

Systematic Review Topic Nomination: Atypical Nevi

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Systematic Review Nomination Questions

This systematic review would analyze current practices for the diagnosis of atypical nevi.

1. Should dermoscopy with or without reflectance confocal microscopy (RFC), compared to no dermoscopy, be utilized as a primary method to identify lesions for biopsy in patients with atypical nevi?
2. Do histologically dysplastic nevi require re-excision (compared to observation)?
3. Is it safe to observe mildly dysplastic nevi biopsied with positive histologic margins rather than performing surgical re-excision?
4. Is it safe to observe moderately dysplastic nevi biopsied with positive histologic margins rather than performing surgical re-excision?

A review on this topic will inform the development of a new clinical guideline or evidence-based practice statement.

While atypical nevi, also known as dysplastic nevi after histologic examination or Clark's nevi, are non-cancerous growths, they may indicate heightened melanoma risk, particularly in individuals with a high number of nevi or a family history of melanoma. [1] Accurate assessment and management of atypical nevi is essential for skin cancer detection and mitigating overaggressive escalation of care. Specific to detection, when melanoma occurs in individuals with skin of color, patients often present with advanced-stage disease and worse prognoses and survival in comparison to white patients. [2][3] Conversely, most dermatopathologists consider overdiagnosis to be a public health issue for atypical nevi.[4] Distinguishing between benign atypical nevi and malignancies can be challenging and no evidence-based standards exist for this assessment and the subsequent management of atypical nevi, especially moderately dysplastic nevi.

Establishing guidelines for the assessment and management of these lesions would reduce practice variability, enhance patient outcomes, and prevent unnecessary treatment. Evidence-based guidance is of particular importance given the disparity in early-stage melanoma detection among individuals with darker skin tones. Guidelines for atypical nevi management can improve early detection, prompt intervention, and ultimately, enhance outcomes for all patients while addressing contemporary concerns about overdiagnosis and unnecessary intervention. A systematic review of the assessment and management of atypical nevi is critical to addressing this gap in clinical knowledge, and variability in practice patterns and patient outcomes.

The American Academy of Dermatology (AAD) is the largest, most influential, and most representative of all dermatologic associations. With a membership of more than 20,000 physicians

worldwide, the AAD is committed to: advancing the diagnosis and medical, surgical, and cosmetic treatment of the skin, hair, and nails; advocating high standards in clinical practice, education, and research in dermatology; and supporting and enhancing patient care for a lifetime of healthier skin, hair, and nails. The AAD is proposing a systematic review of the assessment and management of atypical nevi to support the development of the first evidence-based clinical guidelines in this area.

1. Rosendahl CO, Grant-Kels JM, Que SK. Dysplastic nevus: Fact and fiction. *J Am Acad Dermatol*. 2015;73(3):507-512. doi:10.1016/j.jaad.2015.04.029
2. Cormier JN, Xing Y, Ding M, Lee JE, Mansfield PF, Gershenwald JE, et al. Ethnic differences among patients with cutaneous melanoma. *Archives of Internal Medicine*. 2006;166:1907–1914.
3. Largest study on racial differences in men with melanoma shows men with skin of color have lowest survival rates. News release. American Academy of Dermatology. July 11, 2023.
4. Kerr KF, Eguchi MM, Piepkorn MW, Radick AC, Reisch LM, Shucard HL, Knezevich SR, Barnhill RL, Elder DE, Elmore JG. Dermatopathologist Perceptions of Overdiagnosis of Melanocytic Skin Lesions and Association With Diagnostic Behaviors. *JAMA Dermatol*. 2022 Jun 1;158(6):675-679. doi: 10.1001/jamadermatol.2022.0489. PMID: 35442415; PMCID: PMC9021983.

AAD clinical practice guidelines adhere to industry standards for trustworthy guidelines requiring a systematic review to support recommendation development. Given the absence of an evidence-based clinical guideline for atypical nevi, the proposed systematic review would directly support the development of the first evidence-based guidelines in this area. This systematic review and the subsequent guidelines would serve to enhance clinical practice by filling the existing gap in clinical guidance for atypical nevi and by extension impacting patient-important outcomes. This initiative aligns with the AAD's commitment to evidence-based medicine and improving outcomes for all patients with dermatologic conditions and is fully funded and supported by the organization.

Research Questions:

Question 1: Should dermoscopy with or without reflectance confocal microscopy (RFC), compared to no dermoscopy, be utilized as a primary method to identify lesions for biopsy in patients with atypical nevi?

a. Population of interest: Who are the people that should be studied?

