

**CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL**

Mohs Surgery for the Treatment of Skin Cancer: A Review of Guidelines

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Context and Policy Issues

Skin cancer is an abnormal growth of skin cells – usually caused by exposure to ultraviolet radiation. The two most common types of skin cancers basal cell carcinoma and squamous cell carcinoma (usually grouped under non-melanoma skin cancers - NMSC).^{1,2} Melanoma, a less common but the most deadly form of skin cancer lead to 1,250 Canadian deaths in 2017.^{1,2} Other less common types of skin cancer include Merkel cell carcinoma, dermatofibrosarcoma protuberans, atypical fibroxanthoma and sebaceous carcinoma.³ Skin cancers can be invasive (invading through the basement membrane) or in situ (confined to the epidermis), and tumour characteristics such as size, location, and pathology influence the risk for deep tumour invasion and recurrence after treatment.

Treatment for non-melanoma skin cancer usually includes surgical removal of the tumour, while treatment for melanoma may include surgery, radiation therapy, chemotherapy, and immunotherapy.⁴ Surgery for small skin cancer lesions can include simple excision, electrodesiccation and curettage, or cryosurgery; surgery for larger or recurrent lesions may include conventional wide excision of the tumour, or Mohs surgery.⁴ Mohs surgery, also known as Mohs micrographic surgery (MMS) is a surgical procedure in which thin layers of the tumour are progressively removed and examined until only cancer-free tissue remains, and can be done in a single visit at an outpatient clinic.^{5,6} The increased precision of MMS can also decrease scarring and reduces the likelihood for needing additional treatment or surgeries.⁷ Clinical evidence up to date showed that, compared with conventional surgical excision, MMS led to a significant higher cure rate for treatment of recurrent NMSC, and may have a role in the treatment of melanoma in situ and some other unusual skin cancers such as Merkel cell carcinoma and dermatofibrosarcoma protuberans.^{8,9}

With a noticeable increase in use of MMS and associated expenditures in Canada, this Rapid Response report aims to review the evidence-based guidelines associated with the use of Mohs surgery for the treatment of skin cancer.

Research Questions

What are the evidence-based guidelines regarding the use of Mohs surgery for the treatment of skin cancer?

Key Findings

Nine evidence-based guidelines were identified; two guidelines issued recommendations on basal cell carcinoma, four on squamous cell carcinoma, two on melanoma, and one on Merkel cell carcinoma. Mohs micrographic surgery (MMS) is recommended as a first-line option for high-risk primary or recurrent basal cell carcinoma. For high-risk primary or recurrent squamous cell carcinoma, MMS may be considered as one of the options, especially where tissue preservation or margin controls are challenging, or when the tumour is at a critical anatomical site. For squamous cell carcinoma in situ (Bowden's disease), MMS may be indicated for digital and penile tumours. MMS may also be considered for melanoma in situ (lentigo maligna) and Merkel cell carcinoma especially when the tumour is in a sensitive area and there are concerns of functional impairment from an excision that is too radical.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD), Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit the retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and February 20, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	People diagnosed with skin cancer
Intervention	Mohs surgery (also known as Mohs micrographic surgery)
Comparator	Not applicable
Outcomes	Evidence-based guidelines (including guidance on the appropriate patient populations, disease sites, and clinical settings)
Study Designs	Evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014.

Critical Appraisal of Individual Studies

The included guidelines were assessed using the AGREE II checklist.¹⁰ Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 75 citations were identified in the literature search. Following screening of titles and abstracts, 65 citations were excluded and 10 potentially relevant reports from the electronic search were retrieved for full-text review. Four potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, five publications were excluded for various reasons, while nine publications met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

Nine relevant evidence-based guidelines on the treatment of skin cancers were included.¹¹⁻¹⁹ One guideline was developed by Cancer Care Ontario for all skin cancers,¹¹ guideline content and recommendations were based on a structured review of the literature up to 2017, and the evidence and recommendation ratings were adopted from the classification developed by the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) workgroup. While the methods indicate that the GRADE system was used to assign strength to each recommendation, the grading and strength of recommendations did not seem to be reported in the final document.

