JAMA Dermatology | Review

Impact of Clinical Information on Melanocytic Skin Lesion Pathology Diagnosis A Scoping Review

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IMPORTANCE There is poor accuracy and reproducibility for the histopathologic diagnosis of melanocytic skin lesions, and the provision of clinical information may improve this.

OBJECTIVE To examine the impact of clinical information on the histopathologic diagnosis of melanocytic skin lesions.

EVIDENCE REVIEW PubMed, Embase, and Cochrane Library were searched for new records published from January 2018 to January 2024. References included in the 2018 Cancer Council Australia evidence review were also screened, and forward and backward citation searches were conducted.

FINDINGS From 2224 records screened, 162 full-text studies were assessed, and 7 studies were included. Studies included pathologists from Austria, Germany, the US, Italy, the UK, and Australia. Patient populations had a mean age of 43 to 55 years and a proportion of female participants of 23% to 63%. The risk of bias assessment demonstrated that all studies had domains at unclear or high risk of bias. Clinical images increased diagnostic certainty (3 studies) and agreement between pathologists (2 studies) led to diagnostic upgrades in 7.6% to 16.7% of interpretations. Clinical diagnosis on the pathology requisition form reduced the odds of missing a melanoma with progression (1 study), while more clinical elements on the form correlated with higher re-excision rates (1 study). Among patients with distant metastases on long-term follow-up, a prior consensus diagnosis of melanoma was established on histopathology alone.

CONCLUSIONS AND RELEVANCE Providing clinical information to pathologists may improve diagnostic confidence and interobserver agreement and result in upgrading of the histopathologic diagnosis. While providing the clinical diagnosis may prevent missing a progressive melanoma, more research is needed to determine the appropriateness of histopathology upgrading when clinical images are provided and the impacts on patient outcomes.

JAMA Dermatol. doi:10.1001/jamadermatol.2024.4281 Published online October 30, 2024. Supplemental content
CME at jamacmelookup.com

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elanoma is the most common fatal type of skin cancer and is an important threat to health in many countries.¹ Excluding keratinocyte cancer, cutaneous melanoma was the third most commonly diagnosed cancer and tenth most common cause of cancer death in Australia in 2022.² Significant advances have been made in risk assessment, diagnostic technology, and treatment.³ The accuracy and reproducibility of histopathologic diagnosis remains challenging, however, and ways to improve this remain an active area of research.³

Histopathologic examination of melanoma is the clinical reference standard; however, inherent subjectivity in interpretations results in suboptimal accuracy and reproducibility,⁴⁻⁹ particularly for borderline melanocytic lesions. To prevent underdiagnosis and overdiagnosis of melanoma, strategies to improve accuracy and reproducibility are required.¹⁰⁻¹³ Providing detailed clinical information (including patient demographic characteristics, lesion location and history of change, clinical and dermoscopic images, and prior diagnoses) has been proposed as one such strategy.¹⁴⁻¹⁸

The 2018 Cancer Council Australia clinical guidelines included evidence identified through systematic database searches (PubMed, Embase, and Cochrane Library) to address the question, "What information should the clinician give the pathologist to aid the diagnosis of melanoma?"¹⁹ To inform the current update of these guidelines, we aimed to identify, collate, and synthesize all available evidence on the impact of providing clinical information to pathologists assessing melanocytic skin lesions.

Methods

A detailed description of the prespecified study protocol is provided elsewhere,²⁰ and a summary is provided here. We designed and conducted this review according to the Joanna Briggs Institute Methodology,²¹ and we report our findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.²²

Search Strategy

We used several strategies to identify records for inclusion. We considered the 2018 Cancer Council Australia guidelines' database searches comprehensive, and we screened all records identified by those searches. We undertook new database searches for records published after the time of the 2018 guideline's searches (eTable 1 in the Supplement). We used the same search string for PubMed: melanoma OR (lentigo or naevi or nevi) AND (pathology request form or clinical information of pathology report or pathologist or clinician) AND (staging or clinical management or diagnosis). We adapted these search terms with the aid of the Polyglot Search Translator from The Systematic Review Accelerator^{23,24} for our Embase and Cochrane Library searches. We searched the 3 databases from January 2018 to January 2024 for potentially relevant records. In addition, as well as screening the 14 references in the 2018 Cancer Council Australia guidelines' evidence review, we undertook forward and backward citation searches of these references to identify other potentially relevant records using the SpiderCite tool from The Systematic Review Accelerator.23

Eligibility Criteria

Studies were included if they assessed patients undergoing a biopsy of a melanocytic skin lesion for histopathologic diagnosis and if the clinical information under evaluation was available to requesting clinicians in routine practice (eTable 2 in the Supplement). There were no restrictions by language—Google Translate (Google) was used for non–English-language records.

Study Selection and Screening

One reviewer (B.L.) screened titles, abstracts, and full texts. A second reviewer (K.J.L.B.) checked the full-text articles selected for inclusion to confirm eligibility. Discrepancies were resolved by discussion between these 2 reviewers.

Data Extraction

A data extraction tool was developed by 2 reviewers (B.L. and K.J.L.B.) and piloted on a single journal article. The data were extracted by a reviewer (B.L.) and checked and refined by a second reviewer (K.J.L.B.). For each study, we extracted information about the population, context, and study methods. Where available, we extracted findings on the impact of clinical information on each of the following outcomes: diagnostic certainty, accuracy and reproducibility of histopathologic diagnosis, clinical utility (change in clinical management), and patient health outcomes. Microsoft Excel version 16.89.1 (Microsoft) was used to collect, summarize, and tabulate data.

