Methods of melanoma detection and of skin monitoring for individuals at high risk of melanoma: new Australian clinical practice guidelines

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Abstract

Introduction: The evidence-based national clinical practice guidelines for the management of cutaneous melanoma published in 2008 are currently being updated. This article summarises the findings from multiple chapters of the guidelines on different methods of melanoma detection and of monitoring the skin for patients at high risk of melanoma. Early detection of melanoma is critical, as thinner tumours are associated with enhanced survival; therefore, strategies to improve early detection are important to reduce melanoma-related mortality.

Main recommendations:

- Clinicians who perform skin examinations for the purpose of detecting skin cancer should be trained in and use dermoscopy.
- The use of short term sequential digital dermoscopy imaging to detect melanomas that lack dermoscopic features of melanoma is recommended to assess individual melanocytic lesions of concern.
- The use of long term sequential digital dermoscopy imaging to detect melanomas that lack dermoscopic features of melanoma is recommended to assess individual or multiple melanocytic lesions for routine surveillance of high risk patients.
- The use of total body photography should be considered in managing patients at increased risk for melanoma, particularly those with high naevus counts and dysplastic naevi.
- There is insufficient evidence to recommend the routine use of automated instruments for the clinical diagnosis of primary melanoma.

Management overview: Determining the relative indications for each diagnostic method and how each method should be introduced into the surveillance of a patient requires careful consideration and an individualised approach.

Melanoma significantly contributes to the burden of cancer in Australia, where it is the third most common cancer in adults and the most common cancer in young Australians (aged 15–39 years).[1] The incidence of melanoma in Australia has increased considerably over recent decades, with the age-standardised incidence rate increasing by 181% between 1982 and 2016, from 26.8 per 100 000 annually to an estimated 48.7 cases per 100 000 annually (59.9 for males and 39.2 for females), respectively.[1] In 2017, an estimated 13 941 new cases of melanoma were diagnosed and an estimated 1839 people died of melanoma in Australia.[1] Based on estimates from New South Wales, melanoma costs the Australian health care system about $500 million per year.[2] Early detection of melanoma is critical, as thinner primary tumours are associated with enhanced survival.[3] Therefore, strategies to improve early detection are important to reduce melanoma-related mortality.

The evidence-based national clinical practice guidelines for the management of cutaneous melanoma published in 2008 are currently being updated by a multidisciplinary working group under the auspices of Cancer Council Australia. Sections of the updated guidelines have now been published through an online wiki platform (http://wiki.cancer.org.au/australia/Guidelines:Melanoma). Summaries of other chapters of the updated guidelines — specifically, chapters on melanomas that lack the classical clinical features and chapters on definitive excision margins for primary cutaneous melanoma — have been recently published.[4,5] This article summarises the findings from multiple chapters of the revised guidelines on different methods of monitoring the skin in patients at high risk of developing melanoma. It details the relative indications for each method and outlines when each method should be introduced into the surveillance of a patient at high risk of melanoma.

Methods

The following five study questions were devised by the multidisciplinary Melanoma Guidelines Working Party:

- What is the role of dermoscopy in melanoma diagnosis?
- What is the role of sequential digital dermoscopy imaging (SDDI) in melanoma diagnosis?
- What is the role of total body photography (TBP) in the early diagnosis of patients at high risk of developing melanoma?
- What is the role of automated instruments in melanoma diagnosis?
- What is the role of reflectance confocal microscopy (RCM) in melanoma diagnosis?

A literature search was performed by the Cancer Council Australia Clinical Guidelines Network Working Group using PubMed, EMBASE and the Cochrane databases including particular keywords for each clinical question as per the protocol for guidelines development. A broad range of study designs, including randomised controlled trials and cohort, case–control, cross-sectional, comparative and diagnostic accuracy studies were included. Information from the search was collated, appraised and summarised. Key findings that directly addressed the study questions formed the main evidence summary. The level of evidence for the recommendations was determined using the Australian National Health and Medical Research Council (NHMRC) evidence hierarchy.[6] Box 1 provides an evidence summary with the level of evidence for each method of monitoring the skin surface in individuals at high risk of developing melanoma. Practice points were included based on expert consensus opinion when evidence was lacking (Box 2).

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1 Evidence summary with the level of evidence for each method of monitoring the skin surface in patients at high risk of developing melanoma

Evidence summary	NHMRC level of evidence	References
Total body photography		
Five level III-2 studies have demonstrated that a multimodal approach with the combination of total body photography and sequential digital dermoscopy imaging provides effective surveillance in high risk patients and may assist with early melanoma diagnosis	III-2	7-11
Two level IV studies have demonstrated that total body photography may reduce the number of naevus biopsies and improve diagnostic accuracy in patients at high risk of melanoma	IV	12,13
Dermoscopy*		
From a meta-analysis of nine level II studies, the diagnostic accuracy for melanoma was 15.6 times higher for dermoscopy compared with naked-eye examination. Two subsequent level II studies showed results consistent with the larger meta-analysis	I, II	14-26
Dermoscopy has been shown to reduce the benign to malignant ratio of excised melanocytic lesions and reduce the number of patients referred for biopsy in both specialists and primary care settings	II	15,16,25,27
Sequential digital dermoscopic imaging (SDDI)		
Four level II studies and more recent cohort studies show consistently that SDDI allows the detection of suspicious dermoscopic change in melanomas that lack dermoscopic evidence of melanoma at a particular time	II, III-2	28-33
The routine use of SDDI in both dermatologist and primary care allows the detection of a significant proportion of patients' melanomas. Long term SDDI of multiple naevi in lower risk patients, while allowing detection of melanoma, is less efficacious	II, III-2	25,29,33-39
SDDI has been shown to reduce the benign to malignant ratio of excised melanocytic lesions and reduce the number of patients referred for biopsy in both specialists and primary care	II	25,36
Automated instruments		
To date, only two level II studies have compared specialist clinician diagnosis with an automated machine diagnosis with adequate sample size to assess both specificity and sensitivity for the diagnosis of melanoma	II	40,41