Two guidelines were developed by the Canadian Non-melanoma Skin Cancer Guidelines Committee, one for basal cell carcinoma (BCC)¹² and one for squamous cell carcinoma,¹³ guideline content and recommendations were based on a structured review of the literature up to 2012, the evidence and recommendation ratings were adopted from the classification developed by the GRADE working group.

Three other guidelines make recommendations for the treatment of patients with squamous cell carcinoma. One guideline was developed by the American Academy of Dermatology¹⁴ for the treatment of squamous cell carcinoma, with a structured review of the literature up to 2016. One guideline was developed by the Scottish Intercollegiate Guidelines Network (SIGN)¹⁵ for the treatment of primary squamous cell carcinoma, with a structured review of the literature up to 2012. One guideline was developed by the British Association of Dermatologists¹⁶ for the treatment of patients with squamous cell carcinoma in situ (Bowden's disease), with a structured review of the literature up to 2013. Methods for grading the evidence were not reported in these guidelines.

Two identified guidelines contain recommendations for the treatment of melanoma.^{17,18} One guideline was developed by the American Academy of Dermatology committee,¹⁷ based recommendations for patients with primary melanoma on evidence from a structured review of the literature up to 2017. The available evidence was evaluated using SORT (Strength of Recommendation Taxonomy). One guideline used a structured review of the literature to make recommendations regarding the treatment of patients with melanoma in situ (lentigo maligna) and was developed by the Cancer Council Australia in 2007.¹⁸ The available evidence was evaluated using NHMRC (National Health and Medical Research Council) levels of evidence.

One guideline was developed by the Alberta Cutaneous Tumour Team,¹⁹ for patients with Merkel cell carcinoma, using a structured review of the literature up to 2014. Level of evidence and strength of recommendation were not reported.

Characteristics of the included guideline are detailed in Appendix 2.

Summary of Critical Appraisal

The included guidelines¹¹⁻¹⁹ had a clear scope and purpose, the recommendations are specific and unambiguous, methods used for formulating the recommendations are clearly described, health benefits, side effects, and risks were stated in the recommendations, and the procedures for updating the guidelines provided and target users of the guideline are clearly defined. The methods for searching for and selecting the evidence were clear. This rigour of development and clarity of presentation would

increase the users' confidence in the accuracy and reliability of the recommendations. Potential cost implications of applying the recommendation were included in one guideline,¹⁶ while not included in the rest. It was unclear whether the guideline was piloted among target users, or whether patients' views and preferences were sought, which is particularly important when the procedure may affect patients' appearance.

Details of the critical appraisal of the included studies are presented in Appendix 3.

Summary of Findings

Evidence-based guidelines regarding the use of Mohs surgery for the treatment of skin cancer

Skin cancers

Cancer Care of Ontario recommends MMS for patients with histologically confirmed recurrent BCC of the face and for primary BCC of the face when tumours are >1cm, have aggressive histology, or are located on the critical sites of the face.¹¹ Strength of evidence was not reported. The Guideline Development Group intended to but did not issue recommendations on other types of skin cancers such as squamous cell carcinoma, melanoma, dermatofibrosarcoma protuberans, atypical fibroxanthoma, and sebaceous carcinoma due to lack of strong evidence.

Basal cell carcinoma

The Canadian Non-melanoma Skin Cancer Guidelines Committee recommends that MMS may be considered as a first-line option for high-risk primary BCC, incompletely excised high-risk BCC, and most recurrent BCC amenable to surgery.¹² The strength of the recommendation is strong (desirable effects outweigh undesirable effects).

Squamous cell carcinoma

The Canadian Non-melanoma Skin Cancer Guidelines Committee recommends that MMS may be considered as one of the options for the treatment of high-risk primary or recurrent squamous cell carcinoma.¹³ The recommendation is rated as strong (based on the guideline development group's confidence that the treatment's desirable effects outweigh undesirable effects). The American Academy of Dermatology recommends MMS for high risk squamous cell carcinoma.¹⁴ The recommendation is based on inconsistent or limited-quality evidence. The SIGN guideline recommends that MMS should be considered for patients with high-risk tumours where tissue preservation or margin control is challenging, and on an individual case basis for patients with any tumour at a critical anatomical site.¹⁵ The recommendation is based on the guideline development group's confidence that, for the vast majority of people, the intervention will do more good than harm.

