#### COMMENTARY



# Analyzing Controversies in Management and Surveillance of Early-Stage Melanoma

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### **ABSTRACT**

The incidence of cutaneous melanoma continues to rise dramatically worldwide, presenting a significant burden to the healthcare system. Despite this, there is still controversy in the guidelines regarding follow-up surveillance for patients with thin melanoma. Since there are no randomized clinical trials to support evidence-based guidelines for follow-up surveillance, dermatologic and oncologic organizations have developed their own recommendations based on expert opinion. However, these recommendations differ widely and

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O. Marushchak (⊠) Touro College of Osteopathic Medicine, New York, NY, USA e-mail: omarushc2@student.touro.edu are often vague, resulting in considerable variability in the management of early-stage melanoma among clinicians. The benefits of frequent follow-up visits are early detection of recurrent lesions, lower cost of early-stage melanoma compared to that of late-stage melanoma, decreased need for sentinel lymph node biopsy and adjuvant therapies, and the opportunity to educate patients on self-examination and sun protection. However, the high cost of screening and potential increased rates of biopsy, as well as over-imaging and overtreating, pose serious concerns about this approach. While more rigorous research is needed to resolve this controversy, currently clinicians should follow a relatively universal recommendation to tailor the follow-up regimen based on the patient's relative risk of recurrence and comfort.

**Keywords:** Early-stage melanoma; Follow-up guidelines; Management controversies

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### **Key Summary Points**

Absence of universal guidelines for followup management in patients with earlystage melanoma may be a source of uncertainty among physicians and inconsistency in patient management.

Multiple advantages and disadvantages of different approaches should be addressed to come to a consensus.

A patient-centered plan that is based on individual risk factors and comfort is currently recommended.

The incidence of cutaneous melanoma continues to rise dramatically worldwide [1, 2]. According to the National Cancer Institute, there will be over 100,000 new cases of cutaneous melanoma in the United States in 2020. continuing the trend of a constant increase over almost three decades [3]. Cohort studies in Europe demonstrate similar trends and indicate that a further increase in incidence rates is expected in the future [4]. Melanoma presents a considerable public health and a significant cost burden to the healthcare system, having the highest cost per death and the highest loss of productive life-years among all cancers in countries with high incidence [1, 2]. Despite this, there is still controversy in the guidelines regarding follow-up surveillance for patients with thin melanoma. Thin melanomas are those with a Breslow depth that ranges between 0.1 and 1.0 mm and represent approximately 70% of all new cases [5]. Treatment is surgical excision with a 1-cm margin, while imaging is reserved only for symptomatic cases [6]. Sentinel lymph node biopsy should be discussed and considered for patients with T1b melanomas, which are those with either 0.8-1 mm depth or < 0.8 mm depth with ulceration [6]. The majority of these patients are managed exclusively by their general dermatologist [5]. Because of the limited number of randomized clinical trials to support evidence-based

guidelines for follow-up surveillance, dermatologic and oncologic organizations have developed their own recommendations based on expert opinion [7].

Given the lack of evidence, skin cancer screening for the general population is not currently recommended by the United States Preventive Services Task Force [8]. For the higher-risk groups, which include those with a recent diagnosis of melanoma, leading physician organizations recommend routine skin surveillance, which includes a total-body skin examination, palpation of the primary site and surrounding area for recurrence and metastases, regional lymph node examination, and review of systems [1]. However, the guidelines published by these organizations (listed in Table 1) differ widely in the frequency of the in-office examinations and skin self-examinations as well as the longitudinal duration of the followup period. Moreover, even within each organization, guidelines range widely and are quite vague, resulting in considerable variability in the management of early-stage melanoma among clinicians [7]. The frequency of the follow-up visits ranges from 3 to 12 months. Most local recurrences or secondary melanomas appear within the first 3-5 years after the diagnosis, making an increased frequency during that period more appropriate [1, 6, 9]. A case series of patients with primary melanomas conducted at Duke University showed that about 40% of the patients had at least one recurrence, with the risk of recurrence peaking at 12 months and decreasing over time, but not reaching zero [10]. A large study by Leiter et al. revealed that about 40.5% of secondary melanomas were detected within the first year of the primary diagnosis, 54.4% within the first 2 years, and 25% after 5 years of follow-up [11]. However, late recurrence and secondary melanomas even more than 30 years after the primary diagnosis have been reported, especially in patients initially presenting with early-stage melanoma [6, 11]. Thus, although there are no data directly supporting one schedule over another, and some authors question the cost efficiency of surveillance beyond 10 years, the majority of recommendations deem the lifelong Oncol Ther (2020) 8:191–196