NHMRC = National Health and Medical Research Council. * The studies were classified as III-2 according to the NHMRC 2009 levels and grade of evidence.[6] Using the GRADE approach (www.gradeworkinggroup.org), the studies were then upgraded to level II if the only criterion not meeting level II was that the pathologist was not blinded to clinical information of the patient and/or lesion, as it is established that clinical information is required for an accurate pathological diagnosis of melanocytic lesions. ◆

2 Practice points for methods of monitoring the skin surface in patients at high risk of developing melanoma based on expert consensus*

- Dermoscopy can identify diagnostic features in non-pigmented (amelanotic) lesions
- Only flat or slightly raised lesions should undergo sequential dermoscopy monitoring. Suspicious nodular lesions should not be monitored but should be excised
- The interval for short term sequential digital dermoscopic imaging (SDDI) monitoring is 3 months when any change leads to excision. When lentigo maligna is in the differential diagnosis, it is recommended an additional 3 months of monitoring performed (ie, a total of 6 months)
- The usual interval for long term SDDI monitoring is 6–12 months. Unlike short term monitoring, certain specific changes are required for excision to be indicated
- Total body photography (TBP) allows monitoring of most of the skin surface, including most existing skin lesions. TBP should be the primary imaging intervention for early melanoma detection in patients at elevated risk who have high naevus counts or multiple dysplastic naevi

* These practice points are based on expert consensus opinion, not on evidence. ◆

Recommendations: systematic review evidence

The role of dermoscopy in the diagnosis of melanoma

Dermoscopy (dermatoscopy, skin surface microscopy, epiluminescence microscopy) is a non-invasive, in vivo technique that uses a handheld magnifying device combined with either the application of a liquid interface between the transparent plate of the device and the skin or the use of cross-polarised light. This technique allows for the visualisation of diagnostic features that are not able to be seen with the naked eye.[42,43] Previous meta-analyses that included both clinical and experimental studies have consistently found that dermoscopy improves diagnostic accuracy for melanoma.[44,45]

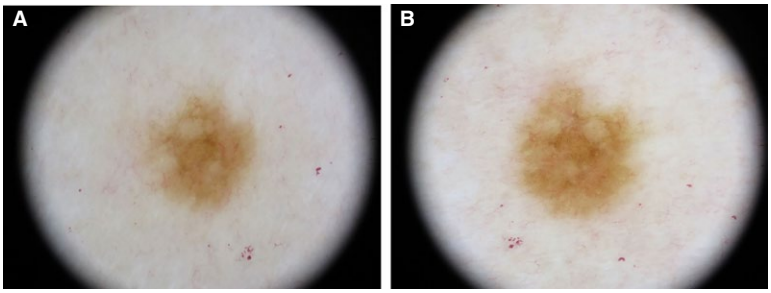
A more recent meta-analysis of high quality clinical studies[14–23] found that the relative diagnostic odds ratio for melanoma was 15.6 times higher (95% CI, 2.9–83.7; $P = 0.016$) for dermoscopy compared with naked-eye (clinical) examination.[24] Following the publication of this meta-analysis, a study indicated that dermoscopy improved the sensitivity of melanoma diagnosis in a primary care setting.[25] Several studies have found reduced rates of excision of benign lesions with the use of dermoscopy, providing indirect evidence for improvement in specificity in both dermatologist[15,16,27] and primary care[25,26] settings. In a study of high risk patients, the use of dermoscopy resulted in 42% fewer excisions.[27] In another study, the benign to malignant ratio improved with the use of dermoscopy from 1:18 to 1:4.3.[16] Dermoscopy has also been shown to detect melanomas at an earlier clinical stage.[46]

While few studies have assessed dermoscopy in primary care settings, the existing literature has consistently shown that dermoscopy improves diagnostic accuracy for melanoma.[14,25,26,47,48] However, it should be noted that all these studies were undertaken by clinicians with some level of training in dermoscopy. Evidence suggests that formal training is required to achieve these improvements in diagnostic accuracy.[49]

The role of sequential digital dermoscopy imaging in the diagnosis of melanoma

SDDI involves the capture and assessment of successive dermoscopic images, separated by an interval of time, of one or many melanocytic lesions to detect suspicious changes (Box 3). SDDI is performed in two settings: short term dermoscopy monitoring (over a period of 3 months) for suspicious melanocytic lesions without dermoscopic evidence of melanoma, and long term monitoring for surveillance of multiple non-suspicious melanocytic lesions (usually at intervals of 6–12 months).[28,50] Long term monitoring is generally used in the surveillance of high risk patients, usually patients with multiple dysplastic naevi. Short term monitoring of individual suspicious lesions is used in multiple clinical settings regardless of patient phenotype (eg, lesions with a banal dermoscopic appearance and a patient-reported history of change, or an atypical lesion without a patient-reported history of change). Only flat or slightly raised lesions should undergo sequential dermoscopy monitoring. Suspicious nodular lesions and lesions with extensive regression are not appropriate for dermoscopic monitoring, but should be excised.