The British Association of Dermatologists recommends that MMS is indicated for digital squamous cell carcinoma in situ (Bowden's disease) and for some cases of genital (especially penile) squamous cell carcinoma in situ for its tissue-sparing benefits.¹⁶ The recommendation is based on evidence from non-analytical studies or extrapolated from well-conducted case-control or cohort studies with a low risk of confounding, bias, or from formal consensus.

Melanoma

The American Academy of Dermatology committee recommends that MMS may be used for melanoma in situ, lentigo maligna type, on the face, ears, or scalp.¹⁷ The recommendation is based on inconsistent or limited-quality evidence. The Cancer

Counsel Australia guideline states that MMS improves complete clearance rates and reduces recurrences over conventional surgical removal of lentigo maligna.¹⁸ The recommendation is based on non-randomized experimental studies.

Merkel cell carcinoma

The Alberta Cutaneous Tumour Team guideline states that MMS is appropriate as a tissue-sparing technique when the tumour is in a sensitive area such as head and neck area and there are concerns of functional impairment from an excision that is too radical.¹⁹ The strength of the recommendation was not reported.

Further detail regarding the included guidelines is presented in Appendix 4.

Limitations

The majority of recommendations on the use of MMS for the treatment of other types of were based on evidence of limited quality; the recommendations should be interpreted with caution. Results from more high-quality trials are needed to elucidate the role of MMS on skin cancers. The identified guidelines are limited on specific types of skin cancers and recommendations should not be generalized to patients with other types of skin cancer.

Conclusions and Implications for Decision or Policy Making

Based on the included guidelines, MMS is recommended as a first-line option for high-risk primary or recurrent basal cell carcinoma. For high-risk primary or recurrent squamous cell carcinoma, MMS may be considered as one of the options, especially where tissue preservation or margin controls are challenging, or when the tumour is at a critical anatomical site. For squamous cell carcinoma in situ (Bowden's disease), MMS may be indicated for digital and penile tumour, or in recurrent or incompletely excised lesions. MMS may also be considered for melanoma in situ (lentigo maligna) and Merkel cell carcinoma especially when the tumour is in a sensitive area and there are concerns of functional impairment from an excision that is too radical. The included guidelines did not address the setting in which MMS was performed.