Key Points

Question What is the impact of providing clinical information to pathologists interpreting melanocytic skin lesions?

Findings In this scoping review including 7 studies, evidence suggests that providing clinical information (including clinical and dermoscopic images) to pathologists may improve their diagnostic confidence and interobserver agreement. Clinical images were more likely to result in an upgrade rather than a downgrade of histopathologic diagnosis, but the impact of this on patient outcomes is unknown.

Meaning Clinical information can increase pathologists' diagnostic confidence and interobserver agreement; however, the appropriateness of histopathology upgrading and its impact on patient outcomes is yet to be determined.

Quality Assessment

Studies were given a quality of evidence rating from 1 to 5, based on a rating scheme modified from the Oxford Centre of Evidence-Based Medicine (eTable 3 in the Supplement). Two quality assessment tools were used to appraise the methodological quality and risk of bias in the included studies. For cross-sectional studies of diagnostic reliability, we used the Quality Appraisal Tool For Studies of Diagnostic Reliability (QAREL) tool to assess the risk of bias in the representativeness of participants and raters, blinding, and appropriateness of statistical measures.²¹ For case series reports, we used the Joanna Briggs Institute Critical Appraisal Checklist for Case Series²² to evaluate the inclusion of participants, measurement and identification of the condition, adequate reporting, and appropriate statistical analysis. Two reviewers (B.L. and K.J.L.B.) independently assessed the risk of bias, with disagreements resolved through discussion.

Results

We retrieved 2224 records for title and abstract screening, assessed the full text of 162 studies for eligibility, and excluded 155 of these. Seven articles^{18,25-30} were included in the review (eFigure in the Supplement).

Included Studies

The 7 studies^{18,25-30} included 4 cross-sectional studies, with participating pathologists located in Austria and Germany (n = 1), the US (n = 1), and Italy, the US, the UK, Austria, and Australia (n = 2). There were also 3 case series reporting on patients in Italy (n = 1), Australia (n = 1) and the US (n = 1) (**Table**). The studies reported on patient populations with a mean age ranging from 43 to 55 years and a proportion of female participants ranging from 23% to 63%. Patients included in these studies had melanocytic lesions that were suspicious of melanoma, were otherwise atypical on clinical assessment, or did not have concordance between the clinical and histopathological diagnosis. Common anatomical locations included the trunk (19% to 77% of cases) and lower limbs (11% to 16% of cases). The proportion of cases with a diagnosis of malignant melanoma ranged from 8% to 45%. Study pathologists worked in dermatology departments or tertiary referral centers. Six studies^{18,25-28,30} included pathologists with dermatopathology expertise and 1 study²⁹

| Source | Setting, country | Patients | Cases | Clinical information | Pathologists |
|---|---|---|---|--|--|
| Cross-sectio | nal studies (quality ratin | ıg, 4) ^a | | | |
| Shi et al, ³⁰ 2021 | Pigmented Lesions Clinic, Northwestern University, Chicago, Illinois | Melanocytic lesions were identified for excisional biopsy due to concerns for melanoma. 89 Patients: median (range) age, 43 (21-74) y; 48% female. Diagnostic grades from real-time clinical care included 63 (46.3%) with low-grade atypia, 35 (25.7%) with severe atypia, and 38 (27.9%) melanomas | 136 Cases including 9 naevi, 89 dysplastic naevi, and 38 melanoma (23 in situ and 15 T1a invasive) | Clinical photographs and polarized and nonpolarized dermoscopic images | 3 Board-certified dermatopathologists |
| Ferrara et al, ¹⁸ 2015 | Cases are from university departments of dermatology in Italy (pathologists from Italy, the US, the UK, Austria, and Australia) | Patients attending a dermatology clinic who had melanocytic neoplasms excised. 96 Patients: male-to-female ratio, 0.6:1; age range, 10-78 y; mean age, 43.4 y; median age, 42 y | 99 Cases, in which the original histopathologic diagnosis was naevus in 54 cases and melanoma in 45 cases | Age and sex, location of the lesion, clinical diagnosis, clinical image, and dermoscopic image available before histopathologic examination | 10 Dermatopathologis all with experience in clinical dermatology |
| Ferrara et al, ²⁶ 2009 | Cases are from a university department of dermatology in Italy (pathologists from Italy, the US, the UK, Austria, and Australia) | Patients attending a dermatology clinic who had melanocytic neoplasms excised. 96 Patients: male-to-female ratio, 0.6:1; age range, 10-78 y; mean age, 43.4 y; median age, 42 y | 99 Cases, in which the original histopathologic diagnosis was naevus in 54 cases and melanoma in 45 cases | Age and sex, location of the lesion, clinical diagnosis, clinical image, and dermoscopic image | 10 Dermatopathologisi including 5 with experience in clinical dermatology |
| Bauer et al, ²⁵ 2006 | 2 University departments of dermatology in Austria and Germany | Patients attending a pigmented skin lesion clinic for excisions to rule out malignancy. Cases were included if they were difficult to diagnose or thought to be a risk of misdiagnosis by dermatopathology. 243 Patients: 119 male and 123 female participants (German participants, 46 male and 53 female; Austrian participants, 73 male and 70 female); age range, 1-87 y | 301 Cases (German center, 141 samples; Austrian center, 160 samples), in which 218 were benign melanocytic tumors, 9 were nonmelanocytic pigmented tumors, and 74 were melanoma | Digital dermoscopic images, and clinical information concerning age and sex and localization of the tumors | 7 Dermatopathologists who were experts in dermoscopy |
| Case series (| quality rating, 4) ^a | | | | |
| Kok et al, ²⁷ 2021 | Statewide tertiary referral center, Victorian Melanoma Service, Melbourne, Australia | Consecutive referrals made to the center from January 2014 to May 2019. 3668 Patients; demographic characteristics not described | 3668 Cases; overall No. of melanoma diagnoses not provided | Specimen type, anatomical site and laterality, history of current lesion (duration, history of change, and size of lesion), suspected clinical diagnosis, clinical evidence of ulceration, the history and timing of lesional trauma (biopsy, irritation or treatment with topical agent, and laser or radiation therapy), dermoscopic findings (clinically suspicious areas) | Dermatopathologists working in the referral center (number not specified) |
| Longo et al, ²⁸ 2015 | A tertiary referral centre in Italy | Atypical skin lesions where good clinicopathologic correlation was missing and required a joint review by referral clinician and referral dermatopathologist | 158 Skin lesions jointly reviewed during the clinic-pathologic meeting | Clinical images, dermoscopic images, reflectance confocal microscopy, and sequential digital dermoscopy imaging | Dermatopathologists working in the referral center (number not specified) |
| Romano et al, ²⁹ 2016 | Department of Dermatology, Mayo Clinic, Rochester, Minnesota | Cases were melanocytic skin lesions that required biopsy for primary diagnosis. Cases that required second opinion consultation, re-excision, rebiopsy specimens, or residual or recurrent lesions were not included. Implied 93 patients with melanocytic lesions. Overall sample of 249 patients; mean (range) age, 58.8 (4-94) y; 51% female (includes inflammatory lesions, melanocytic lesions, nonmelanocytic lesions) | 93 Melanocytic lesions; overall No. of melanomas diagnoses not provided | ABCDE criteria (asymmetry, border irregularity, color variation, diameter >6 mm, evolving or changing features), age, prior dermatopathological diagnosis, anatomic location of biopsy, duration of lesion(s), partial vs complete sampling, pertinent clinical diagnoses, clinical impression, morphologic description, and clinical photographs | Not provided |