3 Sequential digital dermoscopy imaging showing dermoscopic change in a lesion present on the right chest of a 59-year-old woman, separated by a 3-month interval (A and B). The lesion has increased in size, changed shape and the pigment network appeared more atypical. Histopathology from an excisional biopsy showed melanoma in situ of the superficial spreading subtype arising within a lentiginous dysplastic naevus



SDDI allows for the detection of melanomas that lack dermoscopic evidence of malignancy.[28–33] This type of imaging has been shown to diagnose incipient melanomas when they are still dermoscopically featureless by detecting morphological change.[28] In a prospective study of melanomas diagnosed by a variety of methods, 34% were detected exclusively by SDDI and were dermoscopically featureless.[29] In several studies of moderate to high risk patients in specialist settings, SDDI detected 34–61% of the melanomas diagnosed.[29,34,35] In studies conducted in routine dermatological practice settings, 12–55% of melanomas were detected with the use of SDDI[33,36] and 52% in a self-referring dermoscopic telemedicine setting.[10] Dermatologists with access to SDDI show improved sensitivity and specificity of melanoma diagnosis compared with dermatologists using dermoscopy only.[36]

SDDI has also been shown to significantly reduce the benign to malignant excision ratio and the number of excised benign melanocytic lesions in both a dermatologist (both short and long term monitoring)[36] and primary care setting (short term monitoring only).[25] While reducing the benign to malignant ratio may potentially risk missing malignant lesions, there is evidence to suggest that SDDI allows for the detection of incipient melanomas and melanomas diagnosed at an early clinical stage.[28]

While studies evaluating the use of SDDI consistently show an improvement in the sensitivity for melanoma diagnosis,[25,29,30,51] evidence suggests that routine long term SDDI of multiple naevi in lower risk cohorts may be less efficacious.[37,38] Therefore, appropriate selection of patients for SDDI with individualised surveillance plans is important.

The role of total body photography in the early diagnosis of patients at high risk of developing melanoma

TBP describes the use of clinical photography to provide a photographic record of a patient's entire skin surface.[52] TBP typically includes 12–24 baseline photographs of the skin surface (Box 4).[9,53,54] It provides a comparative reference point for subsequent examinations, and its value derives from the knowledge that melanomas are new or show varying rates of progressive, unremitting change, while the majority of benign naevi remain stable.[54] Newness or visual change in a lesion may be helpful in arousing suspicion of lesions that might not otherwise be suspicious for melanoma, while photographic evidence of the skin surface to demonstrate stability minimises the need for unnecessary biopsies.

TBP reduces the biopsy rate of benign naevi and improves diagnostic accuracy of melanoma in high risk patients[9,12] — who are those patients with high naevus counts, multiple atypical naevi and strong personal and family history of melanoma.

The "two-step method of digital follow-up" describes follow-up with TBP and SDDI.[11] Several authors have advocated that this multimodal approach provides optimal surveillance in high risk patients to assist with early melanoma diagnosis.[7–11] Melanomas diagnosed by TBP and SDDI have been found to be thinner compared with those diagnosed by traditional diagnostic methods.[10]