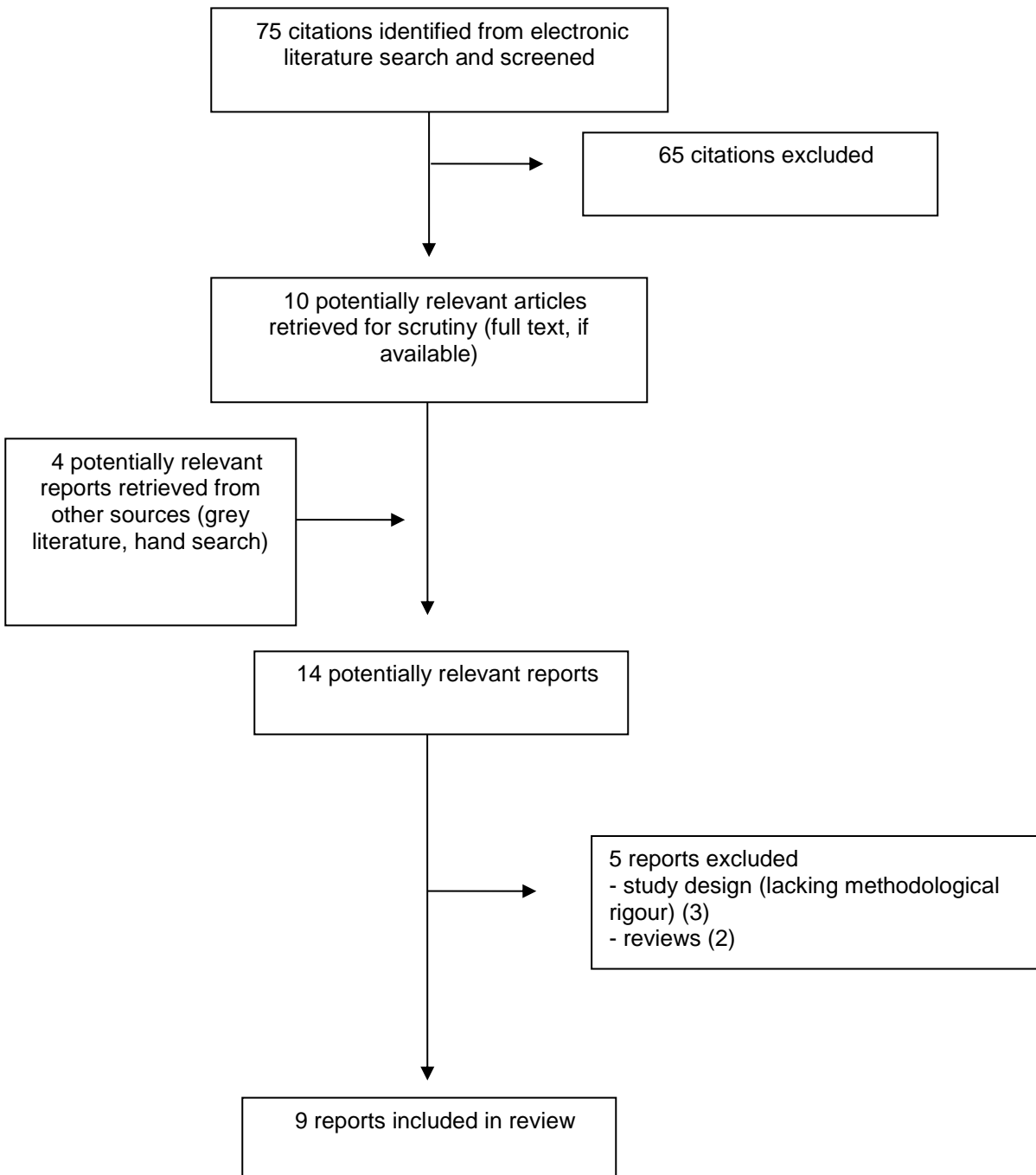
In agreement with the identified guidelines on the advantage of MMS to conventional surgery in the treatment of high-risk, recurrent, or at critical site skin cancers, a review on treatment options for skin cancers²⁰ also found that even though the size of the lesion should be analyzed together with its location and histological pattern, MMS could be a better treatment option for tumours larger than 2 cm which present a higher chance of incomplete removal with conventional surgery. The review also found that MMS lead to a smaller recurrence rate than conventional surgery for dermatofibrosarcoma protuberans.

The majority of the recommendations on the use of MMS for skin cancers were based on evidence of limited quality and need to be interpreted with caution. Results from more high-quality trials are needed to elucidate the role of MMS on skin cancers.