Table 1 Guidelines for screening patients with cutaneous melanoma

Organization	Stage	Office follow-up	Skin self-examination
American Academy of Dermatology [9]	0	At least every 6–12 months for 1–2 years; then annually	Self-examination of the skin and lymph nodes for the detection of recurrent disease or new melanoma lesions is recommended
	IA-IIA	Every 6–12 months for 2–5 years; then at least annually	
	IIB-IV	Every 3–6 months for 2 years; then at least every 6 months for 3–5 years; then at least annually	
British Association of Dermatologists [20]	0	Follow-up exam after excision, interval not specified	Self-examination for the detection of recurrent disease or new melanoma lesions is recommended
	IA	Every 3–6 months over up to 1 year	
	IB-IIIA	Every 3 months for 3 years; then every 6 months for 2 years	
	IIIB–IV (resected)	Every 3 months for 3 years; then every 6 months for 2 years; then annually for 5 years	
Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand [21]	I	Every 6 months for 5 years	Self-examination by patients is essential
	II–III	Every 3–4 months for 5 years; then annually	
National Comprehensive Cancer Network [6]	0	At least annually	Regular post-treatment self- examination of the skin and lymph nodes is recommended
	IA-IIA	Every 6–12 months for 5 years; then annually	
	IIB-IV	Every 3–6 months for 2 years; then every 3–12 months for 3 years; then annually	

follow-up to be justified due to increased risk of recurrence [6, 9].

As with any medical intervention, there are advantages and disadvantages to increased skin surveillance. Gardner et al. analyzed the published works that support multiple benefits of screening, dividing them into a few categories. First of all, multiple case–control studies showed that frequent skin examinations

resulted in earlier melanoma detection [8]. Because lesions are thinner and more manageable, patients with melanoma diagnosed at an early stage have significantly lower mortality and morbidity [1]. Furthermore, surveillance and treatment of early-stage melanoma is significantly less costly than that for advanced-stage melanoma, since thinner melanomas are less likely to require sentinel lymph node biopsy

and adjuvant therapies. A melanoma expense model comparing the overall costs of various stages of melanoma estimated that treatment of a T4b melanoma lesion was about 20 times as expensive as melanoma in situ and ten times as expensive as T1a lesion treatment [8]. Additionally, follow-ups present an opportunity to educate patients on self-examination and sun protection, as well as to identify family members who might be at increased risk and provide ongoing psychosocial support [6, 8, 9].

There are still costs to increased skin surveillance that have to be balanced by those advantages. While earlier-stage diagnosis offers significant cost savings on treatment mentioned above, the cost-effectiveness of screening is a major factor in forming guidelines. A study conducted at the University of Pittsburgh Medical Center estimated a cost of \$32,594 to detect a single melanoma lesion [12]. According to one screening trial, 620 people needed to be screened to find one melanoma, whereas other studies showed that the number of biopsies needed to diagnose one melanoma ranged from 50 to 100 [8, 13]. Another factor against an intense followup regimen is the likely increase in biopsy rates, as well as potential for overdiagnosis and overtreatment, which may or may not end up reducing mortality [8]. Moreover, increased biopsy rates may lead to unnecessary re-excisions, which can cause additional cosmetic, psychological, and functional morbidity [8].

There is no doubt that more rigorous research is needed to resolve these issues. Meanwhile, how should clinicians manage the follow-up for their patients with thin melanomas? A relatively universal recommendation is to tailor the follow-up regimen to the relative risk of recurrence [6–9]. Risk factors presented in guidelines include multiple primary melanomas, familial melanoma with first melanoma diagnosed before 40 years of age, family history of melanoma, documented genetic predisposition to melanoma, personal history of nonmelanoma skin cancer, immunosuppression, and physical features associated with increased risk (blond or red hair, more than 40 nevi, more than two clinically atypical nevi, freckling, and other signs of ultraviolet radiation overexposure) [6–9]. The follow-up surveillance can also be modified in accordance with the perceived difficulty of examination: patients with numerous atypical nevi may be monitored by photography or digital dermoscopy, patients not able to routinely perform skin selfexamination may benefit from more frequent office visits [7]. Lastly, the importance of patient education on thorough skin self-examination should not be underestimated. Multiple studies have shown that about 50% to 62% of patients detect recurrent lesions between office visits [2, 7, 14–17]. In Australia, where melanoma prevention and awareness have been receiving active promotion, the number was even higher, at about 75% of patients [10]. Some studies suggest that due to such a high rate of self-detection, it is reasonable to favor a less intense inoffice surveillance regimen and to focus more on skin self-examination, as it could both significantly reduce the financial burden and save physicians time, allowing for more efficient distribution of resources in the healthcare system [18, 19]. On the other hand, a significant proportion of patients who detect malignant lesions seek evaluation by a professional with delays, consequently presenting with increased tumor thickness, resulting in poorer patient outcomes [2, 14]. Thus, skin self-examination is a cost-effective and essential supplement to the in-office examination, which should approached with caution and understanding that patients' ability to detect malignant lesions may vary greatly and requires sufficient patient education by the healthcare provider and active secondary skin cancer prevention campaigns to promote population awareness [2, 10].

Currently, given the limited number of randomized controlled trials on this matter, management of early-stage melanomas will likely vary from patient to patient. A patient-centered plan that is based on their individual risk factors and comfort is recommended and relies heavily on the clinicians' level of expertise and professional judgment. As we learn more about the specific factors that contribute to mortality in those with thin melanomas, we look forward to more specific and consistent guidelines with regard to patient management and follow-up, which will account for the long-term effect on quality of life, survival, and cost-effectiveness.

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