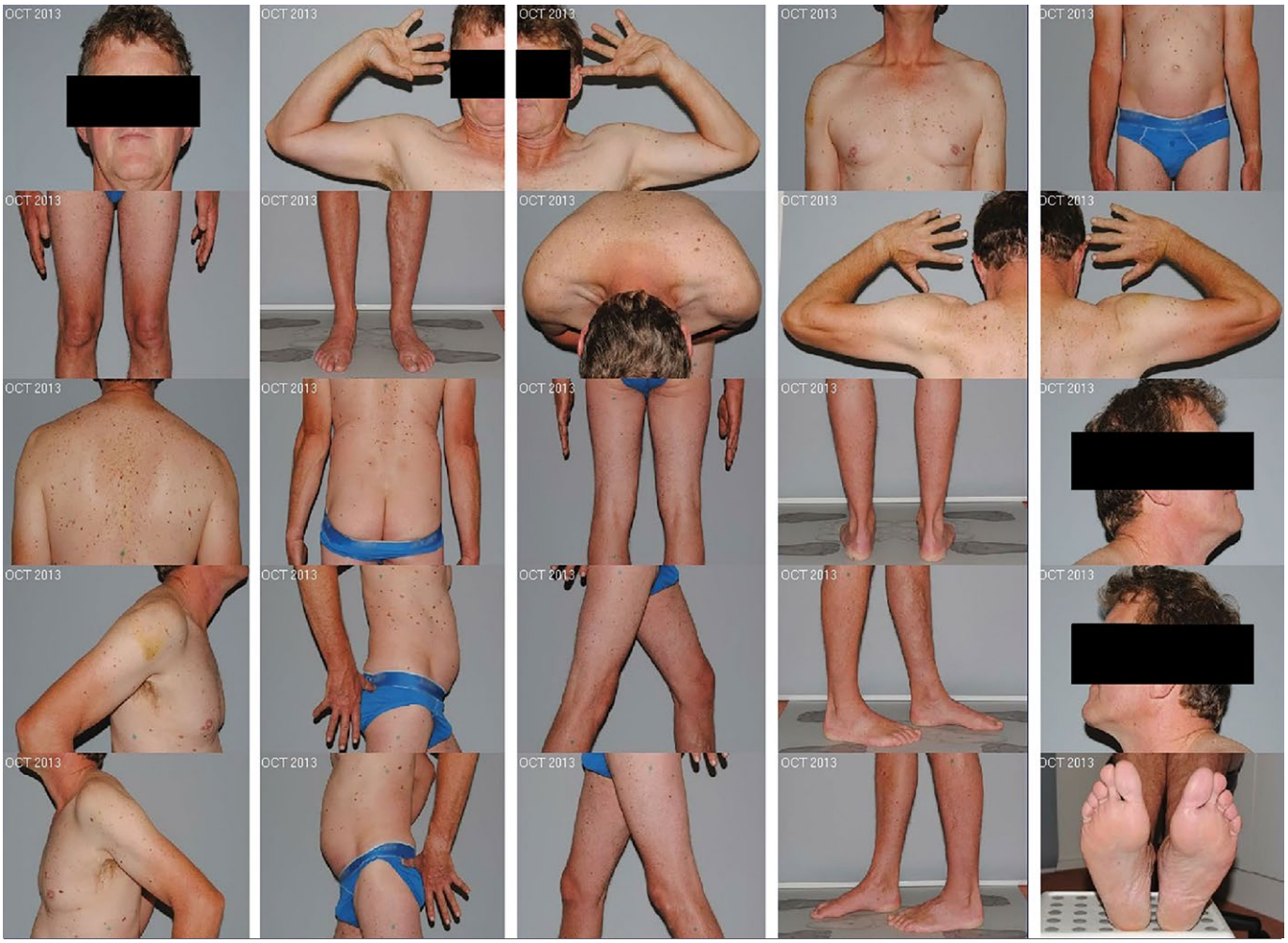
TBP has the advantage of monitoring the patient's entire skin surface, rather than a subset of individual lesions. TBP may reveal interval change in pre-existing lesions that were not initially suspicious or atypical based on clinical or dermoscopic examination, and as such were not included for SDDI, as well as detecting de novo lesions.[35] A cohort study determined that a third of melanomas diagnosed during follow-up of high risk patients corresponded to lesions that were not under digital dermoscopic surveillance.[35] An Australian study, which assessed the impact of TBP and SDDI on melanoma detection in an extreme high risk cohort of patients, found that 38% of melanomas were diagnosed either exclusively or aided by TBP.[9]

A group of investigators evaluated the use of TBP in high risk patients in the context of their prior experience with SDDI in a similar patient population.[13] Monitoring with TBP was associated with lower biopsy rates and lower naevus to melanoma ratios among biopsied lesions compared with SDDI.[13] TBP was found to have a higher rate of melanoma detection than SDDI and to be a more time-efficient approach.[13] There remain no randomised controlled studies that have specifically evaluated the role of TBP in the early diagnosis of melanoma.

The role of automated instruments in the diagnosis of melanoma

An automated diagnostic instrument is defined as one that requires minimal or no input from the clinician to achieve a diagnosis. Each automated instrument offers different technology with differing diagnostic ability. Guidelines for assessing such instruments have been published elsewhere.[55] To date, only two studies have compared clinician diagnosis with automated

4 Total body photography images, which typically include 12–24 baseline photographs of the skin surface



The image is an example courtesy of MoleMap (www.molemap.net.au). ◆

machine diagnosis of melanoma with an adequate sample size to assess both specificity and sensitivity.[40,41]

The MelaFind system (MELA Sciences, Irvington, NY, USA) — an automatic, digital, multispectral image analysis device — was directly compared with the ability of specialists to diagnose suspicious pigmented lesions in a prospective study with a histopathological reference standard.[40] The measured sensitivity of MelaFind was 98.4% (125/127 melanomas) with a 95% lower confidence bound at 95.6%. MelaFind was observed to have a superior specificity to that of clinicians (9.9% *v* 3.7%; $P = 0.02$).[40] However, this study only evaluated lesions with suspicious clinical or dermoscopic features.[40] At present, the use of MelaFind is largely confined to the United States and uptake remains limited.

The Nevisense system (SciBase, Sundbyberg, Sweden) — an electrical impedance spectroscopy device developed to distinguish between benign lesions and melanoma — was assessed in a prospective clinical trial.[41] The observed sensitivity of Nevisense was 96.6% (256/265 melanomas; 95% CI lower bound 94.2%) with an observed specificity of 34.4%.[41]

In both of the above systems, high false positive rates with seborrhoeic keratoses were noted. This may cause a significantly poorer specificity when used by non-experts in the field, which has yet to be fully investigated. Currently, there are no reports on the use of these instruments in clinical trials in a primary care setting.