References

1. Canadian Dermatology Association. 2017 Skin cancer fact sheet; 2017: <https://dermatology.ca/wp-content/uploads/2017/11/2017-Skin-Cancer-Fact-Sheet.pdf> Accessed 2019 Mar 19.
2. Canadian Cancer Society. Melanoma skin cancer statistics; 2019: <http://www.cancer.ca/en/cancer-information/cancer-type/skin-melanoma/statistics/?region=on> Accessed 2019 Mar 19.
3. American Academy of Dermatology. Types of skin cancer; 2018: <https://www.aad.org/public/spot-skin-cancer/learn-about-skin-cancer/types-of-skin-cancer> Accessed 2019 Mar 19.
4. WebMD. Skin cancer. 2019: <https://www.webmd.com/melanoma-skin-cancer/guide/skin-cancer#1> Accessed 2019 Mar 19.
5. Canadian Cancer Society. Mohs surgery; 2019: <http://www.cancer.ca/en/cancer-information/diagnosis-and-treatment/tests-and-procedures/mohs-surgery/?region=on> Accessed 2019 Mar 19.
6. Skin Cancer Foundation. Mohs surgery; 2019: <https://www.skincancer.org/skin-cancer-information/mohs-surgery> Accessed 2019 Mar 19.
7. Nehal K, Lee E. Mohs surgery. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2018: www.uptodate.com. Accessed 2019 Feb 20.
8. Cohen DK, Goldberg DJ. Mohs micrographic surgery: past, present, and future. *Dermatol Surg*. 2018;45(3):329-339.
9. Murray C, Sivajohanathan D, Hanna TP, et al. Patient indications for Mohs micrographic surgery: a systematic review. *J Cutan Med Surg*. 2018;23(1):75-90.
10. Agree Next Steps Consortium. The AGREE II Instrument. [Hamilton, ON]: AGREE Enterprise; 2017: <https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf>. Accessed 2019 Mar 12.
11. Murray C, Sivajohanathan D, Hanna T, et al. Patient indications for Mohs micrographic surgery. *A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)*. Toronto (ON): Cancer Care Ontario; 2018 Jan: <https://www.cancercareontario.ca/en/file/36136/download?token=HCOno4uE> Accessed 2019 Mar 19.
12. Zloty D, Guenther LC, Sapijaszko M, et al. Non-melanoma skin cancer in Canada chapter 4: management of basal cell carcinoma. *J Cutan Med Surg*. 2015;19(3):239-248.
13. Sapijaszko M, Zloty D, Bourcier M, Poulin Y, Janiszewski P, Ashkenas J. Non-melanoma skin cancer in Canada chapter 5: management of squamous cell carcinoma. *J Cutan Med Surg*. 2015;19(3):249-259.
14. Kim JYS, Kozlow JH, Mittal B, Moyer J, Olenecki T, Rodgers P. Guidelines of care for the management of cutaneous squamous cell carcinoma. *J Am Acad Dermatol*. 2018;78(3):560-578.
15. SIGN. Management of primary cutaneous squamous cell carcinoma. (*Sign publication no. 140*). Edinburgh (GB): Scottish Intercollegiate Guidelines Network (SIGN); 2014: <https://www.sign.ac.uk/assets/sign140.pdf>. Accessed 2019 Mar 19.
16. Morton CA, Birnie AJ, Eedy DJ. British Association of Dermatologists' guidelines for the management of squamous cell carcinoma in situ (Bowen's disease). *Br J Dermatol*. 2014;170(2):245-260.
17. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. *J Am Acad Dermatol*. 2019;80(1):208-250.
18. Soyer H, Guitera P, Hong A, et al. What are the most effective treatment/management interventions to improve outcomes in patients with lentigo maligna? *Cancer Guidelines WIKI*; 2018: https://wiki.cancer.org.au/australia/Clinical_question:Effective_interventions_to_improve_outcomes_in_lentigo_maligna%3F Accessed 2019 Mar 19.
19. Alberta Health Services. Merkel cell carcinoma. (*Clinical practice guideline CU-004*). Edmonton (AB): Alberta Health Services; 2015: <https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-cu004-merkel-cell.pdf>. Accessed 2019 Mar 19.
20. Cernea SS, Gontijo G, Pimentel ER, et al. Indication guidelines for Mohs micrographic surgery in skin tumors. *An Bras Dermatol*. 2016;91(5):621-627.

Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Guidelines

Guideline Development Group, Year	Scope and Interventions	Target Population; Intended users	Evidence Collection, Selection, and Synthesis	Recommendations Development and Evaluation	Grading system
Skin cancers					
Cancer Care Ontario, MMS Guideline Development group, 2018 ¹¹	Management of skin cancers	<p>Patients with skin cancers</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	Systematic structured evidence review done by the Cancer of Ontario Guideline Development Group (literature search up to 2017 for Medline, Embase, Cochrane library database)	Clinical recommendations were developed on the basis of the best available evidence	The evidence and recommendation rating were adopted from the classification developed by the GRADE workgroup. The GRADE system primarily involves consideration of the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence.
Basal cell carcinoma					
Canadian non-melanoma Skin Cancer Guidelines Committee, 2015 ¹²	Management of basal cell carcinoma	<p>Patients with basal cell carcinoma</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	Systematic structured evidence review done by the Canadian non-melanoma skin cancer committee (literature search up to 2012 for Pubmed)	The relevant publications were categorized according to type of lesion and treatment modality. Each study was formally evaluated by 3 members of the Committee, using the GRADE (Grading of Recommendations Assessment, Development and Evaluation system)	The evidence and recommendation rating were adopted from the classification developed by the GRADE workgroup. The GRADE system primarily involves consideration of the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence.