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| or Cross-Sectional Relia | | | | |
|--|--|--|--|--|
| | Yes | No Unclear | NA | |
| Item | Bauer et al, ²⁵ 2006 | Ferrara et al, ²⁶ 2009 | Ferrara et al, ¹⁸ 2015 | Shi et al, ³⁰ 2021 |
| Setting | University dermatology department | University dermatology department | University dermatology department | Pigmented lesions clinic |
| Pathologist characteristics | Experts in dermatopathology and dermoscopy | 5 Histopathologists, and 5 other histopathologists with expertise in dermatology | 10 Dual-trained dermatologists and dermatopathologists | 3 Board-certified dermatopathologists |
| Item 1: representative sample of participants | | | | |
| Item 2: representative raters | | | | |
| Item 3: raters blinded to other raters' findings | | | | |
| Item 4: raters blinded to their own prior findings | | | | |
| Item 5: raters blinded to the reference standard | | | | |
| Item 6: raters blinded to clinical information that is not part of the study | | | | |
| Item 7: raters blinded to additional cues | | | | |
| Item 8: varied order of examination | | | | |
| Item 9: suitable time interval between repeated measurements | | | | |
| Item 10: appropriate application and interpretation of test | | | | |
| Item 11: appropriate statistical measures of agreement | | | | |

Figure 1. Quality Appraisal Tool For Studies of Diagnostic Reliability Appraisal of Cross-Sectional Reliability Studies

did not specify the type of pathologist involved. Three studies^{18,25,26} involved dermatopathologists who were dual trained in clinical dermatology and/or dermoscopy. The clinical information that was evaluated in the studies included patient demographic characteristics, lesion history before excision, clinical images, and dermoscopic images.

Risk of Bias

All studies had a quality evidence rating of 4 (case series or cross-sectional studies). The risk of bias assessments for the 4 cross-sectional studies using QAREL are summarized in Figure 1.^{18,25,26,30} Overall, 2 studies were rated as having unclear risk of bias^{26,30} and 2 as having high risk of bias.^{18,25} For the representativeness of participants, 2 studies had a low risk of bias.^{18,30} The other 2 studies had unclear bias, as there was no clear description of the inclusion criteria or study setting.^{25,26} For representativeness of raters, 1 study²⁶ had low risk of bias. The 2 high-risk studies^{18,25} did not have raters representative of the general population of clinicians who would use the clinical information in practice, as both studies had expert dermatopathologists also skilled in dermoscopy and/or dermatology, whereas most pathologists interpreting melanocytic skin lesions in practice would not have these skills. This may limit the applicability

NA indicates not applicable.

of study findings to clinical practice. For appropriate blinding of raters, 1 study had a low risk of bias²⁵ and the other 3 studies had unclear bias due to the possibility of additional cues and/or knowledge of prior findings.^{18,26,30} None of the studies assessing dermoscopic images detailed the diagnostic criteria for dermoscopic interpretation,^{18,25,26,30} and hence, appropriate application of this test was uncertain. All studies used appropriate statistical agreement measures.