The role of reflectance confocal microscopy in the diagnosis of melanoma

In vivo RCM is a non-invasive, real-time technique that allows for the examination of the epidermis and upper layers of the dermis with cellular resolution. A recent meta-analysis, conducted to assess the accuracy of RCM for diagnosing malignant tumours, identified 21 studies involving 3108 patients with a total of 3602 lesions.[56] The corresponding pooled results for sensitivity and specificity were 93.6% (95% CI, 0.92–0.95) and 82.7% (95% CI, 0.81–0.84), respectively, for the diagnosis of malignant lesions. Positive likelihood ratio and negative likelihood ratio were 5.84 (95% CI, 4.27–7.98) and 0.08 (95% CI, 0.07–0.10), respectively. Subgroup analysis showed that RCM had a sensitivity of 92.7% (95% CI, 0.90–0.95) and a specificity of 78.3% (95% CI, 0.76–0.81) for detecting melanoma.[56] This meta-analysis concluded that RCM is an efficient method for identification of malignant skin tumours and a promising technology that can be applied to skin cancer diagnosis.

Of note, lesions located on the head and neck,[57–59] lesions on skin damaged by chronic sun exposure,[57,58] lesions suspicious for melanoma of the lentigo maligna subtype,[57,58] lesions dermoscopically demonstrating regression,[59] and amelanotic tumours[60,61]

5 Recommendations and the associated National Health and Medical Research Council (NHMRC) grade for each recommendation

Recommendations	Grade*
Consider the use of total body photography in managing patients at increased risk for melanoma, particularly those with high naevus counts and dysplastic naevi	C
Clinicians who are performing skin examinations for the purpose of detecting skin cancer should be trained in and use dermoscopy	A
The use of short term sequential digital dermoscopy imaging to detect melanomas that lack dermoscopic features of melanoma is recommended to assess individual melanocytic lesions of concern	B
The use of long term sequential digital dermoscopy imaging to detect melanomas that lack dermoscopic features of melanoma is recommended to assess individual or multiple melanocytic lesions for routine surveillance of high risk patients	B
There is insufficient evidence to recommend the routine use of automated instruments for the clinical diagnosis of primary melanoma. However, this information may aid the clinician, particularly when a benign measurement is found using the cited protocols of Nevisense† and MelaFind‡	D

* The NHMRC grades of recommendation are intended to indicate the strength of the body of evidence underpinning the recommendation. The grade of evidence incorporates the evidence base, consistency, clinical impact, generalisability and applicability of the results to the Australian health care setting. Grade A indicates that the body of evidence can be trusted to guide practice. Grade B indicates that the body of evidence can be trusted to guide practice in most situations. Grade C indicates that the body of evidence provides some support for the recommendations but care should be taken in its application. Grade D indicates that the body of evidence is weak and recommendation must be applied with caution.[6] † Nevisense, SciBase, Sundbyberg, Sweden. ‡ MelaFind, MELA Sciences, Irvington, NY, USA. ◆

represent the best indications for RCM. The addition of RCM to dermoscopy has been shown to reduce unnecessary excisions with a high diagnostic accuracy.[62–64]

Guideline recommendations and practice points

Box 5 displays the final evidence-based recommendations in the new Australian guidelines for the management of melanoma for the aforementioned chapters relating to methods of monitoring the skin in patients at high risk of melanoma. Box 2 displays the practice points based on expert consensus opinion.

Conclusion and directions for future research

Early detection of primary melanoma remains an effective strategy to reduce melanoma-related mortality. This article presents multiple methods of monitoring the skin in patients at high risk of developing melanoma. Determining the relative indications for each method and how each method should be introduced into the surveillance of a patient requires careful consideration and an individualised approach.

TBP and SDDI provide different methods for the detection of change in the context of melanoma surveillance and, therefore, these methods should be applied to different, but overlapping (ie, non-mutually exclusive), settings. TBP permits identification of most new or changed lesions on the skin surface. TBP is particularly suited to patients at elevated risk with high naevus counts and multiple dysplastic naevi. SDDI fulfils a different need for monitoring one or many individual flat lesions of concern that lack diagnostic clinical or dermoscopic features of melanoma. Of note, both TBP and SDDI rely on patient adherence to follow-up appointments, and poor compliance would thus compromise the benefits that these methods confer. It is therefore crucial to emphasise to patients the importance of regular follow-up.

Much of the existing literature has been conducted in high risk patient cohorts; however, these techniques, particularly TBP, are less tested in lower risk populations and may not have the same value. To undertake a randomised controlled trial evaluating these methods in high risk patients would present ethical difficulties; nevertheless, a randomised controlled trial of TBP and SDDI in a large cohort of lower risk individuals might be justifiable. Further research is needed to elucidate the optimal risk thresholds for the introduction of both TBP and SDDI to surveillance programs. Research regarding cost-effectiveness for the above-mentioned diagnostic aids in different risk cohorts is also required. Specialised surveillance with TBP and SDDI has been shown to be a cost-effective strategy for the management of individuals at high risk of melanoma.[65] Notwithstanding the demonstrated cost-effectiveness in high risk patients, these modalities are not currently reimbursed by the Australian Medicare system.