Squamous cell carcinoma					
American Academy of Dermatology, 2018 ¹⁴	Management of squamous cell carcinoma	<p>Patients with squamous cell carcinoma</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	Systematic search and review of published studies (lit search up to 2016 for PubMed and the Cochrane Library databases)	Clinical recommendations were developed on the basis of the best available evidence	The available evidence was evaluated using SORT (Strength of Recommendation Taxonomy)
Canadian non-melanoma Skin Cancer Guidelines Committee, 2015 ¹³	Management of squamous cell carcinoma	<p>Patients with squamous cell carcinoma</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	Systematic structured evidence review done by the Canadian non-melanoma skin cancer committee (literature search up to 2012 for Pubmed)	The relevant publications were categorized according to type of lesion and treatment modality. Each study was formally evaluated by 3 members of the Committee, using the GRADE (Grading of Recommendations Assessment, Development and Evaluation system)	The evidence and recommendation rating were adopted from the classification developed by the GRADE workgroup. The GRADE system primarily involves consideration of the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence.
Scottish Intercollegiate Guidelines Network (SIGN), 2014 ¹⁵	Management of primary squamous cell carcinoma	<p>Patients with primary invasive SCC</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	A systematic review of the literature (lit search up to 2012 for Medline, Embase, Cinahl, PsycINFO and the Cochrane Library)	Clinical recommendations were developed on the basis of the best available evidence	The available evidence was evaluated by SIGN using GRADE system
British Association of Dermatologists, 2014 ¹⁶	Management of squamous cell carcinoma in situ (Bowden's disease)	<p>Patients with Bowen's disease</p> <p>Clinicians involved in the assessment and treatment of patients with skin cancer</p>	A systematic review of the literature (lit search up to 2013 for PubMed, Medline and Embase databases)	Clinical recommendations were developed on the basis of the best available evidence	The available evidence was evaluated by British Association of Dermatologists (tool used unclear)

Melanoma					
American Academy of Dermatology, 2019 ¹⁷	Management of primary melanoma	Patients with melanoma Clinicians involved in the assessment and treatment of patients with skin cancer	Systematic search and review of published studies (lit search up to 2017; databases used unclear)	Clinical recommendations were developed on the basis of the best available evidence	The available evidence was evaluated using SORT (Strength of Recommendation Taxonomy). No details provided.
Cancer Council Australia, 2018 ¹⁸	Management of melanoma in situ (lentigo maligna)	Patients with lentigo maligna Clinicians involved in the assessment and treatment of patients with skin cancer	A systematic review of the literature (lit search from 2007 for Pubmed, Embase, Trip database, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects and Health Technology Assessment)	Clinical recommendations were developed on the basis of the best available evidence	The available evidence was evaluated using NHMRC (National Health and Medical Research Council) levels of evidence
Merkel cell carcinoma					
Alberta Cutaneous Tumour Team, 2015 ¹⁹	Management of Merkel cell carcinoma	Patients with Merkel cell carcinoma Clinicians involved in the assessment and treatment of patients with skin cancer	Systematic search and review of published studies (lit search up to 2014 for The MEDLINE, CINAHL, Cochrane, ASCO abstracts and proceedings, and PubMed databases)	Clinical recommendations were developed on the basis of the best available evidence	No evaluation for level of evidence or strength of recommendations

MMS = Mohs micrographic surgery

Appendix 3: Critical Appraisal of Included Publications

Table 3: Summary of Critical Appraisal of Included Guideline using AGREE II10

First Author, Publication Year	Strengths	Limitations
Skin cancers		
Cancer Care Ontario, MMS Guideline Development group, 2018 ¹¹	<ul style="list-style-type: none"> • scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included
Basal cell carcinoma		
Canadian non-melanoma Skin Cancer Guidelines Committee, 2015 ¹²	<ul style="list-style-type: none"> • scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included
Squamous cell carcinoma		
American Academy of Dermatology, 2018 ¹⁴	<ul style="list-style-type: none"> • scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included
Canadian non-	<ul style="list-style-type: none"> • scope and purpose of the guidelines are 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted

