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Do we need to rethink the diagnoses melanoma *in situ* and severely dysplastic naevus?

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Dear Editor, Many countries have seen a dramatic increase in the reported incidence of cutaneous melanoma in recent decades, largely driven by increased diagnoses of melanoma *in situ* and thin invasive melanoma. The incidences of thick and metastatic melanomas, and melanoma mortality have remained relatively stable. While ageing populations could be

Table 1 Evidence identified to support or reject a change to diagnostic thresholds and/or terminology used for melanoma *in situ* (MIS) and severely dysplastic naevus (SDN)

Study	Country	Study design	Key findings	Overall risk of bias
Natural history studies: observation of MIS or SDN not actively treated or incompletely excised (partial or close margins) for ≥6 months. The collective 127 cases are underlined				
Engeln, 2017	USA	Retrospective chart review	286 people with SDN (140 with negative margins, 47 with close margins, 40 with positive margins, 3 with indeterminate margins, 56 margins not reported) observed for ≥5 years. 0 cases of invasive melanoma at same site, metastasis, or deaths from melanoma	High
Fleming, 2020	USA	Retrospective chart review	30 people with SDN (26 with negative margins, 4 with positive margins) observed for 0.6–17.5 years (median 7.5). 0 cases of invasive melanoma at same site, metastasis, or deaths from melanoma	High
Hocker, 2013	USA	Retrospective chart review	7 people with SDN with close or positive margins observed for mean 14.7 years. 0 cases of invasive melanoma at same site, metastasis, or deaths from melanoma	High
Menzies, 2020	Australia	Statistical modelling study	Estimated risk of progression of lentigo maligna (a type of MIS) to lentigo maligna melanoma (a type of invasive melanoma) is 3.5%, based on population-based cancer registry data and retrospective patient surveys	High
Reproducibility studies: independent readings of the same MIS or SDN histopathological slides by at least three pathologists at the same timepoint for the purpose of diagnostic classification				
Elmore, 2017	USA	Cross-sectional study	187 pathologists provided diagnoses for 240 melanocytic lesions. For MPATH-Dx class III lesions, there was 40% agreement between study pathologists and expert consensus, 45% interobserver agreement and 60% intraobserver agreement	Low
Diagnostic drift studies: at least two independent readings of the same MIS or SDN histopathological slides from at least two timepoints for the purpose of diagnostic classification				
Frangos, 2012	USA	Repeated cross-sectional study	The diagnoses of 40 lesions (29 SDN, 11 superficial spreading melanoma) by 6 dermatopathologists in 1988–90 were compared with diagnoses made by 9 dermatopathologists in 2008–09 who were blinded to the original diagnoses. The mean proportion of lesions upgraded to melanoma in 2008–09 was 7/40 (18%), with no lesions downgraded	High
Hocker, 2013	USA	Repeated cross-sectional study	The diagnoses of 1179 melanocytic lesions (junctional or compound naevus extending to within 0.2 mm of a microscopic border) by pathologists in 1980–89 were compared with diagnoses made by 2 dermatopathologists in 2011–12 who were blinded to the original diagnoses. 117/1179 (10%) of lesions were upgraded to dysplastic naevi (66 mild, 42 moderate, 7 severe, 2 excluded)	High

The full evidence review (including additional papers identified) is available at https://osf.io/bt97e. MPATH-Dx, Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis.

causing some true increase in melanoma incidence, much of this increase may represent overdiagnosis: diagnosis of lesions that would never have caused harm if left undetected and untreated.[1] If it occurs, melanoma overdiagnosis may result in potential psychological and physical harms to individuals, as well as significant costs to the healthcare system from procedures and long-term surveillance.[1–3] The use of new diagnostic labels (e.g. 'melanocytic neoplasm')[2] and/or the recalibration of diagnostic thresholds for the diagnosis of melanoma *in situ* could reduce these harms.[4,5] These strategies could also be applied to the diagnosis of severely dysplastic naevus, whereby the diagnostic label and apparent equivalence to melanoma *in situ* in the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis (MPATH-Dx) reporting schema (with associated treatment recommendations)[6] may also cause substantial anxiety for patients and clinicians.[3]

We undertook a search and review of the published evidence to support or reject a change to the diagnostic thresholds and/or terminology used for these low-risk melanocytic lesions and provide a detailed report on our findings,[7] which we summarize here. Three lines of evidence were evaluated (Table 1). First was evidence on the natural history of these lesions, which we found was sparse as both melanoma *in situ* and severely dysplastic naevus are usually managed with excision. We found four studies on natural history, all at high risk of bias. One statistical modelling study estimated that at most 3.5% of lentigo maligna (a type of melanoma *in situ*) may progress to lentigo maligna melanoma (a type of invasive melanoma) each year. Three retrospective studies reported on patients with severely dysplastic naevi who were observed following incomplete excision. None of the collective 127 patients with positive or close margins developed an invasive melanoma at the same site as the severely dysplastic naevus, or metastases, after follow-up periods of between 6 months and 29.9 years.

Second was evidence on the reliability of diagnostic criteria for the two types of lesions. We found 14 reproducibility studies, three of which were at low risk of bias. The largest of these, by Elmore *et al.*,[8] found poor reproducibility for diagnoses of melanoma *in situ* and severely dysplastic naevus (MPATH-Dx class III), with 40% agreement between study pathologists and an expert panel consensus, 45% interobserver agreement, and 60% intraobserver agreement. Other studies also demonstrated poor reproducibility for diagnoses of both melanoma *in situ* and severely dysplastic naevus.

Third was evidence of diagnostic drift in the diagnostic threshold over time, such that a more 'malignant' diagnostic label would now be applied even though the same melanocytic lesion was judged benign previously. We found two studies providing evidence on diagnostic drift, both at high risk of bias. These provided evidence of a downward shift of the diagnostic thresholds, and expansion of disease definitions, for both melanoma *in situ* and severely dysplastic naevus. The first retrospective study compared the original diagnoses made for 40 melanocytic lesions in 1988–1990 against diagnoses made by dermatopathologists in 2008–2009 who were blinded to the original diagnoses. Of the 40 lesions, 29 were diagnosed as severely dysplastic naevi and 11 as superficial spreading melanomas in 1998–1990. The mean proportion upgraded to melanoma in 2008–2009 was seven of 40 (18%), with no lesions downgraded. In another study, 1179 lesions originally diagnosed as junctional or compound naevus in 1980–1989 were re-reviewed in 2011–2012. Using contemporary histopathological criteria, 117 of 1179 (10%) were reclassified as dysplastic naevi (seven severely dysplastic naevi, 42 moderately dysplastic naevi, and 66 mildly dysplastic naevi; two excluded). These studies both suggest an implicit lowering of the diagnostic thresholds for melanoma and severely dysplastic naevus over time, causing expansion of the disease definition.

In summary, sparse natural history evidence suggests uncertain but likely low risk of progression from melanoma *in situ* to invasive melanoma, and negligible risk of progression from severely dysplastic naevus to invasive melanoma. These types of lesions may be better conceptualized as risk factors for, rather than obligate precursors to, invasive melanoma. There is strong evidence of low reproducibility for diagnosis of both types of lesions, and some evidence that disease definitions have expanded over time. Our review supports the need for robust discussion, in both clinical and pathology communities, on the benefits and downsides of changing diagnostic thresholds and/or terminology to address potential overdiagnosis. Such discussions could be facilitated through an international summit on the topic, which would inform the next steps towards achieving change in policy and practice for pathology diagnosis.

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