The Joanna Briggs Institute Critical Appraisal Checklist for Case Series²² was applied to the other 3 studies (**Figure 2**).²⁷⁻²⁹ Overall, all 3 were rated as having high risk of bias.

Impact on Diagnostic Certainty

Three cross-sectional studies found that the provision of clinical information increased diagnostic certainty (eTable 4 in the Supplement). One study found that pathologists' self-reported diagnostic confidence increased when provided with dermoscopic images to aid histopathologic interpretation.²⁵ Another study reported stepwise increases in diagnostic confidence as increasingly more clinical information was provided (demographic characteristics of the patient, clinical diagnosis, and clinical images; *P* for linear trend = .001).²⁶ In the third study, the same author group found a higher level of diagnostic confidence among pathologists with ac-

| | Yes | No Unclear | |
|--|---------------------------------|-------------------------------|----------------------------------|
| Item | Longo et al, ²⁸ 2015 | Kok et al, ²⁷ 2021 | Romano et al, ²⁹ 2016 |
| Study type | Case series | Case series | Case series |
| Setting | Tertiary referral center | Tertiary referral center | Dermatology department |
| Pathologist characteristics | Dermatopathologists | Expert dermatopathologists | Not provided |
| Item 1: inclusion criteria | | | |
| Item 2: standard measurement of condition | | | |
| Item 3: valid identification of the condition | | | |
| Item 4: consecutive inclusion of participants | | | |
| Item 5: complete inclusion of participants | | | |
| Item 6: reporting demographic characteristics of participants | | | |
| Item 7: reporting clinical information of the participants | | | |
| Item 8: reporting of outcomes or follow-up results | | | |
| Item 9: reporting of presenting site(s)/clinic(s) | | | |
| Item 10: appropriate statistical analysis | | | |

cess to all available clinical information upfront at the time of reading compared with another group who read cases with all clinical information after sequential stepwise access to increasing information (P < .001).¹⁸

Impact on Agreement and Reproducibility

Three cross-sectional studies found that additional clinical information increased agreement among pathologists (eTable 4 in the Supplement). Bauer and colleagues²⁵ reported that the overall Cohen k for 301 cases reported by 7 participating pathologists in 2 referral centers was 0.81 (95% CI, 0.74-0.89) without dermoscopic images and 0.88 (95% CI, 0.82-0.94) with dermoscopic images. Ferrara and colleagues²⁶ reported that agreement across the 10 participating pathologists achieved a Fleiss K of 0.57 (95% CI, 0.54-0.60) when no clinical information was provided and 0.67 (95% Cl, 0.64-0.70) when all clinical information was known (age, sex, location of the lesion, clinical diagnosis, clinical image, and dermoscopic image) (agreement expected by chance: $\kappa = 0$). A third related study, also by Ferrara and colleagues,¹⁸ reported that the proportion of cases with unanimous agreement among 5 pathologists who had access to all clinical information upfront (79 of 99 cases [80%]) was higher than 5 other pathologists who had stepwise access to clinical information (unanimous agreement in 65 of 99 cases [66%]), although the difference was not statistically significant (McNemar test: P = .08).

Impact on Histopathologic Diagnosis

Three cross-sectional studies and 1 case series provided data on changes in histopathologic diagnosis when clinical information was provided (Figure 3; eTable 4 in the Supplement).^{25,26,28,30} Across

all studies, no changes in diagnosis occurred in most readings (76% to 94% of readings).

In 2 cross-sectional studies, when a change in diagnosis did occur, there was a similar proportion of upgrades and downgrades. Ferrara and colleagues²⁶ reported on 10 dermatopathologists who each read 99 cases with stepwise increases in clinical information available, resulting in a total of 990 interpretations in the final with all clinical information available (demographic characteristics, clinical diagnosis, and clinical images including dermoscopic images). The original diagnosis was benign in 54 of 99 cases (54%; naevus) and melanoma in 45 of 99 cases (45%). All available clinical information resulted in an upgrade (benign or unknown to malignant) in 43 of 990 interpretations (4.3%) and a downgrade (malignant to benign or unknown and unknown to benign) in 44 of 990 interpretations (4.4%). One case changed from melanoma to unknown (0.1%). Bauer and colleagues²⁵ reported on 7 pathologists who collectively read 301 cases (1 pathologist per case) with access to dermoscopic images, resulting in a total of 301 interpretations. The original diagnosis was benign in 227 of 301 interpretations (75.4%), including 218 melanocytic naevi and 9 nonmelanocytic pigmented tumors, and was melanoma in 74 interpretations (24.6%). Dermoscopic images resulted in upgrades (benign to malignant) in 8 of 301 interpretations (2.7%) and downgrades in 9 of 301 (3.0%).