First Author, Publication Year	Strengths	Limitations
melanoma Skin Cancer Guidelines Committee, 2015 ¹³	<ul style="list-style-type: none"> clear the recommendations are specific and unambiguous the method for searching for and selecting the evidence are clear methods used for formulating the recommendations are clearly described health benefits, side effects and risks were stated in the recommendations procedure for updating the guidelines provided target users of the guideline are clearly defined 	<ul style="list-style-type: none"> among target users unclear whether patients' views and preferences were sought potential cost implications of applying the recommendation not included
Scottish Intercollegiate Guidelines Network (SIGN), 2014 ¹⁵	<ul style="list-style-type: none"> scope and purpose of the guidelines are clear the recommendations are specific and unambiguous the method for searching for and selecting the evidence are clear methods used for formulating the recommendations are clearly described health benefits, side effects and risks were stated in the recommendations procedure for updating the guidelines provided target users of the guideline are clearly defined 	<ul style="list-style-type: none"> unclear whether the guideline was piloted among target users unclear whether patients' views and preferences were sought potential cost implications of applying the recommendation not included
British Association of Dermatologists, 2014 ¹⁶	<ul style="list-style-type: none"> scope and purpose of the guidelines are clear the recommendations are specific and unambiguous the method for searching for and selecting the evidence are clear methods used for formulating the recommendations are clearly described health benefits, side effects and risks were stated in the recommendations procedure for updating the guidelines provided target users of the guideline are clearly defined potential cost implications of applying the recommendation included 	<ul style="list-style-type: none"> unclear whether the guideline was piloted among target users unclear whether patients' views and preferences were sought
Melanoma		
American Academy of Dermatology, 2019 ¹⁷	<ul style="list-style-type: none"> scope and purpose of the guidelines are clear the recommendations are specific and unambiguous the method for searching for and selecting the evidence are clear methods used for formulating the recommendations are clearly described health benefits, side effects and risks 	<ul style="list-style-type: none"> unclear whether the guideline was piloted among target users unclear whether patients' views and preferences were sought potential cost implications of applying the recommendation not included

First Author, Publication Year	Strengths	Limitations
	<ul style="list-style-type: none"> were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	
Cancer Council Australia, 2018 ¹⁸	<ul style="list-style-type: none"> • scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included
Merkel cell carcinoma		
Alberta Cutaneous Tumour Team, 2015 ¹⁹	<ul style="list-style-type: none"> • scope and purpose of the guidelines are clear • the recommendations are specific and unambiguous • the method for searching for and selecting the evidence are clear • methods used for formulating the recommendations are clearly described • health benefits, side effects and risks were stated in the recommendations • procedure for updating the guidelines provided • target users of the guideline are clearly defined 	<ul style="list-style-type: none"> • unclear whether the guideline was piloted among target users • unclear whether patients' views and preferences were sought • potential cost implications of applying the recommendation not included