Furthermore, RCM may be used to assist with the identification of melanoma for suspicious lesions located on the head and neck, lesions in areas that are subject to chronic sun exposure, lesions dermoscopically typified by regression and amelanotic tumours. At present, there is insufficient evidence to recommend the routine use of automated instruments for the clinical diagnosis of melanoma. Nonetheless, the use of both automatic instruments and of artificial intelligence for the clinical diagnosis of melanoma represents an exciting area for future research. Further research should also be directed at assessing the performance of new methods of skin imaging, such as three dimensional imaging, the role of teledermatology using TBP, dermoscopy and SDDI, and skin self-assessment of suspicious lesions using smartphone applications.[66]

Of note, TBP also has the potential to aid skin self-examination; yet, evidence to date would appear to indicate limited uptake by consumers.[67] An important area for future research might also be to explore barriers to and determinants of skin self-examination, and to investigate appropriate methods of educating consumers with respect to melanoma surveillance.

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1 Australian Institute of Health and Welfare. Cancer in Australia 2017. (Cat. no. CAN 100) Canberra: AIHW; 2017. https://www.aihw.gov.au/reports/cancer/cancer-in-australia-2017/contents/table-of-contents (viewed Oct 2018).

2 Doran CM, Ling R, Byrnes J, et al. Estimating the economic costs of skin cancer in New South Wales, Australia. *BMC Public Health* 2015; 15: 952.

3 Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol* 2009; 27: 6199–6206.

4 Mar VJ, Chamberlain AJ, Kelly JW, et al. Clinical practice guidelines for the diagnosis and management of melanoma: melanomas that lack classical clinical features. *Med J Aust* 2017; 207: 348–350. https://www.mja.com.au/journal/2017/207/8/

clinical-practice-guidelines-diagnosis-and-management-melanoma-melanomas-lack

5 Sladden MJ, Nieweg OE, Howle J, et al. Updated evidence-based clinical practice guidelines for the diagnosis and management of melanoma: definitive excision margins for primary cutaneous melanoma. *Med J Aust* 2018; 208: 137–142. https://www.mja.com.au/journal/2018/208/3/updated-evidence-based-clinical-practice-guidelines-diagnosis-and-management

6 National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Stage 2 Consultation. NHMRC; 2009. https://www.mja.com.au/sites/default/files/NHMRC.levels.of.evidence.2008-09.pdf (viewed Oct 2018).

7 Mintsoulis D, Beecker J. Digital dermoscopy photographs outperform handheld dermoscopy in melanoma diagnosis. *J Cutan Med Surg* 2016; 20: 602–605.

8 Nathansohn N, Orenstein A, Trau H, et al. Pigmented lesions clinic for early detection of melanoma: preliminary results. *Isr Med Assoc J* 2007; 9: 708–712.

9 Moloney FJ, Guitera P, Coates E, et al. Detection of primary melanoma in individuals at extreme high risk: a prospective 5-year follow-up study. *JAMA Dermatology* 2014; 150: 819–827.

10 Rademaker M, Oakley A. Digital monitoring by whole body photography and sequential digital dermoscopy detects thinner melanomas. *J Prim Health Care* 2010; 2: 268–272.

11 Salerni G, Carrera C, Lovatto L, et al. Benefits of total body photography and digital dermatoscopy ("two-step method of digital follow-up") in the early diagnosis of melanoma in patients at high risk for melanoma. *J Am Acad Dermatol* 2012; 67: e17–e27.

12 Truong A, Strazzulla L, March J, et al. Reduction in nevus biopsies in patients monitored by total body photography. *J Am Acad Dermatol* 2016; 75: 135–143.

13 Goodson AG, Florell SR, Hyde M, et al. Comparative analysis of total body and dermatoscopic photographic monitoring of nevi in similar patient populations at risk for cutaneous melanoma. *Dermatol Surg* 2010; 36: 1087–1098.

14 Argenziano G, Puig S, Zalaudek I, et al. Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *J Clin Oncol* 2006; 24: 1877–1882.

15 Carli P, de Giorgi V, Chiarugi A, et al. Addition of dermoscopy to conventional naked-eye examination in melanoma screening: a randomized study. *J Am Acad Dermatol* 2004; 50: 683–689.

16 Carli P, De Giorgi V, Crocetti E, et al. Improvement of malignant/benign ratio in excised melanocytic lesions in the "dermoscopy era": a retrospective study 1997–2001. *Br J Dermatol* 2004; 150: 687–692.

17 Carli P, Mannone F, De Giorgi V, et al. The problem of false-positive diagnosis in melanoma screening: the impact of dermoscopy. *Melanoma Res* 2003; 13: 179–182.

18 Bono A, Bartoli C, Cascinelli N, et al. Melanoma detection. A prospective study comparing diagnosis with the naked eye, dermatoscopy and telespectrophotometry. *Dermatology* 2002; 205: 362–326.

19 Bono A, Tolomio E, Trincone S, et al. Micro-melanoma detection: a clinical study on 206 consecutive cases of pigmented skin lesions with a diameter < or = 3 mm. *Br J Dermatol* 2006; 155: 570–573.

20 Benelli C, Roscetti E, Pozzo VD, et al. The dermoscopic versus the clinical diagnosis of melanoma. *Eur J Dermatol* 1999; 9: 470–476.