Two other studies found that when a change in diagnosis did occur, this was proportionately more likely to be an upgrade than a downgrade. In the third cross-sectional study, Shi and colleagues³⁰ reported on 3 dermatopathologists who each assessed 136 cases with access to clinical photographs and dermoscopic images, resulting in 408 interpretations. The original diagnosis was benign in 98 cases (72.1%), including 9 naevus, 4

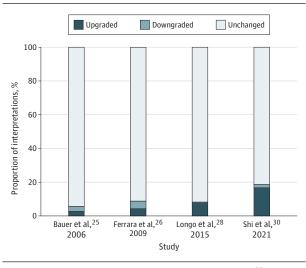


Figure 3. Changes in Histopathologic Diagnosis After Provision of Clinical Information

There were a total of 301 interpretations in the study by Bauer et al²⁵; 990 in the study by Ferrara et al²⁶; 158 in the study by Longo et al²⁸; and 408 in the study by Shi et al.³⁰

dysplastic naevi with mild or moderate atypia, 32 dysplastic naevus with severe atypia, and 3 Reed or Spitz naevus, and melanoma in 38 cases (27.9%). Clinical images resulted in upgrades (low-grade to high-grade atypia or high-grade atypia to melanoma) in 68 of 408 interpretations (16.7%), including 38 of 408 (9.3%) where the diagnosis changed from benign to malignant. Downgrades (melanoma to high-grade atypia or high-grade atypia to low-grade atypia) occurred in 8 of 408 interpretations (2.0%), including 3 (0.7%) where the diagnosis changed from malignant to benign. Longo and colleagues²⁸ reported on a case series of 158 cases lacking clinical-pathologic correlation, where referral clinicians and dermatopathologists jointly read the cases with access to clinical images (overview, close-up, and dermoscopic), resulting in 158 interpretations. The original diagnosis was benign in 127 interpretations (80.4%), including 74 junctional or compound naevus, 22 Spitz or Reed naevus, and 31 other nonmelanocytic tumors, and melanoma in 31 interpretations (19.6%). Clinical images resulted in upgrades (benign to malignant) in 12 of 158 interpretations (7.6%) and downgrades (malignant to benign) in 1 (0.6%).

Impact on Clinical Utility and Patient Health Outcomes

Two case series (Kok and colleagues²⁷ and Romano and colleagues²⁹) and 1 cross-sectional study with follow-up data (Ferrara and colleagues¹⁸) reported on the impact of clinical information on clinical utility (clinical decisions) and patient outcomes (eTable 4 in the Supplement). Kok and colleagues²⁷ assessed the impact of providing adequate clinical information on the accuracy of histopathologic diagnosis of melanoma in a case series of 3668 referrals to an Australian tertiary center (Victorian Melanoma Service; Table). The odds of a false-negative result, according to a dermatopathologists' consensus reference standard, were significantly reduced when the anatomical site (odds ratio [OR], 0.16; 95% CI, 0.04-0.58; P = .002), suspected clinical diagnosis (OR,

0.46; 95% CI, 0.03-0.85; P = .01), or laterality of lesions (OR, 0.41; 95% CI, 0.19-0.90; P = .02) were provided. The odds of a false-negative result, according to a composite reference standard of consensus diagnosis and progression to a higher T stage on definitive diagnostic biopsy, were significantly reduced when the suspected clinical diagnosis was provided (OR, 0.26; 95% Cl, 0.09-0.81; P = .02).²⁷ The odds of a false-positive result, according to dermatopathologists' consensus reference standard, were significantly reduced when any clinical information was provided (OR, 0.10; 95% CI, 0.01-0.79) and when the anatomical site (OR, 0.25; 95% CI, 0.01-0.61; P = .002), suspected clinical diagnosis (OR, 0.41; 95% CI, 0.27-0.63; P < .001), lesion laterality (OR, 0.45; 95% CI, 0.24-0.81; P < .001), specimen type (OR, 0.67; 95% Cl, 0.46-0.98), history of lesional trauma or treatment (OR, 0.43; 95% CI, 0.19-0.99; P = .04), or history of melanoma status (OR, 0.34; 95% CI, 0.18-0.64; P = .001) were provided. The odds of a false-negative result (ORs ranged from 5.19 to 5.56) and of a falsepositive result (ORs ranged from 1.86 to 2.00) were significantly higher for partial/incisional biopsies (incisional punch, partial shave, and incisional elliptical biopsies) compared with complete elliptical excisions. This implies that providing clinical information may be of more value for partial biopsies than complete excisions, although this hypothesis was not directly assessed.

Romano and colleagues²⁹ assessed the completeness of clinical information based on 10 critical elements on skin biopsy requisition forms with health care delivery outcomes in a case series of 83 patients with melanocytic lesions referred to a US tertiary center (Mayo Clinic). They found that on average, there were more elements present on the requisition form in cases that were reexcised (mean of 3.1 elements) than in cases that were not reexcised (mean of 2.7 elements; P = .007).²⁹ Finally, in a report on the long-term follow-up of patients in the cross-sectional study by Ferrara and colleagues,¹⁸ in all cases where the patient developed distant metastases, a consensus diagnosis of melanoma of the index lesion had been achieved whether or not pathologists were provided clinical images. This implies that clinical images may not offer additional prognostic information in clinically aggressive cases.

Discussion

We found 7 studies that provided data on the impact of clinical information on the histopathologic diagnosis of melanocytic skin lesions. Knowledge of the patient history, dermoscopic images, and clinical diagnosis appear to improve pathologists' confidence when diagnosing melanomas and between-pathologist reproducibility. Clinical information, particularly clinical and dermoscopic images, may also change the histopathologic diagnosis, with upgrades more likely than downgrades, but does not appear to provide additional diagnostic value in clinically aggressive cases. Provision of clinical information may reduce the odds of a false-negative (missed) diagnosis, although it may increase re-excision rates.

