Melanoma (MM) is a serious public health problem in the U.S. and many other countries. It is the eighth most common U.S. malignancy and accounts for 1% of all cancer deaths. In addition, the incidence of melanoma has been rising rapidly, approximately 3-4% per year since the 1970s. In 1935 the lifetime risk of melanoma was 1 in 1500, whereas recently it was estimated to be 1 in 75. This increase is due not only to earlier detection, but represents a true increase in the incidence of all stages of the disease. The etiology of the increase is not known with certainty but increases in ultraviolet exposure due to behavioral and ozone changes have been postulated by many. The burden of disease from melanoma is high by several measures. Each year in the U.S., in addition to the approximately 40,000 incident cases, there are about 7500 deaths from melanoma. There have been increases in mortality since the 1970's, though by lesser amounts than the increases seen in incidence. More recent trends suggest the mortality rate has stabilized. Each melanoma death accounts for approximately 17 years-of-life-lost on average, one of the highest rates for all adult-onset cancers. Not all statistics for melanoma are worsening, however. The overall survival from melanoma has increased. The 5-year survival in the 1940’s was 40%, from 1980-82 it was 83%, and from 1992-98 it was 89%. This improvement in survival is thought by most researchers to be primarily due to early detection. Advances in treatment have not dramatically altered the outcome for a given stage of melanoma in
recent years. Thus, primary and secondary prevention strategies have been proposed as a means to reduce the morbidity and mortality of this disease.

Primary prevention strategies aim at eliminating the causes of the disease while secondary prevention strategies aim at early detection. Both primary and secondary prevention could reduce the burden of disease from melanoma substantially. For instance, the link between sun exposure and melanoma is well-established. It has been estimated that the majority of one’s lifetime sun exposure occurs by the early twenties. If so, primary prevention strategies aimed at reducing ultraviolet exposure in this young population may be successful in reducing the development of melanoma. Exactly how to go about affecting change in this population and others is an area in need of research. A recent study suggests that changing knowledge of melanoma risks such as the link between sun exposure and melanoma will be unlikely to affect behaviors dramatically without other interventions\(^6\). Many researchers believe the improvements in survival of melanoma have been due to early detection and thus there is considerable interest in expanding efforts to enhance screening by self-examination and by physicians or other professionals.

Chapter Four “Estimating the effectiveness and cost-effectiveness of melanoma screening” investigates issues in secondary prevention through melanoma screening. This chapter presents a decision analysis model used to estimate the effectiveness and cost-effectiveness of melanoma screening. Because there is a significant difference in survival between early and late disease in patients with melanoma, and because some
early lesions may take months to progress to a late lesion, screening programs are thought to be a means by which melanoma outcomes may be improved. Most dermatologists assume that screening for melanoma is a useful and important service, which they provide. 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 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. The Canadian Task Force on the Periodic Health Examination recommends screenings only for high-risk patients. Many important questions have not been addressed in scientific studies. These questions include: Should physician screening be performed and if so, who should be screened? Should risk factors be used to determine who gets screened and if so, which ones? Beginning at what age should people be screened? How often should people be screened? Should self-screening be promoted and if so, in what manner should it be promoted? Should non-physician health care professionals be used to screen for melanoma? The ideal study to answer these questions, a randomized, controlled clinical trial of melanoma screening, has never been performed but there are sources of data that may be helpful in answering some of these questions.

Measurements of the effectiveness and cost-effectiveness of melanoma screening programs are not available in any comprehensive manner. Given the burden of disease
from melanoma, this is surprising. Since funds spent on melanoma screening could also be spent on other cancer screening programs, it is important to determine and compare the effectiveness and cost-effectiveness of melanoma screening to screening programs for colon, breast, prostate, and other cancers. If screening programs are a cost-effective way to reduce the mortality and morbidity from this disease, they should be funded in the same manner as other funded cancer prevention and screening programs. Eventually, a large-scale, prospective, randomized screening program may be designed to estimate the cost-effectiveness of melanoma screening. However, such a costly and lengthy trial is not likely unless an estimate arrived at via other means determines it is likely to be effective and cost-effective. In addition to calculating cost-effectiveness, evaluating melanoma screening using decision analysis and modeling techniques can lead to greater insights into the design of such a trial in the future.

The characteristics of a good cancer screening program have been previously described.\(^5\)

1) Screening should be highly sensitive and specific.

2) The prevalence of the disease should be high enough to warrant screening.

3) The health implications should be high enough to warrant screening.

4) The disease should be slowly progressing and not immediately life-threatening.

5) The screening procedure should be simple, inexpensive, and acceptable to the population being screened.

6) The disease should be one for which early diagnosis results in improved prognosis.

7) Screening should lead to more effective treatment at an earlier stage.
In addition to these criteria one might add that:

8) The population to be screened should be identifiable and reachable so as to accurately target one’s screening campaign.

9) The campaign’s cost-effectiveness should be comparable to other cancer screening campaigns.

A good case can be made that characteristics 1-3 and 5-8 are true for melanoma. Regarding characteristic number four, the natural history of melanoma has not been clearly elucidated to-date, but melanoma likely progresses more rapidly than many other cancers and this may adversely affect number nine, the effectiveness and cost-effectiveness of screening, which is a function of the other characteristics listed. Having such an estimate is becoming more important as the cost-effectiveness is being determined for many medical interventions and is used to determine public health policy.

Cost-effectiveness calculated as YLS is one measure, perhaps the most important measure in cancer screening, but still not a complete measure of a program’s worth. Further, there is often room for funding many programs geared towards different diseases, which affect health in more ways than just years-of-life saved. Nonetheless, cost-effectiveness is considered important in determining federal funding of specific health programs and when deciding where to spend the marginal dollar on health care, knowing the cost-effectiveness of potential programs can be helpful.
Some researchers have suggested the increases in melanoma incidence and improvements in survival are artifactual and due to a change in the histopathological criteria for diagnosing melanoma, such that some lesions that are biologically benign are now classified as melanoma. They suggest increased screening has led to more biopsies of these biologically benign but histologically malignant lesions thus increasing both incidence and survival. The evidence for these hypotheses is not convincing however. Clearly, the increase in mortality is not explained by these hypotheses. These issues are analyzed in Chapters Two, “The melanoma epidemic: Res ipsa loquitur” and Chapter Three, “Gender differences in melanoma incidence”. The data from these chapters were derived from analyses of the databases of the Surveillance Epidemiology and End Results (SEER) and the California Cancer Registries originally undertaken to generate parameters for modeling melanoma screening. Such necessary parameters were not available with enough specificity in the literature. An analysis of changes in incidence over time for each stage of melanoma revealed results relevant to the debate on whether there has been a “melanoma epidemic”. From an analysis of incidence and life expectancy, we found important patterns of age- and gender-specific incidence not previously described for melanoma. In the final chapter, the implications of this body of research are brought into perspective. These implications are relevant to current screening policy as well as to the design of future studies. Deficiencies in our current knowledge of melanoma screening are discussed along with suggestions for future studies.
It is hoped that this dissertation will inform the debate on the effectiveness and cost-effectiveness of melanoma screening from the research currently available. Knowing that a large body of research that could guide health policy planning for melanoma screening is not currently available, it is hoped that this dissertation will also help to promote further research and guide such research appropriately.

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