MMS = Mohs micrographic surgery

Appendix 4: Main Study Findings and Author’s Conclusions

Table 4: Main Study Findings and Authors’ Conclusions

Recommendations	Strength of Evidence
Skin cancers	
Cancer care Ontario, MMS Guideline Development Group, 2018 ¹¹	
<p><i>“MMS is recommended for those with histologically confirmed recurrent basal cell carcinoma (BCC) of the face, and is appropriate for primary BCC of the face that are >1cm, have aggressive histology, or are located on the H zone of the face”</i> (p2)</p> <p>Note: H zone of the face: eyelids, nose, lips, ears, periorbital/ periauricular skin. The Guideline Development Group did not issue recommendations on other types of skin cancers such as squamous cell carcinoma, melanoma, dermatofibrosarcoma protuberans, atypical fibroxanthoma and sebaceous carcinoma due to lack of strong evidence.</p>	<p>Level of evidence and strength of recommendation not reported</p>
Basal cell carcinoma	
Canadian non-melanoma Skin Cancer Guidelines Committee, 2015 ¹²	
<p><i>“MMS, if available, may be considered as a first-line option for high-risk primary BCC, incompletely excised high-risk BCC, and most recurrent BCCs amenable to surgery”</i> (p244)</p>	<p>Level of evidence: high (further research is very unlikely to change confidence in the estimate of effect)</p> <p>Strength of recommendation: strong (desirable effects outweigh undesirable effects)</p>
Squamous cell carcinoma	
American Academy of Dermatology, 2018 ¹⁴	
<p><i>“MMS is recommended for high-risk cSCC”</i> (p568)</p>	<p>Level of evidence: II, III (II. Limited-quality patient-oriented evidence. III. Other evidence, including consensus guidelines, opinion, case studies, or disease-oriented evidence; ie, evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes).</p> <p>Strength of recommendation: B (recommendation based on inconsistent or limited-quality patient-oriented evidence)</p>
Canadian non-melanoma Skin Cancer Guidelines Committee, 2015 ¹³	
<p><i>“Treatment options for recurrent or otherwise high-risk SCC lesions include the following:</i></p> <ul style="list-style-type: none"> • Mohs micrographic surgery • Surgical excision with a 6- to 13-mm margin • Radiation therapy (in selected patients with contraindications to surgery, when surgery 	<p>Level of evidence: high (further research is very unlikely to change confidence in the estimate of effect)</p>

Recommendations	Strength of Evidence
<i>would be disfiguring, or when radiation therapy is needed for palliation)</i> " (p255)	Strength of recommendation: strong (desirable effects outweigh undesirable effects)
Scottish Intercollegiate Guidelines Network (SIGN), 2014 ¹⁵	
<i>"Mohs micrographic surgery should be considered at the multidisciplinary team meeting, for selected patients with high-risk tumours where tissue preservation or margin control is challenging, and on an individual case basis for patients with any tumour at a critical anatomical site"</i> (p17)	Strength of recommendation: the guideline development group is confident that, for the vast majority of people, the intervention will do more good than harm.
British Association of Dermatologists, 2014 ¹⁶	
<p><i>"Mohs micrographic surgery may be indicated for digital SCC in situ (around the nail in particular) and for some cases of genital (especially penile) SCC in situ for its tissue-sparing benefits. There may also be a role for Mohs in recurrent or incompletely excised lesions"</i> (p250)</p> <p><i>"In the absence of new therapies, and with limited variation in treatment recommendations since the last guideline update, there should be no significant organizational or financial barriers to the treatment recommendations contained in this guideline"</i> (p254)</p>	<p>Level of evidence: 3 (non-analytical studies; for example, case reports, case series)</p> <p>Strength of recommendation: D (evidence level 3 or 4, or extrapolated evidence from studies rated as 2+, or formal consensus)</p>
Melanoma	
American Academy of Dermatology, 2019 ¹⁷	
<p><i>"Mohs micrographic surgery or staged excision with paraffin-embedded permanent sections may be utilized for MIS, LM type, on the face, ears, or scalp for tissue-sparing excision and exhaustive histologic assessment of peripheral margins"</i> (p220)</p>	<p>Level of evidence: II, III (II. Limited-quality patient-oriented evidence. III. Other evidence, including consensus guidelines, opinion, case studies, or disease-oriented evidence; ie, evidence measuring intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes).</p> <p>Strength of recommendation: B (recommendation based on inconsistent or limited-quality patient-oriented evidence)</p>
Cancer Council Australia, 2018 ¹⁸	
<p><i>"Mohs micrographic surgery (MMS) has shown to improve complete clearance rates and reduced recurrences over conventional surgical removal of LM"</i> (p1)</p>	<p>Level of evidence: III – 2 (a comparative study with concurrent controls: non-randomised, experimental trial, cohort study, case-control study, interrupted time series with a control group)</p> <p>Strength of recommendation: not reported</p>

Recommendations	Strength of Evidence
Merkel cell carcinoma	
Alberta Cutaneous Tumour Team, 2015 ¹⁹	
<p><i>“Mohs micrographic surgery is appropriate as a tissue-sparing technique when the tumour is in a sensitive area such as head and neck area and there are concerns of functional impairment from too radical an excision” (p3)</i></p>	Not reported

cSCC = cutaneous squamous cell carcinoma; LM = lentigo maligna; MIS = melanoma in situ; MMS = Mohs micrographic surgery