Towards evidence-based skin checks

Melanoma is often referred to as Australia's national cancer, with the highest incidence per capita in the world due to the combination of high solar ultraviolet radiation levels, a temperate climate, outdoor lifestyle and genetically susceptible population.[1] Melanoma is our third most common invasive cancer, and two-thirds of Australians will be diagnosed with keratinocytic tumours (including basal cell and squamous cell carcinomas).[2] Despite advances in treatment and improved survival over the past decade, one Australian dies about every six hours from melanoma.[3]

Routine skin checks occur widely in Australia, with about one-third of Australian adults aged 45–69 years reporting having a whole-body skin check annually.[4] This form of ad-hoc screening is contrary to national and international recommendations, with both the Australian Government Standing Committee on Screening[5] and United States Preventive Services Taskforce[6] concluding insufficient information on the benefits and harms of skin cancer screening, and lack of data on cost-effectiveness. Herein, we discuss the need for evidence-based approaches to skin cancer detection in Australia. Risk factors and diagnostic techniques for melanoma and keratinocyte carcinoma overlap. This perspective article focuses on melanoma, which is most likely to be associated with mortality, and its detection and cost benefits from an organised screening program.

"Population screening" refers to an organised program to identify disease in asymptomatic populations.[5] Australian clinical practice guidelines recommend "opportunistic screening", that is, patient-driven or clinician-initiated skin checks occurring outside an organised program, for patients at increased risk of melanoma, and six- to 12-monthly skin checks for anyone who has ever had a melanoma (targeted screening).[7] Detection and treatment of melanoma at an early stage is associated with an excellent prognosis, and increased mortality has been demonstrated with each 0.2 mm increment in Breslow thickness at diagnosis.[8]

Skin cancer is Australia's most expensive cancer, with direct costs to the health care system of almost $2 billion per year.[9] The additional cost of skin checks that do not result in a diagnosis of skin cancer is difficult to accurately quantify, as there is no Medicare item or process to collect these data. Current reimbursement models reward high patient volume and high biopsy rates, and community fear of cancer and clinician fear of error can also drive over-servicing. The potential non-financial costs of skin checks include patient anxiety, overdiagnosis and surgical burden.[10] Increasing government spending on skin checks and skin cancer treatments may also exacerbate missed opportunities to focus on primary prevention, which is highly cost-effective.[11] There are geographical and socio-economic inequities in who accesses skin checks,[4] is diagnosed with melanoma, and dies from it, and there is a large variation in the number of surgical procedures per malignant diagnosis by clinical setting and subspecialty.[12] Skin checks in their current form are largely without clear guidelines or quality frameworks. For these reasons, key stakeholders representing consumers, researchers, clinicians and policy makers are supportive of an organised risk-tailored melanoma screening program.[13-16]

The clinical diagnosis of melanoma and other skin cancers is challenging. There are many benign and age-related lesions that can mimic skin cancer, and conversely some melanomas (particularly amelanotic) are subtle or featureless. This challenge is compounded by poor reproducibility of the histopathological diagnosis of borderline malignant melanocytic skin lesions.[17] It is estimated that up to half of melanoma in situ diagnoses and 15% of invasive melanomas are overdiagnosed, that is, if left undetected, they would not have caused morbidity or mortality within a person's lifetime.[18] Thus, consideration of who to screen, and detection and management of low risk skin cancers or their precursors, need careful consideration.

Moving towards accurate melanoma screening that is targeted to individuals most at risk while minimising harm requires consideration of many factors, which ideally need evaluation in high quality studies:

- who: identification of individuals at high risk of developing melanoma using validated risk prediction tools;
- what: non-invasive imaging technologies to improve diagnostic accuracy (particularly specificity);
- when: risk-tailored screening and surveillance intervals;
- where: primary and specialist care, with clearly defined access and shared care protocols;
- how: education and upskilling of health practitioners;
- cost: renumeration models linked to quality of care;
- outcomes: equitable access, quality of care, stage at diagnosis and cost-effectiveness are key outcomes.

Who needs a skin check?

Not all Australians need regular skin checks. Targeting early detection efforts to individuals at high risk of developing melanoma can increase benefits and reduce potential harms of screening. The interplay between risk factors for developing melanoma, such as innate skin colour, mole count, family history, genetic factors and sun exposure, is complex. There are several online validated melanoma risk prediction tools available for the Australian population that facilitate estimation of personal risk of melanoma diagnosis.[19,20] Future developments in risk tools and their interface, such as incorporation of additional risk factors from skin images and medical record data, are expected to further improve accuracy. Individual risk assessment and education for all patients has been

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demonstrated to be acceptable and feasible in clinical care.[21,22] Communicating the lifetime risk of melanoma and other skin cancers is important for primary prevention messaging; however, ten-year absolute risk of melanoma would be more relevant for identification of individuals who may benefit from regular skin checks.[23] The risk thresholds to determine screening eligibility and frequency could be based on modelling and achieving an optimal balance of benefits and harms, along with considerations of cost-effectiveness and resource implications.