Like our findings, the 2018 Australian Cancer Council guidelines' evidence review concluded that although clinical information may alter the pathological diagnosis of melanoma, there was a paucity of evidence correlating this to clinical follow-up data.^{19,31} Clinical information may also improve efficiency outcomes. One study that was identified by our search but did not meet eligibility criteria found that

providing clinical information increased turnaround times for histopathology reporting.³² Clinicians may also communicate with pathologists without directly providing clinical information. For example, punch scoring clinically suspicious foci of excised pigmented lesions may direct the pathologist to examine the area more closely.³³

Providing clinical images appears to result in more upgrades than downgrades in histopathologic diagnosis and more malignant diagnoses. At a population level, the absolute number of upgrades will be substantially higher than downgrades, given the much higher prevalence of benign than malignant lesions among all biopsies.^{34,35} Epidemiologic data suggest that there are increasing incidences of melanoma in situ and thin invasive melanomas across several countries,^{13,36} which has been attributed to overdiagnosis^{11,13,36,37} and, to a lesser extent, aging populations.^{36,37} The extent to which pathology upgrades as a result of clinical information (especially images) mitigate the underdiagnosis of clinically progressive lesions, rather than exacerbate the overdiagnosis of indolent ones, is unknown. Further studies, including those with randomized comparisons, may help elucidate this.³⁸

Providing clinical information may be especially important for partial biopsies, which are associated with a higher risk of both falsenegative and false-positive melanoma diagnoses compared with complete excisions.²⁷ For partial biopsies, providing information on the size of the clinical lesion, the proportion captured by the biopsy, and the representativeness of the biopsy may increase pathologists' diagnostic confidence and negate the need for inclusion of differential diagnoses in the final report or ancillary tests.^{19,39} Future studies may usefully explore the impact of providing clinical information for partial biopsies specifically.

There may be several practical challenges to implementing the incorporation of clinical information in workflows from both the clinician and pathologist side. Key challenges for clinicians may be a lack of time and reimbursement to provide clinical information and clinical or dermoscopic images at the point of request for pathology assessment. These logistical considerations could be addressed through better digital systems for collating and communicating clinical information. For example, a standardized templated

requisition checklist that included key clinical could be implemented within existing health record systems.⁴⁰ Ideally, these fields would be automatically populated to reduce the burden on the clinician. Educational initiatives and case-based feedback in the pathology report itself may also help to raise awareness of the type of clinical information that may be useful to pathologists interpreting skin lesions.^{41,42} From the pathologist's side, as well as lack of time and reimbursement, an additional challenge is unfamiliarity with interpreting clinical or dermoscopic images. This could potentially be addressed by including dermoscopy report that summarizes key features (possibly using artificial intelligence, ⁴⁴ with safeguards to mitigate the risk of automating overdiagnosis).⁴⁵

Strengths and Limitations

Strengths of this scoping review are the multidisciplinary author team, comprehensive search of large databases supplemented by forward and backward citation searches, and a review process involving 2 authors for most steps. Our study also has limitations. The evidence base is limited by the small number of studies that are heterogeneous in their design, with few data on clinical utility and patient health outcomes. All studies had domains that had unclear or high risk of bias, particularly for the representativeness of participants and raters and reporting of key items. There was only 1 reviewer for the title and abstract screening stage, which may have meant some relevant studies were missed.

Conclusions

This scoping review suggests that the provision of clinical information to pathologists interpreting melanocytic skin lesions may improve diagnostic confidence and interobserver agreement and change histopathologic diagnosis. While the provision of key clinical information, such as suspected clinical diagnosis, can improve patient outcomes by reducing the odds of melanoma progression, the clinical value of diagnosis upgrading with the provision of clinical images remains uncertain.

ARTICLE INFORMATION

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shareholder of MoleMap NZ Limited and e-derm

consult GmbH and undertakes regular teledermatological reporting for both companies. Dr Soyer is a medical consultant for Canfield Scientific Inc, Blaze Bioscience Inc, and a medical advisor for First Derm outside the submitted work. No other disclosures were reported. Funding/Support: This project was funded through a National Health and Medical Research Council Investigator Grant (2019/GNT1174523). Dr Soyer holds a National Health and Medical Research Council Medical Research Future Fund Next Generation Clinical Researchers Program Practitioner Fellowship (APP1137127) and is a recipient of a National Health and Medical Research Council Synergy Grant (APP2009923). Dr Scolyer is supported by a National Health and Medical Research Council Investigator Grant (APP2018514) and was previously supported by a National Health and Medical Research Council Practitioner Fellowship (APP1141295). Dr Bell is supported by a National Health and Medical Research Council Investigator Grant (2019/GNT1174523)

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Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Bolick NL, Geller AC. Epidemiology of melanoma. *Hematol Oncol Clin North Am*. 2021;35(1):57-72. doi:10.1016/j.hoc.2020.08.011

2. Australian Institute of Health and Welfare. Cancer data in Australia. Accessed September 26, 2024. https://www.aihw.gov.au/reports/cancer/ cancer-data-in-australia/contents/about

3. Long GV, Swetter SM, Menzies AM, Gershenwald JE, Scolyer RA. Cutaneous melanoma. *Lancet*. 2023;402(10400):485-502. doi:10.1016/S0140-6736(23)00821-8

