Inquiry into skin cancer in Australia

A submission prepared by:

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1. Introduction

There are three main types of skin cancer; the most numerous are the **keratinocyte cancers** (**BCC** and **SCC**), so named because the cells of origin are the abundant, keratin-producing cells of the epidermis. **Melanomas**, arising from melanocytes (the pigment-producing cells of the skin), tend to be more rapidly invasive than the keratinocyte cancers, and can metastasise widely.

This submission makes a number of recommendations to the Parliamentary Committee, with particular reference to two terms of reference:

- the need to increase levels of awareness in the community and among healthcare professionals;
- strategies to enhance early diagnosis;

2. Background

Keratinocyte cancers impose the highest costs of any cancer on the Australian health system. Each year, nearly 400,000 Australians develop at least one keratinocyte cancer (1), resulting in more than 750,000 Medicare claims for treatment, and an annual cost of $511 million(2). These figures are predicted to rise to ~ 1 million treatments in 2015 at a cost of $703 million(2). While commonly thought to be ‘trivial’ cancers, they cause considerable mortality and morbidity; each year in Australia keratinocyte cancers account for 450 deaths(3) and

85,000 hospital admissions (more than twice the number of admissions for each of bowel, breast or prostate cancers)(4). The principal treatment modality is surgery, which while highly effective in the majority of cases, inflicts pain, scarring, risks and costs. The enormous burden of skin cancer underscores the priority for research efforts to find better ways to control these cancers.

The approach to minimising the health burden from keratinocyte cancers and melanomas involves three strategies, broadly defined as follows:

1. ***Primary prevention***: preventing the onset of skin cancer by reducing population exposure to sunlight.
2. ***Secondary prevention***: preventing the onset of suffering from skin cancers by early detection and effective treatment.
3. ***Tertiary prevention***: preventing premature death from skin cancer by implementing effective treatments.

These strategies are complementary, and a coordinated plan for controlling these cancers must balance them all.

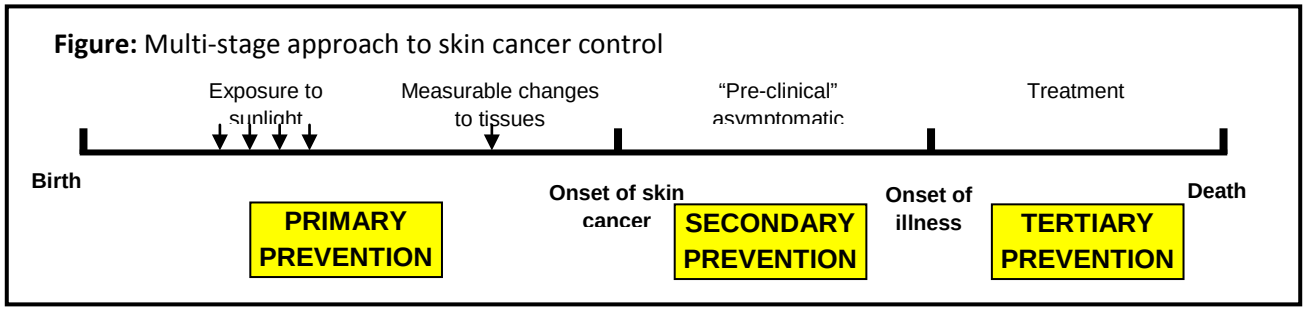


Figure: Multi-stage approach to skin cancer control

3. Primary prevention

3.1 Context and current issues

Primary prevention has been the favoured approach to skin cancer control in Australia, and great efforts have been made to reduce population exposure to sunlight. (I understand that the Cancer Councils and other agencies will be making submissions to this Inquiry, and will be providing details of the components of successful primary prevention campaigns. As such, I

will not describe them further here). However, there are some who question the impact of primary prevention activities for skin cancer, arguing that the continuing increases in skin cancer incidence provide evidence that primary prevention has failed. Some go further to argue that primary prevention of skin cancer is not only not effective, but that it is also not cost-effective, and that society would be better off just letting skin cancers develop and then to excise them (inexpensively?) once they come to clinical attention.