We anticipate some reluctance for low risk groups to not screen or de-escalation of existing screening. Anxiety related to melanoma diagnosis is common and needs to be systematically identified and addressed with specific psychological interventions to reduce fear of cancer, rather than addressed with increased skin surveillance.[24]

What diagnostic technologies should be used in a skin check?

A key obstacle to melanoma screening is the variable diagnostic accuracy of standard care. Dermoscopy reduces the benign to malignant ratio of excised melanocytic lesions and the number of patients referred for biopsy, but requires training.[7] New non-invasive diagnostic technologies will be fundamental in improving and standardising diagnostic accuracy.[14] These require evaluation in randomised controlled trials to establish diagnostic accuracy, reduction in unnecessary biopsies and cost-effectiveness in real-world settings. Validated technologies include total body photography (for individuals at high risk of developing melanoma), and sequential dermoscopic imaging (for equivocal lesions).[25] Photographic medical records require robust privacy protection. The role of advanced and emerging diagnostic technologies, including in vivo reflectance confocal microscopy, optical coherence tomography, line-field optical coherence tomography, artificial intelligence decision support, and biomarker analysis of tape-stripped samples, is to be determined. The effect of health apps that facilitate direct patient interaction with unregulated software requires evaluation.

The quality of skin checks and health outcomes could be improved through the introduction of an organised screening program, by standardising the screening and diagnosis process, including:

- extent of examination: whether special sites (such as scalp, mucosa) are included;
- lesion selection: identification of appropriate lesions for dermoscopy and non-invasive diagnostic technologies;
- criteria for biopsy: it is time to move beyond the common message of "if in doubt, cut it out" and establish monitoring protocols and objective biopsy criteria based on lesion malignancy risk in context of individual patient risk and clinical history — emerging diagnostic technologies mentioned above may assist in creating such an algorithm;
- biopsy technique: different factors will guide the choice of biopsy technique; however, partial and shave biopsies are associated with the underestimation of melanoma thickness by a mean 0.25 mm.[26]

When to get a skin check?

The frequency of skin checks should be tailored to individual risk, while considering growth trajectories of melanoma subtypes. Cost-effective screening intervals are yet to be determined, and modelling may provide guidance, but could vary from every three to six months for individuals at extremely high risk of developing melanoma to every five years or more for individuals at lower risk.[21,23]

Where to get a skin check?

In Australia, most diagnoses and management of skin cancers, including melanoma, occur in primary care,[4] where we have a skilled workforce. Currently, opportunistic melanoma detection leads to the inequitable allocation of health care resources, creating or exacerbating health inequalities.[10] Referral to specialist facilities should be based on risk and complexity rather than socio-economic status, with defined shared care roles and priority access pathways based on clinical need.

How to make skin checks evidence-based?

Improving skin check quality, equity and cost-effectiveness requires major investment in infrastructure and workforce upskilling. Investment is needed in education on multiple levels, including: (i) medical student curriculums to increase dermatology content, specifically including skin cancer diagnosis and management, which should be examinable; (ii) general practice education to involve expert-level teaching including morphological identification of high risk lesions (such as amelanotic and desmoplastic melanomas), differentiation from inflammatory dermatoses, understanding of non-invasive technologies and competency assessment; (iii) increased numbers of dermatologists, and dermatologist upskilling in advanced non-invasive diagnosis (eg, confocal microscopy); and (iv) effective community education on sun protection and early detection, highlighting the importance of seeking medical review for new or changing lesions. Skin cancer prevention brings cost benefits to governments and society[11] and should be embedded in the skin cancer screening and detection processes. In addition, quality assurance frameworks need to be established to ensure equitable access to good quality skin checks, and should consider clinical and patient reported outcomes.

How should skin checks be funded?

Medicare reimbursement models need re-evaluation. Specific item numbers for skin checks and differentiation of skin biopsy item numbers where the intention is for investigation of possible cutaneous malignancy would assist in the evaluation of real-world skin cancer management. Ideally models of care

would not financially penalise time spent on patient education and judicious biopsy use, but reflect the time and expertise required for complex pigmented lesion diagnosis and quality patient care.

The state of the nation report into melanoma and the Melanoma Institute Australia position statement highlighted improving early detection and building evidence for a national targeted screening program as a major strategy for reducing the burden of melanoma in the community.[15] Consideration of the challenges outlined in this perspective article will help us to achieve that goal.

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