen depending on the frequency of the screen and the actual length of the preclinical period for melanomas. Often in public policy decisions however, changes are made and implemented one step at a time and the results analyzed prior to expanding the program (e.g. to involve recurrent screen). Thus, our estimate of the cost effectiveness of an initial melanoma screening provides useful information.
Future studies should focus on developing a screening program that minimizes melanoma mortality while meeting “reasonable” cost-effectiveness constraints. The definition of “reasonable” is best determined by what the cost-effectiveness estimates are for other medical interventions which save lives and in particular cancer screening interventions. Clearly, further analyses should be completed on age and gender-specific recommendations for melanoma screening, the frequency of screens, and the impact on screening recommendations of other risk factors such as family history of melanoma in a first degree relative, numerous nevi, or history of nevi with architectural disorder and atypia.

It will take a clinical trial of screening with good data collection and prospective cost and effectiveness data collected to truly estimate the cost-effectiveness accurately. This study makes a strong case for pursuing such a trial in the near future. A trial such as this would give more accurate data on both the costs and the effectiveness of screening. For instance, it would not require assumptions about the survival of patients with tumors detected by screening being similar to stage-adjusted tumors detected without screening. Rather, the survival for screened and non-screened groups would simply be observed. Assumptions on the cost of the screen would also be avoided by calculating the actual costs as best as possible. It would also provide valuable information on interval cancers and the duration of the preclinical stage. Such a randomized trial should be considered ethical given that the current default standard is not to initiate screening of individuals for melanoma.
Although a melanoma screening program such as the one analyzed here is important, there are also other interventions, which may reduce melanoma mortality and deserve further attention. These include educational campaigns aimed at primary and secondary prevention. Should screening be tied to educational campaigns and should self-screening be taught? These are also important issues deserving of investigation.

In this study, I provide estimates for the effectiveness and cost-effectiveness of a melanoma screening program with and without accounting for the impact of non-melanoma skin cancer. In addition, some age- and gender-specific estimates were determined. Melanoma screening appears effective and relatively cost-effective. The elderly and males appear to be particularly good candidates for screening. These estimates are based on the best evidence-to-date on melanoma screening, but further work is needed to make clear and specific recommendations.

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