To address these criticisms requires an understanding of the process through which skin cancers arise as well as a thorough analysis of recent Australian data. It is well accepted that the incidence of skin cancer in a population is determined strongly by the ambient exposure in which the population resides, the patterns of outdoor exposure in that population, as well as the overall susceptibility of the population to the carcinogenic effects of ultraviolet radiation. Skin cancers have long latency, and sun exposure in early life appears particularly important for BCC(5) and melanoma(6)). This means that primary prevention efforts must be directed towards the young, and benefits are likely to accrue only after decades have elapsed since the intervention. The corollary is that evidence for an effect of primary prevention activities can only be detected in those who stand to benefit (that is, young people who have been targeted by primary prevention activities since birth), and for whom sufficient time has elapsed to be able to measure a difference in skin cancer incidence.

3.2 Keratinocyte cancer incidence trends by age group

My research group recently analysed Medicare claims data to monitor trends in the diagnosis and treatment of BCC and SCC in Australia during the period 2000-2011. (The manuscript has recently been accepted for publication in the *Journal of the American Academy of Dermatology*) (7). Overall, we found sizeable and statistically significant increases in excision rates for keratinocyte cancers (3.3% p.a. for men and 2.2% p.a. for women). However, when we examined the data separately for younger and older Australians, we found clear differences in the time trends. Among those aged less than 45 years, rates of diagnoses and treatments for keratinocyte cancers declined by between 2-3% p.a. between 2000 and 2011. In marked contrast, rates of diagnoses and treatments rose steadily among older age groups, with the highest increases observed among men aged 75-84 years (8.6% p.a.).

Of particular relevance to this Inquiry was the observation that rates of skin biopsies for non-malignant lesions increased substantially in all age groups over the same period (2000-2011).

Such data suggest strongly that medical practitioners have been increasingly vigilant in monitoring their patients for the development of skin cancer, yet have not detected more skin cancers among the young. Taken together, these population-based data provide strong ecological evidence that the primary prevention campaigns initiated in Australia in the 1990s are now beginning to show their effects within the subgroups of the population most likely to benefit.

3.3 Melanoma incidence trends by age group

Melanoma is the third most commonly occurring cancer in Australia, and is the most common cancer among young adults aged 20-39 years, accounting for 23% of all cancer diagnoses in that age group in 2009 (8). As for keratinocyte cancers, the overall incidence of melanoma has been climbing in Australia for decades, but recent studies have documented the declining incidence of melanoma in young people (9). These trends are consistent with a birth-cohort effect, in which those born after about 1965 have experienced consistently lower rates of melanomas than earlier generations. In most other fair-skinned populations (including USA, UK, Scandinavia), rates of melanoma are continuing to increase steadily in all age groups and birth cohorts (9). The most plausible explanation for the recent declines in melanoma incidence seen in young Australians is that the targeted primary prevention campaigns implemented since the 1980s are beginning to exert a beneficial effect upon the rates at which melanomas develop in the population. To date, the gains have been modest, and it remains an open question whether they will be sustained into the future.

Conclusion:

> **The effects of primary prevention activities for skin cancer in Australia are beginning to manifest through lower incidence rates for both melanomas and keratinocyte cancers among the most recent birth cohorts.**

Recommendation:

1. **Continued monitoring is essential to document the trends in skin cancer incidence and mortality into the future.**

Australia leads the world in developing and implementing campaigns directed towards the prevention of skin cancer. There is evidence that awareness of skin cancer is high in the general population of Australia, however the prevalence of **preventive behaviours** (e.g.

wearing hats, sunscreen, avoiding sunburns) in the community is labile, and appears to correlate with the level of investment in conducting campaigns. When investment wanes, the prevalence of poor preventive behaviour increases (10). Thus the major challenge for public health is to translate the high levels of community awareness into sustained behaviour change.

Recommendation:

2. **Primary prevention activities should be supported and extended to benefit current and future generations of Australians.**
3. **Cancer Councils in each state and territory are best placed to advance efforts in this area, based on their consistent record of innovative research and effective translation.**

4. Early detection

4.1 Population screening

Mortality from melanoma is correlated strongly with tumour thickness; as the thickness of melanomas increase, so does the probability of death. Patients with thin melanomas (less than 1mm in thickness) have 20 year survival approaching 96% whereas survival for thicker lesions is substantially lower (11) (12). Because of the well-documented relationship between melanoma thickness and mortality, there has been a strong motivation to identify potentially malignant lesions before they have invaded the dermis.