21 Cristofolini M, Zumiani G, Bauer P, et al. Dermatoscopy: usefulness in the differential diagnosis of cutaneous pigmentary lesions. *Melanoma Res* 1994; 4: 391–394.

22 Dummer W, Doehnel KA, Remy W. Videomicroscopy in differential diagnosis of skin tumors and secondary prevention of malignant melanoma [German]. *Hautarzt* 1993; 44: 772–776.

23 Stanganelli I, Serafini M, Bucch L. A cancer-registry-assisted evaluation of the accuracy of digital epiluminescence microscopy associated with clinical examination of pigmented skin lesions. *Dermatology* 2000; 200: 11–16.

24 Vestergaard ME, Macaskill P, Holt PE, et al. Dermoscopy compared with naked eye examination for the diagnosis of primary melanoma: a meta-analysis of studies performed in a clinical setting. *Br J Dermatol* 2008; 159: 669–676.

25 Menzies SW, Emery J, Staples M, et al. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. *Br J Dermatol* 2009; 161: 1270–1277.

26 Koelink CJ, Vermeulen KM, Kollen BJ, et al. Diagnostic accuracy and cost-effectiveness of dermoscopy in primary care: a cluster randomized clinical trial. *J Eur Acad Dermatol Venereol* 2014; 28: 1442–1449.

27 van der Rhee JI, Bergman W, Kukutsch NA. Impact of dermoscopy on the management of high-risk patients from melanoma families: a prospective study. *Acta Derm Venereol* 2011; 91: 428–431.

28 Kittler H, Guitera P, Riedl E, et al. Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. *Arch Dermatol* 2006; 142: 1113–1119.

29 Haenssle HA, Krueger U, Vente C, et al. Results from an observational trial: digital epiluminescence microscopy follow-up of atypical nevi increases the sensitivity and the chance of success of conventional dermoscopy in detecting melanoma. *J Invest Dermatol* 2006; 126: 980–985.

30 Altamura D, Avramidis M, Menzies SW. Assessment of the optimal interval for and sensitivity of short-term sequential digital dermoscopy monitoring for the diagnosis of melanoma. *Arch Dermatol* 2008; 144: 502–506.

31 Robinson JK, Nickoloff BJ. Digital epiluminescence microscopy monitoring of high-risk patients. *Arch Dermatol* 2004; 140: 49–56.

32 Menzies SW, Gutenev A, Avramidis M, et al. Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. *Arch Dermatol* 2001; 137: 1583–1589.

33 Salerni G, Terán T, Alonso C, Fernández-Bussy R. The role of dermoscopy and digital dermoscopy follow-up in the clinical diagnosis of melanoma: clinical and dermoscopic features of 99 consecutive primary melanomas. *Dermatol Pract Concept* 2014; 4: 39–46.

34 Moloney FJ, Guitera P, Coates E, et al. Detection of primary melanoma in individuals at extreme high risk: a prospective 5-year follow-up study. *JAMA Dermatol* 2014; 150: 819–827.

35 Salerni G, Carrera C, Lovatto L, et al. Characterization of 1152 lesions excised over 10 years using total-body photography and digital dermatoscopy in the surveillance of patients at high risk for melanoma. *J Am Acad Dermatol* 2012; 67: 836–845.

36 Tromme I, Sacré L, Hammouch F, et al. Availability of digital dermoscopy in daily practice dramatically reduces the number of excised melanocytic lesions: results from an observational study. *Br J Dermatol* 2012; 167: 778–786.

37 Schiffner R, Schiffner-Rohe J, Landthaler M, Stolz W. Long-term dermoscopic follow-up of melanocytic naevi: clinical outcome and patient compliance. *Br J Dermatol* 2003; 149: 79–86.

38 Haenssle HA, Korpas B, Hansen-Hagge C, et al. Selection of patients for long-term surveillance with digital dermoscopy by assessment of melanoma risk factors. *Arch Dermatol* 2010; 146: 257–264.

39 Fuller SR, Bowen GM, Tanner B, et al. Digital dermoscopic monitoring of atypical nevi in patients at risk for melanoma. *Dermatol Surg* 2007; 33: 1198–1206.

40 Monheit G, Cognetta AB, Ferris L, et al. The performance of MelaFind: a prospective multicenter study. *Arch Dermatol* 2011; 147: 188–194.

41 Malvehy J, Hauschild A, Curiel-Lewandrowski C, et al. Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multicentre, prospective and blinded clinical trial on efficacy and safety. *Br J Dermatol* 2014; 171: 1099–1107.

42 Kittler H, Marghoob AA, Argenziano G, et al. Standardization of terminology in dermoscopy/dermatoscopy: results of the third consensus conference of the International Society of Dermoscopy. *J Am Acad Dermatol* 2016; 74: 1093–1106.

43 Argenziano G, Giacomel J, Zalaudek I, et al. A clinico-dermoscopic approach for skin cancer screening: recommendations involving a survey of the International Dermoscopy Society. *Dermatol Clin* 2013; 31: 525–534.