 Farmer ER, Gonin R, Hanna MP. Discordance in the histopathologic diagnosis of melanoma and melanocytic nevi between expert pathologists. *Hum Pathol*. 1996;27(6):528-531. doi:10.1016/ S0046-8177(96)90157-4

 Elmore JG, Barnhill RL, Elder DE, et al. Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study. *BMJ*. 2017;357:j2813. doi: 10.1136/bmj.j2813

6. Braun RP, Gutkowicz-Krusin D, Rabinovitz H, et al. Agreement of dermatopathologists in the evaluation of clinically difficult melanocytic lesions: how golden is the 'gold standard'? *Dermatology*. 2012;224(1):51-58. doi:10.1159/000336886

7. Hawryluk EB, Sober AJ, Piris A, et al. Histologically challenging melanocytic tumors referred to a tertiary care pigmented lesion clinic. *J Am Acad Dermatol*. 2012;67(4):727-735. doi:10. 1016/j.jaad.2012.02.036

8. Gerami P, Busam K, Cochran A, et al. Histomorphologic assessment and interobserver diagnostic reproducibility of atypical spitzoid melanocytic neoplasms with long-term follow-up. *Am J Surg Pathol.* 2014;38(7):934-940. doi:10. 1097/PAS.0000000000198

9. Piepkorn MW, Barnhill RL, Elder DE, et al. The MPATH-Dx reporting schema for melanocytic proliferations and melanoma. *J Am Acad Dermatol.* 2014;70(1):131-141. doi:10.1016/j.jaad.2013.07.027

 Kutzner H, Jutzi TB, Krahl D, et al. Overdiagnosis of melanoma - causes, consequences and solutions. *J Dtsch Dermatol Ges*. 2020;18(11):1236-1243. doi:10.1111/ddg.14233
Semsarian CR, Ma T, Nickel B, et al. Do we need to rethink the diagnoses melanoma in situ and severely dysplastic naevus? *Br J Dermatol*. 2022; 186(6):1030-1032. doi:10.1111/bjd.21010

12. Bell KJL, Nijsten T. Melanoma overdiagnosis: why it matters and what can be done about it. *Br J Dermatol.* 2022;187(4):459-460. doi:10.1111/bjd. 21750

 Welch HG, Mazer BL, Adamson AS. The rapid rise in cutaneous melanoma diagnoses. *N Engl J Med*. 2021;384(1):72-79. doi:10.1056/NEJMsb2019760
Comfere NI, Peters MS, Jenkins S, Lackore K, Yost K, Tilburt J. Dermatopathologists' concerns and challenges with clinical information in the skin biopsy requisition form: a mixed-methods study. *J Cutan Pathol*. 2015;42(5):333-345. doi:10.1111/cup. 12485

15. Sleiman R, Kurban M, Abbas O. Maximizing diagnostic outcomes of skin biopsy specimens. *Int J Dermatol*. 2013;52(1):72-78. doi:10.1111/j.1365-4632. 2012.05731.x

16. Scope A, Busam KJ, Malvehy J, et al. Ex vivo dermoscopy of melanocytic tumors: time for

dermatopathologists to learn dermoscopy. Arch Dermatol. 2007;143(12):1548-1552. doi:10.1001/ archderm.143.12.1548

17. Elmore JG, Eguchi MM, Barnhill RL, et al. Effect of prior diagnoses on dermatopathologists' interpretations of melanocytic lesions:

a randomized controlled trial. *JAMA Dermatol*. 2022;158(9):1040-1047. doi:10.1001/jamadermatol. 2022.2932

18. Ferrara G, Annessi G, Argenyi Z, et al. Prior knowledge of the clinical picture does not introduce bias in the histopathologic diagnosis of melanocytic skin lesions. *J Cutan Pathol*. 2015;42(12):953-958. doi:10.1111/cup.12589

19. Scolyer RA, Soyer HP, Kelly JW, et al. Improving diagnostic accuracy for suspicious melanocytic skin lesions: new Australian melanoma clinical practice guidelines stress the importance of

clinician/pathologist communication. *Aust J Gen Pract.* 2019;48(6):357-362. doi:10.31128/AJGP-11-18-4759 **20**. Lai B, Bell K. The effect of the provision of clinical information on the histopathologic diagnosis of cutaneous melanoma: a scoping review protocol. Accessed January 10, 2024. https://osf.io/ v9zkb

21. Lucas NP, Macaskill P, Irwig L, Bogduk N. The development of a quality appraisal tool for studies of diagnostic reliability (QAREL). *J Clin Epidemiol*. 2010;63(8):854-861. doi:10.1016/j.jclinepi.2009.10. 002

22. Munn Z, Barker TH, Moola S, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. *JBI Evid Synth*. 2020;18(10):2127-2133.