Adults 18+ with atypical nevi, inclusive of patients with skin of color

b. Interventions/options: What options should be compared? These are the decisions the research is intended to inform. Please include specific interventions, treatments or delivery models.

1. Dermoscopy alone
2. Dermoscopy + reflectance confocal microscopy
3. Clinical examination without dermoscopy

c. Outcomes: How will evidence generated from this topic make a difference for patients, providers, health systems, policy makers, or other stakeholders? For example, will the evidence generated improve individual outcomes (e.g., pain control), save time, or improve access to care?

Patient-important outcomes are the focus of AAD guidelines.

1. Potential for melanoma progression at site of lesion
2. Potential for melanoma progression anywhere
3. Unnecessary biopsy

4. Nevi recurrence
5. Patient anxiety
6. Biopsy site morbidity

Questions 2-4: Do histologically dysplastic nevi with clear margins require re-excision (compared to observation)?

a. Population of interest: Who are the people that should be studied?

Adults 18+ with histologically dysplastic nevi, inclusive of patients with skin of color.

-Subgroup considerations for severity of dysplasia (mild, moderate, severe)

-Subgroup considerations for positive margins by severity:

Mildly dysplastic nevi with positive margin

Moderately dysplastic nevi with positive margin

Severely dysplastic nevi with positive margin

b. Interventions/options: What options should be compared? These are the decisions the research is intended to inform. Please include specific interventions, treatments or delivery models.

1. Observation
2. Surgical re-excision

c. Outcomes: How will evidence generated from this topic make a difference for patients, providers, health systems, policy makers, or other stakeholders? For example, will the evidence generated improve individual outcomes (e.g., pain control), save time, or improve access to care?

Patient-important outcomes are the focus of AAD guidelines.

1. Dysplastic nevi recurrence
2. Development/occurrence of melanoma at site of biopsy
3. Rate of melanoma detection/change in diagnosis as a result of re-excision
4. Biopsy site morbidity
5. Treatment burden/ Quality of life

Recent Guidance:

Consensus statement

Kim CC, Swetter SM, Curiel-Lewandrowski C, et al. Addressing the Knowledge Gap in Clinical Recommendations for Management and Complete Excision of Clinically Atypical Nevi/Dysplastic Nevi: Pigmented Lesion Subcommittee Consensus Statement. *JAMA Dermatol.* 2015;151(2):212–218. doi:10.1001/jamadermatol.2014.2694

Important studies completed in this area:

1. Condorelli AG, Farnetani F, Ciardo S, Chester J, Kaleci S, Stanganelli I, Mazzoni L, Magi S, Mandel VD, Mirra M, Pampena R, Raucci M, Longo C, Pellacani G. Dynamic dermoscopic and reflectance confocal microscopic changes of melanocytic lesions excised during follow up. *J Am Acad Dermatol.* 2022 May;86(5):1049-1057. doi: 10.1016/j.jaad.2021.03.081. Epub 2021 Apr 3. PMID: 33823198.
2. Guitera P, Pellacani G, Longo C, Seidenari S, Avramidis M, Menzies SW. In vivo reflectance confocal microscopy enhances secondary evaluation of melanocytic lesions. *J Invest Dermatol.* 2009 Jan;129(1):131-8. doi: 10.1038/jid.2008.193. Epub 2008 Jul 17. PMID: 18633444.
3. Engeln K, Peters K, Ho J, Jedrych J, Winger D, Ferris LK, Patton T. Dysplastic nevi with severe atypia: Long-term outcomes in patients with and without re-excision. *J Am Acad Dermatol.* 2017 Feb;76(2):244-249. doi: 10.1016/j.jaad.2016.08.054. Epub 2016 Nov 9. PMID: 27838051.
4. Reddy KK, Farber MJ, Bhawan J, Geronemus RG, Rogers GS. Atypical (dysplastic) nevi: outcomes of surgical excision and association with melanoma. *JAMA Dermatol.* 2013 Aug;149(8):928-34. doi: 10.1001/jamadermatol.2013.4440. PMID: 23760581.
5. Strazzula L, Vedak P, Hoang MP, Sober A, Tsao H, Kroshinsky D. The utility of re-excising mildly and moderately dysplastic nevi: a retrospective analysis. *J Am Acad Dermatol.* 2014 Dec;71(6):1071-6. doi: 10.1016/j.jaad.2014.08.025. Epub 2014 Sep 26. PMID: 25262175.
6. Fleming NH, Egbert BM, Kim J, Swetter SM. Reexamining the Threshold for Reexcision of Histologically Transected Dysplastic Nevi. *JAMA Dermatol.* 2016 Dec 1;152(12):1327-1334. doi: 10.1001/jamadermatol.2016.2869. PMID: 27542070.