44 Kittler H, Pehamberger H, Wolff K, Binder M. Diagnostic accuracy of dermoscopy. *Lancet Oncol* 2002; 3: 159–165.

45 Bafounta ML, Beauchet A, Aegerter P, Saiag P. Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. *Arch Dermatol* 2001; 137: 1343–1350.

46 Haenssle HA, Hoffmann S, Holzkamp R, et al. Melanoma thickness: the role of patients' characteristics, risk indicators and patterns of diagnosis. *J Eur Acad Dermatol Venereol* 2015; 29: 102–108.

47 Westerhoff K, McCarthy WH, Menzies SW. Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. *Br J Dermatol* 2000; 143: 1016–1020.

48 Dolianitis C, Kelly J, Wolfe R, Simpson P. Comparative performance of 4 dermoscopic algorithms by nonexperts for the diagnosis of melanocytic lesions. *Arch Dermatol* 2005; 141: 1008–1014.

49 Binder M, Puespoeck-Schwarz M, Steiner A, et al. Epiluminescence microscopy of small pigmented skin lesions: short-term formal training improves the diagnostic performance of dermatologists. *J Am Acad Dermatol* 1997; 36: 197–202.

50 Salerni G, Terán T, Puig S, et al. Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society. *J Eur Acad Dermatol Venereol* 2013; 27: 805–814.

51 Kittler H, Pehamberger H, Wolff K, Binder M. Follow-up of melanocytic skin lesions with digital epiluminescence microscopy: patterns

of modifications observed in early melanoma, atypical nevi, and common nevi. *J Am Acad Dermatol* 2000; 43: 467–476.

52 Feit NE, Dusza SW, Marghoob AA. Melanomas detected with the aid of total cutaneous photography. *Br J Dermatol* 2004; 150: 706–714.

53 Kelly JW, Yeatman JM, Regalia C, et al. A high incidence of melanoma found in patients with multiple dysplastic naevi by photographic surveillance. *Med J Aust* 1997; 167: 191–194. https://www.mja.com.au/journal/1997/167/4/high-incidence-melanoma-found-patients-multiple-dysplastic-naevi-photographic

54 Banky JP, Kelly JW, English DR, et al. Incidence of new and changed nevi and melanomas detected using baseline images and dermoscopy in patients at high risk for melanoma. *Arch Dermatol* 2005; 141: 998–1006.

55 Rosado B, Menzies S, Harbauer A, et al. Accuracy of computer diagnosis of melanoma: a quantitative meta-analysis. *Arch Dermatol* 2003; 139: 361–367.

56 Xiong YD, Ma S, Li X, et al. A meta-analysis of reflectance confocal microscopy for the diagnosis of malignant skin tumours. *J Eur Acad Dermatol Venereol* 2016; 30: 1295–1302.

57 Menge TD, Hibler BP, Cordova MA, et al. Concordance of handheld reflectance confocal microscopy (RCM) with histopathology in the diagnosis of lentigo maligna (LM): a prospective study. *J Am Acad Dermatol* 2016; 74: 1114–1120.

58 Guitera P, Pellacani G, Crotty KA, et al. The impact of in vivo reflectance confocal microscopy on the diagnostic accuracy of lentigo maligna and equivocal pigmented and nonpigmented macules of the face. *J Invest Dermatol* 2010; 130: 2080–2091.

59 Borsari S, Pampena R, Lallas A, et al. Clinical indications for use of reflectance confocal microscopy for skin cancer diagnosis. *JAMA Dermatol* 2016; 152: 1093–1098.

60 Ludzik J, Witkowski AM, Roterman-Konieczna I, et al. Improving diagnostic accuracy of dermoscopically equivocal pink cutaneous lesions with reflectance confocal microscopy in telemedicine settings: double reader concordance evaluation of 316 cases. *PLoS One* 2016; 11: e0162495.

61 Guitera P, Menzies SW, Argenziano G, et al. Dermoscopy and in vivo confocal microscopy are complementary techniques for diagnosis of difficult amelanotic and light-coloured skin lesions. *Br J Dermatol* 2016; 175: 1311–1319.

62 Alarcon I, Carrera C, Palou J, et al. Impact of in vivo reflectance confocal microscopy on the number needed to treat melanoma in doubtful lesions. *Br J Dermatol* 2014; 170: 802–808.

63 Ferrari B, Pupelli G, Farnetani F, et al. Dermoscopic difficult lesions: an objective evaluation of reflectance confocal microscopy impact for accurate diagnosis. *J Eur Acad Dermatol Venereol* 2015; 29: 1135–1140.

64 Stanganelli I, Longo C, Mazzoni L, et al. Integration of reflectance confocal microscopy in sequential dermoscopy follow-up improves melanoma detection accuracy. *Br J Dermatol* 2015; 172: 365–371.

65 Watts CG, Cust AE, Menzies SW, et al. Cost-effectiveness of skin surveillance through a specialized clinic for patients at high risk of melanoma. *J Clin Oncol* 2017; 35: 63–71.

66 Janda M, Loescher LJ, Soyer H. Enhanced skin self-examination: a novel approach to skin cancer monitoring and follow-up. *JAMA Dermatol* 2013; 149: 231–236.

67 Secker LJ, Bergman W, Kukutsch NA. Total body photography as an aid to skin self-examination: a patient's perspective. *Acta Derm Venereol* 2016; 96: 186–190. ■