23. Clark J, Glasziou P, Del Mar C, Bannach-Brown A, Stehlik P, Scott AM. A full systematic review was completed in 2 weeks using automation tools: a case study. *J Clin Epidemiol*. 2020;121:81-90. doi: 10.1016/j.jclinepi.2020.01.008

24. Clark JM, Sanders S, Carter M, et al. Improving the translation of search strategies using the Polyglot Search Translator: a randomized controlled trial. *J Med Libr Assoc*. 2020;108(2):195-207. doi: 10.5195/jmla.2020.834

25. Bauer J, Leinweber B, Metzler G, et al. Correlation with digital dermoscopic images can help dermatopathologists to diagnose equivocal skin tumours. *Br J Dermatol.* 2006;155(3):546-551. doi:10.1111/j.1365-2133.2006.07342.x

26. Ferrara G, Argenyi Z, Argenziano G, et al. The influence of clinical information in the histopathologic diagnosis of melanocytic skin neoplasms. *PLoS One*. 2009;4(4):e5375. doi:10. 1371/journal.pone.0005375

27. Kok Y, Scott K, Pham A, et al. The impact of incomplete clinical information and initial biopsy technique on the histopathological diagnosis of cutaneous melanoma. *Australas J Dermatol*. 2021; 62(4):e524-e531. doi:10.1111/ajd.13697

28. Longo C, Piana S, Lallas A, et al. Routine clinical-pathologic correlation of pigmented skin tumors can influence patient management. *PLoS One*. 2015;10(9):e0136031. doi:10.1371/journal.pone. 0136031

29. Romano RC, Novotny PJ, Sloan JA, Comfere NI. Measures of completeness and accuracy of clinical information in skin biopsy requisition forms: an analysis of 249 cases. *Am J Clin Pathol*. 2016;146 (6):727-735. doi:10.1093/ajcp/aqw186

30. Shi K, Compres E, Walton KE, et al. Incorporation of dermoscopy improves inter-observer agreement among dermatopathologists in histologic assessment of melanocytic neoplasms. *Arch Dermatol Res.* 2021; 313(2):101-108. doi:10.1007/s00403-020-02079-w **31.** Scolyer R, Taing C, Kelly J, et al. Clinical information for the pathologist. Clinical Practice Guidelines for the Diagnosis and Management of Melanoma. Accessed January 30, 2024. https://app.magicapp.org/#/guideline/Lkk3pL/section/LpRMY8

32. Ali SMH, Kathia UM, Gondal MUM, Zil-E-Ali A, Khan H, Riaz S. Impact of clinical information on the turnaround time in surgical histopathology: a retrospective study. *Cureus*. 2018;10(5):e2596. doi:10.7759/cureus.2596

33. Grogan J, Cooper CL, Dodds TJ, Guitera P, Menzies SW, Scolyer RA. Punch 'scoring': a technique that facilitates melanoma diagnosis of clinically suspicious pigmented lesions. *Histopathology*. 2018;72(2):294-304. doi:10.1111/his. 13342

34. Lott JP, Boudreau DM, Barnhill RL, et al. Population-based analysis of histologically confirmed melanocytic proliferations using natural language processing. *JAMA Dermatol*. 2018;154 (1):24-29. doi:10.1001/jamadermatol.2017.4060

35. Bell KJL, Cust AE, Scolyer RA. The importance of population-based estimates of melanocytic pathology. *JAMA Dermatol*. 2018;154(1):15-17. doi: 10.1001/jamadermatol.2017.4061

36. Glasziou PP, Bell KJ, Barratt AL. Estimating the magnitude of cancer overdiagnosis in Australia. *Med J Aust*. 2020;213(4):189-189.e1. doi:10.5694/mja2.50578

37. Bjørch MF, Gram EG, Brodersen JB. Overdiagnosis in malignant melanoma: a scoping review. *BMJ Evid Based Med*. 2024;29(1):17-28. doi: 10.1136/bmjebm-2023-112341

38. Bell K, Lai B. A protocol for a feasibility study investigating the effect of clinical images and dermoscopy report on the histopathology diagnosis of melanocytic skin lesions amongst expert dermatopathologists: the Melanocytic Histopathology Reading study. *OSF Registries*. Published online July 17, 2023. doi:10.17605/OSF.IO/ PCR23

39. Witheiler DD, Cockerell CJ. Sensitivity of diagnosis of malignant melanoma: a clinicopathologic study with a critical assessment of biopsy techniques. *Exp Dermatol*. 1992;1(4): 170-175. doi:10.1111/i.1600-0625.1992.tb00184.x

40. Smith SDB, Reimann JDR, Horn TD. Communication between dermatologists and dermatopathologists via the pathology requisition: opportunities to improve patient care. *JAMA Dermatol.* 2021;157(9):1033-1034.

41. Wong C, Peters M, Tilburt J, Comfere N. Dermatopathologists' opinions about the quality of clinical information in the skin biopsy requisition form and the skin biopsy care process: a semiqualitative assessment. *Am J Clin Pathol*. 2015;143(4):593-597. doi:10.1309/ AJCPHPG6DOFBKKUR

42. Sellheyer K, Bergfeld WF. "Lesion," "rule out...," and other vagaries of filling out pathology requisition forms. *J Am Acad Dermatol*. 2005;52(5): 914-915. doi:10.1016/j.jaad.2004.11.073

43. Wu X, Marchetti MA, Marghoob AA. Dermoscopy: not just for dermatologists. *Melanoma Manag.* 2015;2(1):63-73. doi:10.2217/ mmt.14.32

44. Beltrami EJ, Brown AC, Salmon PJM, Leffell DJ, Ko JM, Grant-Kels JM. Artificial intelligence in the detection of skin cancer. *J Am Acad Dermatol.* 2022;87(6):1336-1342. doi:10.1016/j.jaad.2022.08. 028

45. Adamson AS, Welch HG. Machine learning and the cancer-diagnosis problem - no gold standard. *N Engl J Med*. 2019;381(24):2285-2287. doi:10. 1056/NEJMp1907407