Australian guidelines do not recommend **population screening** for melanoma (13). The formal recommendation is as follows:

> *In the absence of substantive evidence as to its effectiveness in reducing mortality from melanoma, population-based skin screening cannot be recommended.*

The absence of substantive evidence refers to an absence of randomised trials that have tested whether screening is effective in reducing mortality from melanoma. At the present time, there are only observational data available to inform decision making. Observational studies can be criticised as being open to various biases, and readers will draw different conclusions depending upon their points of view. Thus, the scientific evidence necessary to revisit this Australian guideline can only come from a randomised trial. The challenge is that it is

extremely unlikely that a randomised trial can ever be performed in Australia, given the high prevalence of opportunistic screening in the community, and the costs involved.

Despite no randomised trial evidence to assess the performance of population-based skin screening, Germany has implemented has implemented a screening program following a pilot study in the northern state of Schleswig-Hollstein (14, 15). The pilot program was not a controlled trial, and evaluation was imperfect. Nevertheless, the pilot was judged to be successful and a national screening program was rolled out in Germany commencing in 2008 (16). While German data will be of interest to Australian researchers, it is difficult to gauge how applicable they will be given the profound differences in the incidence of skin cancer, the differences in medical training, and very different health systems operating in the two jurisdictions.

Recommendation:

4. **If 'early detection' of melanomas is to be considered as a public health strategy to reduce melanoma mortality, then more Australian research (possibly including large-scale, population-based, randomised controlled trials) is necessary to provide an evidence base with which to make informed judgements about efficacy, effectiveness and costs.**

3.2 Opportunistic screening and risk prediction

In the absence of a systematic population-based screening program for skin cancer, a strategy of early detection must rely on **opportunistic identification of lesions**. This requires high levels of awareness in the community coupled with rapid access to clinical care for patients with suspicious skin lesions. There has been some evidence that opportunistic early detection has been successful in Australia, with a pronounced 'leftward shift' in lesion thickness such that the vast majority of melanomas are now diagnosed as thin lesions. However, there have been worrying trends of increasing rates of thicker melanomas in recent years (17), which may be considered "failures" of early detection.

A strategy to enhance early detection might include targeted screening for skin cancer. The current Australian guidelines state (13):

> *It is reasonable to posit that successful and timely diagnosis of melanoma will be enhanced if clinicians are aware of high-risk groups in the population, and that people in these groups are aware of their status.*

Further, the guidelines recommend that:

> *Individuals at high risk of melanoma and their partner or carer be educated to recognise and document lesions suspicious of melanoma, and to be regularly checked by a clinician with six-monthly full body examination supported by total body photography and dermoscopy as required.*

While well-intentioned, putting these guidelines into practice is not straightforward since there are no validated clinical tools for reliably identifying patients at high risk of skin cancer. Instead, clinicians must make subjective assessments of risk.

In the field of preventive medicine, risk prediction tools that have been developed for other chronic diseases. For cardiovascular disease, for example, epidemiologists combined primary data from observational studies and trials to develop charts which convey the absolute risks of suffering from heart disease within a given time frame. Considerable evidence has accumulated that these tools can be correctly applied and interpreted by physicians and nurses, and that they are used reliably to improve decision-making by patients and their carers.

Such approaches are less well developed in cancer prevention, and although a number of risk prediction tools for melanoma have been published in the international literature, very few have been validated (18). Further, most such tools have been developed from small datasets sampled from low incidence populations which have questionable relevance to the Australian population. To overcome these problems, my group at the QIMR Berghofer Cancer Research Centre is conducting the **QSkin Study**, a prospective cohort of 43,794 people being followed through Medicare records for the next 10 years for the development of skin cancer (19). (More information about the QSkin Study is available at www.qskin.qimrberghofer.edu.au). We aim to develop accurate and valid tools which can be used by Australian patients and doctors to assess their future risks of keratinocyte cancers and melanomas. Such data are essential if the Australian guidelines are to be followed. Our study will provide one source of data, but will need to be replicated by other studies using other patient samples to ensure validity.

Ultimately, we aim to develop a tool similar to the New Zealand risk factor chart for cardiovascular disease (20) that provides a visual image of the absolute risk of melanoma for an individual according to their profile of risk factors (see **Figure** below). In this 'hypothetical' chart, we have stratified levels of risk using factors that are widely accepted as independent determinants of melanoma, namely, current age, place of residence, number of melanocytic nevi, and skin type (21). In recognition of the rapidly moving field of genetic epidemiology and the expectation that the insights so derived may offer additional information for risk counseling, we have included a putative marker of melanoma risk, the status of the melanocortin-1-receptor (*MC1R*) gene. It is too early yet to be definitive about the final content of the chart – this hypothetical version is intended to convey the form that we expect the chart to take.

Recommendation:

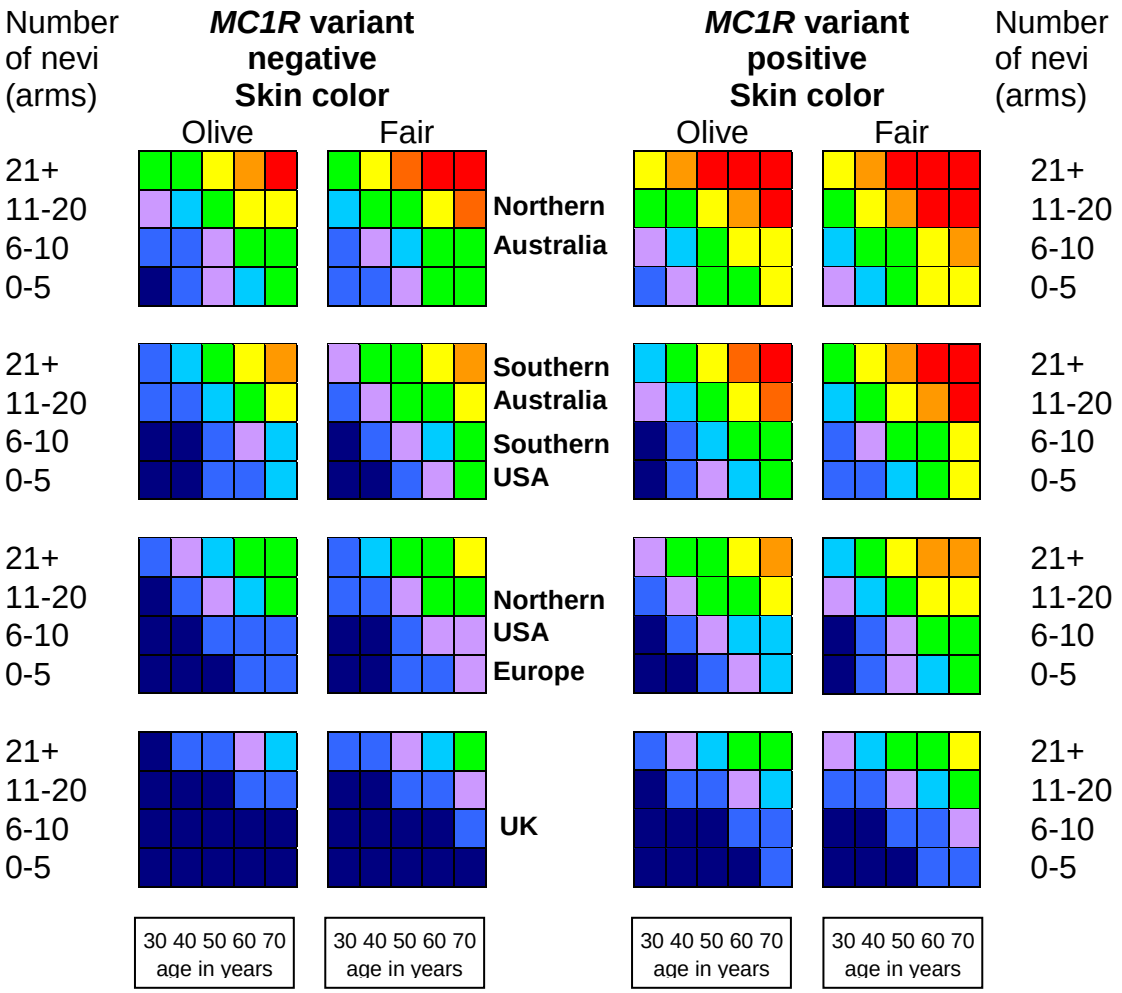
5. **Validated tools need to be developed with which doctors and patients can predict future risk of skin cancer.**

3.3 Shortcomings of early detection

3.3.1 Mortality from thin melanomas

There is a perception that most people who die from cutaneous melanoma are those who initially present to clinical care with thick tumours. Early detection aims to reduce melanoma mortality overall by encouraging patients and clinicians to identify lesions early, before they become thick, and is predicated on the observation that the 10-year survival for patients diagnosed with thin melanomas approaches 95%. While this survival is far superior (and inherently preferable) to the 40% survival experienced by patients diagnosed with thick melanomas (those greater than 4mm) (12), the fact remains that 5% of patients with thin melanomas will not survive 10 years. So even though early detection aims to bring forward the time of diagnosis for melanoma and thereby reduce the risk of fatality, early detection will never stop melanoma deaths entirely.

Figure: Hypothetical table of absolute risks for melanoma among Caucasians, combining information on environmental, phenotypic and genotypic causal factors (originally published in *Cancer Epidemiol Biomarkers Prev (21)*).



10 year risk of cutaneous melanoma

Very high	> 10%
	6-10%
High	4-6%
Moderate	2-4%
	1.5-2%
Low	1-1.5%
	0.5-1.0%
	<0.5%

To explore this issue further, my group at the QIMR Berghofer Medical Research Institute sought to document, in absolute terms, the numbers of people who have died from thin vs thick melanoma in Queensland in the past 3 decades. Using mortality data from the Queensland Cancer Registry, we analysed the characteristics of all persons who died between 1982 and 2009 and for whom the cause of death was "melanoma". We linked these records to obtain the histological details of their melanomas, and then compared the number of deaths according to thickness category. We found that in the most recent decade (2000-2009) more Queensland residents died after being diagnosed with thin melanomas (<1mm, n=466, 19.1% of all melanoma deaths) than died following thick melanomas (4+mm, n=402 deaths, 16.5%).

These data highlight the limitation of all early detection programs; namely, that a proportion of thin melanomas are lethal. Even if a diagnosis of melanoma is made earlier than might otherwise have been the case because of a detection program, it still does not eliminate the risk of dying from melanoma.

Recommendation

6. **Primary prevention should remain the principal strategy for melanoma control in high incidence populations, since thin lesions confer substantial mortality in absolute terms when their incidence is high.**

3.3.2 Overdiagnosis

A related problem for early detection programs is the phenomenon of overdiagnosis. In a recent *Br Med J* article, Moynihan and colleagues defined the issue as (22):

> *Overdiagnosis occurs when people without symptoms are diagnosed with a disease that ultimately will not cause them to experience symptoms or early death. More broadly defined, overdiagnosis refers to the related problems of overmedicalisation and subsequent overtreatment, diagnosis creep, shifting thresholds, and disease mongering, all processes helping to reclassify healthy people with mild problems or at low risk as sick.*

For lesions of the skin, it is likely that as people are encouraged to examine their skin through early detection campaigns, more and more will present to their doctors with suspicious lesions. This is likely to prompt greater numbers of excisions or biopsies for many benign or borderline lesions, a proportion of which might be overdiagnosed as melanomas. An analysis

of US data has found evidence of overdiagnosis by demonstrating a strong correlation between melanoma incidence and skin biopsy rates, without any appreciable decline in mortality (23). In essence, they cautioned against over-zealous detection, implying 'the more you look, the more you find'.

Another form of overdiagnosis which might occur through early detection strategies is the potential for uncovering a reservoir of 'indolent' melanomas that have no risk of metastasis. Analyses of data from the Hunter Region of NSW in the 1980s provide some evidence that such a phenomenon exists (24-26). The authors of that study observed a sudden increase in the incidence of thin melanomas in that region, that was then sustained. The authors concluded:

> *Advancement of the time of diagnosis and a real increase in incidence were likely explanations for some of the observed trends. Increasing diagnosis of a non-metastasising form of thin melanoma, consequent upon increasing removal of pigmented skin lesions by medical practitioners, may also explain some of the observed increase in the incidence of the disease. This possibility has important implications for proposed population screening programs, and methods are needed to distinguish such lesions, if they exist, from potentially fatal melanoma*

Recommendation

7. **The potential hazards of overdiagnosis arising from early detection programs must be quantified.**
8. **Primary prevention should remain the principal strategy for melanoma control.**

5. Summary and conclusions

Cancers of the skin impose a formidable burden on Australians in terms of health and costs. These cancers are largely avoidable through reducing the population's exposure to the sun. Every effort should be made to reduce individual sun exposure through wearing appropriate clothing, rescheduling activities, seeking shade, and applying sunscreen to exposed skin surfaces. Other strategies for controlling the burden of skin cancer, including early detection and evidence-based management, are secondary in importance to reducing incidence.

5. References

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